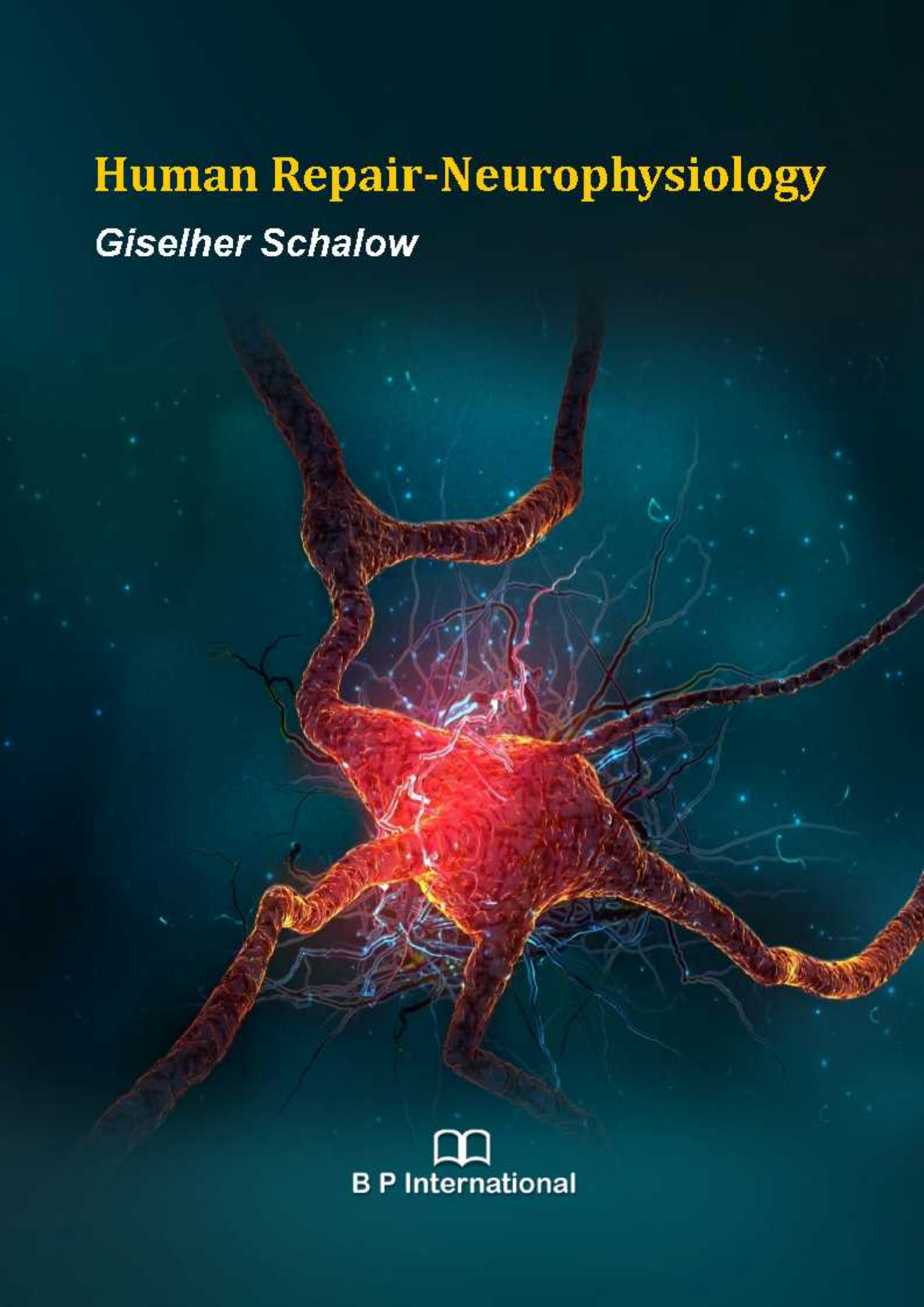
Human Repair-Neurophysiology

Giselher Schalow



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India ▪ United Kingdom

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Edited by

Giselher Schalow

NGOMR: Non-Government-Organized-Medical-Research, Switzerland.
E-mail: g_schalow@hotmail.com;

FIRST EDITION 2022

ISBN 978-93-5547-205-2 (Print)
ISBN 978-93-5547-216-8 (eBook)
DOI: 10.9734/bpi/mono/978-93-5547-205-2

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PREFACE

Human Repair-Neurophysiology is a new discipline in medicine which is not organized and funded. It combines human anatomy, human neurophysiology and the repair of the human central nervous system. The repair of the human nervous system is achieved through movement-based learning. A therapy was developed, called Coordination Dynamics Therapy, which is based on the functioning of the human nervous system, measured by human electrophysiology. To explore the human nervous system by electrophysiological methods is logic because the nervous system is functioning mainly via voltages and currents. The repair of the injured, malfunctioning or degenerating nervous system is achieved through the improvement of the coordinated firing of neurons and the plasticity of the human nervous system. In animals, as for example the rat, repair is achieved through the nerve fiber growing strategy and in human through learning. The main difference between the animal and the human nervous system is the complexity of their neural networks. In animals the nervous system needs a few months to develop and in human nearly 20 years. Through the tremendous complexity of the human nervous system, the human neural networks can nearly learn everything, including its repair. Since the nervous system is involved in nearly all body functions, the repair or the improvement of neural network functioning improves health in general. Many diseases can be treated by coordination dynamics therapy.

In Chapter 1 a partial repair (regeneration) of the human spinal cord is achieved by movement-based learning. When in Chapter 2 an orthopedic surgeon tried to compete with the natural repair by an operation, the spinal cord injury patient got worse. Already Hippocrates had the opinion that the true healer is the body itself. In Chapter 3, a malformation or degeneration of the cerebellum and pons got partly repaired through movement-based learning and in Chapter 4 the basal ganglia and the cortex. All the patients were children. In boys and girls under 10 years of age nearly everything is possible through repair if the patients can be motivated to train at their limits. But how to motivate a child to train very hard. They want to play and not train something what they do not understand. Mothers are most successful to administer the therapy if they know what they have to train with their child.

In brain-injured patients the higher mental functions are most important to be repaired. According to the System Theory of Pattern Formation, there is learning transfer from movements to the cognitive functions. In Chapter 3 and 4 also the higher mental functions of the patients improved through learning.

To administer movement-based learning with 15 to 20 hours per week for a few years, the repair progress has to be measured to motivate the patient and be sure that the treatment works. When exercising on the special coordination dynamics therapy device, the improvement of the coordinated firing of neurons can also be measured by one value, namely the arrhythmicity of exercising. When a subject is exercising on a special coordination dynamics therapy device, the coordination between arm and leg movements changes from pace to trot gait. The central nervous system functioning is then measured by the arrhythmicity of exercising through ‘Movement Pattern Change’ according to the System Theory of Pattern Formation. The improvement of nervous system functioning can be judged by the coordination dynamics value and the improvement of movement patterns.

This progress in the repair of the human nervous system was achieved because of the development of the single-nerve fiber action potential recording method. By recording with two pairs of wire electrodes from thin sacral nerve roots in the cauda equina, it is measured simultaneously what impulse patterns are conducted into the central nervous system and what are conducted out of it; that means the functioning of the human nervous system can be analyzed under physiologic and pathologic conditions at the single-neuron level. It was measured that the phase and frequency coordination among neuron firings becomes impaired through injury, malformation and degeneration. By improving this organization principle of the human central nervous system, when exercising on the special coordination dynamics therapy device, and training movement patterns, especially movement automatisms, other parts of the brain will take function over by plasticity. The human nervous system can be repaired or improved in its functioning at all ages.

To live longer with a better quality of life by 10 to 20 years is already achieved now through coordination dynamics therapy because cardio-vascular performance and nervous system functioning can be improved and cancer grows inhibited.

Giselher Schalow

Print ISBN: 978-93-5547-205-2, eBook ISBN: 978-93-5547-216-8

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Giselher Schalow [a*]

DOI: 10.9734/bpi/mono/978-93-5547-205-2/CH0

ABSTRACT

The human neurophysiology is introduced for repairing spinal cord injuries. Based on the recordings with a new electrophysiologic method, the single-nerve fiber action potential recording method, and morphometry of nerve roots, a classification of human peripheral nerve fibers is developed and used for the identification of neurons from which was recorded to analyze spinal cord functions. The restrictions of basic human right are ethically only justified, if the mistakes of medical research of the past are uncovered and investments in infrastructure and implementation of the clinical research, apart from statistic, are executed. It will be analyzed in detail that the orthopedic surgeon operated without sufficient knowledge in human repair-neurophysiology, necessary especially in SCI. Sophies cerebellar and pons repair is compared with the repair of a traumatic cerebellar and pons injury and her repair-stimulated development is compared with the development of healthy children in the age range between 3 and 18 years, quantified by coordination dynamics values and the ontogenetic landscape for locomotion, based on the System Theory of Pattern formation. More causal cancer treatment is needed, including progress in genetics and epigenetics. Interdisciplinary research and treatment have to be improved. Existing conventional cancer treatment has to be administered more thoroughly.

Keywords: Human neurophysiology; epigenetics; traumatic cerebellar; pons injury.

[a] *NGOMR: Non-Government-Organized-Medical-Research, Switzerland.*
**Corresponding author: E-mail: g_schalow@hotmail.com;*

Chapter 1
Print ISBN: 978-93-5547-205-2, eBook ISBN: 978-93-5547-216-8

Regeneration of the Human Spinal Cord via Coordination Dynamics Therapy

DOI: 10.9734/bpi/mono/978-93-5547-205-2/CH1

ABSTRACT

In the Introduction, the human neurophysiology is introduced for repairing spinal cord injuries. Based on the recordings with a new electrophysiologic method, the single-nerve fiber action potential recording method, and morphometry of nerve roots, a classification of human peripheral nerve fibers is developed and used for the identification of neurons from which was recorded to analyze spinal cord functions. Simultaneous impulse patterns of several single neurons, evoked by natural stimulations, running in and out of the spinal cord, are used to analyze spinal cord functions under rather physiologic and pathologic conditions. By combining the electrophysiology with the "System Theory of Patterns Formation", the movement-based learning method "Coordination Dynamics Therapy" (CDT) is developed to repair the human spinal cord. In the first part of the Results, the achieved repairs in spinal cord injury (SCI) through CDT are given in a group of patients and the single cases of 50% and 95% cervical SCI. In 50% SCI, urinary bladder functions, walking and running were repaired. In 95% SCI, bladder functions and trunk control were repaired, but free walking was not achieved. In the second part, **first time in history, the regeneration of the human spinal cord** of the 10-year-old Nefeli **was measured** by the re-innervation of segment-indicating muscles below the injury level of Th10. It turned out that most of the approximate one-year lasting regeneration time was needed to cross the injury site. Then, the fastest nerve fibers regenerated with a speed of 1mm/day down to the muscles. In the third part, details of the case report to repair the spinal cord by movement-based learning are given. Emphasis is put on the repair of the urinary bladder function, because its repair is most important for patients with SCI. In the Discussion, the deficits of animal research and clinics are given. Possible reasons for the regeneration of the human spinal cord may be that the power of regeneration is higher below an age of 10 and efficient aggressive treatment has to be administered continuously for more than one year. A permanent coma patient started to speak through 6 years of CDT with 20 hours efficient therapy per week.

Keywords: Human repair-neurophysiology; Electrophysiology; Single-nerve fiber action potentials; Surface EMG; Oscillatory firing; Phase and frequency coordination; Coordination dynamics therapy; Regeneration; Spinal cord injury repair.

1.1 INTRODUCTION

1.1.1 Urinary Bladder Functions are Most Important to be Repaired in Spinal Cord Injury

Before World War II, most patients with a spinal cord injury (SCI) died because of recurrent urinary tract infections. Nowadays, in India the life expectancy time of a patient with a severe SCI, after leaving the clinic, is 1 year because at home bladder and other infections cannot be managed sufficiently. Needless to say, that one of the most important functions to be repaired in patients with SCI is the control of the urinary bladder, followed by the sexual function, walking, spasticity, pressure ulcers and other functions. Most functions below the injury level (Fig. 1.1) are lost or impaired.

Patients are often reluctant to undergo urodynamic evaluation in a rehabilitation center, because of the fear of contracting urinary tract infection with antibiotic resistant bacteria. Development of urinary tract infection is a major set-back to the therapy, as optimal therapy is not possible in the presence of such an infection. If urodynamic assessment is not available, some good practical indicators of

improvement in urinary bladder function are the reduction in the incidence of urinary bladder infections and the significant reduction in the volume of post-voidal residual urine in the bladder. Residual urine can be measured by emptying the bladder with a catheter, after the patient has passed urine voluntarily. Residual urine of less than 50 ml indicates good physiological functioning of the bladder.

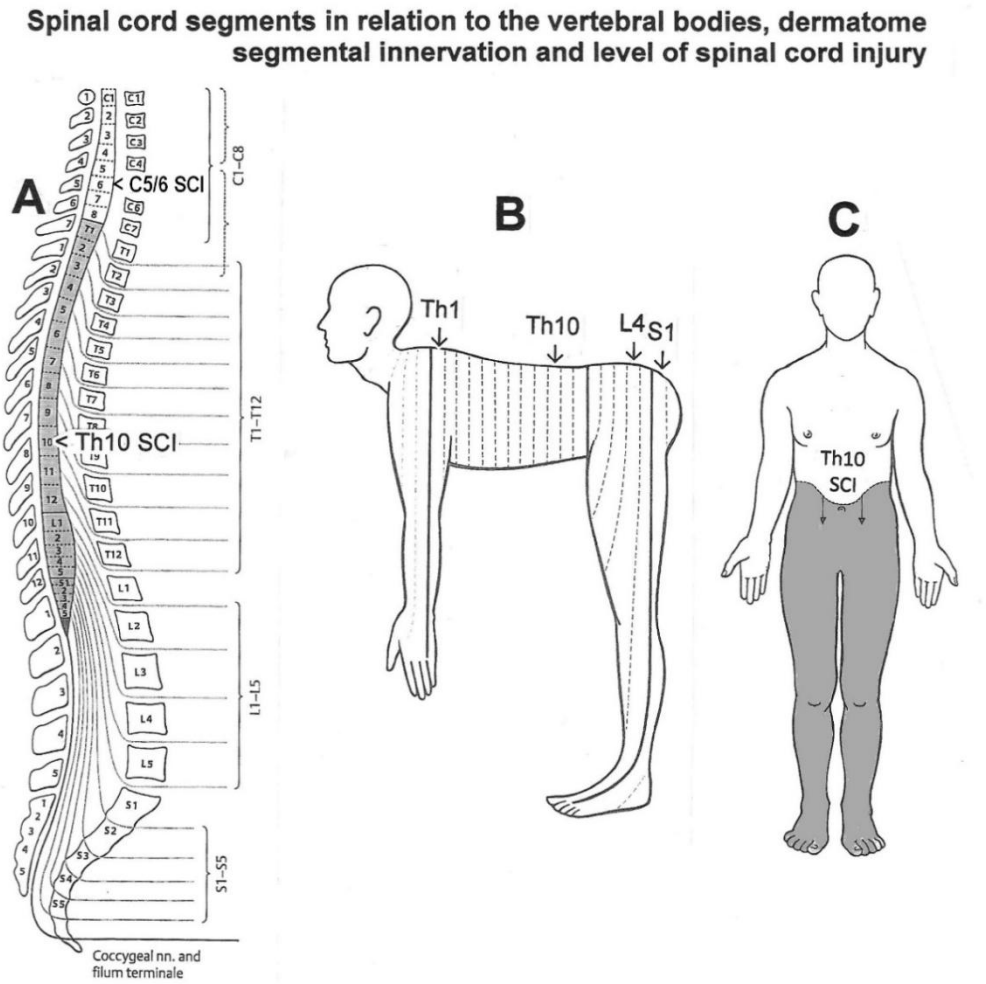


Fig. 1.1. A. Spinal cord segments and their relation to the vertebral bodies. Note the Ascensus of the spinal cord, giving rise to the long cauda equina nerve roots. B. Approximate segmental innervation of the skin. C. Below the SCI level there is loss of sensitivity and loss of connectivity to muscle and other functions

After World War II, Guttmann from Breslau [1] introduced intermitted catheterization to keep SCI patients alive. The neurosurgeon L.W. Freeman (USA) stated in the 1960's after performing very many SCI repair experiments on dogs, "it is difficult to find persons who do research in paraplegia and to get money for such research; probably World War II is already too far away". By cutting only one half of the spinal cord in animal experimentation, one is not getting urinary bladder and skin nutrition problems, but the repair in a 50% SCI is already solved in human [2] (Fig. 1.19G,H).

1.1.2 Spontaneous Recovery from Spinal Cord Injury

In incomplete SCI (Fig. 1.19D), the patients can also re-learn running and jumping (Fig. 1.19G,H), besides proper breathing and urinary bladder control and can improve cardio-vascular performance. Such a repair can be mainly achieved by a functional reorganization. In almost complete cervical SCI, there is nearly no spontaneous recovery. In incomplete SCI there is some spontaneous recovery,

especially during the following weeks after the spinal shock. Most spontaneous recovery occurs in the first 6 months following the injury. One year after the injury there occurs normally no further spontaneous recovery. Conventional rehabilitation centers, which are concerned with care and not with cure, 'sell' the mainly spontaneous recovery as treatment-induced repair. In a case report it was explained how an 18-year-old boy, who suffered an incomplete SCI at the cervical 5/6 segments, could achieve a near-complete recovery within 3 years of CDT and improved further in the following 3 years [2].

1.1.3 Human Spinal Cord Injury Treatment Situation

For judging SCI repair, one needs to know how much percent of the spinal cord was damaged, what treatment was used and the improvement of functions with treatment has to be quantified objectively. SCI's are known for hundreds of years and all easy treatments will have been tried out, including electrostimulation and interponats placed into the injured spinal cord site to re-connect the cord. The main drawing back in repair is that the injured adult spinal cord does not regenerate spontaneously. Placing a piece of nerve to the injury site to reconnect the proximal and distal spinal cord parts will not help, because the human nerve fibers cannot grow from the cord into the nerve transplant and vice versa. In rat, nerve fibers of the cord can cross a gap up to 12mm. By using an olfactory transplant with stem cells, may be some fibers can cross the transplanted site, but the damage to the still existing fibers is probably higher than the gained new connections, because the injured spinal cord is very vulnerable. The only successful treatment so far is the CDT [3], as is shown here. The nervous system is functionally repaired by movement-based learning, including some regeneration. In this paper it is reported about the enhancement of the limited regenerative capacity of the human spinal cord. Some details of human anatomy and human electro-physiology are given to make the reader understandable on what level of research treatment has to be designed to be successful on the long term. A combination of CDT and stem-cell therapy should be tried in the future. "The medical promise of stem cells remains real, but largely unrealized for now. The excitement must not be left to dissolve into a muddle of disappointment, frustration and fear because of the practices of a few irresponsible profiteers" [4].

1.1.4 Animal and Human Research/Treatment in SCI

It has been reported that SCI is a devastating condition for which there is as yet no cure [5,6 (2006)], even though it has been published that SCI can partly be repaired through CDT [7,8 (2003),2,9]. A century step forward was that also in a motoric complete cervical SCI, which is really a devastating condition when there are nearly no motor functions remained, the most important urinary bladder function could be repaired and this repair included some regeneration of the human spinal cord besides a functional repair [9].

Basic scientific research (including human research) should provide a rational basis for tailoring specific combinations of therapies [5]. Reviewers cite human work without a scientific basis and argue then, that neuro-rehabilitation methods should have a scientific basis.

The main difference with respect to repair between animal and human is the power of regeneration and learning. In animals the nerve fiber growing strategy is used for repair because of the high regenerative capacity and in human the re-learning is used for functional reorganization because in human the regenerative capacity is small and the learning capacity high. Therefore, the animal research in SCI is by-passing the interests of human patients with SCI. But in animal and human, both, regeneration and learning are needed to a certain extent.

For sure: Specialist journals and general audience media need to set reasonable expectations of the safety and efficacy of potential therapies to avoid raising and then dashing the hopes of those living with SCI or those in government, those carrying out research, or the general public [5]. High ethical standards are required by researchers, clinicians and journalists to ensure that results are communicated to the general public in a manner that honestly reflects the safety and efficacy of a potential therapy [5].

1.1.5 Anatomy of the Spinal Cord and Nerve Roots

The level of a SCI is diagnosed by the segmental innervation of the skin (Fig. 1.2) and the segment-indicating muscles (Fig. 1.37), that means till what caudal skin-segment the patient can feel and till what caudal muscles he/she can activate on volition. There is some variation of the segmental innervation of the skin and the muscles.

Since in animal research and clinics original pictures of the human spinal cord and magnetic resonance images (MRI) are seldomly shown, it will be done here. Fig. 1.3 shows the human spinal cord, dissected by the Author. It can be seen that the cauda equina nerve roots are much longer than the thoracic roots. In Fig. 1.6A the spinal cord is shown in connection with the brain. The cauda equina, after opening the dura mater, is shown in Fig. 1.6C in a cadaver dissection and during an operation in Fig. 1.6B.

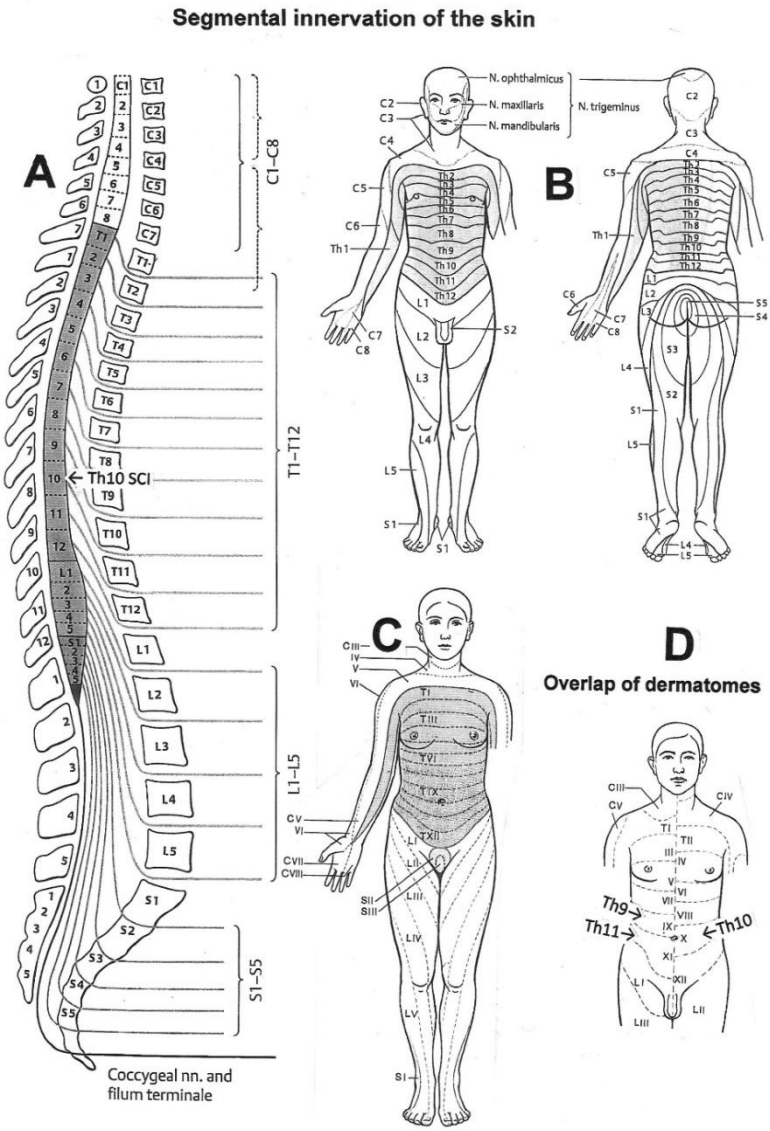


Fig. 1.2. Spinal cord (A) and dermatome segments (B-D). The segmental innervation of the skin in B is according to Hansen-Schliack and in C after Keegan and Garret. The overlap of dermatomes (D) is according to Foerster. Note the different location of the T1 dermatome in B and C. There is variation of the segmental skin innervation, especially in the lower sacral range

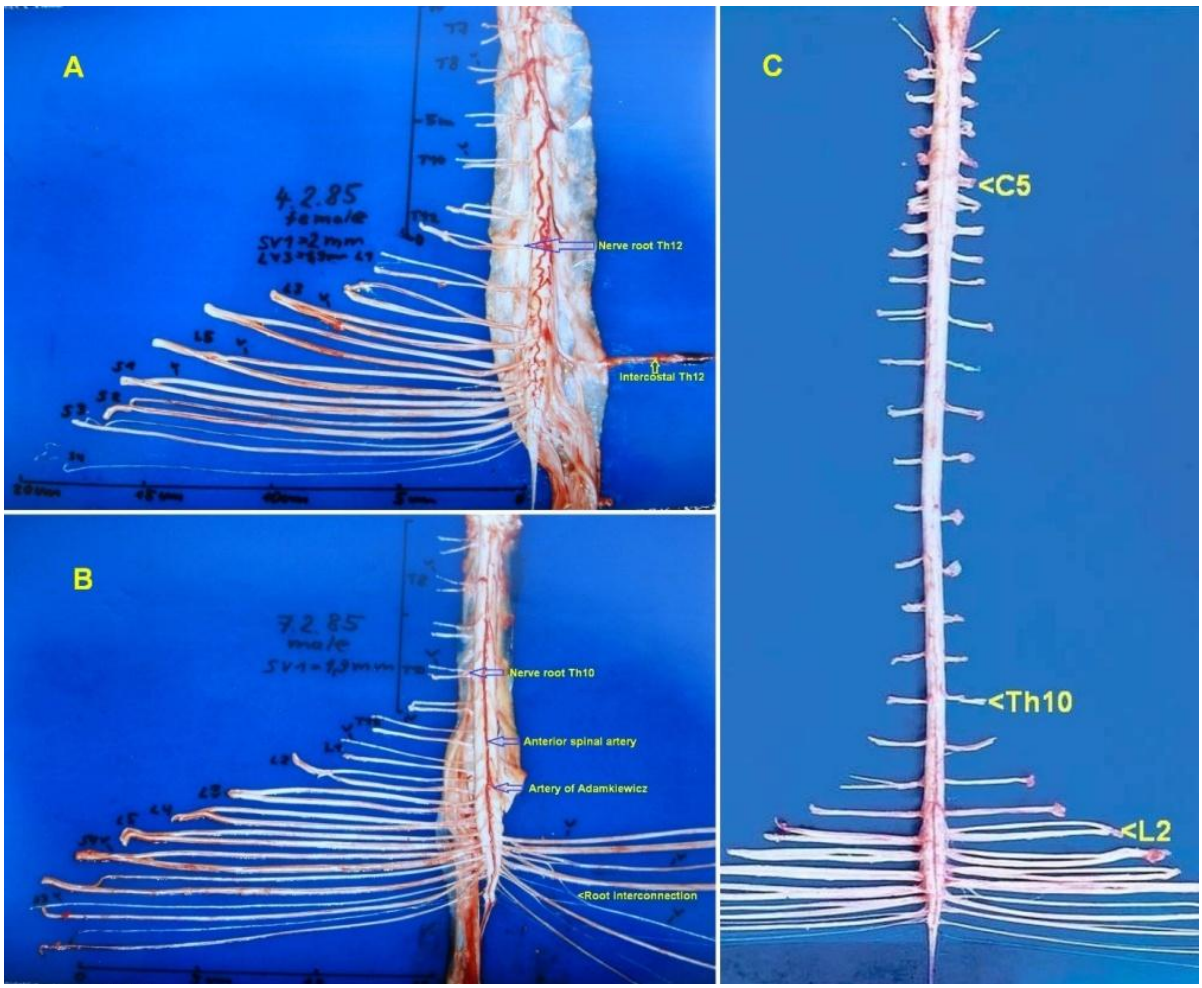


Fig. 1.3. Human spinal cord from dorsal (A) and ventral (B,C). Intumescentia cervicalis and lumbosacralis are visible in C. The caudal ventral roots are thinner than the dorsal roots. The passage of the artery spinalis magna (Artery of Adamkiewicz) and the anterior spinal artery are indicated. The C5, Th10 and L2 roots and the intercostal nerve Th12 are indicated. Dissection by the Author

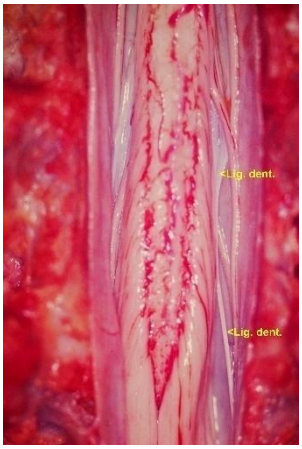


Fig. 1.4. Caudal part of the human spinal cord from dorsal. Lig. dent. = denticulate ligament. Dissection of the Author

The vascularization of the lower spinal cord and nerve roots can be seen in Fig. 1.4. A compression of the spinal cord will not only damage the spinal cord tissue directly, but also indirectly by impairing its blood supply. The spinal cord is protected by the spinal canal and is hold in place in the spinal fluid via the denticulate ligaments (in Fig. 1.4). When in an accident the spine brakes and presses onto the spinal cord (Fig. 1.5A), the cord has to be decompressed as quickly as possible, not to increase the pressure damage with ongoing time. The decompression has to be performed within the 8 hours following the accident, especially in cervical SCI. Wrong handling during the transport of the injured patient has to be avoided, especially in cervical SCI, not to increase the damage. Often further spinal cord damage takes place by wrong transport and too late spine operations.

1.1.6 A Too Late Decompression of the Spinal Cord Steels the Patient the Future

Fig. 1.5 demonstrates the tremendous consequences of a too late decompression of the spinal cord. Since repair is mainly achieved by functional reorganization of the brain, it is of importance to reduce secondary damage due to wrong handling and care and too late spinal cord decompression.

In Switzerland on a Sunday a motorcyclist suffered a SCI. In the hospital in 'Lausanne' the surgeons wanted to operate the patient immediately, probably within 8 hours after the accident to reduce quickly the spinal cord compression (Fig. 1.5A). The mother wanted the best for her child and took her boy to a well-known rehabilitation center in Switzerland. The orthopedic surgeon of the rehabilitation center decided on the basis of the MRI of Fig. 1.5A to postpone the operation to the Monday morning. One can see from the MRI of Fig. 1.5A that there was already an injury of approximately 70%. But by postponing the operation to the next day and leaving the pressure onto the cord the injury increased from the probable 70% to 99% (Fig. 1.5B). Because of this additional loss of spinal cord matter, due to the late removal of the pressure exerted from the vertebras onto the cord, the 18 years old patient lost part of his quality of life for the rest of his life. It will be shown below that with an injury of 70% you can relearn walking and get most functions repaired below the injury level C5/6. Only hand and finger functions would be impaired because of the loss of the grey matter at the injury site C5/6, where motoneuron cell bodies are located.

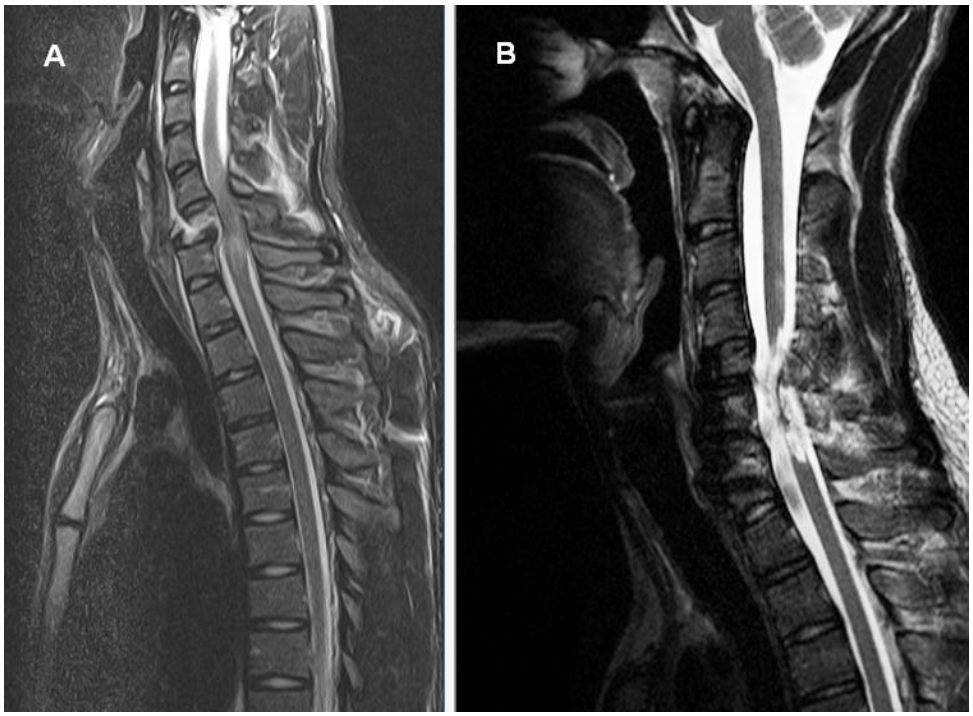


Fig. 1.5. Cervical SCI of an 18-year-old man approximately 8 hours after a motor cycle accident (A) and one year later (B)

1.1.7 Human Electrophysiology for Understanding Repair

With the single-nerve fiber action potential recording method one can record simultaneously at the neuron level natural impulse patterns (Fig. 1.6) running in and out of the spinal cord [10-15].

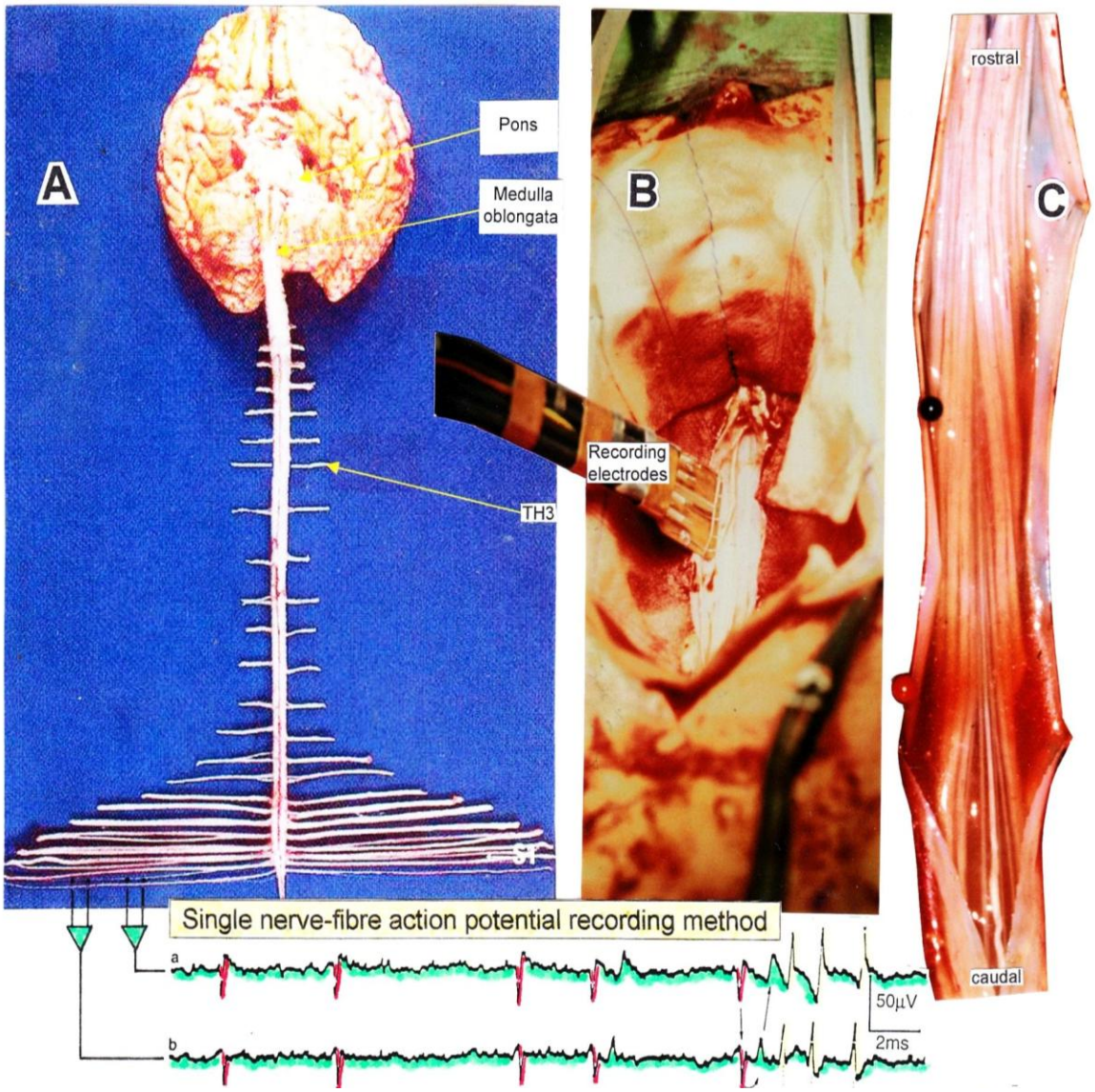


Fig. 1.6. Layout of the recording of single-nerve fiber action potentials to measure the self-organization of neuronal networks of the human CNS under physiologic and pathophysiologic conditions. By recording with two pairs of wire electrodes (B) from sacral nerve roots (cauda equina, C), containing between 200 and 500 myelinated nerve fibers, records were obtained in which single-nerve fiber action potentials (APs) were identified from motoneuron axons (main action potential (AP) phase downwards) and afferents (main AP phase upwards)

The impulse patterns of single-nerve fibers can be separated by splitting the multi-unit recording into impulse patterns of single-fibers by waveform comparisons, conduction times of single action potentials and impulse patterns. Fig. 1.7 shows such a splitting of the impulse traffic of several fibers into the impulse patterns of single fibers. The multi-fiber recording of Fig. 1.6 is split into the activity of single fibers.

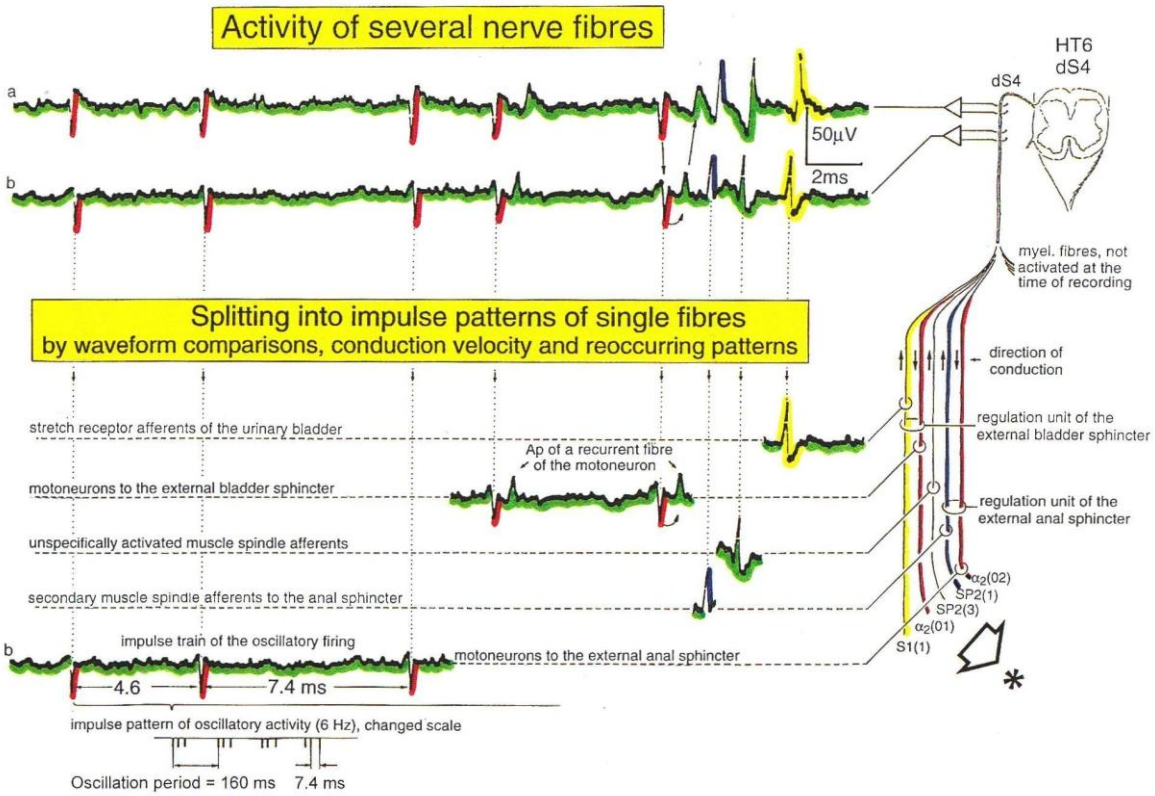


Fig. 1.7. Schematic splitting of the activity of several nerve fibres into simultaneous impulse patterns of single fibres by comparing waveforms, conduction velocities and reoccurring characteristic impulse patterns (rhythmic firing of sphincteric motoneurons). The different conduction times and waveforms were recognized on an expanded time scale. Stretch receptor and secondary muscle spindle afferents contribute to the drive of sphincteric motoneurons and form, together with other afferents, regulation units

But to identify from what nerve fibers the action potentials originate, a classification scheme for human nerve fibers is needed.

By measuring the conduction times and with the known electrode pair distance of 10mm, conduction velocity could be calculated and distribution histograms constructed in which the myelinated nerve fiber groups larger than 4µm could be characterized by group conduction velocity values. After the recording, the roots were removed, fixated, stained and morphometry was performed. Distributions of nerve fiber diameters for different myelin sheet thicknesses were constructed and nerve fiber diameter groups were characterized by the peak values of asymmetrical distributions. By correlating the peak values of the velocity distributions with those of the diameter distributions, obtained for the same root, a classification scheme was constructed for the human peripheral nervous system (Fig. 1.8) [16]. A group of nerve fibers is thus classified by a group conduction velocity and a group nerve fiber diameter. This classification scheme (Fig. 1.9) is the only existing one for the human nervous system. With this classification scheme it became possible to record natural impulse patterns simultaneously from identified single afferent and efferent nerve fibers and analyze self-organizing mechanisms of the human CNS under physiologic and pathologic conditions [17-19]. Since conduction velocities depend on the temperature, a calibration relation is needed. Such a calibration relation is for the lower sacral nerve roots that the secondary muscle spindles afferent fibers conduct with the same velocity as the α_2-motoneuron axons for different temperatures, marked in Fig. 1.9 with red. For the classification of human nerve fibers, it is further important that the nerve fibers taper only very little. As measured, if there is no splitting or branching of fibers, the tapering is 0.2% per 13cm [20]. A 100cm long fiber, for example of the pyramidal tract, would only reduce the diameter from 10µm to 9.8µm.

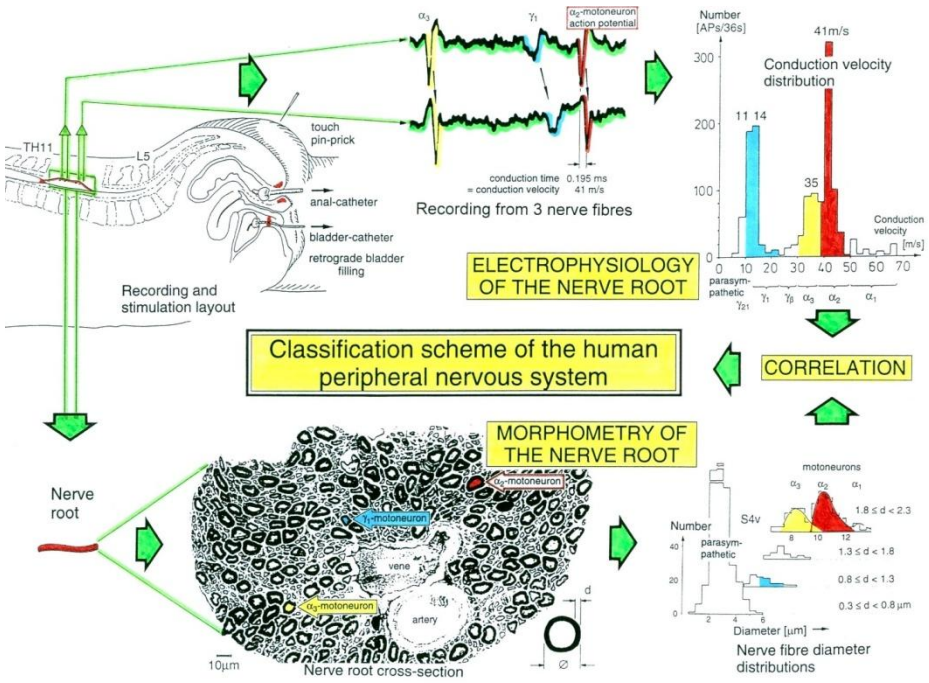


Fig. 1.8. Development of a classification scheme for human peripheral nerve fibers. Conduction velocities (V) and nerve fiber diameters (∅) of afferent and efferent nerve fiber groups in normal humans and in patients with a traumatic SCI for 0.5 to 6 years

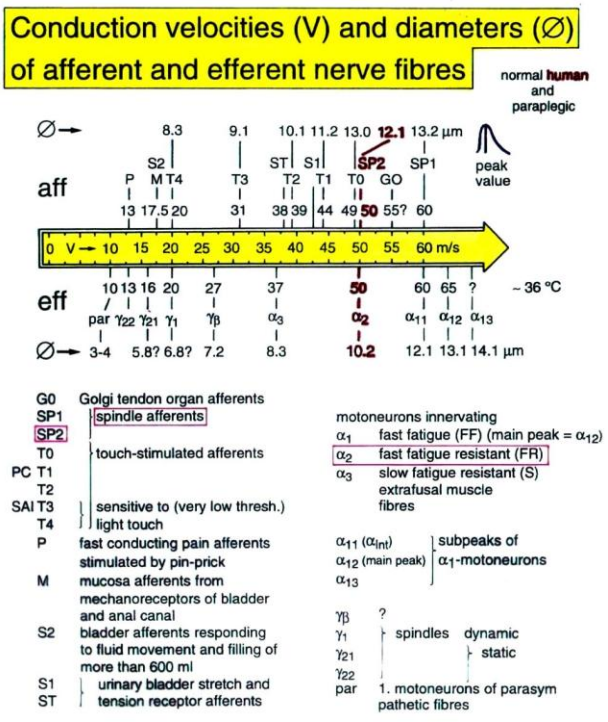


Fig. 1.9. Classification scheme for human peripheral nerve fibers. Conduction velocities (V) and nerve fiber diameters (∅) of afferent and efferent nerve fiber groups in normal humans and in patients with a traumatic spinal cord lesion for 0.5 to 6 years. The splitting of the α_1-motoneurons into the 3 subgroups, α_{11}, α_{12}, α_{13}, has not yet been confirmed. This is the only existing classification scheme for human nerve fibers!

1.1.8 Electrostimulation Cannot Simulate Natural Impulse Patterns, is Unphysiological and May Damage Neural Network Functions and Learning Transfer from Movements to Urinary Bladder and Sexual Functions

Electrostimulation is unphysiological because the applied patterns cannot simulate the natural impulse patterns conducted in the different nerve fibers. Fig. 1.10 shows the impulse patterns evoked by touch or pin-prick conducted in up to 22 skin afferent fibers. An electrostimulation of the skin cannot simulate such naturally generated impulse patterns caused by touch or pin-prick. Such impulse patterns inform the CNS about the outside world, which means in this case about touch and pin-prick. The by the electrostimulation generated patterns the CNS cannot understand.

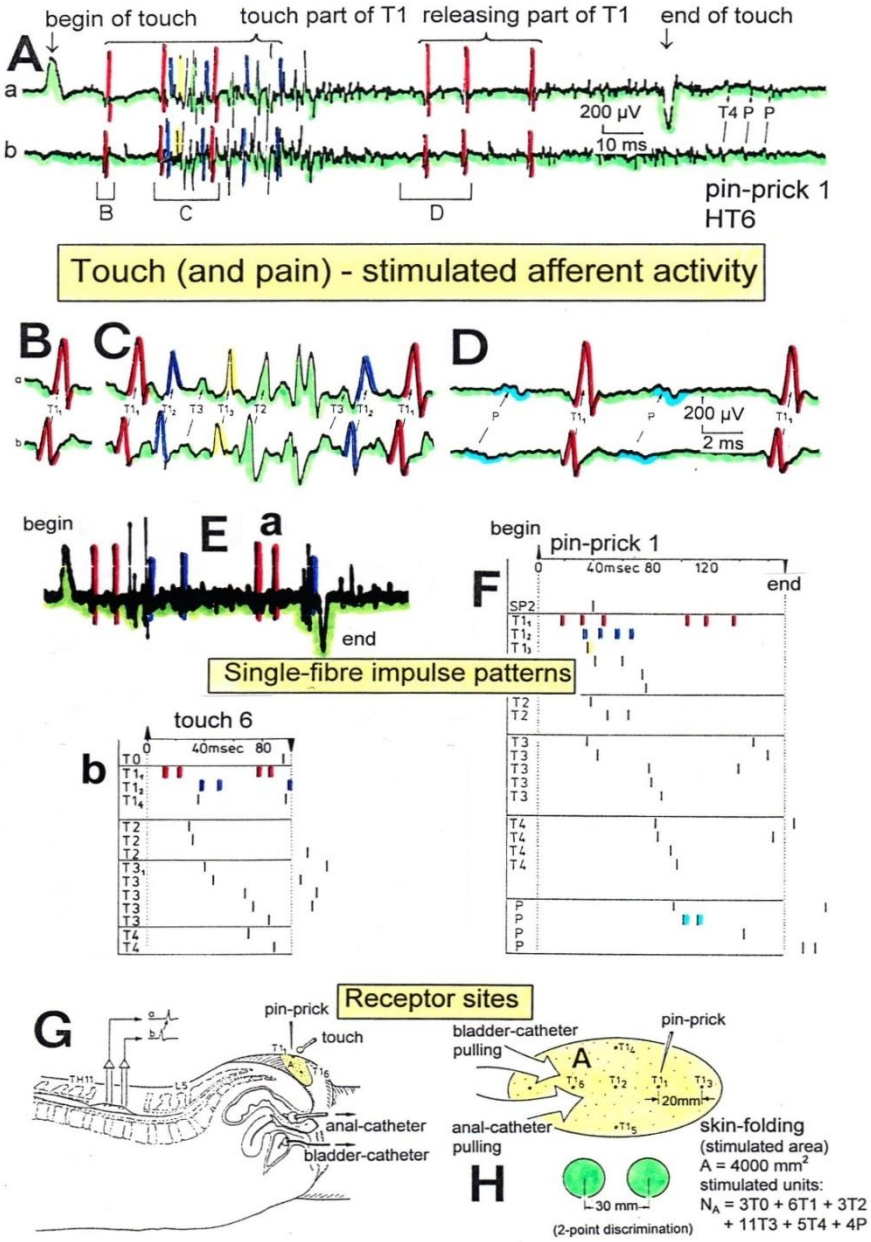


Fig. 1.10. Touch (and pain)-stimulated afferent activity. Touch and pain activity, stimulated by pin-prick (A) and touch (Ea) of S5 or Co dermatomes and recorded extracellularly from a dorsal coccygeal root (brain-dead human HT6). T1, T2, T3, T4, P = mark action potentials (APs) from single touch and pain fibers. Subscripts 1, 2, 3 mark single fibers

In Fig. 1.10A a whole sweep following pin-prick 1 is shown at a slow time base. The large upward artifact on trace 'a' marks electronically the beginning of the pin-prick. The large downward artifact on trace 'a' marks the end of the pin-prick. Note that 2 intervals of high activity of large APs occur, one after the beginning of the pin-prick with 1 AP in front, and a second before the end of the pin-prick; potentials with large amplitude are followed by potentials of small amplitude. Time intervals B, C and D are shown in a time-expanded form in B, C and D. Identified APs are indicated. Note that the APs from the $T1_1$ touch unit can be safely identified by the waveforms in B, C, D.

AP occurrence patterns of single touch and pain fibers following short touch 6 and pin-prick 1 are shown in Fig. 1.10 Eb, F. No pain afferents are stimulated upon touch 6. Upon pin-prick 1, the single-fiber AP activity of the different touch and pain groups is identified by the AP waveforms on traces 'a' and 'b', and by the conduction times. The single touch afferents of the T1 group are marked with subscripts. One active secondary muscle spindle afferent fiber (SP2) could always be identified in F. Note that for pin-prick 1, touch and pain afferents are stimulated whereas for touch 6 only touch afferents.

Recording and stimulation arrangement for simultaneous recording of several single touch and pain units are shown in Fig. 1.10G. The area A stimulated by skin folding is drawn in H in more detail. $T1_1$, $T1_6$ = suggested touch points of the $T1_1$ and $T1_6$-units. A drawing of the very approximate skin area stimulated by skin folding is shown in Fig. 1.10 H. $T1_{1\text{-}6}$ = suggested focal T1 touch points. Two-point discrimination indicated for the sake of comparison. N_A = number of stimulated units in the dorsal coccygeal root. Skin tractions evoked by anal and bladder-catheter pulling are indicated by the large open arrows in Fig. 1.10H.

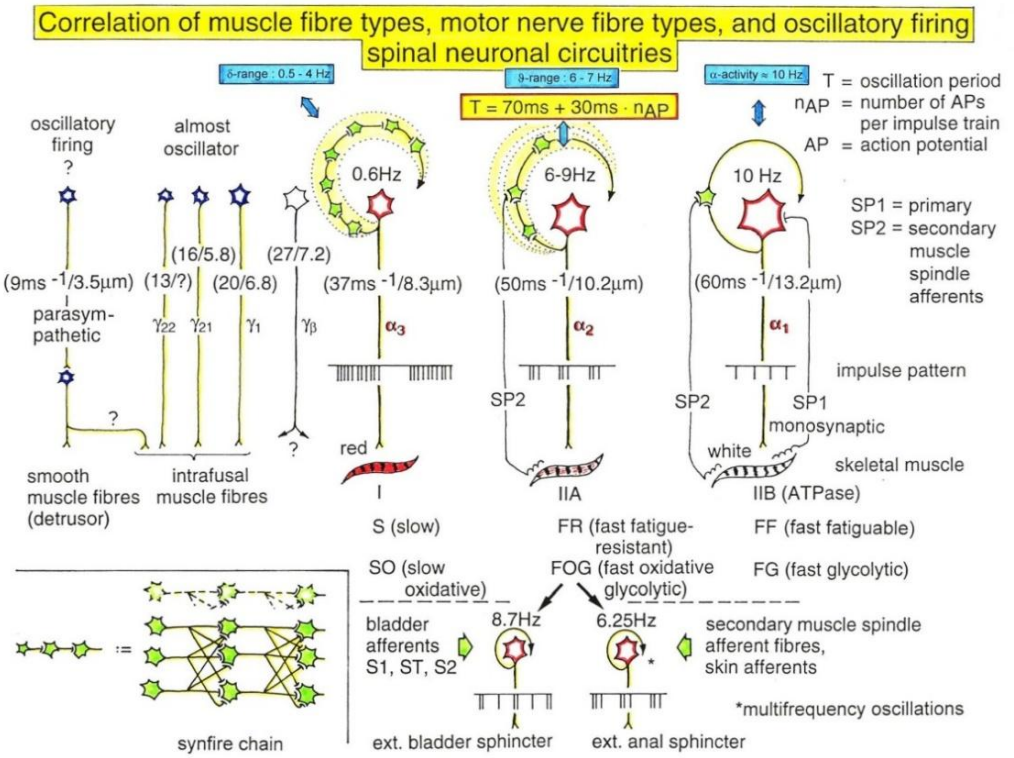


Fig. 1.11. Correlation of muscle fiber types, motor nerve fiber types, and oscillatory firing spinal neuronal networks, based on histochemical, morphological and physiological properties. This figure provides a simplified correlation between muscle fiber, motoneuron and sacral oscillator types. No additional subtypes have been included. α = motoneuron, γ_1, γ_2 = dynamic and static fusimotors, parasympathetic = parasympathetic preganglionic motoneuron. S1, ST, S2 = stretch, tension and flow receptor afferents

The electro-stimulation of motoneurons or motor units is also unphysiological. Firstly, as Fig. 1.11 shows, the three different kinds of motoneurons, innervating the three kinds of muscle fibers (FF, FR, S), have different activation frequencies and patterns. An electrostimulation can only serve a certain muscle fiber type at the surface of the muscle. Secondly, the motoneurons and the motor units do not fire physiologically in a synchronized manner to avoid tremor. They fire coordinately distributed to avoid synchronization of motor units and therefore tremor (Fig. 1.12). The electrostimulation of muscles may enhance tremor in patients with Parkinson's disease.

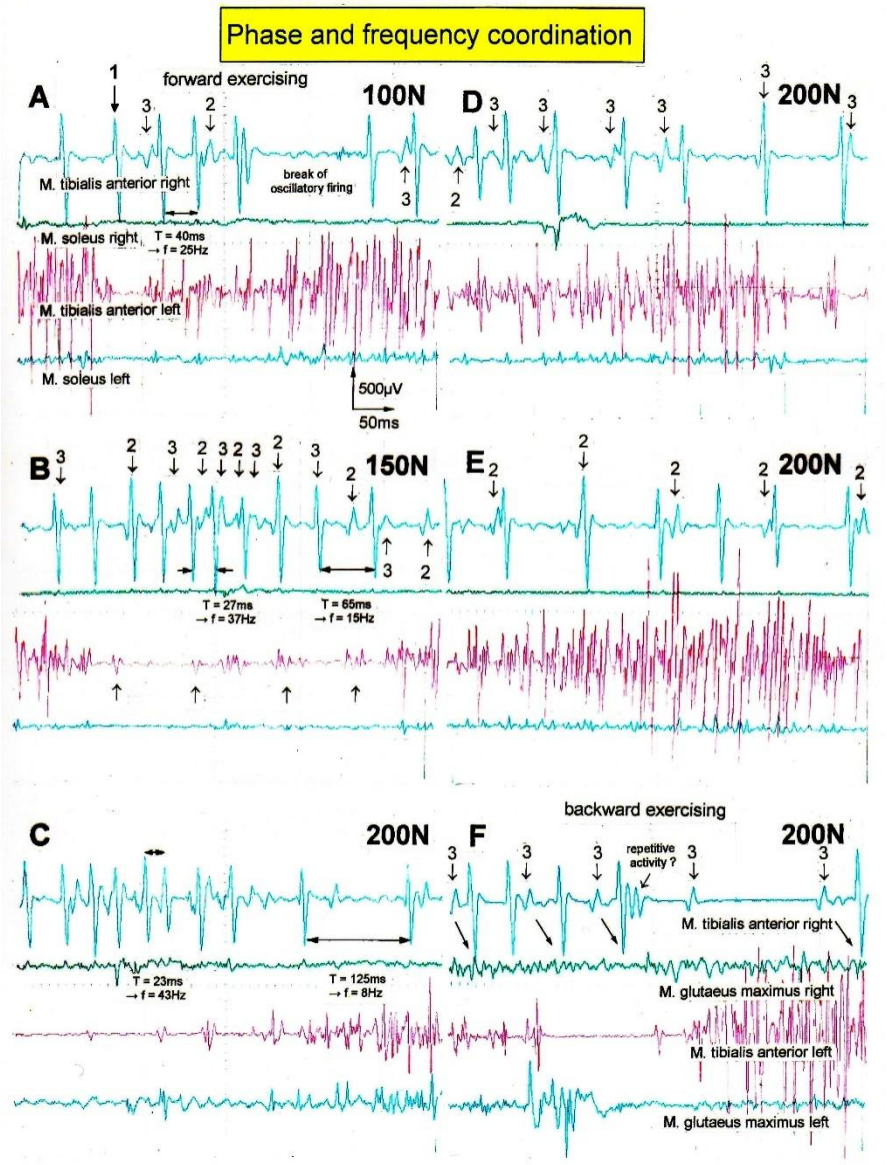


Fig. 1.12. Phase and frequency coordination between oscillatory firing motor units (FF-type) during the generation of a motor program during exercise on the special CDT device at loads increasing from 100 to 200N. Oscillation periods (T) and oscillation frequencies (f [Hz]) of oscillatory firing motor unit 1 are partly indicated. 'A,B,D,E' same recording situation as in Fig. 1.23; 'C,F' soleus electrodes shifted to gluteus muscles to check early re-innervation upon therapy. The waveforms of the 3 identified FF-type motor unit potentials '1', '2', and '3' are the same as in Fig. 1.23; motor units '2' and '3' are partly marked. In 'F', some coordination's between motor unit '3' and '1' are marked

In patients with an incomplete SCI there is some tendency for a synchronization of motoneurons because of loss of inhibitory tract fibers. Tremor can normally not be seen. But clonus is often observed in patients with SCI. In clonus, the feet perform consecutive dorsal and plantar flexions. The reason for that rhythmic dorsal and plantar flexion is probably a rhythmic activation of the very sensitive regulation loop between the feet and the spinal cord rather than synchronization of oscillatory firing motor units as in tremor.

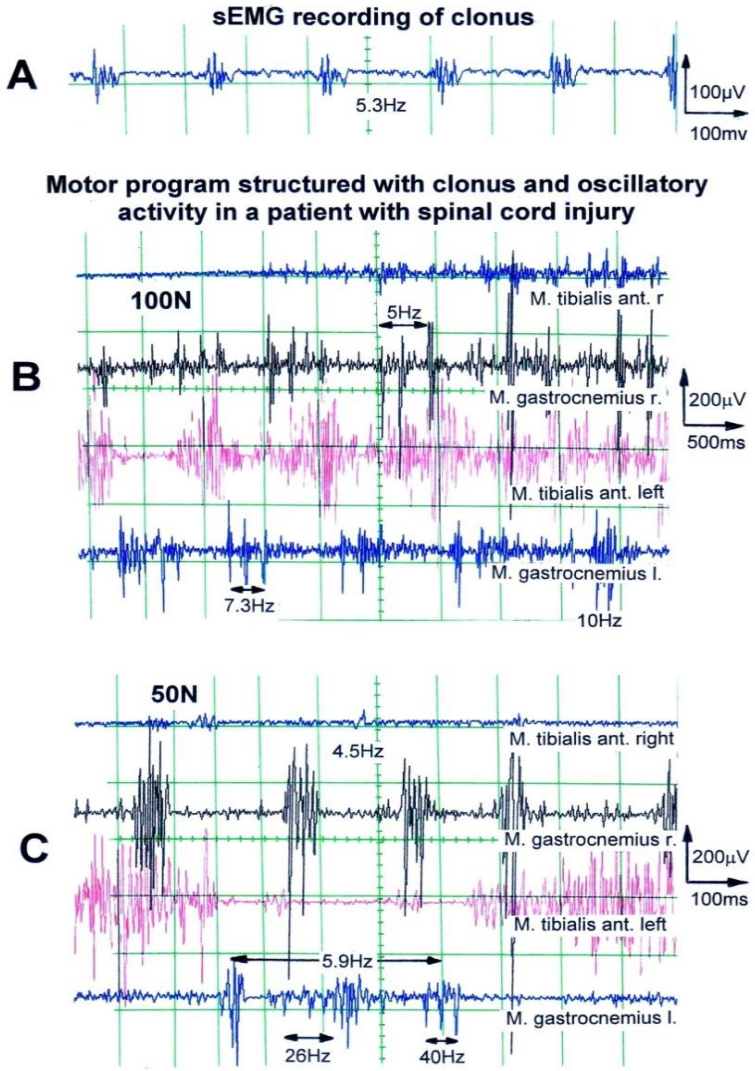


Fig. 1.13. Motor program bursts in patients who suffered a SCI, structured with clonus activation and rhythmic firing of FF-type motor units A. EMG recording of a clonus (f = 5.3Hz) in the right tibialis anterior muscle of a patient who suffered a complete SCI sub Th5/7; the patient was not exercising. B, C. Motor programs of a patient who suffered an incomplete SCI sub Th4 upon exercising on the special CDT device at 50N and 100N (medium to high load). In B, motor program bursts are structured by rhythmicity; frequencies of 5 and 7.3Hz are suggested. No motor program in the right tibialis anterior muscle; some motor program structure in the right gastrocnemius muscle. In C (faster sweep), there is no motor program in the right tibialis anterior muscle. Mainly clonus activity at a frequency of 4.5Hz can be seen in the right gastrocnemius muscle. Two physiologic motor program bursts can be seen in the left tibialis anterior muscle (not structured by rhythmicity). In the left gastrocnemius muscle, a motor program burst can be seen which is structured by 5Hz rhythmicity (clonus frequency, see clonus in the right gastrocnemius muscle) and higher frequency rhythmicity (26 and 40Hz)

Fig. 1.13 shows EMG recordings of a patient with an incomplete SCI, having clonus and a pathologic motor program. The motor program is poor, because there is no motor program in the right tibialis anterior muscle and the motor bursts in the right and left gastrocnemius muscle are structured with rhythmicity, i.e. with clonus activity. A typical clonus recording when no exercising can be seen in Fig. 1.13A. On a stretched time scale the clonus can clearly be seen in the right and left gastrocnemius muscles of Fig. 1.13C. In the left gastrocnemius muscle, the motor program burst is structured with three clonus bursts, which are in turn structured by rhythmic activity at 26 and 40Hz which may originate from the oscillatory firing of FF-type motor units innervated by α_1-motoneurons.

The unphysiological electrostimulation, applied to SCI patients, may increase the clonus and the synchronization of motor units (tremor) and ruin in this way the functional reorganization of neural networks and inhibit physiologic repair. The repair of urinary bladder and sexual functions by learning transfer from movements may become impaired.

1.2 METHOD

1.2.1 Coordination Dynamics Therapy (CDT)

CDT is a movement-based learning therapy to repair the human central nervous system (CNS) to regain lost functions back. For a recent review see [3]. In short, following brain, brain stem or SCI, the self-organization of neural networks by phase and frequency coordination becomes impaired besides the loss of functions due to damage or loss of nervous tissue. Through CDT this impaired phase and frequency coordination has to be improved through exercising on a special CDT device (Fig. 1.16) and other movements. Some lost functions re-appear already then. To regain lost functions, movements have to be trained to repair impaired functions and other brain and spinal cord parts have to take function over by plasticity. The trained movements include creeping, crawling, up-righting, walking, running and jumping. Only those movements can be administered to the patient which the patient can perform with or without support. The main CNS repair is achieved through a functional re-organization. The capacity for a regeneration of the spinal cord and the building of new nerve cells is very limited in human. In this report it is tried to increase the capacity of regeneration and neurogenesis and to understand its induction. It is the first time in history that a regeneration of the human spinal cord could be achieved, based on human neurophysiology and clinics and documented by diagnostic.

1.2.2 System Theory of Pattern Formation for Understanding Neuronal Network Organization and Learning and Measure Repair Progress

To apply successfully CDT, the System Theory of Pattern Formation is needed to understand better the repair and measure the improvement of CNS organization. In a complex system like the human CNS, patterns are generated by the nervous system which seeks cooperative stability. Stability is what defines collective states. The system has the tendency to slip into the collective states to which it is attracted. When an infant crawls (Fig. 1.14), its arms and legs are strongly attracted to the ‘pace’ and ‘trot’ gait coordination patterns. The attraction is so strong that intermediate crawling patterns seemingly do not exist, as if the patterns are hard-wired. But with the help of the special CDT device, the CNS can generate intermediate coordination patterns. A patient with a CNS injury often crawls with intermediate arm and leg coordination patterns and has to re-learn the pace and trot gait coordination’s for CNS repair and shifts in this way the attractors for crawling to the pace and trot gait coordination’s. Attractive states and attractors of CNS organization can be pictured as a ball in a potential well or more generally in an attractor layout (Fig. 1.15). Changes in CNS functioning are characterized as continuous stabilization and destabilization, over time, of preferred attractor states.

Fig. 1.14. Trot gate crawling of a cerebral palsy girl in interpersonal coordination with the therapist. The crawling performance of the therapist is not optimal. The right arm is leading with respect to the left knee. The crawling performance of the patient is also not optimal; the knees are too much apart

To reduce for understanding the complexity of human neural networks of the many billions of neurons, **order parameters** or **collective variables** are introduced for the generation of certain movements. An equation of motion describes the coordination patterns dynamics. However, coordination patterns are not only determined by the task or biological function. Patterns adjust continuously to requirements from the environment (transmitted by impulse patterns from stimulated receptors in the periphery), memory, intention, and support given by a therapist. The specific requirements are captured by the concept of behavioral information and are made part of a vector field that attracts toward the required patterns. The coordination pattern dynamics, characterized by equations of motion of collective variables (the vector **X**), takes the general following form [21].

$$d\mathbf{X}/dt = \mathbf{F}_{intr}(\mathbf{X}) + \sum c_{inf}\mathbf{F}_{inf}(\mathbf{X},t) \quad (2)$$

where $\mathbf{F}_{intr}$ designates the **intrinsic dynamics** of the nervous system. These intrinsic dynamics capture the anatomical (neuronal network structure), physiological and pathological states of the CNS and its muscular-skeletal elements. $\sum c_{inf}\mathbf{F}_{inf}(\mathbf{X},t)$ represents the sum of external influences ($\mathbf{F}_{inf}(\mathbf{X},t)$) with their relative strength (c_{inf}) pertaining to each influence. The so-called **behavioral information** $\mathbf{F}_{inf}(\mathbf{X},t)$ includes cognitive states, emotional states, intentions, motivations, instructions, inter-personal coordination, movement support etc. During motor learning or while applying therapy to a patient these extrinsic influences become extremely important, because the intrinsic (pattern) dynamics can be changed with these extrinsic influences by altering the equation of motion. By modulating the behavioral information, the intrinsic dynamics of the neuronal networks can be influenced further, that is if CDT is no longer efficient in repairing the injured CNS, requiring the therapy to be updated. With respect to a healthy athlete, the movement performance can be improved by modulating the behavioral information by for example including in the training program the exercising on a special CDT device to improve CNS functioning.

If the behavioral information includes the exercising of extremely coordinated, integrative movements, like exercising on the special CDT device, then the quality of CNS self-organization can be enhanced by improving the exactness of self-organization, namely the precision of phase and frequency coordination between neuron and neural assembly firings. By improving the precision of organization of the intrinsic dynamics, that is the specific variability of the injured networks, certain patterns do eventually re-appear in the case of repairing the injured CNS by movement-based learning.

1.2.3 Learning Implications for Treatment Derived from the Equations of Motion of the Collective Variables

From the repair by learning in the severely injured CNS we learn about learning in the healthy CNS, because the impact on the learning mechanisms is higher than in animal experimentation.

1. Behavioral requirements $\mathbf{F}_{inf}$ (like intention, support, and instruction) affect the whole coordination dynamics, including stability, rather than only certain coordination patterns. The **change of the whole coordination pattern dynamics** of the CNS by the behavioral information **is one scientific basis for learning transfer** [22] between different patterns and **stability changes of patterns** (as for example the reduction of spasticity). The other scientific basis for learning transfer is followed from human neurophysiology, namely that nerve cells or neural sub-networks are involved in different neural network organizations [23].

2. The intrinsic dynamics $\mathbf{F}_{intr}$ include vegetative and higher mental functions (these are also patterns of the coordination dynamics), which indicate that via exercising coordinated movements with support and/or instructions ($\mathbf{F}_{inf}$), urinary bladder function, intelligence and speech can be partly repaired or improved following CNS injury or malformation.

3. When in an injured CNS with a certain set of behavioral information ($\sum c_{inf}\mathbf{F}_{inf}$) the intrinsic coordination dynamics ($\mathbf{F}_{intr}$) can no longer be influenced during CDT, then this set of behavioral information has to be changed (using different $\mathbf{F}_{inf}$), or balanced differently (using different $\mathbf{c}_{inf}$), to further improve CNS organization dynamics.

4. However, the equations of motion of the coordination pattern dynamics (formula 2) provide no information about the specific behavioral information ($\mathbf{F}_{inf}$) and training intensity ($\mathbf{c}_{inf}$) with which the CNS can be efficiently repaired by learning in a patient. We need to have detailed knowledge of the human CNS at the single neuron and neural assembly level, as well as knowledge at the integrative level, to find the specific behavioral information for the repair by learning of the human CNS.

A **first novel step** in CDT is the inference derived from the equation of motion. It suggests that the movement learning not only improves the performance of that particular movement, but also improves the other non-trainable functions by **transfer of learning** [22,23]. These functions include vegetative functions like bladder control, speech and higher mental functions.

Furthermore, we have means by which the stability of physiological network states can be increased (e.g. movements, continence, continuous concentration in performing certain tasks, speech etc.) and simultaneously the stability of pathological network states, like spasticity, decreased. The coordination (pattern) dynamics therapy partly based on the System Theory of Pattern Formation in combination with human neurophysiology thus offers us an important theoretical basis and a practical tool to diagnose, quantify and repair/improve the functioning human nervous system at the macroscopic level.

1.2.4 Geographical Landscape of Attractors

The drawback of the equation of motion of the order parameters (formula 2) is that it is normally not possible to find a mathematical solution to it. But by defining a potential function and by picturing the attractive states and attractors by a ball in a potential well or rather by a ball moving in a geographical landscape of attractors (Fig. 1.15), we form a theoretical basis to understand and measure stability of

certain coordinated movement patterns (i.e., the deepness of the potential well of an attractor) in patients with CNS injury who receive on-going therapy.

To make the strategy of pattern formation, pattern stability, pattern assessment, and pattern picturing understandable, the procedure is demonstrated for the simple movement 'jumping on springboard' (Fig. 1.15D), which is used during CDT, especially for the repair of the urinary bladder and training in the up-right weight-bearing posture (very important in patients with SCI).

For the special movement 'jumping on springboard' with no behavioral information ($\sum c_{inf}\mathbf{F}_{inf}(\mathbf{X},t) = 0$) the equations of motion (formula 2) take the form $d\varphi/dt = f_{intr}(\varphi)$, where φ is the relative phase between the two moving legs and is the only collective variable of this special movement.

The mathematical solution of $d\varphi/dt = f_{intr}(\varphi)$ in the Haken-Kelso-Bunz model [24,25] gives the equation of motion for jumping on a springboard for the symmetric case. The obtained potential function $V(\varphi,t) = -a(t)\cos\varphi - b(t)\cos 2\varphi$ can be plotted for different φ and certain ratios of the parameters a and b and is shown in Fig. 1.15.

The potential function shows two attractor states, namely the jumping in in-phase ($\varphi = 0$) and the jumping in anti-phase ($\varphi = \pm \pi$). Especially for higher frequencies (smaller b/a) the jumping in-phase has a higher stability (the potential well is deeper) than the jumping in anti-phase. Asymmetry (not tackled mathematically here) strongly changes the stabilities of the attractor states (depths of potential wells) (Fig. 1.15).

The human CNS, seeking for cooperative stability, slips into the collective states to which it is attracted. For jumping on springboard these attractive states are the jumping in in-phase and in anti-phase. For crawling (Fig. 1.14) the attractive states are the pace (in-phase) and in trot gait coordination's (anti-phase). When introducing the variability of phase and frequency coordination of strength Q, the potential function takes the form $d\varphi/dt = -dV(\varphi)/d\varphi + (Q\xi_t)^{1/2}$, where ξ_t is Gaussian white noise of unit variance.

The behavioral changes when jumping on springboard (Fig. 1.15) are represented by the over-damped movement of a rolling ball in the potential landscape for the physiologic (Fig. 1.15A, Q small = little fluctuation of phase and frequency coordination) and the pathologic case (Fig. 1.15B,C; Q large = large variability). The increased fluctuation in the rather stable state, due to increased variability of phase and frequency coordination, will have greater probability of "kicking" the system out of attractor the basin (Fig. 1.15B,C), especially in the asymmetric case.

In the healthy CNS, the phase and frequency variability is small (short arrows) and the jumping in-phase and anti-phase is stable (Fig. 1.15A). Following injury, the potential landscape is deformed and the fluctuation of the network states, generating jumping, is high (Fig. 1.15B). The in-phase jumping is still stable in spite of the increased fluctuation, because the basin of attraction is deep. The jumping anti-phase became unstable because the basin of attraction is shallow and the increased fluctuation in the state has a greater probability of "kicking" the system out of the basin. A switch into a spastic state is also possible. In severe CNS injury or malformation, the patient cannot jump any more in anti-phase because of the missing of attractors for anti-phase jumping (Fig. 1.15C). Support is needed for anti-phase jumping. The jumping in-phase is still possible but unstable.

Upon performing very exact coordinated movements, imposed by devices (Fig. 1.16), the nervous system of the patient learns to reduce the variability of phase and frequency coordination and achieves in this way a small fluctuation of the network states again as shown in Fig. 1.15A. The progress in treatment (learning) is that the in-phase jumping in Fig. 1.15C and the anti-phase jumping in Fig. 1.15B become stable again (Fig. 1.15A). Also, the potential landscape will change due to the reduction of the phase and frequency variability. The important consequence for treatment is that when exercising on special CDT devices and reducing in this way the variability of phase and frequency coordination, the patient can induce the formation of patterns again, without having trained them (learning transfer). Upon improving the coordinated firing of neurons, a cerebral palsy child my become able to speak or may develop social behaviors.

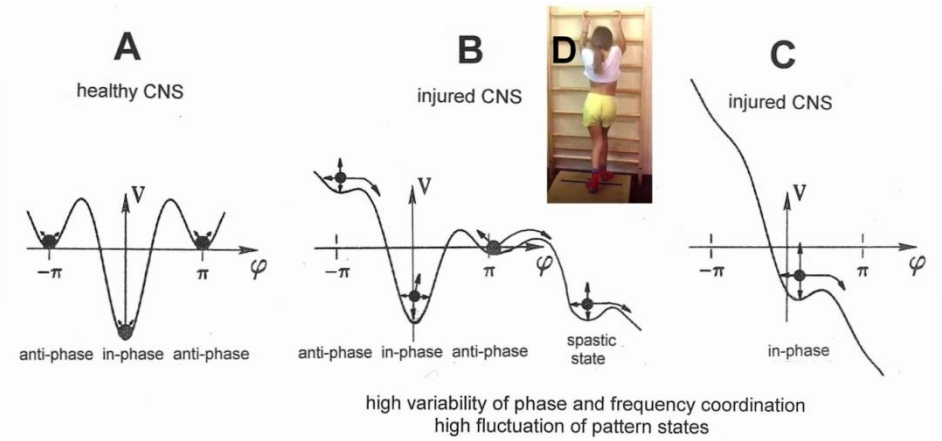


Fig. 1.15. The potential, V(φ), of the coordination dynamics for jumping on springboard (D, Nefeli) of a healthy (A) and injured CNS (B,C). The region around each local minimum acts like a well that weakly traps the system into a coordinated state. Behavioral changes are represented by the over-damped movement of a rolling ball in the potential "landscape". High fluctuations (indicated by long arrows attached to the ball (network state)) in the stable state, due to high variability of phase and frequency coordination (in the injured case), will have a greater probability of "kicking" the system out of the basins of attraction (B,C) than for low fluctuations (short arrows) (A), due to small variability of phase and frequency coordination (in A). In B, only the in-phase jumping is stable, even though the fluctuation is high. In C there is only an attractor basin for the in-phase jumping, but the fluctuation is so high that there is a high probability that the system is kicked out of the basin of attraction. The patient can no longer jump in anti-phase and has difficulty with jumping in-phase. The stability of jumping depends on the motor program (deepness of basin of attraction) and the fluctuation of the pattern state (moving of the ball) caused by the increased variability of phase and frequency coordination due to the injury

Fig. 1.16. The 11-year-old Nefeli with an incomplete SCI during exercising coordinated arm, leg and trunk movements to improve the coordinated firing of neurons and sub-neural networks. This special CDT device for measuring and therapy (int.pat.) is produced by the firm: Giger Engineering, Martin Giger dipl.Ing.ETH/SIA, Herrenweg 1, 4500 Solothurn, Switzerland, www.g-medicals.ch.

In conclusion, the impairment of phase and frequency coordination caused by CNS injury, measured at the single-neuron level in human, can be included in the coordination pattern dynamics at the collective variable level. The decrease of the variability of phase and frequency coordination (one kind of coordination repair) is an essential part of CNS development and repair by movement-based learning.

1.2.5 Quantifying the Improvement of CNS Functioning by Measuring Pattern Stability upon Pattern Change when Exercising on the Special CDT Device

Experimentally, the underlying dynamics of coordinated movements can be found in the temporal stability of coordination patterns and can be assessed through pattern change (second novel step). A change of the coordinated movement patterns is generated, when a subject is exercising on the special CDT and recording device (Fig. 1.17), where the coordination between arms and legs, imposed by the device, changes continuously between pace (P) and trot gait (K) and backwards. The stability of the intrinsic coordination pattern tendencies is measured by the deviations and differential stability during the performance of these rhythmic movements. When the differential stability of the movement pattern is high, the arrhythmicity of exercising is small and when the stability is low the arrhythmicity of exercising in that pattern is high. From standard coordination dynamics trace it can be seen that in the healthy case the arrhythmicity is low for the pace and trot gait coordination's and is high for the intermediate coordination's between pace and trot gate. The pace and trot gait coordination's between arm and leg movements have a high stability (low amplitude arrhythmia) and the intermediate coordination patterns have a low stability (high arrhythmia).

The mean stability per minute can be measured by the arrhythmia of exercising (df/dt:f, f = frequency; or dv/dt, v = angular velocity). Such differential stability value per minute, the so-called coordination dynamics (CD) value, quantifies CNS functioning objectively, integrative and non-invasively. The practical assessment of quality of CNS organization by pattern change is a **third novel step in CDT**.

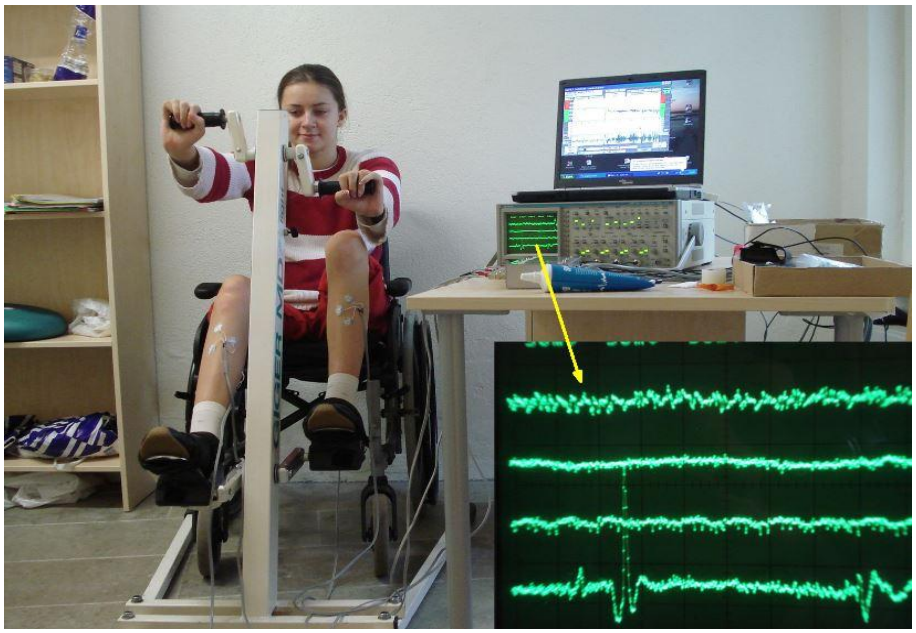


Fig. 1.17. Layout for measuring coordination dynamics (arrhythmicity of exercising) between arm and leg movements, displayed on the laptop; for the intermediate coordination's between pace and trot gait, the fluctuation of the network states is larger. The recording of sEMG activity (displayed on the oscilloscope) from the tibialis anterior and other muscles is also shown. The inset shows single motor unit action potentials on the lowest trace. The recordings are taken from a patient (Kadri) with a motoric complete cervical SCI C5/6 (95% injury)

In Fig. 1.18 it is shown for a patient with a very severe brain injury (Sotiris) following a car accident that brain repair, quantified by high-load coordination dynamics (CD) values, needs years. This patient needed 4 years to reach comparable good high-load CD values. The repair time in SCI depends strongly on the severance of the injury and is longer. For comparison, the rate of repair (the improvement curves of the high-load coordination dynamics values) of an athlete (C) and a healthy pupil (B) is inserted. Note that the brain-injured patient needed much more time to achieve similar good (low) CD values. The athlete and the pupil needed for the substantial improvement of brain functioning approximately 1 month. For roughly the same nervous system improvement the patient with the very severe brain injury needed 4 years, that means the efficiency of movement-based learning was lower by approximately a factor of 50. This means, CNS repair through learning needs years.

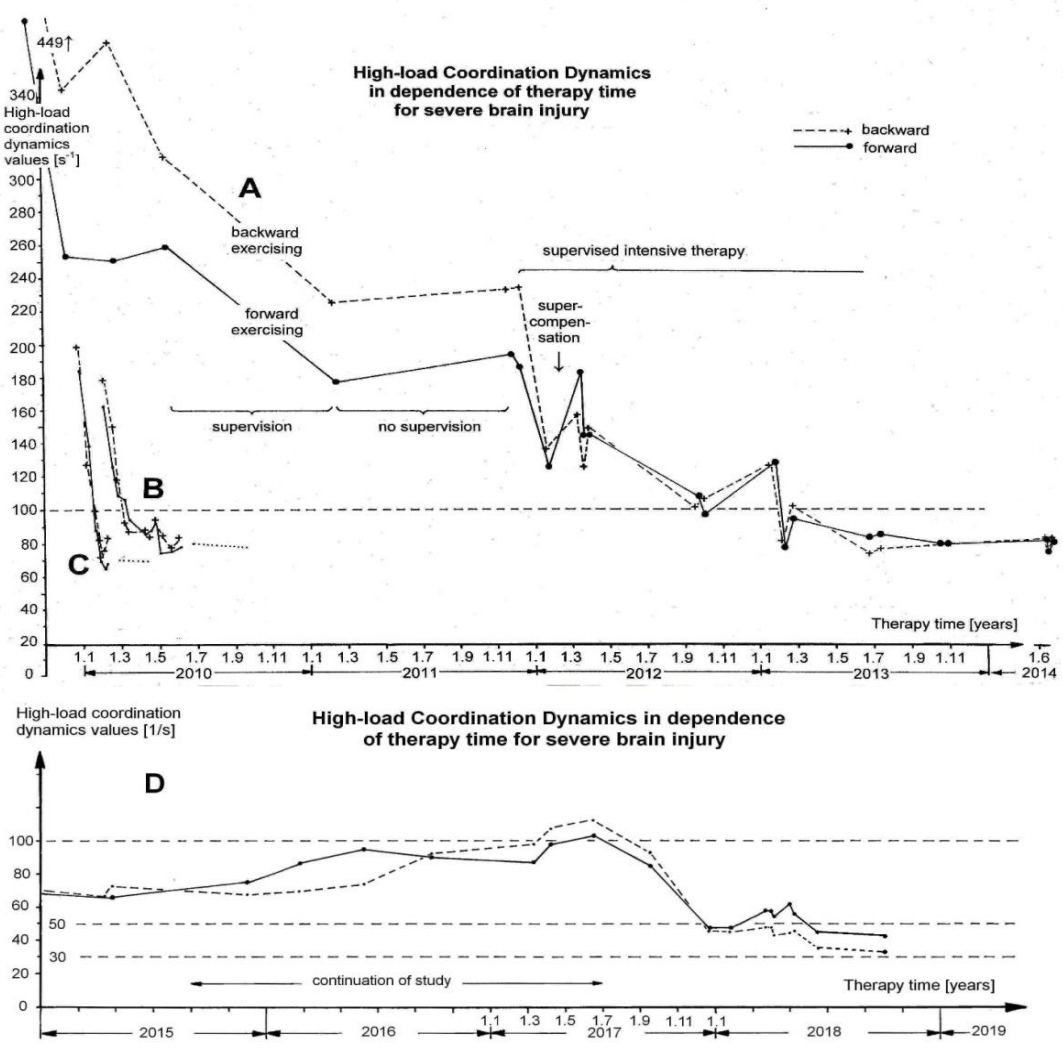


Fig. 1.18. A. Improvement of high-load coordination dynamics (CD) values in a patient with severe brain injury upon CDT for several years. The high-load CD values were obtained by summing up the single CD values for forward and backward exercising, Δ (high-load CD value) = Δ20N + Δ50N + 100N + Δ150N + 200N + Δ150N + Δ100N + Δ100N + Δ50N + Δ20N + Δ20N). B, C. For comparing the rate of repair, the improvement curves of the high-load coordination dynamics values of an athlete (C) and a healthy pupil (B) are inserted. Note that the brain-injured patient needed much more time to achieve similar good CD values. D. Continuation of therapy. The substantial improvement of the high-load CD values (lower values), in the middle of 2018, motivated the patient Sotiris to continue his therapy at the limit.

1.3 RESULTS

1.3.1 Review of Spinal Cord Injury Repair via Coordination Dynamics Therapy

1.3.1.1 Repair in a group of spinal cord injury patients through 3 months of CDT

CDT was applied to 18 patients (average age 31 years, after a SCI between C4/5 and L4/5; the therapy was administered on average 5 years after the injury for a minimum of 3 months. The injuries were due to car accidents, working accidents, jumping into the water, motor-cycle accidents, playing ice hockey, a parachute accident and erroneous surgery. All (almost) complete SCI became incomplete, i.e. motor functions improved below the injury level, including trunk stability and arm, hand and leg functions. The organization of the CNS, quantified by the CD values, improved by 42% for forward and by 49% for backward moving when exercising on a special CDT device. The improvements of the CD were 53%, 32% and 48% for injuries in the cervical, thoracic, and lumbar range, respectively. Since the CD values did not change substantially prior to CDT, it did further improve with continued therapy, and worsened when the therapy was terminated, it is concluded that the improvement of CNS functioning above and below the SCI level was due to the therapy. As will be shown below SCI can partly be repaired if CDT is administered intensively with an efficient Therapy for a few years. With the improvement in single patients, details of repair will be given.

1.3.1.2 Spinal cord repair depends on the severance of the injury

A SCI is followed by a spinal shock of approximately 2 to 4 weeks and a spontaneous recovery. Following a complete SCI there is only little spontaneous recovery and following an incomplete injury, the main spontaneous recovery takes place in the following 6 months. One year after the injury the spontaneous recovery in mainly finished. The mainly spontaneous recovery is ‘sold’ by rehabilitation centers as SCI repair. Efficient movement treatment has to start as early as possible, best in the spinal shock phase.

The improvement of CNS functioning depends on the injury level, the severance of the SCI and the efficiency of the treatment. The repair is mainly a functional one and is achieved by a re-wiring of the remained tract fibers. The functional repair is therefore mainly achieved by a reorganization of the brain. As more tract fibers remained as more functional repair is possible.

Fig. 1.19 shows the CNS repair in dependence on the extent of the injury, quantified by MRI. In a 50% C5/6 injury (Fig. 1.19D), the patient can learn to walk, run and jump (Fig. 1.19G,H). Hand functions became quite good. Urinary bladder functions were repaired within 2 months. The patient had with some deficits a normal life. In a 95% C5/6 injury (Fig. 1.19B,C), the patient could not learn to freely walk and jump through 5 years of CDT. With substantial support walking and jumping was possible (Fig. 19E,F). The patient had very little hand and finger functions as is typical for severe C5/6 injury, because the motoneurons are mainly destroyed in the grey matter. But the urinary bladder functions were repaired through 3 years of intensive CDT. The bladder repair is firstly the most important function to be repaired and secondly, because of nearly no finger functions, the patient cannot empty the bladder by himself through intermittent catheterization. The patient loses the intimism sphere, because somebody else has to do the catheterization. In a 99% injury (Fig. 1.19A), the repair situation is worse. The urinary bladder could not be repaired within 3 years of rather intensive therapy.

It is obvious from Fig. 1.19 that possible repair depends strongly on the severance of the injury. In SCI repair the damage has to be documented.

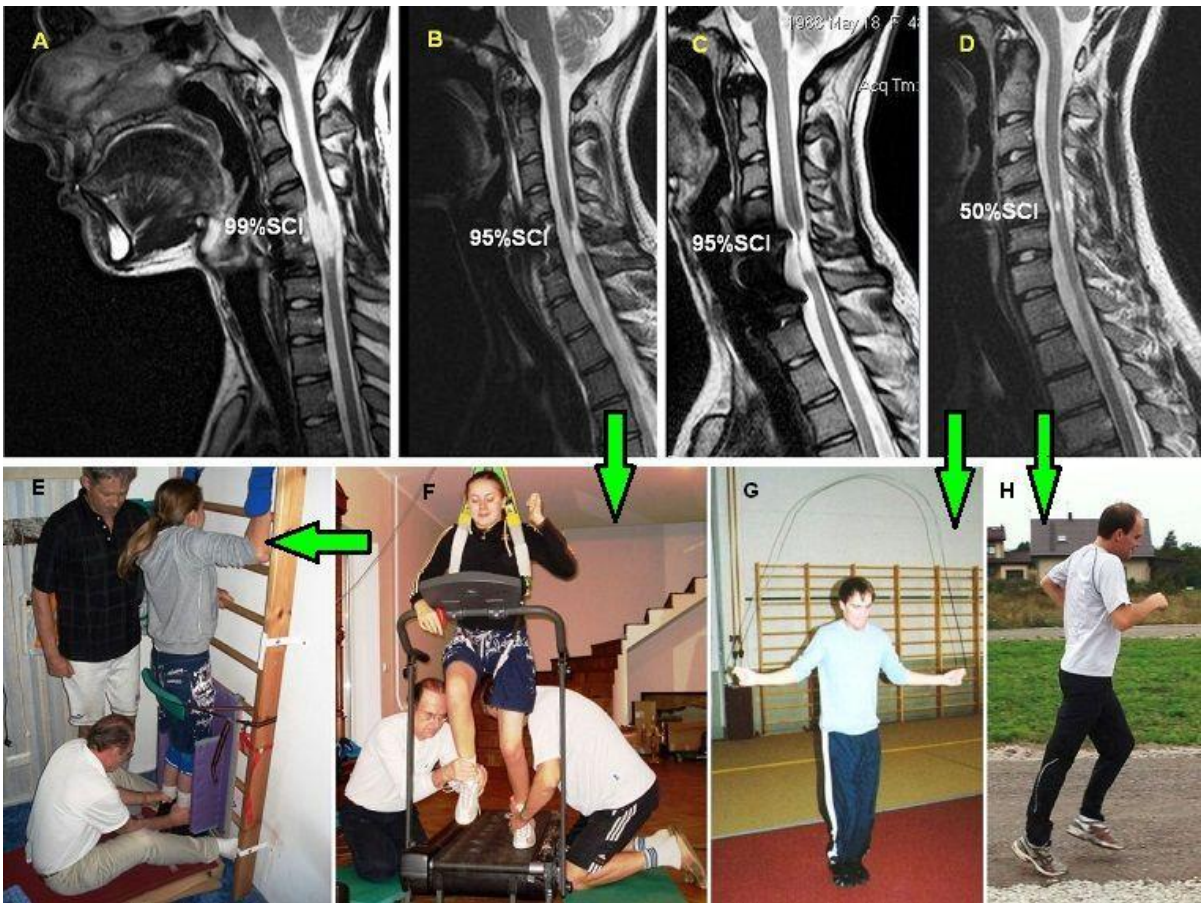


Fig. 1.19. The outcome of a SCI repair depends strongly on the severance of the injury. A-D. MRI's of approximately 99%, 95% and 50% injury. C shows the 50% injury with titan fixation and B without. The severance of an injury can also be estimated with a fixation in place. G,H. In 50% injury, the patient can relearn walking, running and jumping. E,F. In 95% (and 99%) the patient cannot re-learn free walking and jumping

1.3.1.3 Motor Improvement in 50% SCI

The 17.5-year-old male patient Sten suffered a cervical SCI at C5-6 levels in a diving accident. The SCI was incomplete (ASIA grade D). Some sensory-motor functions were preserved below the level of injury. Initially the patient received conventional rehabilitation treatment and then CDT was started, 5 months after the injury. At the time of initiation of CDT, this patient needed a stick as support for walking, was wearing an orthosis on the left foot and emptied the bladder with intermittent catheterization. During walking, the left heel was not touching the ground. While jumping on the springboard, his feet had to be supported by the therapist. While turning on the special CDT devise, the left hand had to be fixed.

He received nearly three years of non-optimal CDT. One year after the injury, the metal support, used for spine fixation, was removed. At the end of the 3rd year of CDT, he was able to walk, run, and even jump independently and did not need any internal or external support. He was continent again and off of all medications. In that sense it can be safely said that the patient is almost cured from his quadriparesis.

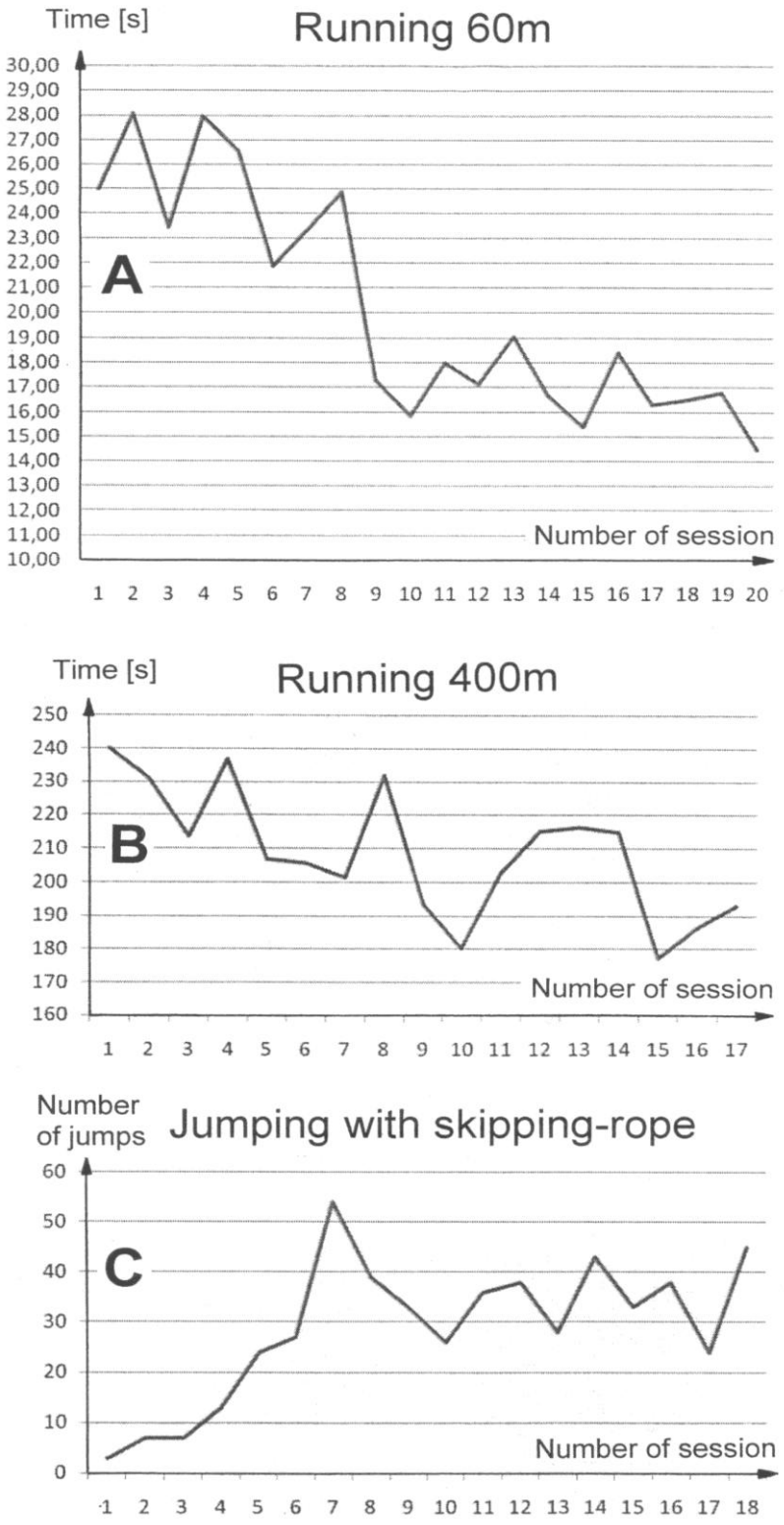


Fig. 1.20. Improvement of times for running 60 and 400m (A,B) and increase of jumps with a skipping-rope per single session (C) in relation to on-going therapy sessions. Therapy period = second half of 2006 (see Fig. 1.21)

In Sten with the 50% SCI at the level of C5/6, the coordination dynamics (CD) values for 20N had improved strongly after approximately one year of CDT (Fig. 1.21). For 100N, when going deeper into the complexity of CNS organization, good CD values were reached only after 2 to 3 years. For 150N, going even more deep into the complexity of CNS organization, good baseline CD values were only achieved after 4 to 5 years of non-optimal CDT (Fig. 1.21).

Such high-load CD values improvement should also have visible improvement in motor performance. The motor training of the patient (which included crawling, walking and running on treadmill in the forward and backward direction, jumping on spring-board,) was guided by the therapist to correct abnormal movement patterns. At the end of the 3 years of therapy, the significant improvement of coordination dynamics values (Fig. 1.21) was accompanied by a substantial improvement in the performance of running and jumping with the skipping rope (Fig. 1.19G). The times required for running 60 and 400 meters decreased and the number of jumps per series increased (Fig. 1.20). Even later on, the patient took part in Marathon with healthy people. He was one of the last ones, but among healthy participants.

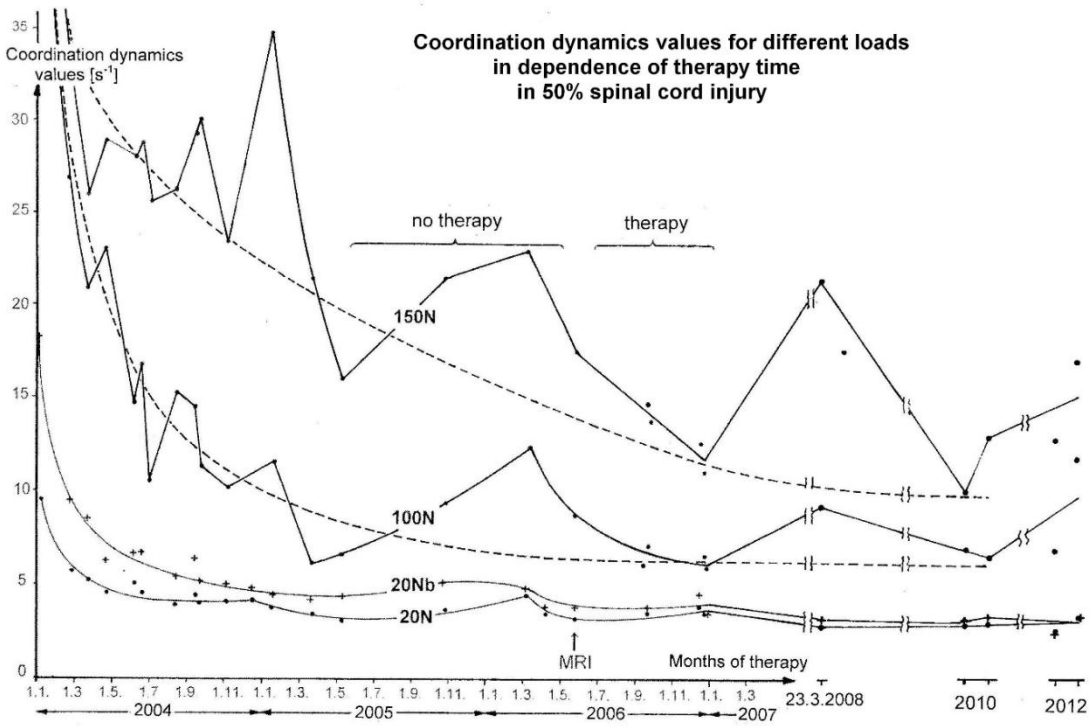


Fig. 1.21. Relation of coordination dynamics values to therapy length for increasing load between 20 and 150N. The loads for forward exercising (dots, 20N, 100N, 150N) are marked at the curves (20Nb = backward exercising (crosses) at 20N). Note that with no therapy the coordination dynamics values got worse and upon administering therapy again the values improved again even 2 years after the accident. After stopping therapy, the coordination dynamics values for 100 and 150N increased again (23.3.2008). When the patient (Sten) trained himself intensively (including running and jumping), he further improved his high-load CD values (8.9. and 23.9.2010)

By comparing the improvement of the coordination dynamics values for higher loads (150N) of the patient with a 50% SCI (Fig. 1.21) with those of the patient with a severe brain injury (Fig. 1.18), it can be seen that they are similar. This means that the repair of a 50% SCI is mainly a functional one and is taking place in the brain. Regeneration of tract fibers will have contributed only little.

1.3.1.4 Motor Improvement in 95% and 99% SCI at C5/6 Levels

In an almost complete cervical SCI, the caudal spinal cord is disconnected from the cerebral cortex and brain stem. Following the spinal shock some reflexes, such as the stepping automatism and urinary bladder reflex (similar to those in infants), may re-appear, especially when stimulated. Pathologic reflexes or automatisms also appear as for example extensor spasticity. With very limited regeneration upon CDT, motor and vegetative functions partly re-appear in a cephalo-caudal direction and movements become controlled first proximally and then distally; spasticity reduces. This cephalo-caudal and proximal to distal scheme only partly holds, because the injured CNS uses all existing repair and adaptation mechanisms upon movement-based learning, including plexus connections outside the spinal cord. But with respect to the improvement of trunk stability and breathing the repair in cephalo-caudal direction seems to hold.

1.3.1.5 Comparison between repair and development in two almost complete SCI patients with respect to administered therapy time

To improve the efficiency of SCI repair through CDT, it may be helpful to compare the improvement of trunk control and antigravity movements between development and repair. For the comparison two patients with similar severe cervical SCI were used. The MRIs are shown in Fig. 1.22J,K. Through 2 years of therapy, the boy (99% injury) mainly regained some trunk control and the breathing improved; the urinary bladder function could not be repaired within 2 years. To the young lady Kadri (95% injury) 5 years of CDT were administered. Bladder function was repaired and many movements improved including breathing. The MRIs of the patient's SCI are shown in Fig. 1.22J,K and the two treatment stages are compared with the development in Figs. 1.22 and 1.23.

Through one year of CDT, the patient regained little trunk control and had big problems with the trunk rotation. Arms and legs could not be flexed for the rotational movement (Fig. 1.22A). Through 5 years of CDT, the patient Kadri could easily roll from supine to prone position and backwards. The movement performance with slightly flexed arms and legs (Fig. 1.22B) looks much healthier and more similar to those of an infant (Fig. 1.22C). The un-sustained sitting (Fig. 1.22F) following 0.5 years of therapy was also very poor. No leg flexion was possible. The back was not straight and the hand could not be opened (Fig. 1.22D). Following 5 years of therapy, the un-sustained sitting (Fig. 1.22E) was more similar to the pattern of the infant (Fig. 1.22F). The four-point kneeling (Fig. 1.22I) (crawling position) was poor following one year of treatment (stretched arms are not possible without support) (Fig. 1.22G) and better following 5 years of treatment (Fig. 1.22H). But the main weight was still on the arms (unsupported crawling was not possible). The feet and leg positioning was much better than in the other patient (Fig. 1.22G) and the arms could be stretched.

The hands to knees positioning of the infant (Fig. 1.23C) could be achieved in the patient upon one years of therapy (Fig. 1.23A). The wheelchair was necessary for hands to knees touch. But this position helps the patient to exercise the pace gait coordination and co-movement can be induced in the legs by the synchronous touch of the hands. Upon 5 years of CDT, the 'hands to knees' position could be achieved (Fig. 1.23B) and the abdominal muscles were activated, but very little power was in the legs and there was no (or not enough) dorsal flexion of the feet.

The supported standing of the infant with leg movements (Fig. 1.23F,I) was not possible in the patients, even following 5 years of CDT. The leg muscles had still too little muscle power. But with different supports, both patients could train upright movements with full weight-bearing, such as swinging/jumping on springboard and sky-walking (Fig. 1.23D,E). For walking on treadmill upon one year of therapy, weight-bearing and feet support was needed (Fig. 1.23G). Upon 5 years of CDT, the patient still needed weight-bearing support, but was able to move the legs volitionally without support (Fig. 1.23H), even though the dorsal flexion of the feet was missing. Upon walking bare foot on treadmill, the stepping automatism was stimulated strongly. The supported standing pattern of the infant (Fig. 1.23I) was still a dream for both SCI patients. But development lasts 17 years. The patients could not catch up with the development, because for organizational reasons optimal CDT was stopped after 3 and 5 years respectively.

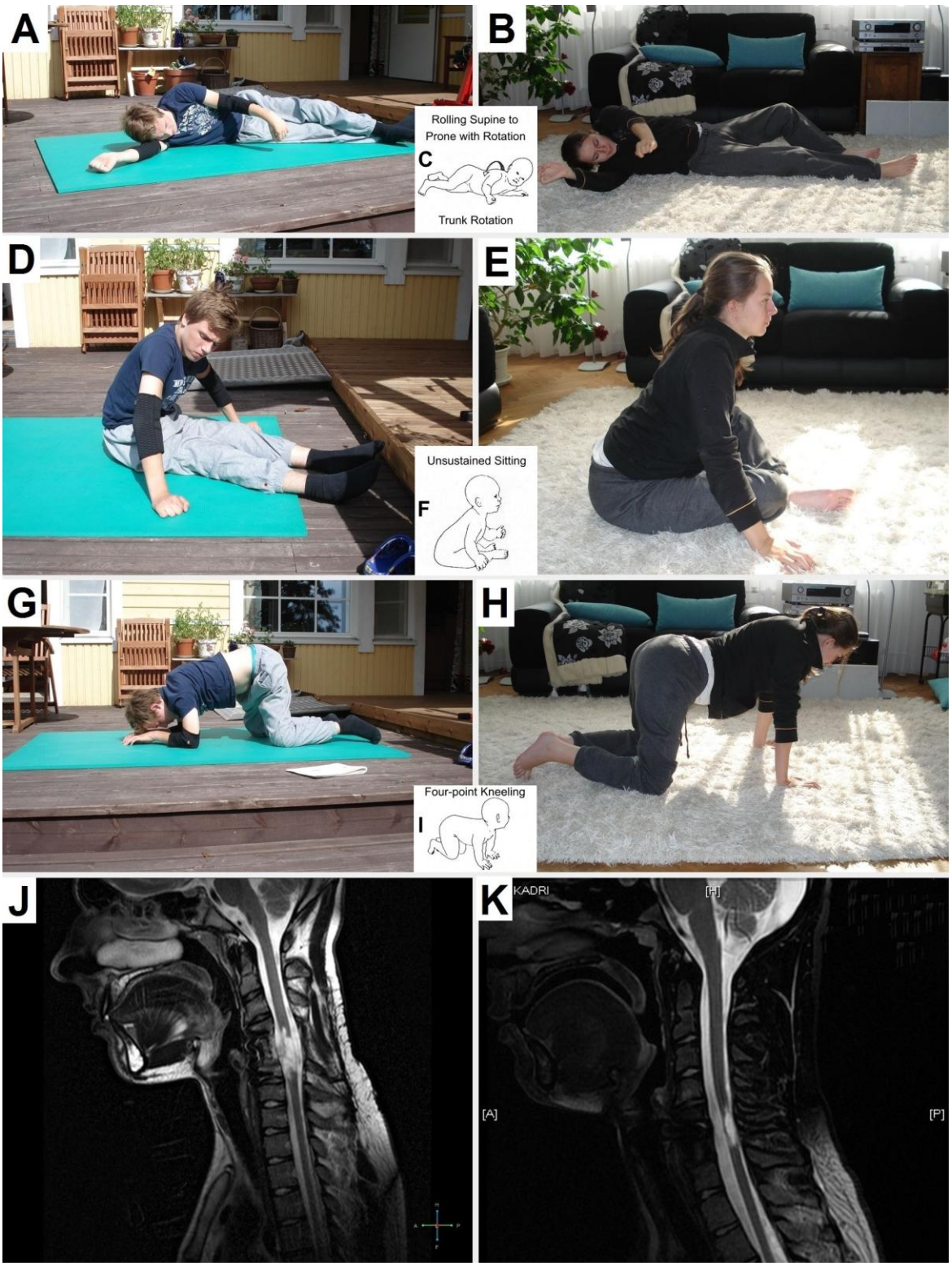


Fig. 1.22. Comparison between development and the repair of an almost complete cervical SCI upon one year (A,C,G) (therapy started at an age of 15.5 years) and 5 years of CDT (B,E,H) (CDT started with 17 years). The MRI of the SCI of the patient of the left panel is shown in 'I' and those one of the right panel in 'K'. Trunk rotation (A,B,C), un-sustained sitting (D,E,F), and four-point kneeling (G,H,I) is compared between one year and 5 years of CDT and with the positioning of an infant

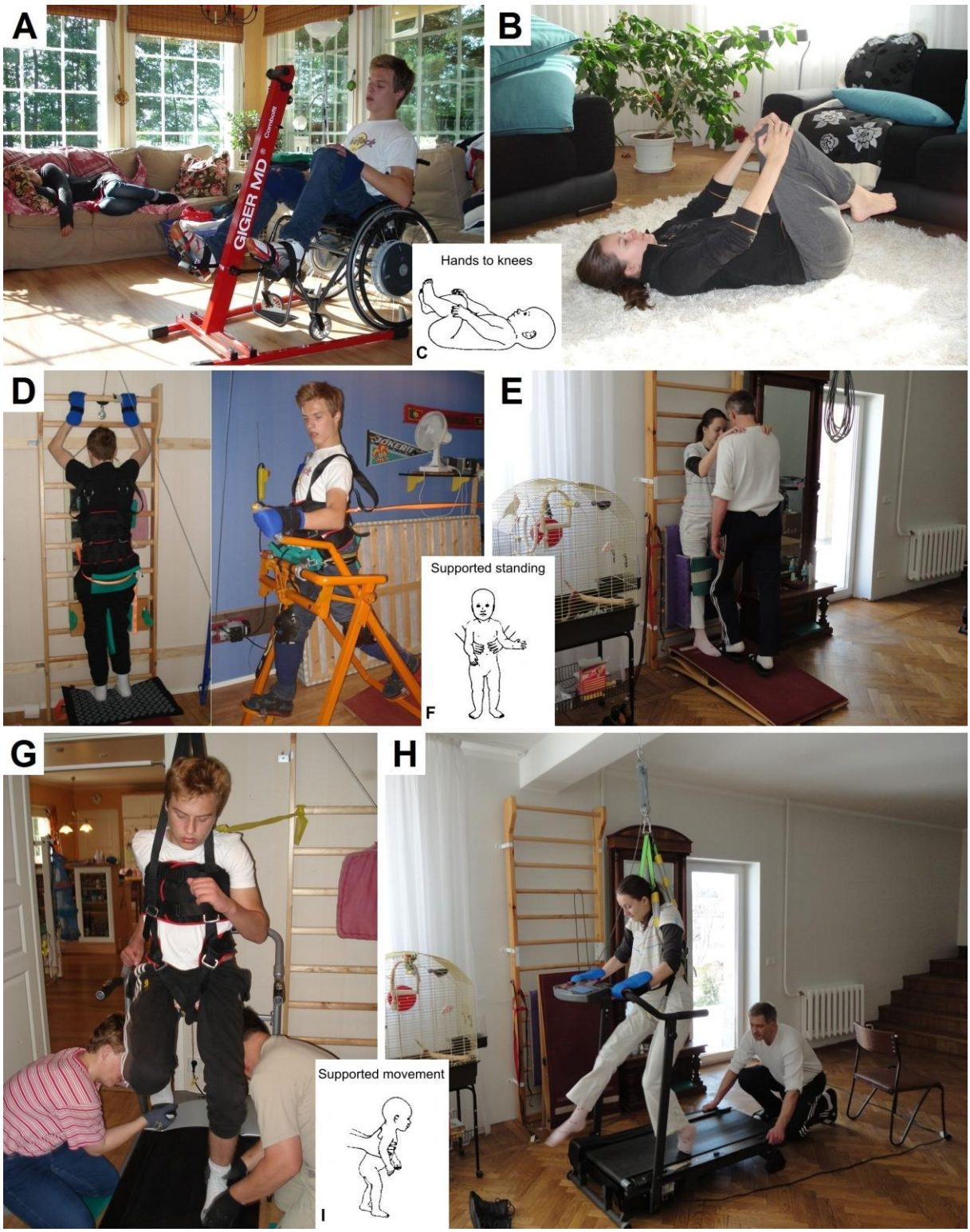


Fig. 1.23. Comparison between the development of an infant and repair of a cervical SCI upon CDT. Left penal, positioning upon 0.5 years of therapy and right penal after 5 years of therapy. Same patients as in Fig. 1.36. Reaching of hands to knees, supported standing, and supported walking are compared

In conclusion, in 95% and 99% SCI's, the motor possibilities are very limited and in no comparison to the 50% injury case. In 95% injury, Kadri could swing a bit with the legs under weight reduction (Fig. 1.23H) and jump a bit without support of the Author (Fig. 1.19E). In 99% injury (Fig. 1.23A,D,G), the patient could perform supported treadmill walking like in Fig. 1.23F, but could not learn within 3 years to swing the legs by himself (Fig. 1.23H). Also on floor movements, Kadri with a 95% injury was better than the patient with the 99% injury (Fig. 1.22). Both patients with the 99% and the 95% injury had no chance to re-learn walking like the patient Sten with a 50% injury. Probably one needs at least 20 % of the cord remained to re-learn a bit of walking.

1.3.1.6 Quantifying Spinal Cord Repair in 95% Injury

In 50% SCI it was shown that CNS repair could be quantified by the improvement (lowering) of the coordination dynamics (CD) values (Fig. 1.21) when exercising on the special CDT device. In 95% injury at the level of C5/6, the patients do not have sufficient muscle power to exercise at higher loads. Still it is helpful to record the CD values, because it can be seen that with every improvement of CNS functioning the CD values get worse, due to the transient impairment of the phase and frequency coordination following neural network change, before they get better again through therapy (Fig. 1.24). With every bit of repair or change of neural networks, the CD values get transiently worse.

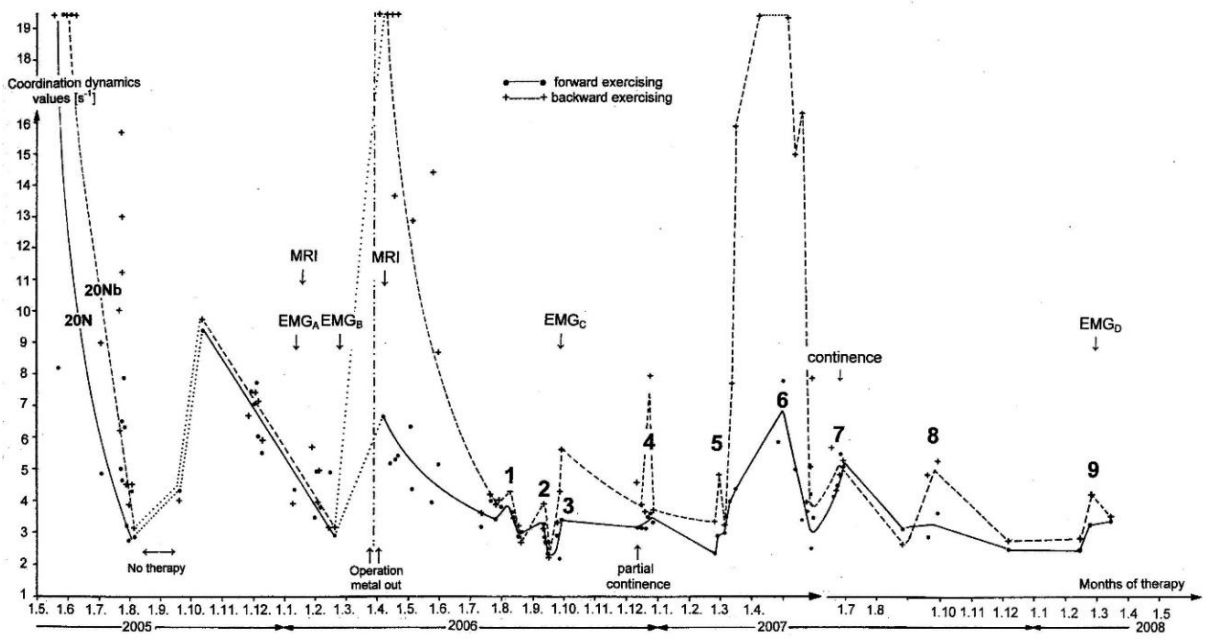


Fig. 1.24. Relation of coordination dynamics values to therapy duration for a load of 20N and for exercising in the forward (lines and dots) and backward directions (20Nb; dashed line and crosses) in a patient with a SCI sub C5/6 (Kadri). Note that with no therapy the coordination dynamics values got worse (increased) and upon therapy they improved again. Upon metal removal the coordination dynamics values increased strongly. The transient coordination dynamics value increases (peaks) '1' through '9' fall together with the re-appearance of certain muscle functions or specific improvements of motor and autonomic functions and indicate therefore most likely small bits of regeneration. After the large peak '6' of transient coordination dynamics value increase, urinary bladder functioning was re-learned

1.3.1.7 Comparison of urinary bladder repair between 50% and 95% spinal cord injury

The most important functions to be repaired in SCI are firstly the bladder repair, followed by the sexual function. The walking is on place 3 followed by spasticity and scoliosis.

In the patient with a 50% SCI (Sten) the bladder was fully repaired through 2 months of CDT. In the patient Kadri with a 95% SCI for the repair through CDT 2.5 years were needed. In the 99% injury the bladder was nor repaired within 2.5 years.

Because in 50% SCI the bladder is somehow functioning, the animal researcher cut only 50% of the cord in animals to avoid urinary bladder problems, even though it is the most important function to be repaired in SCI.

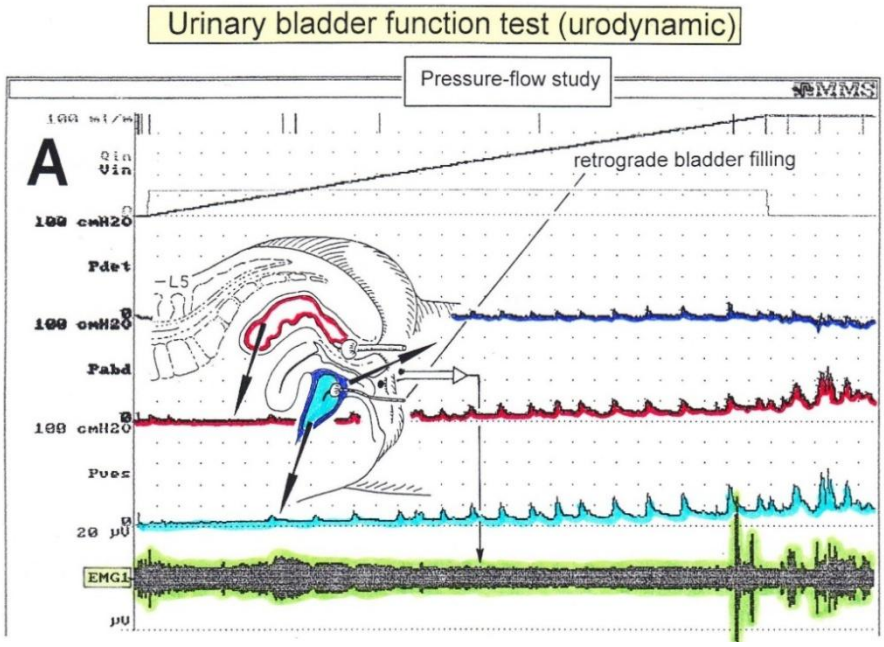
1.3.1.8 Clinical urinary bladder function test (Urodynamics)

The functioning of the urinary bladder can be evaluated by measuring the pressure in the bladder and in the abdomen (colon) and the electromyographic (EMG) activity of the external sphincters and/or functionally associated pelvic floor muscles. Such bladder diagnosis is called urodynamics (Fig. 1.25). Especially the simultaneous activation of the detrusor (line detrusor pressure in Fig. 1.25B) and the sphincteric and/or pelvic floor muscles (line pelvic floor EMG in Fig. 1.25B), the so-called detrusor-sphincter-dyssynergia, can be measured, which may destroy the kidneys on the long term.

Upon retrograde filling of the bladder in a patient with a SCI, the pressure in the bladder and colon is measured and the electromyographic activity (EMG) of the pelvic floor is recorded with surface electrodes (Fig. 1.25). The detrusor pressure is obtained by subtracting the abdominal pressure from the bladder pressure. The continence status of the patient is diagnosed by the reports of the first feeling of bladder fullness, the desire to void, and the leaving of fluid out of the bladder. The EMG activity of the pelvic floor informs when the external bladder and anal sphincters are activated. Upon knocking, pressing, coughing, and stimulating bladder reflexes, the bladder status is obtained. This patient of Fig. 1.25 with a SCI subTh12 had a detrusor-sphincteric-dyssynergia of the bladder, because the EMG activity of the external sphincters increased (the sphincters became activated) with the increase of the detrusor pressure (activation of the detrusor). Improvement of urinary bladder function mainly due to therapy can be quantified by repeated urodynamics measurements (Fig. 1.25AB).

1.3.1.9 Limitation of urodynamics and need for human electrophysiology for causal repair

The evaluation of bladder functioning by means of urodynamics gave the information that the patient had a dyssynergia of the bladder. Repeated testing informed about changes in bladder functioning. But such bladder function tests are giving no information on the pathology of the CNS organization and how to repair urinary bladder functioning causally.



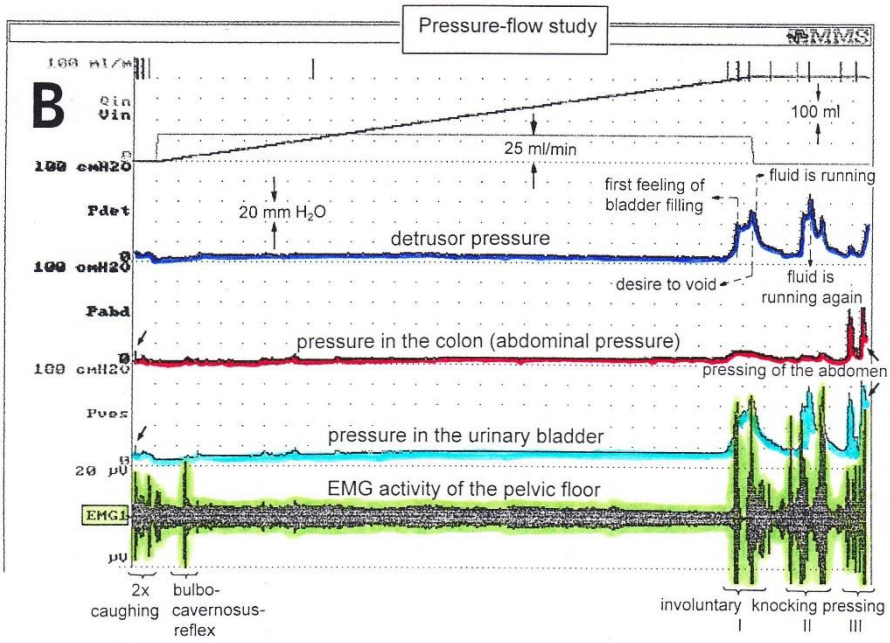


Fig. 1.25. Clinical urinary bladder function test (Urodynamics). Improvement of the urinary bladder functions, quantified by urodynamics in a 30-year-old female patient. A. 3 months after the accident resulting paraplegia sub Th12 following spinal cord lesion. B. 12 months after the accident (lesion level lowered to sub L3). In A, the detrusor pressure (P_{det}) is generated by the contracture of the bladder wall, as the pressure difference between abdominal pressure (P_{abd}, measured in the rectum) and the bladder pressure (P_{ves}, measured in the bladder). Electromyographic recording obtained with surface electrodes from the sphincters and the pelvic floor (EMG) is shown; the external sphincters and the functionally correlated pelvic floor muscles show similar sEMG activity (the rhythmic pressure peaks in A do not originate in the bladder). In A, the detrusor shows nearly no activity with retrograde bladder filling at 25 ml/min; in B, the detrusor shows first activity at 360 ml bladder filling. A detrusor-sphincteric-dyssynergia occurs, because the detrusor pressure peaks occur at the same time as the sphincter EMG activity peaks (B) (bladder and sphincter contract at the same time, so that fluid can only emerge from the bladder at high bladder pressure; there is a danger of reflux through the ureter into the kidneys). The EMG peaks are a bit irregular, probably because the fluid, leaving the bladder, shunts transiently the EMG electrodes. Exact functional description of B: 2x coughing (B below) increases the EMG activity and passively the pressure in the abdomen and in the bladder (marked by the small arrows, physiologic). The bulbocavernosus reflex (induced by pressure applied to the clitoris) increased the EMG activity of the sphincters (physiologic). Conclusion: The reflex arch is in order; sacral nerve roots and nerves have not been damaged in the accident. I (bottom right): The patient feels an increase of unvolitional detrusor pressure (first feeling of bladder pressure at 360 ml). She tries to contract the sphincters to stop the bladder emptying. Shortly after the desire to empty the bladder, as the detrusor pressure decreases, fluid is leaving the bladder. II: Due to tapping onto the bladder, the bladder reflex is activated (detrusor activated, nearly no abdominal pressure); fluid is leaving the bladder. III: Due to the abdominal muscular pressure the pressure in the abdomen increases as does passively the pressure in the bladder (the detrusor is not activated); fluid left the bladder. With a delay, the detrusor was activated by the bladder reflex. - The urinary bladder of the patient is partly functioning. It has to be further improved by therapy induced reorganization of the CNS: (1) An earlier feeling of bladder filling, (2) an increase of the time difference between the feeling of the first bladder filling and the un-volitionally emptying of the bladder (for the time being, approx. 10 min, in dependence on whether the patient is physically active (such as walking) or not, (3) further learning how to activate the detrusor on volition, and (4) the physiologic coordination between the bladder and the external sphincter functioning (to stop the detrusor-sphincter-dyssynergia)

By performing similar bladder tests under operational conditions and recording single-nerve fibre action potentials from sacral nerve roots (Fig. 1.6), the pathology of CNS organization can be explored in patients with SCI and ideas can be found how to repair the injured CNS causally. Since humans have a high capability for learning it is possible to repair the injured networks by learning and learning transfer from exercising on the special CDT device and jumping. By comparing bladder and motor functions at the neuron level, it may be understandable why learning transfer from movements to bladder functions is possible.

1.3.1.10 Bladder functioning at the neuron level

With the single-nerve fiber action potential recording method (Fig. 1.6) it has so far been possible to record single-nerve fiber action potentials from nerve fibers down to a diameter of approximately 3.5 µm in undissected thin long sacral nerve roots/fascicles. It has therefore also been possible to record natural impulse patterns from parasympathetic efferents (par) (Fig. 1.26), urinary bladder stretch and tension receptor afferents (S1, ST), mucosa afferents from mechanoreceptors of the bladder, the urethra and the anal canal (M), from afferents responding to fluid movement (S2), and from α_2, α_3 and γ-motoneurons and muscle spindle afferents innervating the external striated urinary bladder and anal sphincters (or functionally associated pelvic floor muscles), and to analyze regulatory and organizational mechanisms of parasympathetic neurons and motoneurons in the human CNS (Fig. 1.27).

It has been reported that the sacral autonomic outflow is sympathetic [26]. This report is not fully convincing, because in the publication electrophysiological (functional) recordings are missing. But if the sacral autonomic outflow is really sympathetic, this would not change the considerations, when just replacing the word parasympathetic by sympathetic.

Following a laminectomy, natural impulse traffic (somatic and autonomic) to and from the CNS can be recorded from sacral nerve roots (Fig. 1.26). The summed impulse traffic can be split into the natural impulse patterns of single afferent and efferent fibers. Upon retrograde bladder filling as in clinical diagnostic (Fig. 1.25) and the identification of the neuron type, with the use of the classification scheme for human nerve fibers (Fig. 1.9), the natural impulse patterns of identified afferent and efferent fibers can be obtained and analyzed. The obtained natural impulse patterns running in and out of the CNS answered an old question: Is it the firing rate of a neuron that codes the information transmitted and processed or does the precise timing of cell discharge codes information? It is shown here that the information from and to the periphery is coded by specific impulse patterns, including the precise timing and the firing rate.

In response to retrograde bladder filling as during urodynamics (Fig. 1.25) of a brain-dead human, the self-organization of a premotor spinal α_2-oscillator innervating the external striated urinary bladder sphincter is shown in Fig. 1.28D. Because the motoneuron axon of O1 had a recurrent fiber (Fig. 1.28A) at the recording site, each single AP of this motoneuron could be identified safely by the action potential (AP) of the recurrent fiber. The function of the motoneuron was to secure bladder continence. The activity from urinary bladder receptors, i.e. the activity of bladder stretch (S1), tension (ST) and flow receptor afferents (S2) (Fig. 1.28E), was an adequate afferent input to the motoneuron. Phase relations between the firing patterns of bladder afferent fiber S1(1) and oscillatory firing urinary bladder sphincteric motoneuron O1 can be seen in the schematized firing patterns in Fig. 1.28B. They were an indicator that the natural impulse pattern of the S1(1) fiber was an adequate drive of the sphincteric motoneuron O1. For retrograde bladder filling up to 550 ml, motoneuron O1 only fired occasionally (Fig. 1.28D,F). This was the storage phase of the bladder, during which the intravesical bladder pressure increased only little. For higher bladder filling volumes, the motoneuron switched via the transient oscillatory firing mode to the continuous oscillatory firing mode (Fig. 1.28D) to generate a higher activity level (Fig. 1.28F) for a stronger drive of the urethral sphincter to more strongly secure continence when the storage phase was nearly passed and the bladder pressure increased. For bladder filling volumes higher than 800 ml, the activity of the spinal oscillator decreased again; probably, the oscillator became inhibited (Fig. 1.28D). Pain fibers (not shown in Fig. 1.28G) may have inhibited the oscillatory firing to protect the bladder from mechanical damage. The overflow

mechanism was initiated. Probably, fluid entered the trigonum vesicae to activate flow receptors, so that the flow receptor activity (S2) increased strongly (Fig. 1.28E). The premotor spinal oscillator O1, of which motoneuron O1 is probably a part, was organized by the adequate afferent input (S1, ST, S2, ...) induced by bladder filling.

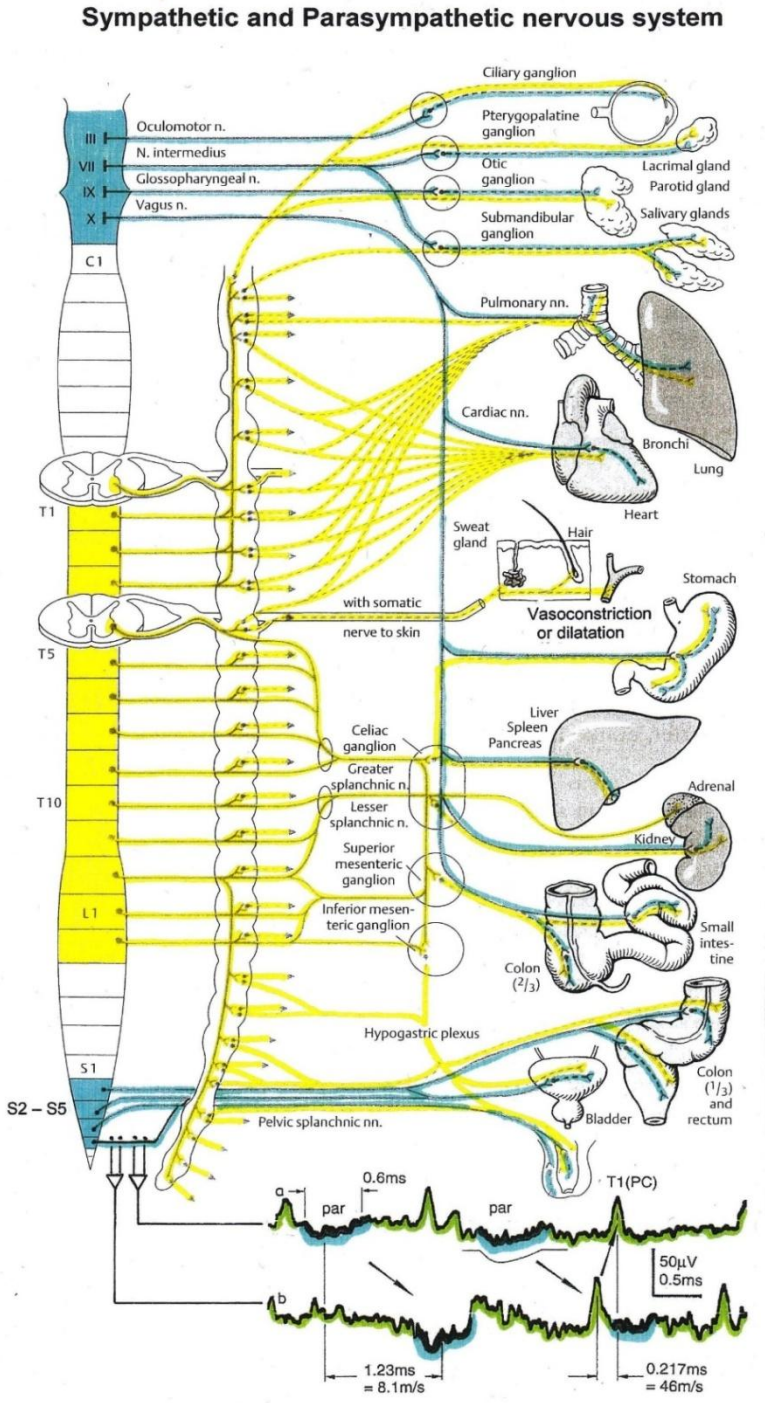


Fig. 1.26. Schematic diagram of the sympathetic and parasympathetic nervous system. Yellow = sympathetic, blue = parasympathetic. The recording from a sacral root shows single action potentials of preganglionic neurons (par) and a skin afferent fiber

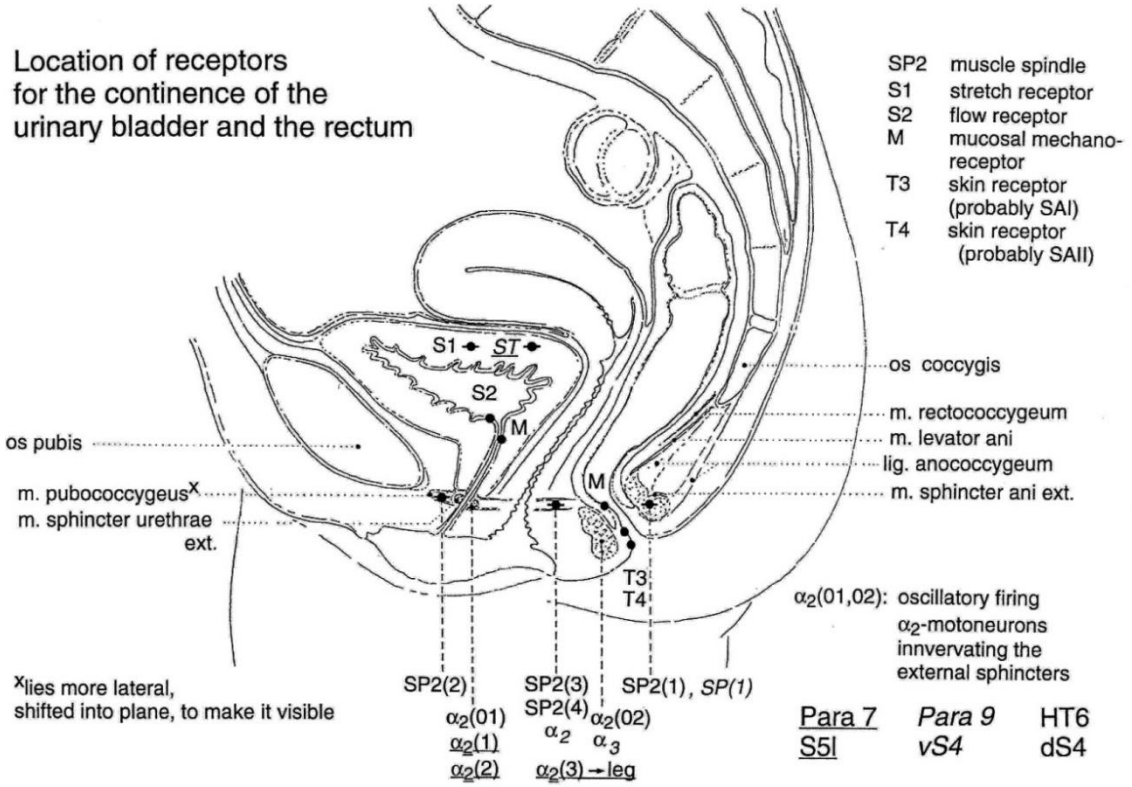


Fig. 1.27. Location of receptors and muscles for the continence of the urinary bladder and the rectum, innervated by motoneurons the activities of which were recorded, in the brain-dead human HT6 (dS4 root), paraplegic 9 (vS4 root) and paraplegic 7 (nerve root S5)

A. Recordings from α_2-motoneurons O1 and O2, firing in the oscillatory mode with impulse trains of 2 (upper recording) and 3 (lower recording) action potentials (APs). The durations of the oscillation periods were 110 (O1) and 164ms (O2). The interspike intervals of the impulse trains were 5.9ms (O1) and 4.6 and 7.4ms (O2). Motoneuron O1 conducted at 36 m/s; its recurrent fiber conducted at 21 m/s. The measurement layout is shown schematically. The inserts show the oscillatory firing modes; they have not been drawn to scale.

By recording from the dorsal S4 root of the brain-dead human HT6, impulse trains from another oscillatory firing motoneuron and its driving afferents were measured, which served quite a different function (Fig. 1.28F). The α_2-oscillator O2 (Fig. 1.28A,B) innervating the striated external anal sphincter was activated by secondary muscle spindle afferent activity, induced by the anal catheter-stretched muscle spindles, probably located in the anal sphincter or functionally associated pelvic floor muscles. Also, mucosal and skin receptors within the anal reflex area will induce self-organization of premotor oscillators activating the external anal sphincter to secure anal/rectum continence. It is evident from the impulse patterns, shown schematically in Fig. 1.28B, that the impulse trains of this oscillator O2 show a phase relation and an interspike interval relation to its driving spindle afferent APs. But no synchronized firing can be seen between the sphincteric α_2-motoneurons, innervating the external bladder sphincter (O1) and anal sphincter (O2). Probably the CNS networks tried to avoid an increased physiologic tremor. Important for the application of human neurophysiology to neurotherapy is the duality of the functions of the sphincteric motoneurons and secondary muscle spindle afferents, sub-serving somatosensory and autonomic (parasympathetic) functions. In animals it was found that also sympathetic fibers innervate intrafusal muscle fibers in muscle spindles [27]. It is likely that also parasympathetic efference innervate intrafusal muscle fibers in muscle spindles in the parasympathetic innervation area (S2-S5).

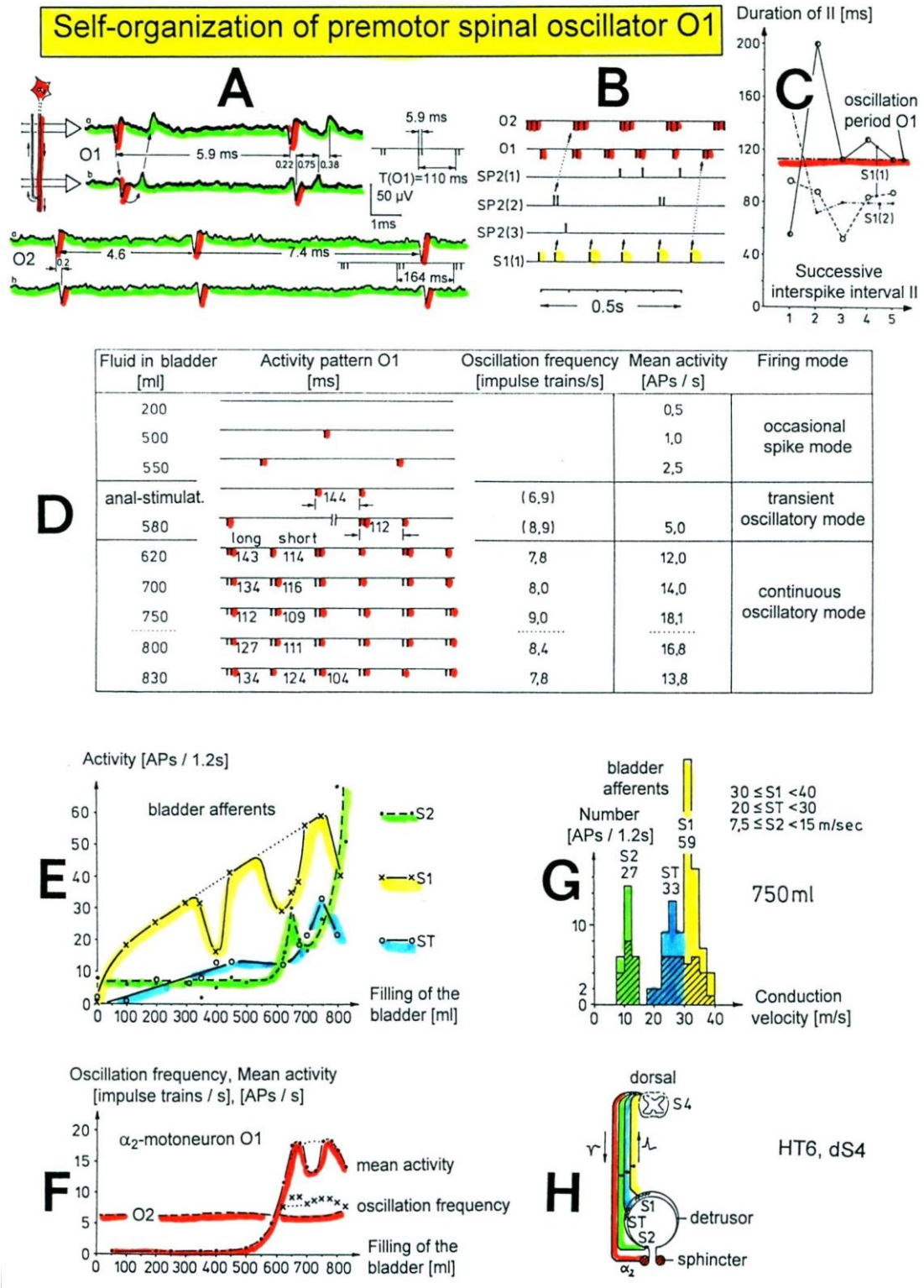


Fig. 1.28. Self-organization of premotor spinal α_2-oscillator O1, which innervates the external urinary bladder sphincter (skeletal muscle). Brain-dead human HT6; recording from a dorsal S4 nerve root

Motoneurons innervating the external sphincters of the bladder and the anal canal sub-serve somatic functions (contraction of the sphincters on volition or for protection reaction) and parasympathetic functions for the coordination of the detrusor function (parasympathetic) and the external sphincter function (somatic). This duality of the sphincteric motoneurons (and spindle afferents in the parasympathetic domain) makes the pattern change from continence to protection reaction understandable and makes learning transfer between somatic and parasympathetic patterns likely. The motoneurons build up two phase relations per oscillation cycle with other motoneurons and secondary spindle afferents for somatic activation [28], and build up 3 phase relations per oscillation cycle when also the parasympathetic division is activated [28]. The neuronal networks of the somatic and the parasympathetic nervous systems are interlaced and interact with each other. It should therefore be possible to improve parasympathetic functions when improving somatic functions by CDT (neural network learning [19]), especially as there is indication that also parasympathetic efferents fire rhythmically [29].

The repair of urinary bladder functioning by reorganization of networks seems to be most difficult because there is false neuronal network organization in the parasympathetic nervous system (overactive (spastic) detrusor) and the somatic division (spastic external (striated) bladder sphincter), and there is false interaction of the interlacing somatic and parasympathetic networks (detrusor-sphincteric dyssynergia: when the detrusor contracts, the external sphincter is also contracting instead of opening (relaxing)) [29-31].

But how can the neural networks be repaired, so that the bladder is functioning physiologically again and SCI and other patients have a rather normal life again. As will be shown below, this will be achieved through neural network repair [19] induced by movement-based learning (CDT) and learning transfer [23] from movements to urinary bladder functions. The most efficient movements to cure urinary bladder functions [9] are exercising on the special CDT device and jumping on springboard. But before coming to the repair of the bladder, more knowledge is needed concerning the neural network organization for physiologic bladder functioning.

1.3.1.11 Time course comparison between the proposed parasympathetically induced muscle spindle afferent activity and the detrusor pressure

In detrusor-sphincter dyssynergia of the urinary bladder, the somatic external bladder sphincter is activated at the same time as the detrusor (smooth muscle) with the consequence that the bladder cannot be emptied. This dyes-coordination between the somatic and parasympathetic nervous system divisions in the human sacral micturition center is reflected urodynamically (clinically) in the simultaneous increase of the detrusor pressure and the electromyographic activity of the pelvic floor (Fig. 1.25). Before analyzing the detrusor-sphincter dyssynergia at the neuron level an important **correlation between muscle spindle activity and detrusor pressure,** measured urodynamically, has to be done, namely that muscle spindles, also driven by the autonomic nervous system, show very similar activity changes than the detrusor pressure.

It was shown that the activity in parasympathetic efferents can be measured, identified and distinguished from the activity of γ-motoneurons in conduction velocity distribution histograms. Since the action potential amplitudes of parasympathetic efferents is small (Fig. 1.26), it would still be very difficult to analyze the organization of the parasympathetic nervous system and it's coordinated functioning with the somatic nervous system as in the control of the urinary bladder. But some secondary muscle spindles in the parasympathetic range are also innervated by parasympathetic efferents besides somatic efferents (γ-motoneurons). In animals it was found that also sympathetic fibres innervate muscle spindles [27]. The activation of the parasympathetic nervous system can therefore also be measured by the activity of secondary muscle spindle afferents. Since the action potentials of secondary spindle afferents are comparably large (thick fibers), the activation of the parasympathetic nervous system can be easily indirectly assessed. It will be shown now that at least some secondary muscle spindles in the parasympathetic range are innervated by parasympathetic efferents (parasympathetic fusimotors, with the above reassignment sympathetic fusimotors). The evidence is obtained by measuring the parasympathetic activation of the detrusor by detrusor pressure changes and by measuring activity changes of secondary muscle spindle afferent fibers and

compare the form of the changes of detrusor pressure with the activity changes of a secondary muscle spindle afferent fiber.

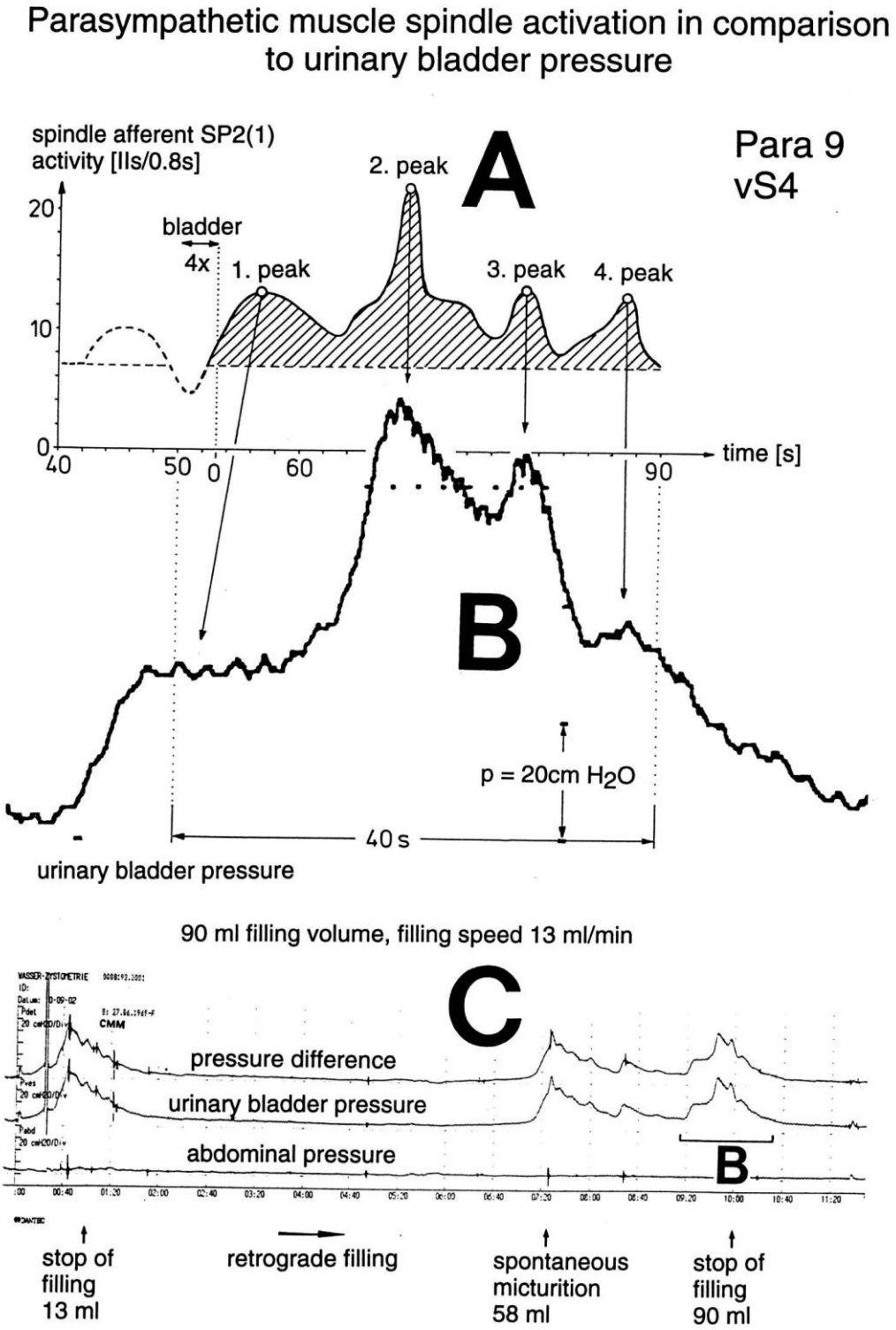


Fig. 1.29. Comparison between changes in secondary muscle spindle afferent activity and detrusor pressure (measured before the surgery; for the implantation of a sacral anterior root stimulator). Paraplegic 9

A. Activity changes of the afferent fiber SP2(1) following bladder catheter pulling (Fig. 1.37Ba). Approx. mean activity level is represented by a dashed line at 7.5 IIs/0.8s ((APs -1)/0.8s). The activity above the mean is cross-hatched and is proposed to be due to parasympathetic activation. Root vS4.

B. Detrusor pressure (pressure difference) changes taken from 'C'. Note that changes in the detrusor pressure show almost exactly the same time course as do the activated changes of the secondary muscle spindle afferent fiber SP2(1) of 'A'. Corresponding peaks are correlated by arrows.

C. Abdominal pressure (measured as rectal pressure), intravesical pressure (urinary bladder pressure) and detrusor pressure (pressure difference) during retrograde filling before the surgery. One transient detrusor pressure increase, marked 'B', is used, after enlargement in 'B', to compare with the spindle afferent activity.

In Fig. 1.29, the increase in detrusor pressure upon retrograde bladder filling before surgery is compared with the activity increase of the secondary muscle spindle afferent fiber SP2(1) during the operation following 4 times bladder catheter pulling. Fig. 1.29A shows the undulating activity increase of a SP2(1) fiber. In Fig. 1.29C the cystogram is shown. Upon bladder filling spontaneous micturition occurred several times. If parasympathetic fibers really activated muscle spindles, then the activity increase of the secondary muscle spindle afferent fibers following bladder catheter pulling may have a similar time course as does the bladder pressure increase due to detrusor activation following retrograde bladder filling. To check this similarity of time course, one undulating increase of detrusor pressure (Fig. 1.29C) has been brought to the same time scale as the measured changes in muscle spindle afferent activity (Fig. 1.29A) and transferred into Fig. 1.29B for a direct comparison with Fig. 1.29A. By comparing Fig. 1.29A with Fig. 1.29B, it can be seen that the occurrence of activity peaks of secondary spindle afferents is very similar in its time course to that of the peaks of the detrusor pressure. From the similarity of changes of spindle afferent activity and detrusor pressure (4 peaks) it can be concluded that some muscle spindles in the domain of the sacral parasympathetic nucleus are partly controlled by the parasympathetic division and that the muscle spindle and the detrusor activation have similar time courses.

Thus, there is indication that some muscle spindles are partly driven by the parasympathetic division. The drive can be by parasympathetic fusimotor activity or more indirectly by somatic fusimotors. Since in HT6, the somatic fusimotors did not change their activity levels strongly with the activation of preganglionic parasympathetic fibres and the activity increase of the secondary muscle spindle afferent fibre SP2(2) followed the transient increase of parasympathetic activity, it is likely that some muscle spindles are directly controlled by parasympathetic fusimotors. For further details see Chapter V of [17].

1.3.1.12 Detrusor-sphincter synergy of the bladder in the brain-dead human HT6 and dyssynergy in paraplegic 9

The measurement of parasympathetic activation of the detrusor by activity changes of secondary muscle spindle afferent fibers (the spindle is innervated by autonomic fusimotors) allows an analysis of detrusor-sphincter dyssynergia using the natural simultaneous impulse patterns of secondary muscle spindle afferents and sphincter α_2-motoneurons (and γ-motoneurons).

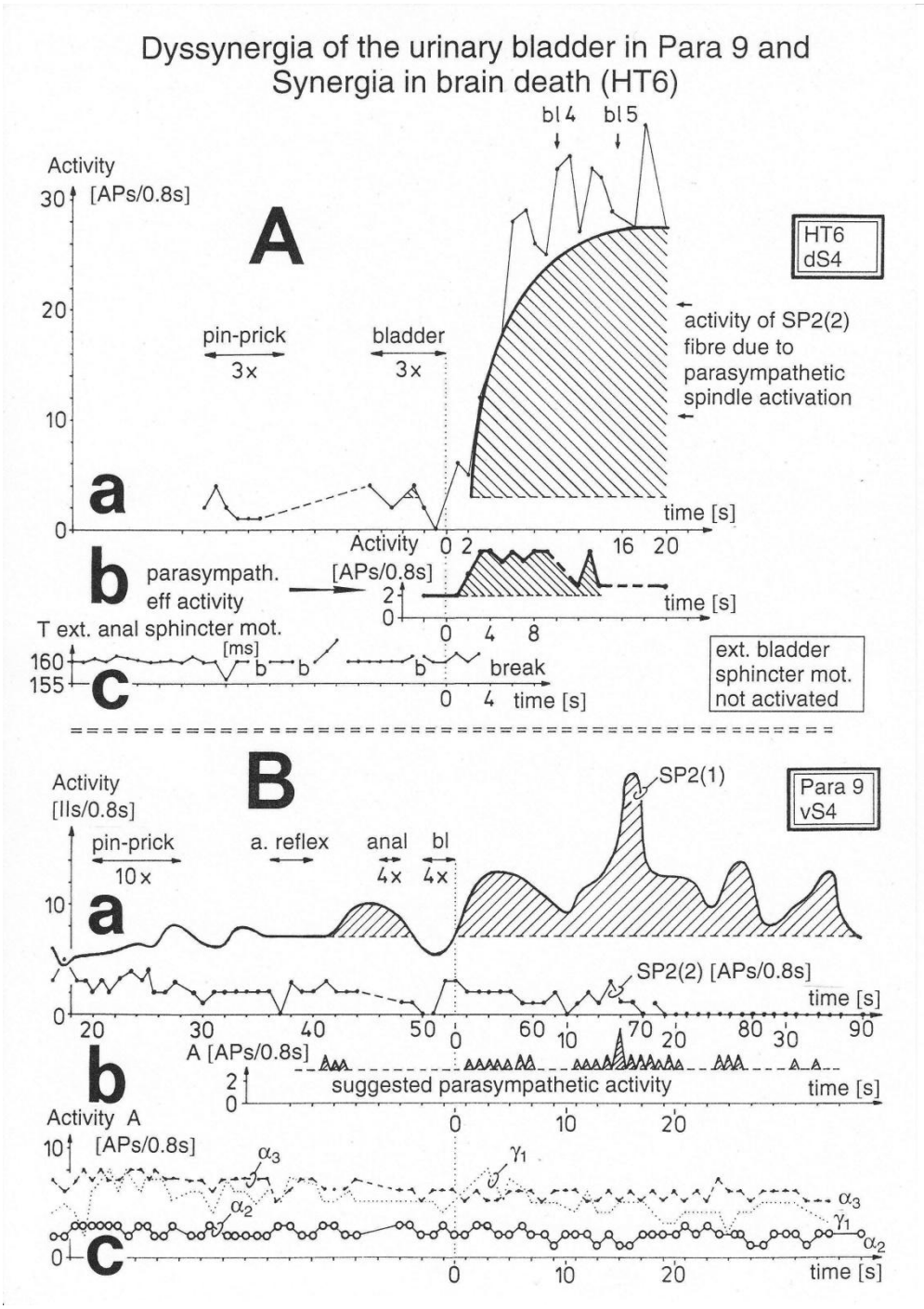


Fig. 1.30. Direct comparison of secondary muscle spindle afferent activity and motoneuron activity between the brain-dead human HT6 with a synergy of the bladder (A) and the paraplegic 9 with a dyssynergia of the bladder (B)

A. Simultaneous measurements of activities of secondary muscle spindle afferents (a), parasympathetic preganglionic motoneurons (b) and oscillatory firing (high activity mode) of a sphincter motoneuron innervating the striated anal sphincter (c). Note that with the transient activity increase of the parasympathetic fibers (b) the secondary muscle spindle afferent fiber increased strongly its activity (a) for minutes, and the oscillatory firing sphincter motoneuron discontinued its oscillation (c) to reduce strongly its activity. bladder 3x = 3 times bladder catheter pulling. T ext. anal

sphincter mot. = oscillation period of the sphincter α_2-motoneuron innervating the anal sphincter. For further details, see Chapter V of [1].

B. Simultaneous measurements of activity of secondary muscle spindle afferent fibers SP2(1) and SP2(2) following anal (anal 4x) and bladder catheter pulling (bl 4x) (a), and the activity changes of an α_2-motoneuron (FR) and α_3-motoneuron (S) and a dynamic fusimotor fiber (γ_1) (c). Note that following bladder catheter pulling (and probably parasympathetic activity increase), the spindle afferent fiber SP2(1) (most likely contributing to continence) increased its activity in an undulating manner (a), whereas the SP2(2) fiber did not (probably not connected to continence) (a), and the α-motoneurons did not reduce their activity (c). The dynamic fusimotor γ_1 transiently increased its activity similarly as in HT6 measurements. In similarity to 'Ab', the suggested parasympathetic activity increase is pictured (b). a. reflex = anal reflex stimulation. IIs = interspike intervals; IIs/0.8s = (APS – 1)/0.8s (the activity measures IIs/0.8s and APs/0.8s differ by '1').

Fig. 1.30A shows that in the brain-dead human HT6, whose parasympathetic preganglionic neurons increased activity (Fig. 1.30Ab) upon bladder catheter pulling, the SP2(2) fiber activity increased strongly (Fig. 1.30Aa), whereas the α_2-motoneuron innervating the external anal sphincter discontinued its oscillatory firing (Fig. 1.30Ac), which is a measure for a strong activity decrease. An α_2-motoneuron, innervating the external (striated) bladder sphincter, was not activated. This means that with the activation of the detrusor the sphincter motoneurons were relaxed by inhibition. Thus, the brain-dead human HT6 had a detrusor-sphincter synergy of the bladder.

In paraplegic 9 who showed a strong activity increase of the SP2(1) fiber, there was no sphincter relaxation following bladder catheter pulling (Fig. 1.30B). The secondary muscle spindle afferent fiber SP2(1) increased its activity in an undulating manner (Fig. 1.30Ba). The parasympathetic fusimotors, driving the muscle spindle, innervated by the SP2(1) fiber, probably were not continuously active as suggested by Fig. 1.30Bb, in contrast to the parasympathetic activity observed in HT6 (Fig. 1.30Ab). The other secondary muscle spindle afferent fiber in paraplegic 9 (SP2(2), Fig. 1.30Ba) slowly reduced its activity upon bladder catheter pulling. This spindle afferent fiber was not connected to the continence of the bladder. It is likely that its spindle was not parasympathetically innervated and was sited in leg muscles or parts of the pelvic floor muscles not contributing to continence. The α_2 and α_3-motoneurons (Fig. 1.30Bc) showed a high activation, which is expressed in their oscillatory firing, and probably contributed to the continence of the bladder and the rectum. These likely sphincter motoneurons did not reduce their activity following parasympathetic activation, as can be seen from the SP2(1) fiber activity (monitoring parasympathetic activity). These motoneurons were not inhibited and the external sphincters were probably not relaxed. The somatic fusimotor γ_1 (Fig. 1.30Bc) increased its activity transiently and slightly upon painful bladder catheter pulling, in similarity to a γ_1 fiber in HT6 [33]. The measurements in paraplegic 9 indicate a loss of the inhibitory action of the detrusor onto the sphincter motoneurons.

The time constant for the activity decrease of a spindle afferent fiber following parasympathetic activation was 31s in a paraplegic and approx. 40s in a brain-dead human (Chapter V of [17]). It is concluded that the muscle spindles are unchanged following SCI. The pathologic firing patterns of the SP2 fibers are thus probably a result of neuronal network changes in the parasympathetic and somatic nervous system divisions of the sacral micturition center.

In conclusion, in a brain-dead human (HT6) the sphincter motoneurons sub-serving continence were inhibited at a time, when preganglionic parasympathetic efferents increased their activity (physiologic) for 10s and an SP2 fiber increased its activity for several minutes. In a paraplegic with a strong bladder dysfunction, the SP2 fiber activity increased, due to parasympathetic activation, lasted for approx. one minute, showed undulations, and its amplitude was smaller than that measured in a brain-dead human. The sphincter motoneurons were not inhibited (pathologic).

By comparing the detrusor pressure curve and the sEMG of the pelvic floor of Fig. 1.25B with the single-neuron recordings of Fig.1.30B, it can be seen that both diagnostics gave the same result, namely that the parasympathetic activation of the detrusor was undulating and not strong continuously

and that the external bladder sphincter was not inhibited when the detrusor was activated. Therefore, the clinical urodynamics is a good clinical diagnostic for judging urinary bladder functioning. But the measurements at the single-neuron level gave more information, namely that the neural networks of the sacral micturition center in cooperation with the pontine micturition center were strongly dysfunction, including the impairment of phase and frequency coordination for neural network self-organization. But neural networks can be repaired through CDT, which means urinary bladder functions can be repair by movement-based learning, as will be shown below. For further details of the dysfunction of the neural networks of the sacral micturition center see Chapter V of [17] and a review of coordination dynamics therapy [3].

1.3.1.13 Urinary bladder repair in 95% spinal cord injury

A 17-year-old female patient (Kadri) suffered a severe cervical SCI in a car accident. No motor functions remained below the injury level of C5/6 and the patient had impaired feelings. From the MR images the author estimated that approximately 5% of the spinal cord matter was spared (Fig. 1.19B,C). When the spinal shock faded away, it became obvious that no motor functions remained below the injury level but spot wise sensitivity remained more or less all over the lower body. Two months after the accident CDT was started. Upon 2.5 years of CDT the sensitivity improved and some motor functions returned below the injury level, indicating that some regeneration of the spinal cord had occurred. Urinary bladder functions were repaired. Details of the repair are given below (Fig. 1.31). The connectivity over the injury site, according to the magnetic resonance imaging (MRI), may have increased to 8%.

Generally, a urinary bladder repair is very important in rather complete C5/6 SCI. The tetras are not able to perform intermittent bladder catheterization by themselves, because of the mainly lost finger functions due to the lost finger-function-motoneurons in C5/6 spinal cord segments. Through urinary bladder repair, the patients get their private sphere back.

1.3.1.14 Transient increases of the coordination dynamics values fall together with the recovery of motor and urinary bladder functions

The changes of the coordination dynamics values of Kadri are shown in Fig. 1.24 for 2.5 years of therapy. Transient worsening of the coordination dynamics (higher values) fall together with the improvement of motor functions and probably indicate successful regeneration of small amounts of nerve fibres. Following the largest peak of transient increase of the coordination dynamics values (indicating the strongest transient regeneration), the urinary bladder started to function rather physiologically again through 2.5 years of CDT.

1.3.1.15 The time course of the improvement of urinary bladder functions upon CDT

It is reported about the stages of bladder repair through 2 years of therapy. The changes of functions of the detrusor (bladder) and the external and internal bladder sphincters are extracted from a detailed anamnesis and are pictured by an evolution of the attractor layout (in similarity to motor function of Fig. 1.15) with the re-learning of bladder functions (Fig. 1.31).

1. After the operation (fixation and alignment of the broken cervical spine) a lying catheter was installed in the patient. The patient was suffering continuous infections and fever.

It is understood that the bacteria are ‘creeping up’ the lying catheter into the bladder (especially in female, because of the anatomy of the urethra) to give rise to ongoing infections in spite of antibiotic therapy. Before World War II (time of no antibiotics), patients were dying of such infections. It is the benefit of Sir Guttmann from Breslau [1] who stopped or reduced these infections by introducing sterile intermittent catheterization. The introduction of antibiotic therapy helped further.

2. One month later (at a time when the spinal shock weaned) a suprapubic catheter was installed and no more infections occurred. But the bladder did not show any physiologic functions. The patient had no feeling of bladder fullness, no desire to void and did not feel when the fluid was leaving the

bladder. The catheter was used for emptying (when opened) and storing (when closed) the urine. Since no fluid was leaving the bladder through the sphincters, the external striated sphincter was spastic (continuous contraction) and the internal sphincter (smooth muscle), as a part of the detrusor, was probably not working.

Physiologically, the internal sphincter (smooth muscle, slowly acting, probably a part of the detrusor) is keeping the continence for low and medium bladder pressure. For high bladder pressure and sudden bladder pressure increases (as for example during coughing), the rather fast-external sphincter (innervated by α_2-motoneurons and consisting of fast fatigue resistant muscle fibers (FR), Fig. 1.11) is contracting to secure continence. If the striated external sphincter does not work properly, patients suffer the so called 'stress incontinence'.

3. Seven to eight months after the accident (end of 2005), the fluid was leaving the bladder by itself after a small storage phase. This means that therapy had reduced the spasticity of the external sphincter. The patient was now incontinent. So far, the spastic external sphincter had mainly stopped the fluid from leaving the bladder by its spasticity. The internal sphincter started to work a bit to allow a small storage phase. When the fluid was leaving the bladder, there was first no feeling of fluid movement. Later on, the patient had some feeling of fluid movement. Probably flow receptor afferents (S2) (Fig. 1.27) started to work. Three months later the suprapubic catheter was removed. The patient started to use diapers.

4. 20 months after the accident (beginning of 2007, upon 18 months of therapy) the patient felt bladder fullness and the desire to void. Probably stretch (S1) and tension receptor connections (ST) (Fig. 1.27) started to work again. The vegetative symptoms of bladder fullness information (sweating and sudden heard rate increases, probably transmitted by plexus connections) were replaced by bladder fullness feeling and the desire to void.

5. The patient became able to press the fluid out of the bladder. To get all fluid out, the reflex bladder had to be activated a bit, by tapping, touching or massaging the skin above the urinary bladder, which is the reflex skin area for the bladder reflex (Zones of Head, Fig. 1.64). Sometimes body positioning was used to influence the bladder reflex. With these maneuvers the desire to void reappeared and the patient could empty the bladder further.

Often patients (to whom no CDT is administered) are training the bladder reflex for emptying. The reflex is stimulated by tapping the skin above the bladder. But if, for example, the external sphincter is spastic (as in this patient), it may not be possible to generate a good functioning reflex bladder. The neural networks of the sacral micturition center are working too pathologic.

6. After the appearance of the desire to void, the patient became able to hold the fluid for 30s till 1min. Sometimes she could keep the continence better and sometimes not so good. This means that the external bladder sphincter (which can be controlled volitionally) started slowly to work, but irregularly. The feeling of bladder emptying became similar to those before the SCI.

7. 24 months after the accident (spring 2007), the bladder started to function rather physiologically again. After a storage phase the fluid came out on volition. The detrusor started to work fully. But if the patient was pressing too much at the end of bladder emptying to get all fluid out (to reduce the residual urine, not to get bladder infections), the external sphincter contracted. The external sphincter co-contracted with the detrusor. Detrusor-sphincteric dyssynergia of the urinary bladder occurred. But when she then activated the reflex bladder by tapping or touching the reflex bladder area, the desire to void reappeared and she could empty the bladder fully. The residual urine was not measured.

At this stage of bladder repair two patterns existed: the synergy of the bladder, in which the detrusor and external sphincter contracted antagonistically, and the dyssynergia of the bladder, in which the detrusor and the external sphincter co-contracted (Fig. 1.25B). The synergy pattern was for emptying the bladder and the dyssynergia pattern was the pathologic pattern. The pathologic co-contraction of the external sphincter with the detrusor occurred more easily when there was less fluid in the bladder and the patient had to press more (inducing stress to the CNS).

Physiologically both bladder emptying patterns do exist. The synergy pattern is for emptying the bladder and the dyssynergia function is for stopping the micturition. But both patterns are under volitional control.

8. Upon two years of CDT (26 months after the accident) the patient was full continent again and could empty the bladder on volition. The time interval from the first feeling of the desire to void to the situation that the fluid was coming out by itself (including 4 times of occurrence of the desire to void) was one hour. The patient did not use diapers any more. The patient had never used drugs which are supposed to improve urinary bladder functions. The repair of urinary bladder functions was achieved by the re-learning of urinary bladder functions including transfer of learning from the movements jumping on springboard, treadmill walking (Fig. 1.19EF) and exercising on the special CDT device. The strong improvement of urinary bladder functions occurred, when the coordination dynamics values strongly increased (got worse) (Fig. 1.24), indicating a bit of regeneration.

For patients with incomplete spinal cord injuries, it is very important how long they can hold the urine from the first desire to void till to the moment when the fluid comes spontaneously. Can they safely reach the WC or not? The improvement of bladder functioning can also be judged by how long the patient can hold the fluid following the first desire to void. In this case it was 1 hour after 2 years of CDT.

The feeling of the lower abdomen, which was poor after the accident, improved also strongly at the time of nearly full bladder repair. The patient felt again the lower abdomen very good (inside and outside as the patient reported) and felt also again the working of the abdominal muscles. At that time, also the finger functions got a tiny bit better and her supported treadmill walking improved (Fig. 1.23H). During walking on treadmill, and during other movements, the patient got goose-pimples all over the body. It seems that an overall improvement of vegetative and somatic functions occurred at the time of full bladder repair.

1.3.1.16 Attractor layout changes during urinary bladder repair

Within the framework of System Theory of Pattern Formation, the repair of the urinary bladder functions can be understood and pictured by the changes in the attractor layout.

One month after the injury, when the spinal shock faded away (Fig. 1.31A, only the pathologic bladder pattern ‘spasticity of the external sphincter’ was present (Fig. 1.31B). Six to 10 months later, the spasticity of the external sphincter reduced and a small storage phase of the bladder re-appeared as a first sign of bladder repair (Fig. 1.31C). 20 months after the operation, the reflex bladder pattern organized itself with bladder fullness feeling and the desire to void (Fig. 1.31D). 24 months after the accident, the attractor layout showed two attractors, the bladder synergy (the detrusor action inhibits the external sphincter) and the dyssynergia (co-contraction of detrusor and external sphincter) (Fig. 1.31E). The state of the system (pictured by the ball) switched easily from the attractor synergy to the attractor dyssynergia. 26 months after the accident, the stability of the attractor synergy had increased and the stability of the attractor dyssynergia had decreased (Fig. 1.31F). On volition (intention), the micturition could be induced and stopped as in healthy individuals.

1.3.1.17 Conclusion

Upon 2.5 years of CDT urinary bladder functions could be cured in severe (95%) cervical SCI. Since the injury was motoric complete and the cord was ‘free’ in the spinal canal (Fig. 1.19BC, the cord does not touch the vertebrae), some regeneration in the human spinal cord should have occurred.

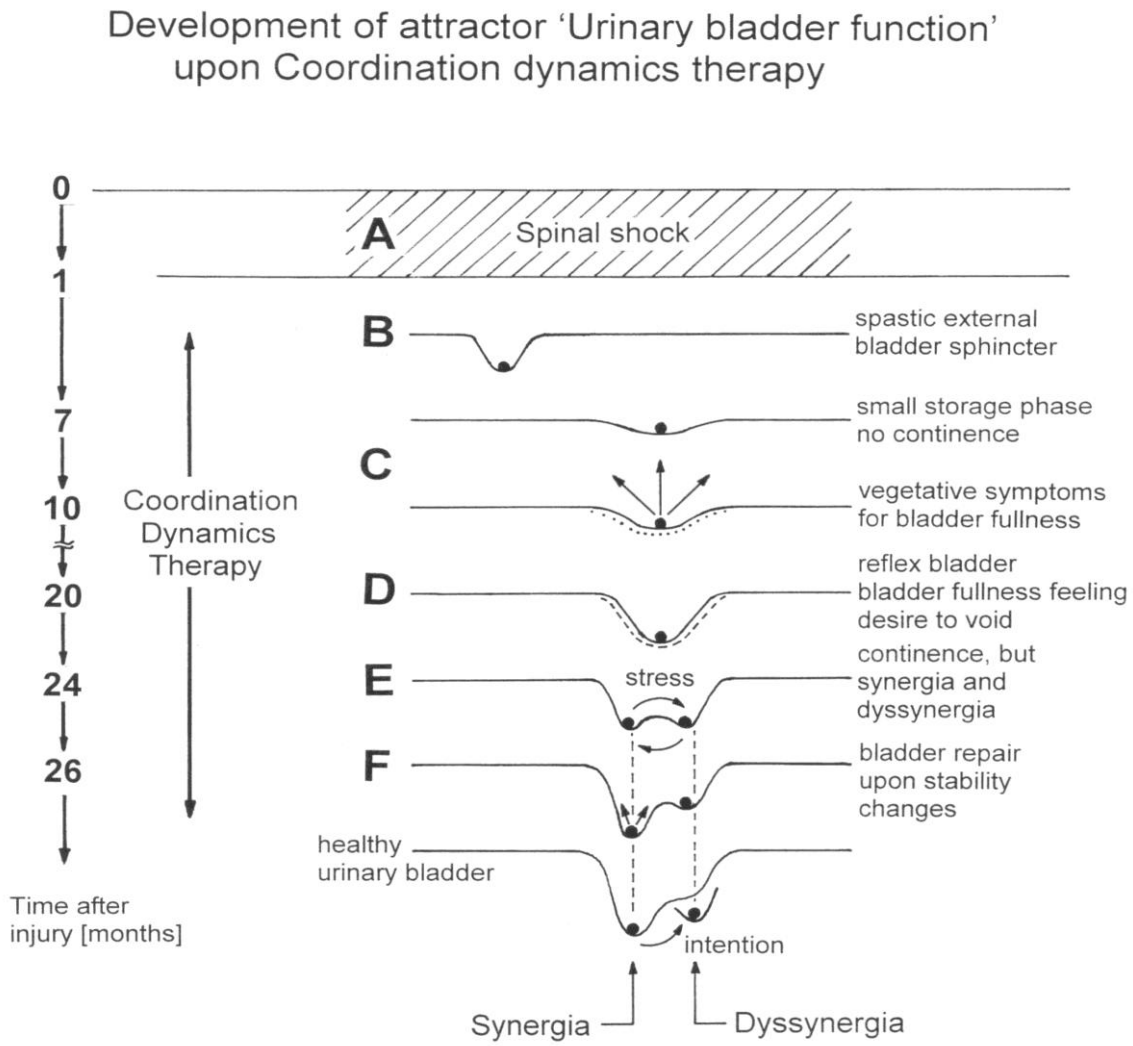


Fig. 1.31. Evolution of the attractor layout of bladder functioning induced by learning transfer from movements to bladder functions upon CDT. The region around each local minimum of the potential landscape acts like a well that weekly traps the system into a coordinated state. Black balls correspond to stable minima of the potential. With learning, the pattern 'spasticity of the external bladder sphincter' vanishes and the patterns for bladder functioning ('synergy' and dyssynergia') appear anew and gain their physiologic stability (physiologic deepness of each basin of attraction). The corresponding attractor layout for physiologic bladder functioning is given. Fluctuation of pattern state (the black ball) (C), and their decrease (F), due to the impairment of phase and frequency coordination of neuron firing, is pictured in 'C' and 'F' by long and short arrows. Dotted and dashed lines indicate the re-occurrence of bladder sensation. Note that more than two years of optimal continuous CDT were needed for bladder repair

1.3.1.18 Integrative functions and central pattern generators for urinary bladder repair

It was shown in this patient Kadri with a 95% SCI that urinary bladder functions could be cured upon 2.5 years of CDT. Three important steps were achieved. First, the patient got the bladder under volitional control again. Second, a physiologic attractor layout for bladder patterns could be generated; and third, the dyssynergia of the urinary bladder could be cured by increasing the stability of the synergy pattern and decreasing the stability of the dyssynergia pattern. The stability changes of the two bladder functioning patterns can be understood within the framework of system theory of pattern

formation and human neurophysiology [17-19] but not in the framework of central pattern generators (CPG's). This knowledge is used below for the bladder repair of the 9-year-old Nefeli with an SCI of approximately 70% at the level of Th10. In Nefeli a transient regeneration of the spinal cord could be achieved and quantified by segment-indicating muscles (Fig. 1.37).

1.3.1.19 A spinal cord injury up to 80% may still allow the re-learning of walking

The repair of a SCI depends on the severance of the injury, the efficiency of the repair treatment and how aggressive the therapy is applied. In Fig. 1.19 it was shown that in a patient with a 50% SCI, the urinary bladder function was fully repaired via 2 months of CDT and the patient Sten could re-learn walking and running through 2 years of CDT. In the patient Kadri with a 95% SCI, 2.5 years of CDT were needed for the bladder repair and the walking could not be achieved. The question is now, up to what severance of injury a re-learning of walking is possible through an efficient, aggressively and continuously applied treatment. The believe is that up to an injury of 80% a re-learning of waking is possible. The repair of the bladder is anyway possible though a long-lasting CDT. Plexus connections and the sympathetic chain (Fig. 1.26) are probably contributing to get the lower body partly under control again.

Below it will be shown that the patient Nefeli with an approximately 70% SCI (30% of the cord remained) could re-learn walking. The importance of this case report and the upper considerations is that most spinal cord injuries are incomplete and substantial repair is possible.

1.3.2 Regeneration of the Human Spinal Cord during Development

1.3.2.1 Summary of the repair of a 70% spinal cord injury at the level of Th10 (10-year-old girl Nefeli)

In the 5.5-years-old Nefeli a neuroblastoma was found to grow from the Th10 ganglion. With the surgery to remove the cancer she suffered a SCI at Th10/11 levels by medical malpractice. An 8-months-rehabilitation in Switzerland brought only little progress. Most of the repair was probably due to spontaneous recovery. When Nefeli started school, she was incontinent and could not walk. An assistance helped her to manage at school (Fig. 1.32B).

At an age of 9 Nefeli started CDT with the Author. Spasmolytic drug and urinary bladder medications were stopped. Following four weeks of aggressive CDT, supported walking and jumping improved. The crawling became better. Following three years of CDT, Nefeli became mainly continent and she learned to walk (Fig. 1.32) with some balance problems. She learned to creep, crawl and jump. Even a bit of running became possible. At an age of 12.5 years, following 3.5 years of CDT, Nefeli learned to ride a normal two-wheel bicycle.

Fig. 1.32. A. The 5.5-year-old Nefeli after suffering an incomplete SCI Th10 by medical malpractice. B. Nefeli after eight months of conventional children rehabilitation in Switzerland (Affoltern). Sticks and orthosis were needed. C,D. Ten-year-old patient Nefeli after six months of CDT. At school she can walk again and can write at the white board

1.3.2.2 Upgrading of coordination dynamics therapy

Above it was stated that CDT consists of the improvement of phase and frequency coordination for an improved neural network organization and the re-learning of movements like creeping (Fig. 1.33AB), crawling, walking, running, jumping and other to the patient adapted movements so that other brain parts can take function over from the injured ones by plasticity. The right-left communication of the hemispheres via the corpus callosum (Fig. 1.33D) can be improved, which is especially important in stroke patients, by especially exercising on the special CDT device with crossed arms (Fig. 1.33C).

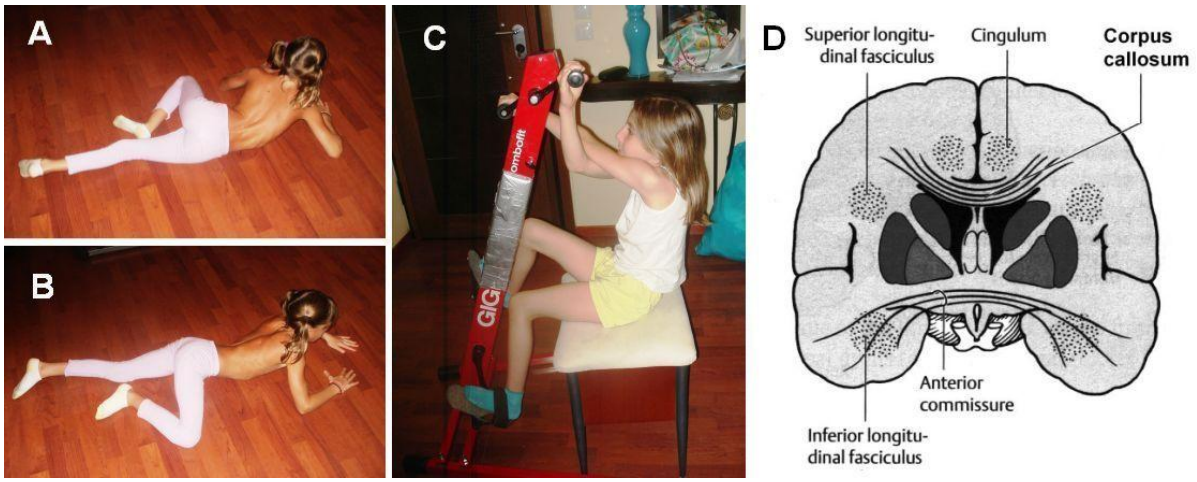


Fig. 1.33. A, B. Ten-year-old patient with an incomplete SCI at the Th10 level during creeping. Note, because of the severe scoliosis, the creeping is not symmetrical. The rotation to the left is limited because of the scoliosis. C. Training of right-left symmetry via the corpus callosum (D) when exercising on the special CDT device with crossed arms

In the patient Nefeli additional trained movements were the phylogenetic old movements like pushing forward movements as Tiktaalik's may have used 375 million years ago (Fig. 1.34) and Salamander crawling (Fig. 1.35). Hula-hoop for improving trunk movements and stability and reduce scoliosis was also used (Fig. 1.81).

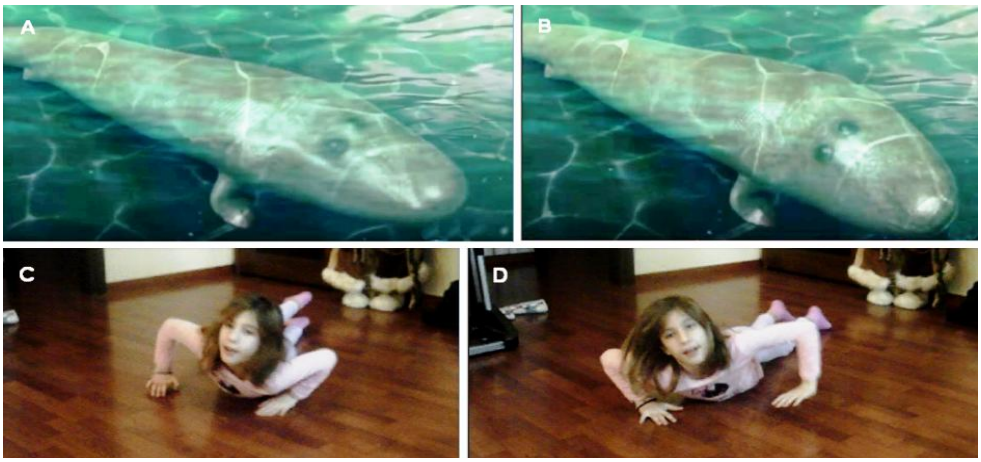


Fig. 1.34. A, B. Possible rotational body movement of Tiktaalik, caused by alternately using one front limb for forward locomotion. C, D. This front limb movement is simulated by a patient with a SCI (Nefeli) by using alternately the right and left arm. Tiktaalik roseae is a lobe-finned fish from the late Devonian period, about 375 million years ago, having may be features akin to those of four-legged animals (tetrapods). Tiktaalik has a possibility of being a representative of the evolutionary transition from fish to amphibians

Fig. 1.35. Salamander-crawling (C, D) in similarity salamander-walking (A, B) of the 10-year-old Nefeli with a SCI (Th10). In D the bending is disturbed because of the scoliosis and spasticity

1.3.2.3 Revised treatment strategy to enhance spinal cord regeneration

The first 10 months of therapy, the strategy of Nefeli's CNS repair was mainly to use optimally what was spared following the SCI. This means activating and re-wiring the remained tract fibers at the injury site with the help of plasticity of the brain to use the spared fibers for all the necessary functions below the injury level. But when it turned out that her damaged spinal cord partly regenerated, the CNS repair had to be seen in a more general way. Now it had to be considered additionally what performed movements and other patterns enhance the regeneration of nerve fibers in the spinal cord. It had to be clarified at what site the regeneration was mainly impeded and how can nerve fiber grows induced and guided and false growing (mismatch) reduced. The contribution from stem/progenitor cells to the regeneration had to be considered.

The improvements of motor and bladder functions during the first six months were probably mainly due to a functional repair (functional reorganization in the brain) of the spared tract fibers 4 years after the injury. But after 10 months of therapy there was indication that motor functions of the legs were re-appearing, caused by a regeneration of the spinal cord. To clinically follow up the regeneration of Nefeli's spinal cord, the human anatomy, including the functional anatomy [34-36], had to be taken into account to see how the regeneration was taking place and how the therapy could be further optimized. The speed of regeneration will be measured below and it will be considered what has to be done to enhance regeneration.

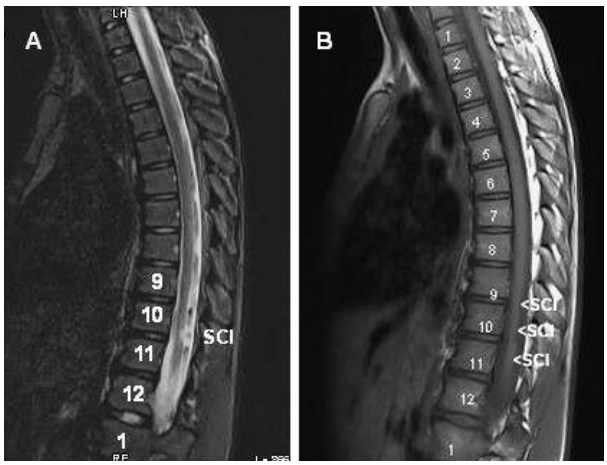


Fig. 1.36. MRI of the 10-year-old patient Nefeli with a SCI at the levels around Th10. Because of scoliosis, the spinal cord is not fully in the plane. The injury of the spinal cord is mainly from the dorsal site

Nefeli suffered an incomplete SCI at the level of Th10/11 (Fig. 1.36). Approximately 30% of the spinal matter was spared. Figs. 1.1 and 1.2 show the spinal cord with the spinal segments and the corresponding dermatomes of the body. To identify the re-innervated cord level and calculate the speed of cord regeneration, segment-indicating muscles should be activated on volition again in the cephalo-caudal direction. Sensory innervation changes may not be characteristic for the identification of regenerated cord levels because Nefeli had an incomplete SCI and the remained sensory distributions were complex. Still sensory repair is as important as motor repair. Especially in the lower sacral range there is a large overlap and variation of the dermatomes [37]. The segment-indicating muscles seemed to be suitable for identifying the level of the re-innervation for certain tract fibers. A muscle starts to contract when sufficient motor units are activated to counteract movement resistance. In the peripheral nervous system (PNS) of the frog the thickest myelinated nerve fibers regenerated fastest [17]. In human it will probably be the same. Fig. 1.9 shows the conduction velocities and nerve fiber diameters of human nerve fibers of the PNS. Classification schemes for the human tract nerve fibers in the spinal cord do not exist. It is therefore assumed that there are similarities between the human CNS and PNS. Further it is not clear whether tract neurons regenerate and/or relay neurons are built at the injury site or even new tract neurons are built anew from stem cells in the sensory-motor cortex. Newly built neurons are most suitable for repair. Also, mismatch has to be considered. Neuron grows along wrong pathways, which has to be compensated for by brain plasticity. Occurring mismatch has to be reduced. The repair and regeneration mechanisms are very complex. Still it is astonishing that some reasonable results will be obtained, when analyzing the speed of regeneration in Nefeli's spinal cord.

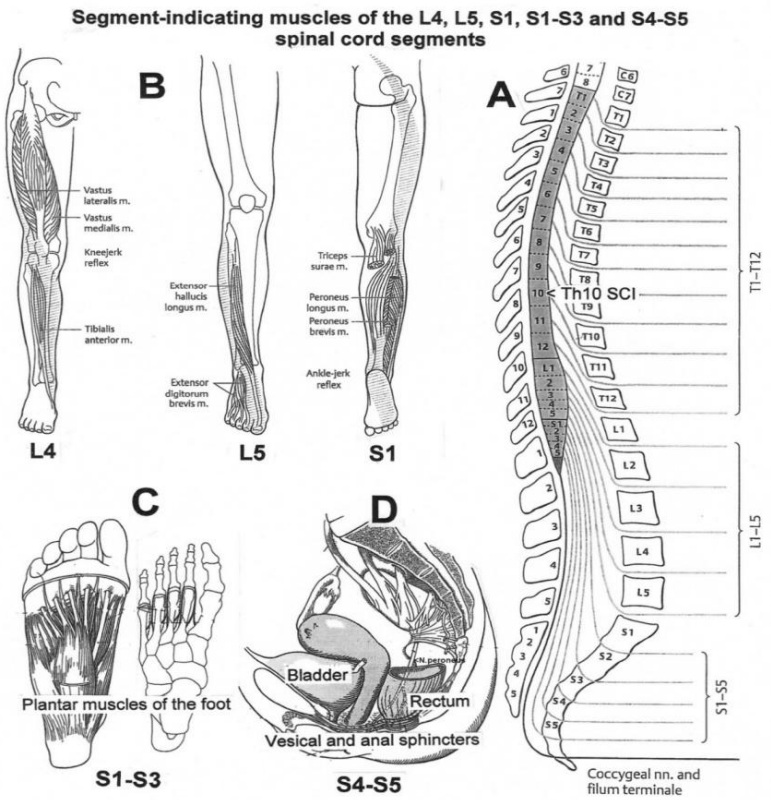


Fig. 1.37. Segment-indicating muscles of the L4, L5, S1, S2/S3 and S4/S5 spinal cord segments for measuring the level of spinal cord regeneration. A. Relation between spinal cord and vertebra segments. B. The spinal cord segment L4 indicating muscle is for example the quadriceps. The extensor halluces longus is characteristic for the L5 segment. C. The plantar muscles of the foot represent S1 to S3 spinal cord segments. D. The vesical and anal sphincters are activated from the S4/S5 spinal cord segments. The skeletal muscles of the leg are innervated by α_1, α_2 and α_3-motoneurons, but the external bladder and anal sphincters are innervated only by α_2-motoneurons

1.3.2.4 Speed of regeneration of the human spinal cord in children

Fig. 1.37 shows the segment-indicating muscles and partly cutaneous sensory distributions of the L4, L5, S1, S2/3 and S4/5 nerve roots or spinal cord segments.

It was measured in Nefeli at what times the different segment-indicating muscles started to work again in cephalo-caudal direction. At the second of February Nefeli was able to lift substantially the knees and dorsal flex a bit the feet (Fig. 1.60) but could not activate the big toes separately or abduct the small toes. The quadriceps femoris and the tibialis anterior could therefore be activated again. A part of spinal cord regeneration had reached the L4 level (Fig. 1.37). At the 12th of February she could activate the extensor halluces longus muscle (Fig. 1.38), which activates the big toe for dorsal flexion and represents the L5 spinal segment. At the 18th of February she could first time in the morning after sleep abduct and adduct the small toes (Fig. 1.39) which represent the S1-S3 segments. The fastest regenerating fibers had reached the motoneurons of the S1-S3 segments for muscle activation. The external bladder and anal sphincters (S4/S5) could not be activated substantially so far. The sphincter muscles (somatic) are not innervated by fast conducting α_1-motoneurons, but only by the thinner and probably slower regenerating α_2-motoneurons (Fig. 1.9).

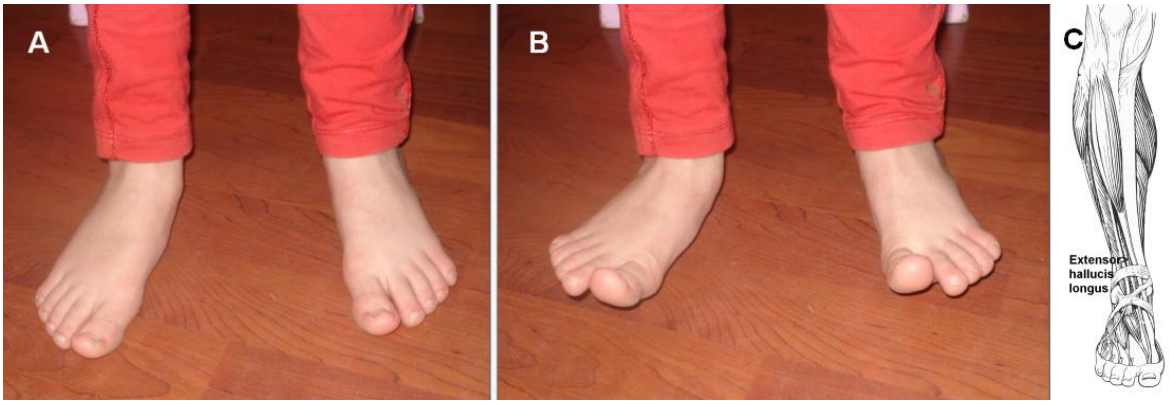


Fig. 1.38. Activation of the halluces longus muscle (C) when dorsal flexing the big toes separately (B). Spinal cord regeneration reached the L5 level

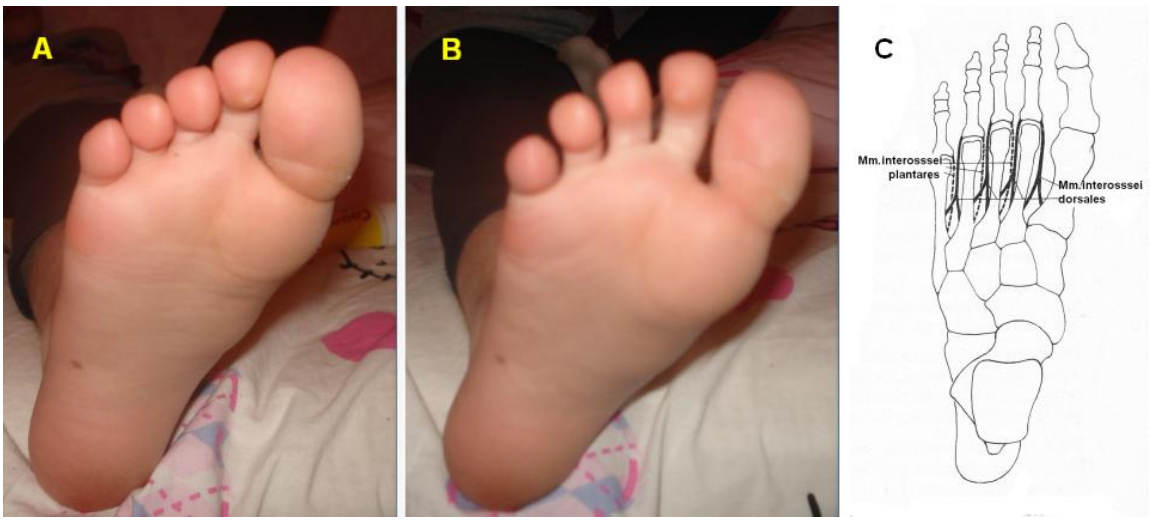


Fig. 1.39. A-C. Volitional abduction and adduction of the toes becomes possible again in the SCI patient Nefeli. With the activation of the Mm. interrossei dorsales and plantares (C), the regeneration of the spinal cord has reached the S1 to S3 spinal cord segments

The distance between the rootlets vL4 and vS2 (Fig. 1.3B) is 20mm in adults. The growing of the nerve fibers from the segment vL4 to vS2 spinal segments needed 13 days. The time for building functional synapses are the same for all muscles indicating segments. But Nefeli is smaller (130cm) than adults, the cord distance is reduced therefore to 20mm • 130/180 = 14mm. The **regeneration** needed 13 days for the 14mm that means approximately **1mm/day**. In the peripheral nervous system, the fastest regenerating fibers need 1 to 2 mm per day for regeneration [17].

Now the time is calculated which the nerve fibers probably needed to grow down from the injury site Th10 to the S2 segment. The cord distance from vTh10 to vS2 (Fig. 1.3B) is approximately 90mm • 130/180 = 65mm. With 1mm/day regeneration speed we obtain 65 days for growing. Assumed that the building of functional synapses needed approximately 35 days, the regeneration down the spinal cord till to the foot muscles and the building of functional synapses needed 100 days. The administered CDT time was ten and a half months that means approximately 320 days. Therefore, before the regenerating fibers grew down the human spinal cord, 220 days were needed. That means, approximately two thirds of the regeneration time were needed to start the regeneration in the spinal cord below the injury level.

Assumed that tract fibers regenerated from above the injury site, the time needed for crossing the 2 to 10mm large gap (Fig. 1.36) was 200 days, which is quite a long time. In rat the longest observed growing distances are a few mm up to 20 mm. In human we expect much shorter possible growing distances, because in the PNS in nerve sutures the nerves have to be adapted for enabling nerve fibers grows into the distal nerve part. A substantial regeneration of tract fibers is therefore unlikely.

If we assume that relay neurons were built from stem cells at the injury site and neural networks were built in the gap from which the spinal cord regeneration started, then this neural network building process needed 200 days. But where are the neural network stem/progenitor cells are migrated from? Are some stem cells in the spinal cord or did they migrated from other places or were they transported in blood vessels?

A neural network building is likely, because Nefeli could contract the muscles only slowly. Further, the building of neural networks for spinal cord re-connection will take more time if the gap is larger. By comparing the SCI site of Nefeli (Fig. 1.36 left) with that of the 17-year-old patient Kadri with a cervical SCI, it can be seen that Kadri's SCI gap was much larger (longer) (Figs. 1.19B,C) and a bit of regeneration in the cephalo-caudal direction needed three to five years.

To understand the cause of repair in humans is of importance because it may have consequences for the treatment to be administered. If neural networks are built at the SCI injury site, then the building of these networks has to be enhanced by training those movements of which the activated neurons lie in and around the injury site. To activate and stimulate neural network growing at the Th10/11 injury site, Nefeli was training with the hula hoop (Fig. 1.72,81), trained trunk rotation on the special CDT device (Fig. 1.56A,B) and trained several rotational movements of the Tiktaalik (Fig. 1.34). Stem/progenitor cells do only proliferate if the membranes are depolarized [68]. That means, the neurons around the injury site have to be activated by certain movements. Further, the tract fibers for all functions below the injury level have to be activated to make them growing into the neural networks at the injury site and stimulate the relay neurons to grow into degenerated tract fibers below the injury site.

The regeneration considered is very complex and only the fastest growing fibers reaching caudal spinal cord segments were measured so far. Many more fibers and thinner/slower regenerating fibers have to grow down to the caudal spinal cord and bring more motoneurons (motor units) and interneurons under supra-spinal control to generate more functional muscle power.

The improvement of the sensory innervation has not been analyzed so far. To get more feeling in the soles of the feet for better walking and balance performance, sensory fibers, entering the lumbar-sacral spinal cord, have to regenerate in the caudal-cephalon direction across the injury site.

Conclusion, even though much more knowledge about the regeneration of the human spinal cord is needed, this documented regeneration of the human spinal cord is a **history progress**. It is the first

time, documented with sufficient diagnostic, that the **human spinal cord** partly **regenerated** by movement-based learning. Through 320 days of therapy, nerve fibers grew from the Th10 spinal segment down to the S2 segment. With a growing velocity of 1mm/day, the 65mm of the cord were covered in 65 days. Assuming 35 days for the building of functional synapses, 100 days were needed for growing caudally. This means that that 220 days of the 320 were needed to start the regeneration process at the Th10 level. The critical area of the regeneration process is located at the injury site and needs special considerations with respect to treatment.

Also, the plasticity of the brain is strongly involved in SCI repair. Whatever neurons are built anew and fibers are growing caudally or rostrally in the cord, the brain has to make the neural network changes functionally correct.

1.3.2.5 Repair of sexual functions

In the sensory-motor cortex the toe functions are sited close to genital and bladder functions (Fig. 1.40). The repair of toe functions may help therefore with the functional repair of bladder and sexual functions. Most spinal cord injuries occur in man between 20 and 25 years and their biggest problem is the disturbed sexual function even though the repair of the bladder functions is more important. The conventional management of the sexual function in SCI is given in [38,39]. But a causal therapy of the disturbed sexual function is the repair of the nervous system. The Author is telling the male patients with a SCI that if the urinary bladder functions are repaired by aggressive CDT, then also the caudal sexual function will improve because both functions are located in the S2 to S5 segments (Fig. 1.26) and there is learning transfer from movements to vegetative functions including sexual functions. Also, in the sensory-motor cortex (Fig. 1.40) the sexual and bladder functions are close to leg and foot functions, making a learning transfer from foot function repair to bladder and sexual function repair easier. With the improvement of leg, foot and toe functions by movement-based learning as for example jumping on springboard in antiphase, also the adjacent neural networks, that means sexual and bladder functions will improve.

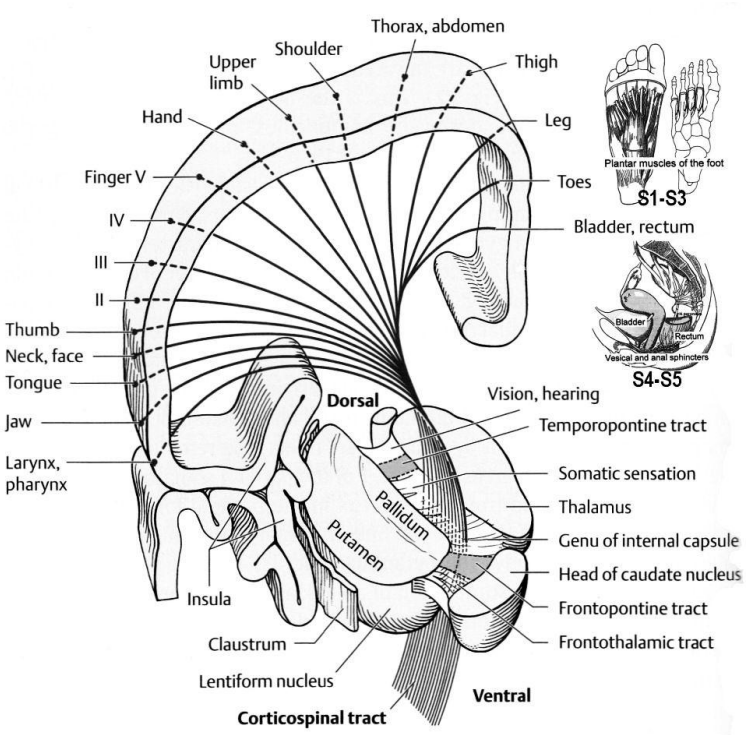


Fig. 1.40. Primary motor areas (homunculus of the brain). Note that the toes are close to urinary bladder and rectum areas

1.3.2.6 Power of reparative regeneration

The capacity for reparative regeneration is smaller, the higher an animal is on the phylogenetic scale [40, 41]. Rats and dogs can have their nerves severed and not sutured together, yet their regenerative efforts are so strong that nerve continuity is restored and motor and sensory return will occur [40, 42]. For a gap of 8mm after transection more than 50% of the nerve fibers could be counted in the distal stump of the rat sciatic nerve [44]. In the dog, nerve fibers can cross a gap of 4 to 5 cm [43].

In human the power of regeneration is much smaller and the distances of regeneration are much larger than in most laboratory animals. The power of regeneration is small in the CNS and in the PNS it is different in different body parts. Well known for dentists is, that the nervous alveolaris always regenerates if the nerve is damaged with an injection needle. The Author experienced himself that in the head touch afferents were able to cross a gap of a few millimeters. Pain afferents seem to be more powerful in regeneration than touch afferents. But from nerve sutures of arm and leg it is known, that the nerves have to be adapted for regeneration. The radial, median and ulnar nerves have a different capacity for regeneration.

To draw conclusions from the regeneration capacity of the rat brain or tissue culture to the human PNS or CNS is therefore only justified, if differences in the regeneration capacity are taken into consideration. On the other hand, in animals one has all possibilities for research. However, comparable studies are necessary to know to what extent animal data can be used in human cases.

Short regeneration distances seem to be important in the human CNS, since there are no leading structures in the CNS as in the PNS. The oligodendrocytes do not guide in the same way as Schwann cells.

In spite of all the problems in repairing the human CNS, still the human CNS can be repaired by movement-based learning. May be the capacity of repair is increasing dramatically if new cells could be built from stem cells with aggressive and long-lasting therapy.

1.3.2.7 Increase of motor units for repair

There are also differences in the increase of motor units after partial denervation of muscles between rats and monkeys. The rat can increase the motor unit by collateral sprouting of nerve fibers in the muscle by about 400%, but the monkey only by about 50% to 100% [45]. This means the monkey (and most likely also the human), needs nearly the whole number of motor fibers to keep important functions [46] and muscle power.

1.3.2.8 The problem of muscle power generation

In incomplete cervical SCI (50% injury) sufficient muscle power can be developed by the patient to walk, run and jump. In nearly complete cervical SCI (95% injury), the generation of sufficient muscle power is a fundamental problem. Due to limited regeneration, the patient can move different leg muscle and can even walk/move on treadmill (Fig. 1.23H). But the patient is still far away from walking without weight-bearing support. The problem of muscle power generation can partly be quantified by the maximum load against which a patient can exercise on the special CDT device. In 95% cervical SCI, upon 0.5 years of CDT the patient can turn on the special device against a maximum load of 30 Newton and upon 5 years of CDT against 50N. The patient with the 50% cervical SCI could exercise already against a load of 200N after 2 years. For 50% cervical SCI, Fig. 1.21 shows the different reductions (improvement) of the coordination dynamics (CD) values for exercising against loads between 20 and 150N. At a load of 20N good values were achieved after 0.5 years and for a load of 150N more than 3 years were needed.

The patient Nefeli with a SCI of approximately 70% became able to exercise against a load of 50N after 8 months of CDT. But good values for 20 and 50N CD were not achieved within 8 months.

1.3.2.9 Plasticity

Sperry transposed the nerve supply of flexor and extensor muscles in the rat [61] and in the monkey [62]: the monkey relearned the task, the rat did not. Monkeys also differ from dogs [47] and rats [62] in the physiotherapy they need. In Sperry's experiment on monkeys, their learning to flex or extend the elbow in one situation did not necessarily become generalized to other performances. This indicates that the neural readjustment was not localized solely in the spinal centers, but involved reorganization at the supraspinal levels [48]. Surprisingly few trials were required for poliomyelitis patients to use transposed tendons successfully. The visualization of the task seemed to be the prime aid to the patients [63]. Intensive neurotherapy gives more useful functions of the to be re-innervated body parts [63,49,50].

1.3.2.10 Loss of spinal cord plasticity due to pressure and ischemia

A loss of interneurons and spinal cord plasticity can occur directly with the spinal cord trauma, when the blood supply of the spinal cord [64] is interrupted [51-53], or with edema or cord pressure which causes ischemia mainly within the first 6 hours following the acute trauma (Fig. 1.5). In the patient Nefeli mainly the bleeding following the surgery (and some tissue) caused pressure which gave rise to an incomplete SCI (Th10/11, Fig. 1.36) after 3 days. Up to the level of Th9 also nervous tissue was lost dorsally (Fig. 1.44C). Probably additional loss of interneurons and plasticity occurred.

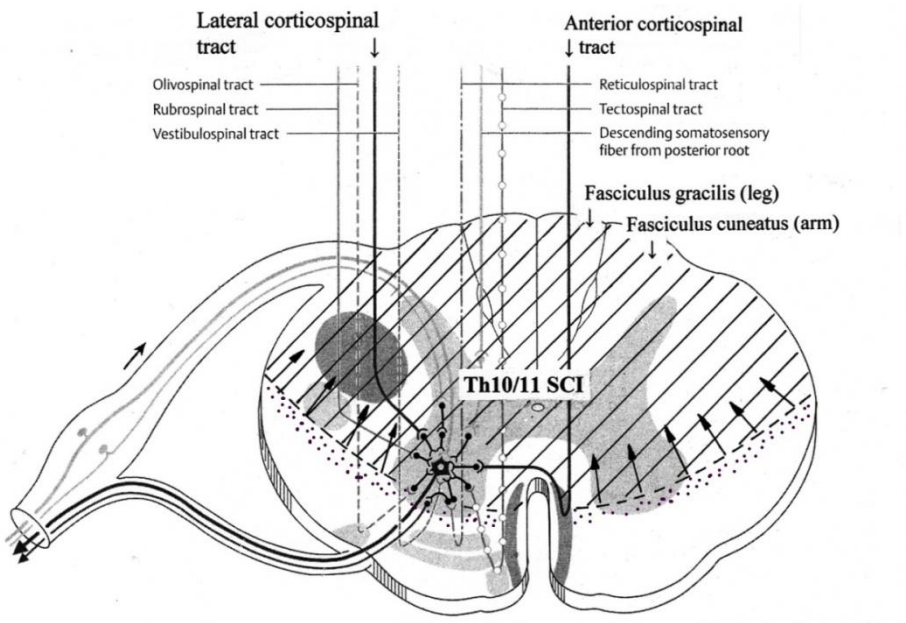


Fig. 1.41. Spinal cord cross section with indicated approximate injury (cross-hatched) and loss of interneuron (dotted area) of the patient Nefeli. Synapses of descending motor tracts onto anterior horn neurons are shown

In animal experiments it has been shown, that the motor cells located at the circumference of the anterior horn are more resistant to ischemia than those at the venter [54]. The motoneurons are nearer the arterial end of the capillaries, and the interneurons are nearer to the venous end. In slowed circulation, the peripheral cells use up the oxygen first, and the central cells are subjected to low oxygen levels. It may therefore happen that monosynaptic reflexes are still present, whereas the polysynaptic responses are lost [55], since they need the interneurons. Interneuron connectivity can partly be measured by polysynaptic reflexes in animals [56]. The secondary destruction of the spinal cord, following the first 6 to 8 hours after acute injury by edema or other pathologic processes, can possibly be reduced by localized cord cooling [56], or by hyperbaric oxygen [57], methylprednisolone, naloxone or dimethyl sulfoxide treatment [57,58].

Interneuron connectivity [59] may also decrease in the following months or years after the spinal cord trauma because of the denervation of interneurons by the injury of the spinal cord tracts. Interneurons may need trophic substance and activity [60] from afferents, other interneurons (mainly) or spinal cord tracts. Maybe the missing trophic effect of other neurons can be compensated transiently by an increased activity input. Partly damaged cord parts with loss of interneurons (Fig. 1.41, indicated with dots), mainly surrounding the injury site, have to be activated by movement-based learning for not losing interneurons and spinal cord plasticity.

Even though the human CNS repairs itself by movement-based learning, the therapist has to understand the repair processes to optimize the repair, or, to enhance the efficiency of repair.

1.3.2.11 Repair of the injury site

The repair of the SCI has to bring the caudal spinal cord under supraspinal control again and the injury site has to be repaired. The repair of the injury site is especially of importance if the intumescentia cervicalis (arm and hand movement) and the intumescentia lumbosacralis (leg movements) (Fig. 1.3C) are damaged, which was not the case in Nefeli. Her damage was mainly located in the thoracic spinal cord with the consequence of impaired trunk and pelvis control. Several movements for trunk and pelvis control had to be trained. These movements are those ones which patients have to train for disk prolapse repair and back pain reduction. Especially the up and down movement of the trunk is important (Fig. 1.42) besides rotational movements.

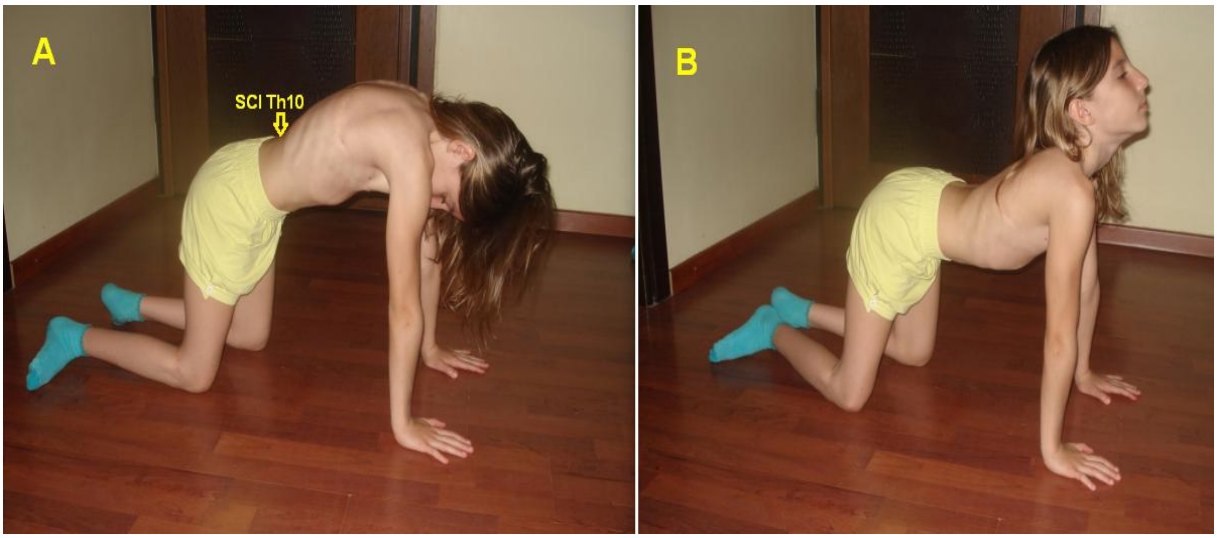


Fig. 1.42. Up and down movements of the trunk to arch the patient's back and to activate neurogenesis at the SCI level Th10. The impaired arch is marked with SCI Th10

1.3.2.12 Motor tract damage and its repair

Fig. 1.41 displays a cross-section of the spinal cord. Some tracts and the approximate cord damage of the patient Nefeli are shown. The motor tracts in the spinal cord are anatomically and functionally segregated into two groups: a lateral group, comprising the corticospinal and rubrospinal tracts, and a medial group, comprising the reticulospinal, vestibulospinal, tectospinal tracts. The lateral tracts mainly project to the distal musculature (especially in the arms) and also make propriospinal connection. They are primarily responsible for voluntary movements of the forearms and hands, i.e., for precise, highly differentiated, fine motor control. Since the SCI is at the level Th10 (Fig. 1.1C), the patient Nefeli can perform like a normal person precise, highly differentiated voluntary arm and hand movements. The medial tracts, in contrast, innervate motor neurons lying more medially in the anterior horn and make relatively long propriospinal connections. They are primarily responsible for movements of the trunk and legs (stance and gait). These medial tracts are more ventral in the

anterior horn (Fig. 1.41) and are probably only little damaged. They will activate the motoneurons in the intumescentia lumbosacralis (not damaged) for stance and gait. Therefore, Nefeli has spared tracts to activate on volition leg and foot muscles. But the contributions from the medial group, lying in damaged cord area (Fig. 1.41), are strongly reduced below the level Th10.

Many motoneurons in the intumescentia lumbosacralis to activate foot and leg muscles (Fig. 1.41) are not reaching the threshold to generate an action potential because of too little input. Improving the coordination of the afferent input (Fig. 1.43) by exercising on the special CDT device will help to reach the threshold. The improvement of the coordination of the afferent input will only partly help. Enhancing the strength of the several thousand synapses onto the motoneuron (Fig. 1.41), by exercising, will additional help. Still more input from the medial and lateral motor groups are needed. As found above, the spinal cord of Nefeli partly regenerated. More tract fiber input made the motoneurons to reach the threshold and activate leg and foot muscles.

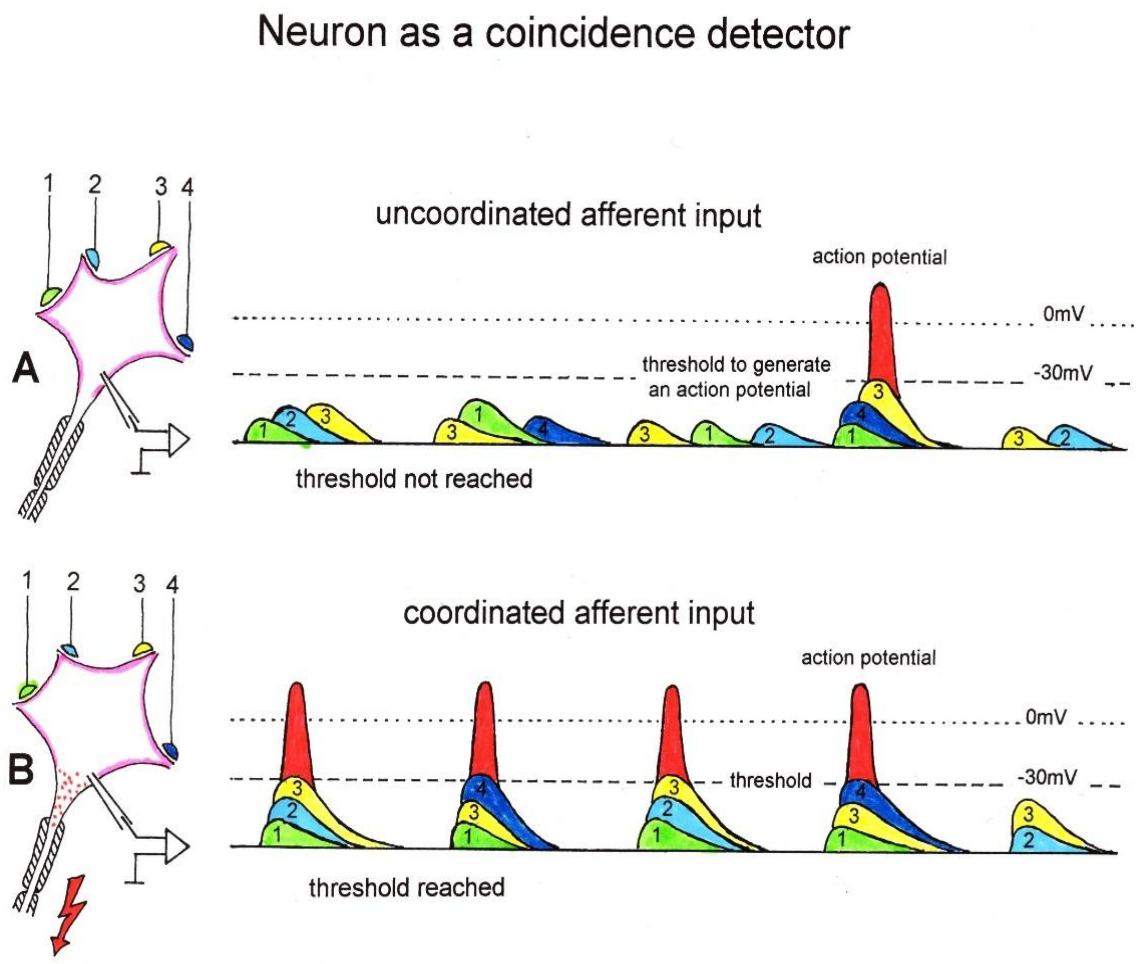


Fig. 1.43. Neuron operating as a coincidence or coordination detector. A. Afferent input is reaching rather uncoordinated the cell soma. Only sometimes an action potential is generated, because the threshold of action potential generation is mostly not achieved. B. The action potentials in fibers 1 through 4 are reaching time-coordinated the dendrites or the cell soma. The postsynaptic potentials add up and the threshold is achieved at approximately –30mV, and action potentials are generated time-coordinated at the axon hillock. In the real CNS mostly, many more smaller postsynaptic potentials will contribute to the generation of an action potential and passive conduction from the dendrites to the cell soma has to be taken into account. Coordinated afferent input may thus induce or enhance (coordinated) communication between neuronal network parts following CNS injury

As analyzed above, it unlikely that a substantial number of fibers, of the for example pyramidal tract (lateral corticospinal tract), regenerated over the injury site to grow down to the motoneurons in the intumescentia lumbosacralis. Probably relay neurons or neural networks were partly built at the injury site. Axons from these new neurons grew down to the motoneurons. The problem with this assumption is, where are the stem/progenitor cells are coming/migrating from.

Another possibility is that new tract neurons were built anew in the somatosensory cortex. Their axons may grow along the anterior corticospinal tract fibers, passing though the not damaged cord part at the injury site and reaching thus the motoneurons in the intumescentia lumbosacralis (stance and gait) and the conus medullaris (urinary bladder and sexual functions). The regeneration times are not against the building of new tract neurons. But these repair possibilities would need more than a year to contribute to the repair. But there are many patients with a SCI for decades and regeneration or improvement of function did not occur. First, many spinal cord injuries are quite complete and there is not much space for the growing of nerve fibers through the injury site. Second, for the wanted afferent and efferent integration intensive efficient therapy is needed so that the axons of the newly built neurons grow to the wanted place. But third, in the developing (pediatric) CNS more nerve cells are built anew especially with aggressive efficient movement-based learning therapy.

1.3.2.13 Sensory tract damage and its repair

The posterior columns consist of the fasciculus cuneatus (arm) and fasciculus gracilis (leg) and transmit impulses arising in the proprioceptors and cutaneous receptors from arms and legs. As we can see from Fig. 1.41, these columns are damaged because of the pressure injury of the spinal cord from dorsal at the level of Th10 (Fig. 1.36). Since the pressure was exerted from dorsal and the spinal cord is fixed by the dentate ligaments (Fig. 1.4), the damage is primarily dorsal. Therefore, the patient Nefeli should have problems in feeling the position of her legs (proprioception) and should no longer securely feel the floor under the feet (cutaneous receptors; touch and pressure). As a result, both stance and gait should be impaired (gait ataxia), particular in the dark or with closed eyes.

Indeed, Nefeli wants to train bare foot or wants to wear only socks to enhance the afferent input necessary for improving standing, walking and balance. She clearly said, when I started to feel more the soles of my feet my balance improved during walking and standing. Obviously, the sensitivity also improved with the regeneration of the cord and reorganization of the brain. With ongoing therapy, she managed also to walk with shoes at school (Fig. 1.32); even though the sport teacher sometimes let the pupils walk and run with socks to include Nefeli better in the sports program. The two-point-discrimination of the sole of the foot was 15-25mm and in the healthy sister approximately 10mm.

Fig. 1.44 shows the fasciculus cuneatus and the fasciculus gracilis. The SCI Th10 is indicated and is sited caudally to the start of the fasciculus cuneatus. As Fig. 1.44C indicates, a regeneration is rostral more difficult because the gap at the injury site is broader there. Also, leading structures for regeneration are missing. Regeneration and or building of neuronal networks at the injury site will start from ventral; where the distance for regeneration is shorter, where healthy cord tissue remained as a leading structure for nerve fiber growing and may be where neurogenesis could be induced by membrane depolarizations from the remained by movements activated cord tissue.

Regenerating sensory fibers from the legs would have to cross the injury gap and grow along myelin sheaths, generated by the oligodendrocytes, to the nucleus gracilis. As for the regeneration of motor fibers across the gap, mismatch will occur. The nucleus gracilis contains the second neurons, which project their axons by way of the medial lemniscuses to the contralateral thalamus (Fig. 1.44B). The somatotopy will be disturbed and has to be compensated for by the plasticity of the brain. The sensory information processing from the arms through the nucleus cuneatus is not impaired (Fig. 1.44).

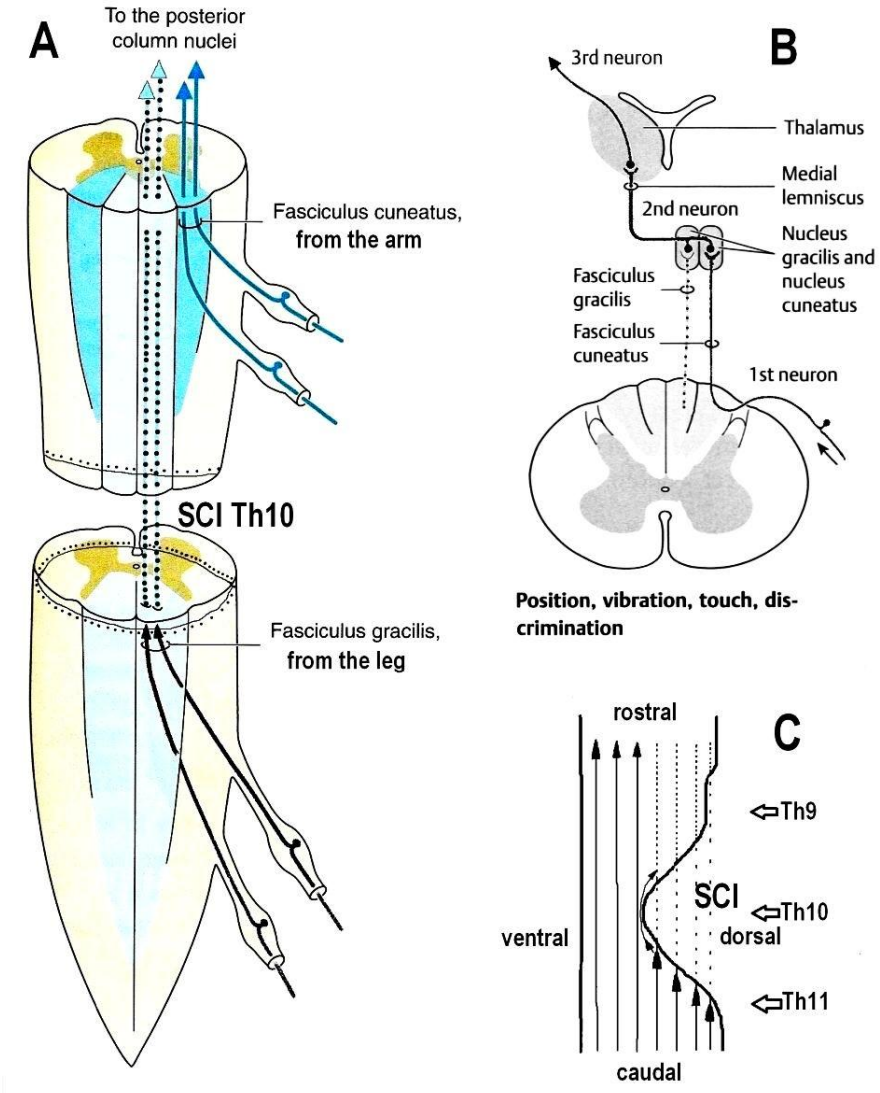


Fig. 1.44. A. Posterior funiculus, containing the posterior columns fasciculus gracilis (medial, afferent fibers from the leg) and fasciculus cuneatus (lateral, afferent fibers from the arm). Afferent fibers sub-serving different sensory modalities traverse the root entry zone and enter the posterior horn (B). The type of myelin changes from peripheral to central, and the myelinating cells are no longer Schwann cells, but rather oligodendrocytes. The SCI at the level of Th10 is indicated. The afferent fibers from the arm join the cord at cervical levels and lie more laterally and dorsally to the SCI. The action potentials derived from receptors in muscles, tendons, fasciae, joint capsules and skin are conveyed in the distal processes of pseudo-unipolar neurons in the spinal ganglia. The central processes of the cells, in turn, ascend in the spinal cord and terminate in the nucleus gracilis of the medulla oblongata. The impulses derived from receptors in the leg are conveyed similarly to the caudal spinal cord. But in the spinal cord the central processes are mainly destroyed at the injury site and the action potentials cannot reach the second neurons in the nucleus gracilis of the medulla oblongata (dotted lines) (B). B. Central continuation of posterior column pathways. The posterior column nuclei contain the second neurons of the afferent pathway, which project their axons to the thalamus. Due to the SCI the second neurons in the nucleus cuneatus are partly de-afferented (dotted line). C. Pictured SCI site. Soled lines are functional, dotted lines not. To understand the regeneration of the human spinal cord, induced through CDT, more knowledge of the regeneration in human is needed

1.3.3 Case Report of Spinal Cord Repair in the Patient Nefeli (70% SCI) via Coordination Dynamics Therapy (CDT) up to 1 Year

1.3.3.1 Cancer and spinal cord injury treatment till CDT was started

After documenting details of the regeneration of the spinal cord in the patient Nefeli, the improvement of CNS functions via movement-based learning will be given.

When Nefeli was 5.5 years, it seemed that she suffered pneumonia because of coughing. She got antibiotics and the coughing stopped within two days. Because this was a too quick recovery a thorax picture was made. A carcinoma was found paravertebral. It was a neuroblastoma growing from the ganglion Th10 on the right side. The cancer was therefore quite close to the spinal cord and the vascularization is high in this area, especially when a tumor was growing there. The tumor, 8cm in diameter, was removed in Greece. The father asked for an additional neurosurgeon in addition to the orthopedic surgeon, because the tumor was connected to the spinal canal. He wanted to pay for the additional costs. Both surgeons refused for a combined operation, even though when removing an acusticus neurinom sometimes a neurosurgeon and an HNO physician do cooperate. After the operation Nefeli complained because of pain in the legs and was crying all the time. The other five children in that hospital room could not stay this continuous crying of Nefeli and moved out of the room. The physicians argued that it is normal after an operation. Clinical knowledge is that if a patient continuously complains of pain one has to check the cause, even if the physician does not believe that the patient has really pain. After three days of pain, the pain disappeared; but the urinary bladder stopped working and Nefeli could not stand any more. The parents took her to another hospital to get an MRI done. The MRI showed a spinal cord compression at Th10/11 levels from bleeding and some tissue. The spinal cord was freed to enable complete decompression, 3.5 days after the first operation. The decompression was re-assessed the following day with a new MRI. But Nefeli had suffered already an incomplete SCI at Th10/11 levels (Fig. 1.36). From disk prolapses it is known that if soft pressure onto the spinal cord lasts longer than 24 hours, the spinal cord becomes damaged. The medical malpractice was mainly not to check for bleeding into the spinal canal at a time when the child was crying and complaining because of pain.

With four months neuro-rehabilitation in Switzerland, which cost approximately 150000US Dollar, Nefeli improved a bit, but mainly due to spontaneous recovery according to the knowledge of the Author. A year later Nefeli was send again from Greece to Switzerland for another four months neuro-rehabilitation. The costs were again approximately 150000US Dollar. The special CDT device was not used in that children s neuro-rehabilitation place (Affoltern), even though they knew about it. Urinary bladder function did not improve and the progress in movements was limited. Nefeli refused to have conventional physiotherapy at home in Greece. At school she had to use sticks and orthosis (Fig. 1.32B). Because of no physiologic bladder functions, she was using diapers. An assistance helped her to manage at school.

At an age of 9 years, three years after the first operation with medical malpractice , the father was advised by a professor in Greece to try CDT and started it. Spasmolytic drug and urinary bladder medication were stopped. Following four weeks of aggressive CDT, supported walking and jumping improved. The crawling became better.

Urinary bladder functions started to improve. The sacral micturition center started to work. When the urinary bladder automatism (S2-S5) was activated by the CNS, the residual urine became less than 10ml as measured by catheterization. Mostly the patient felt the wish to void. But the time from the first desire to void till to the activation of the bladder emptying automatism was one to three seconds. All bladder functions were working unregularly. With regeneration mostly functions re-appear unregularly. The patient still had bladder infections.

When the Author controlled the data of the cancer removal, he found out that the cancer treatment had been far from optimal. Probably the neuroblastoma of the ganglion was not fully removed, even though this would have been possible. In the Authors cancer extirpation, the whole cancer was removed and 1cm healthy tissue around the glioblastoma to be sure that the whole cancer tissue was

taken out. In Nefeli four lymph nodes were removed in the cancer area; three had a metastasis. In the Author, the two lymph nodes with metastasis were removed and further four ones leading away from the cancer (in this case the neck) with no metastasis. Radiation and chemo therapy was administered to the Author but not to the 6-year-old child, mainly because of the SCI. Obviously, the cancer operation in Switzerland (Author) was much more thoroughly performed than those in Greece (Nefeli). As the urine test of decreasing catecholamine metabolites indicated, there seem to be no active growing of the neuroblastoma and/or metastases in Nefeli. A newly made MRI indicated that there might be tumor tissue remained, but no active grows could be found in the area of the former Th10 ganglion. The intensive CDT may have activated tumor suppressor genes. But the movement-based learning therapy is most likely not sufficient efficient to stop aggressive cancer growing. Pathologists had the opinion that the cancer was not very aggressive. In the Author two check-ups of the whole body for metastasis were performed (PET). Nothing was done so far in Nefeli. As stimulated by the Author, more diagnostic of possible tumor growing should be done to be on the safe side. But to think that the Author obtained optimal cancer treatment, is also wrong. When the region of the former cancer below the upper lip was radiated, the eyes and the brain were not protected against radiation. The Author asked for protection, but it was refused.

More causal cancer treatment is needed, including progress in genetics and epigenetics. Interdisciplinary research and treatment have to be improved. Existing conventional cancer treatment has to be administered more thoroughly.

1.3.3.2 Repair within 6 months of CDT

The repair of the SCI of Nefeli involved the repair of movements below the injury level, especially the walking, the repair of urinary bladder functions, the reduction of scoliosis and spasticity and last not least the repair of the sexual functions which will become relevant after puberty. Additionally, it has to be controlled whether the tumor is growing again.

As can be seen from Fig. 1.36A the most loss of spinal cord tissue was at vertebra levels Th10/11. Fig. 1.36B further indicates (spinal cord is white) that there was additional loss of spinal cord matter rostral to the Th10/11 levels. The loss of spinal cord matter was up to the vertebra Th8. Probably because of this additional loss of spinal cord matter, caused by the compression, Nefeli got a severe scoliosis (Fig. 1.45), which is a medical problem and not just a cosmetic one, because of possible spinal nerve root compression in the intervertebral foramen in the future. Most SCI patients get a scoliosis, but not such a severe one.

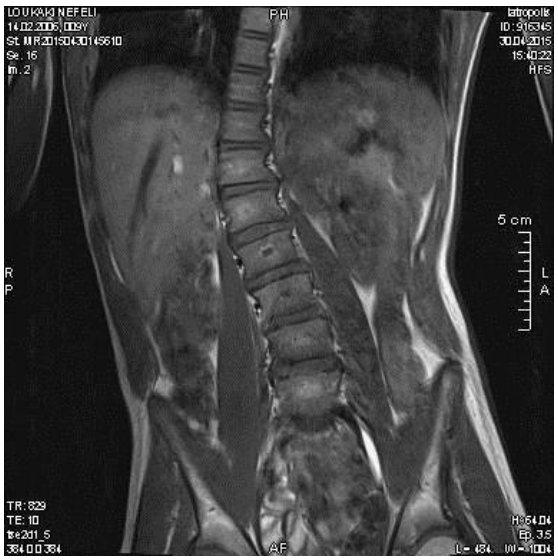


Fig. 1.45. Severe scoliosis of the SCI patient Nefeli caused by the SCI and the cancer removal. With the removal of the neuroblastoma at least one intercostal was removed

Fig. 1.46 shows once more the starting position of CDT. After conventional neuro-rehabilitation she needed sticks and orthosis and had to sit quite often. The urinary bladder was not functioning. A normal school life was not possible. Nefeli often said, I want to be again like the other children at school. Following 6 months of therapy, she could walk again (Fig. 1.47) and could manage much better at school. She could walk to the white-board and write there (Fig. 1.32C,D).

Fig. 1.46. The six-year-old Nefeli (sitting), who acquired a SCI, following 8-months-therapy in a rehabilitation center in Affoltern in Switzerland (one day costs approximately 2000 US Dollar). Note, Nefeli had problems to manage at school in the first class

The walking performance was still far away from normal. As can be seen from Fig. 1.47B, the right knee is inwardly rotated. The outward rotation of the right foot during walking cannot be seen in this picture. The scoliosis can even be seen through the clothes. When walking with sticks (Fig. 1.47A), no scoliosis is apparent, because of the stretching of the upper trunk.

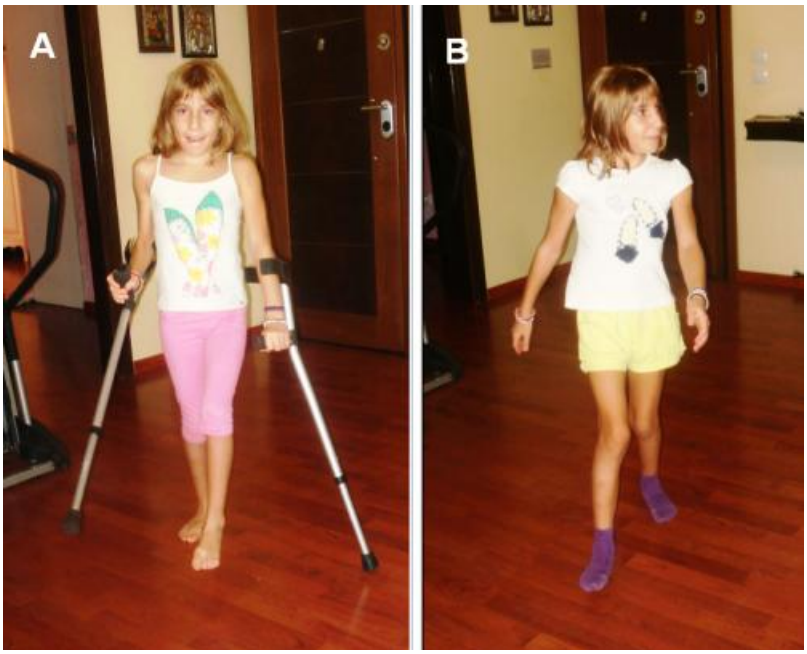


Fig. 1.47. The girl Nefeli, who acquired a SCI at the levels Th10/11 during walking with sticks and free walking. Note the pathologic walking pattern in B

Nefeli had in the legs extensor spasticity, flexor spasticity and rigor. As a consequence of these pathologic patterns, she was spontaneously not standing straight, as can be seen in Fig. 1.32C. On volition she could straighten herself, but she would need too much power to do it continuously. Astonishing, she could still easily walk and train on the special CDT devices.

Because of balance problems, Nefeli was often falling during free walking. But she was used to fall and the protection automatisms were working well; the arms and hands were working normal, as can be expected from the injury level Th10. With ongoing therapy, the balance improved.

The **urinary bladder** of Nefeli was not functioning physiologically. She had no spared sacral tract fibers to the bladder (in German: keine sacrale Aussparung). But she had no dyssynergia of the urinary bladder (co-contraction of the detrusor muscle and the external bladder sphincter), which made it easier to improve bladder functioning. Exercising on the special CDT device and the jumping on springboard strongly activates and trains urinary bladder and bowel functions. Because of the rhythmic and dynamic load changes, exerted onto the pelvic floor during jumping, the external bladder and anal sphincters (somatic muscles), as a part of the pelvic floor, are rhythmically and dynamically activated and relaxed, and passively stretched for movement-based learning. The inner sphincter (smooth muscle) is probably trained and activated by the pressure changes in the detrusor muscle.

At school Nefeli was using diapers. When going to the WC for disabled, a helper was assisting. At home during CDT she was not using diapers. Often, she got wet and the trousers had to be changed. The time from the urge/desire to void and reaching safely the WC improved. Fig. 1.48 shows the improvement of urinary bladder functioning by the times she reached the WC safely and could keep the fluid. The times to hold the fluid longer improved but varied quite much. Once she was even be able to hold the fluid for 20min. Also, the emptying of the colon and rectum (defecation) became more regular.

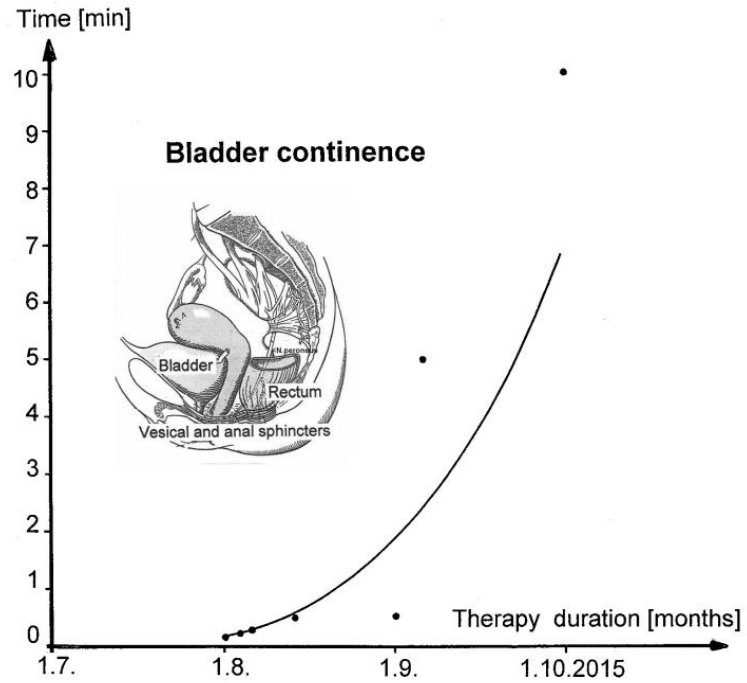


Fig. 1.48. Improvement of urinary bladder functioning quantified by the time from the urge/desire to void until micturition

When training regularly, Nefeli had no dyssynergia of the bladder. That means, when the detrusor (smooth muscle) contracted and the inner sphincter (smooth muscles) opened, the external sphincter (striated (somatic) muscle) relaxed and the fluid could leave the bladder via the urethra (Fig. 1.27).

But when she was performing the program unregularly (not according to the program), it happened sometimes that she got very spastic in the legs and pelvis. Then also the external bladder sphincter got spastic and she could not void even though she had the desire to void. By exercising a bit on the special CDT device and jumping on springboard, the external bladder sphincter relaxed and she could empty the bladder physiologically again.

This shows that even though the bladder functioning improved, still a physiologic storage and emptying was not established in the long-term memory. The repairs of the vegetative nervous system and especially those activating bladder functions (in coordination with the somatic nervous system division) need time. SCI treatment for children should be able to repair the urinary bladder so that they have a private sphere in five or ten years.

The improvement of motor functions from wearing orthosis and walking with sticks (Fig. 1.46) to free walking without orthosis (Fig. 1.47) is quantified by the re-learning of free walking and supported jumping on springboard.

Fig. 1.49 shows the beginning and improvement of free walking on treadmill in the forward direction. After improving the walking on treadmill at a speed of 2.5km/h, it was changed to a higher speed (4km/h), which is more difficult but closer to a real walking speed. The walking period was limited by losing the balance. The problem was therefore not to stay in the walking pattern, but to keep the balance for a longer time. Another 13-year-old cerebral palsy patient (Rafaelena), training partly together with Nefeli, could not learn to keep the balance during free walking on treadmill. One has to remember that treadmill walking is different to normal walking (more difficult for patients), because the kinetic energy in the forward direction is missing with the consequence that it is more difficult to keep balance. This can be observed in the mountains. If an ibex or mountain goat has to cross a difficult and steep piece of ground, it is running. If one or two steps cannot be performed properly, they will not fall down the steepness, because the kinetic energy is bringing them further to a not so difficult piece of ground.

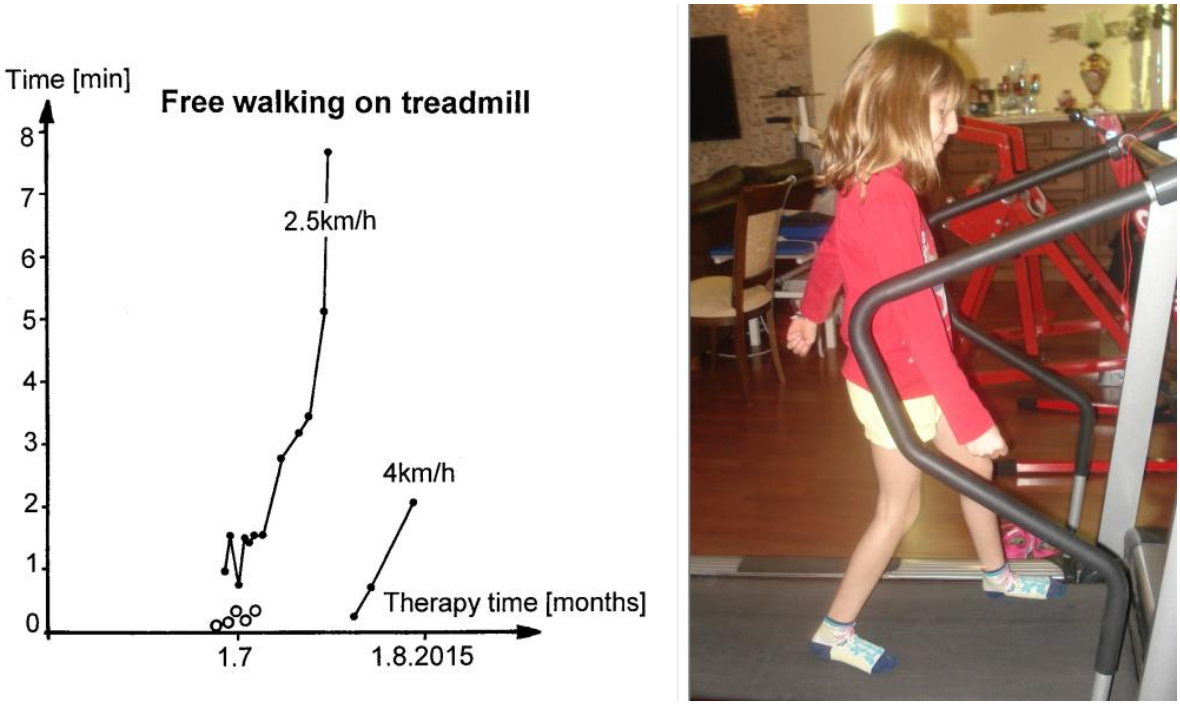


Fig. 1.49. Improvement of free walking on treadmill of the 10-year-old patient Nefeli with a SCI. At the beginning a walking speed of 2.5km/h was only possible, later on a speed of 4km/h became possible. The patient walked without shoes to have a better sensory input and in this way a higher stability, which was the limiting factor of continuous walking

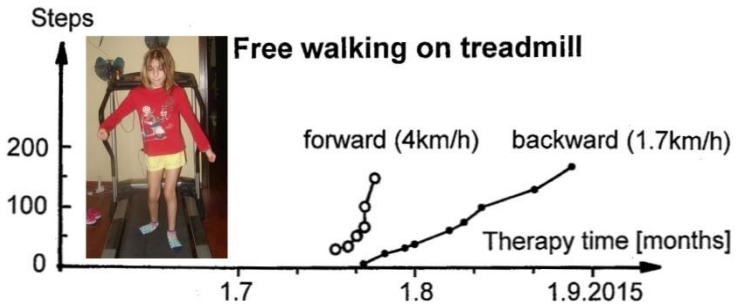


Fig. 1.50. Free walking on treadmill in the forward and backward direction of a patient with a SCI. Note the pathologic inward rotation of the left knee and the not straight upper body because of the scoliosis

To improve the forward walking, the backward walking was also trained for symmetry improvement. Forward and backward walking were trained together. Fig. 1.50 shows the improvement of forward and backward walking quantified by the number of performed steps till the patient lost the balance. It was much more difficult to walk backwards and the speed had to be much lower (1.7km/h) than for forward walking (4km/h). Still it seemed that the backward walking improved the forward walking. Since it was for Nefeli much more difficult to walk on treadmill than walk freely, she later on refused to train the free walking on the treadmill. But she further trained the normal free walking in the forward (Fig. 1.47) and backward direction. The beginning of walking was hard work for the patient and the therapist (Author). Often Nefeli was falling during normal free walking. She never complained and was mostly laughing. As a para with an injury level of Th10, she had no problems with good protection reactions. And, of course, she had no overweight, which would make the walking of a patient with a SCI more difficult. With ongoing therapy, the balance of Nefeli during walking improved, but she still fell quite often (and the Author could not always catch her) because she liked to move fast and risked more. Her far goal in mind was the re-learning of running.

As can be seen from the Fig. 1.47 till 50, Nefeli preferred to walk during training without shoes, because she could walk better then. The enhanced input from the soles of the feet improved her walking performance. At school she had to walk with shoes. But, as can be seen from Fig. 1.32D, she managed quite well also to walk with shoes. But the jumping was easier when she jumped without shoes (Fig. 1.51).

Fig. 1.51 shows the improvement of supported jumping in anti-phase. Even though Nefeli could jump without support, the supported jumping was preferred, because the movement-induced afferent input was then more physiologic. More physiologic afferent input makes it probably easier to re-learn physiologic movement patterns. But moving sometimes without support is also good, to tell the CNS what is has to learn.

To repair the SCI as much as possible, Nefeli had to be made to train at her limits (aggressive therapy). But she also wanted to play with her sister and other children and she wanted to have an easier life like the other children. It was therefore difficult to push her to limits. Especially when a parent was missing, the Author was often not sufficient patient and struggled with her. In spite of all the hard work together, she well understood that she had to train to get better and she liked to train with the Author. She wrote into the protocol book that she likes the Author (Fig. 1.52). Later on, she clearly said why she liked the Author, because he was fighting with her to make her a better life. In spite of all the fighting, Nefeli was clever and understood exactly what was going on with the treatment; but she was still a child. Mothers with cerebral palsy children are in a much worse situation. They are fighting very much, are tremendously patient with the child, but only little is coming back from the child.

When the Author asked Nefeli, how was it in the rehabilitation center in Affoltern in Switzerland, she answered: It was nice there, I liked very much there – but it was a bit like in a playing school.

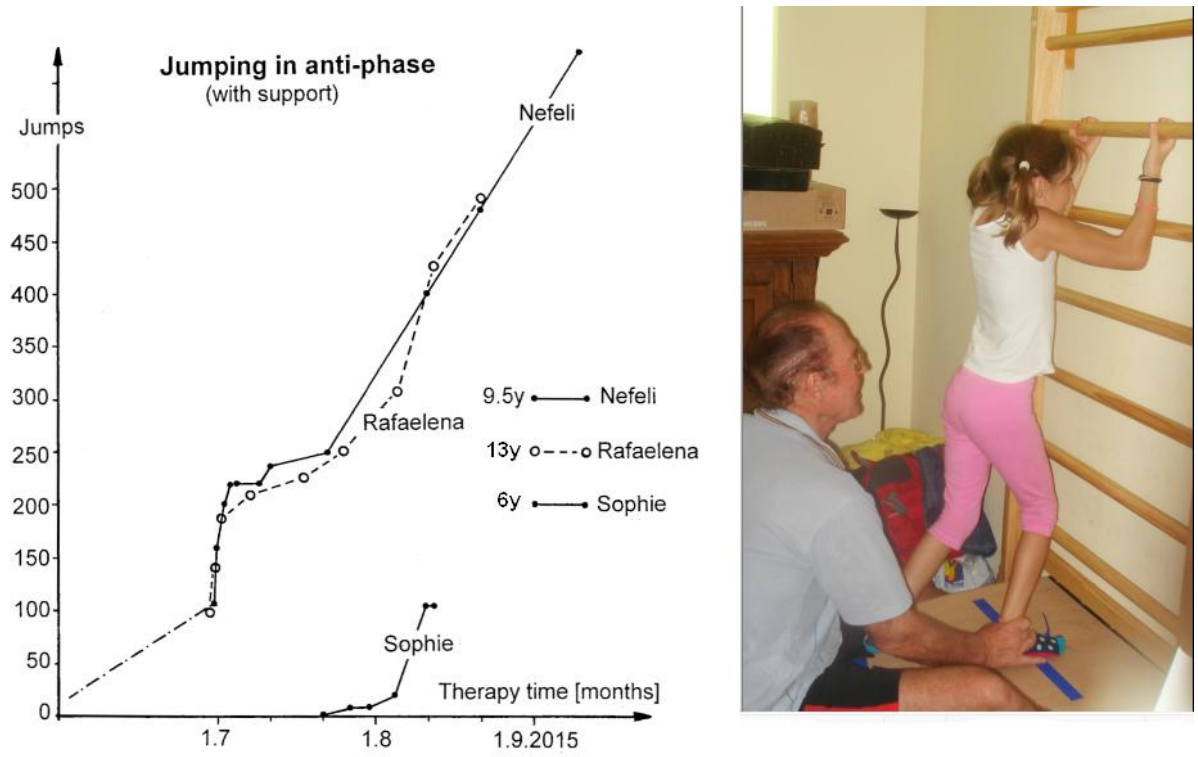


Fig. 1.51. Supported jumping in anti-phase of the 9.5-year-old Nefeli with SCI in comparison to other girls. Note, with the right small finger the therapist (Author) is trying to keep the right foot of Nefeli in a physiologic position. The progress in jumping is quantified by the increase of jumps per series. y = age in years

Fig. 1.52. In spite of all the struggles the Author had with the patient Nefeli when pushing her to the limits of exercising, she wrote into the control book that she likes the Author

In spite of all the hard work, Nefeli got much better and she appreciated that. The question remained, to what extent can a SCI be repaired in children.

1.3.3.3 Repair within 12 months

The CDT was continued. When the Author trained with the patient, there was progress. When the Author was not training with her, there was little or no progress. Stability of standing and walking improved. Urinary bladder functions improved further. Apart from bladder function repair, the main problem seemed to be the foot functions. The induction of the stepping automatism (Fig. 1.53), located mainly in the intumescentia lumbosacralis, for improving leg functions by learning, was not

possible following 9 months of CDT. She could not lift sufficiently the knees and dorsal flex the feet for heel strike.

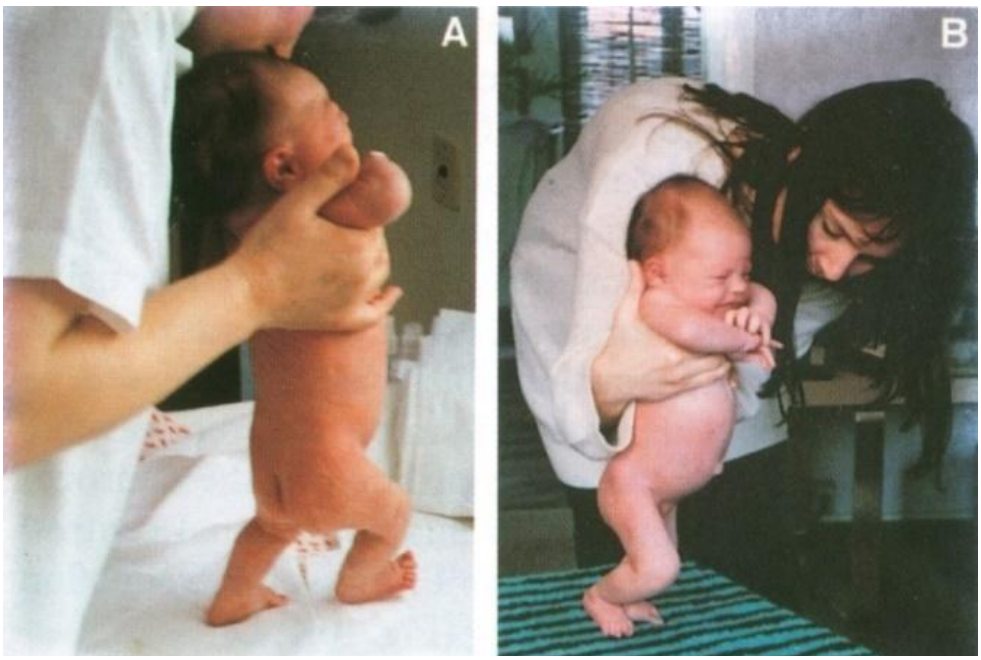


Fig.1.53. Automatic stepping in a newborn infant. A. The 5-day-old infant, Juliane, performing primary automatic stepping; slight backward posture. The heel of the right foot touched the ground first. B. Infant Juliane, 8-day-old, performing automatic stepping

After 10 months of CDT, the sensitivity of the soles of the feet improved (dermatomes L4 to S1, (Fig. 1.1)), which is important for controlling walking and jumping. She became able to dorsal flex the feet (Fig. 1.54) with little power. She became able to move a bit the toes, but all together. But standing on the forefoot was only possible with the help of the extensor spasticity. The use of spasticity for certain functional aspects is not of interest for a full functional repair which was the far goal.

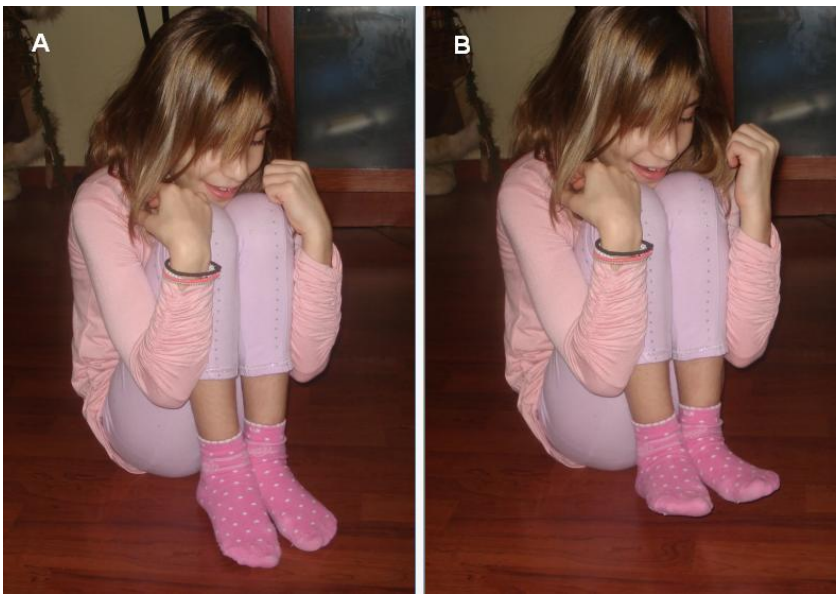


Fig. 1.54. Volitional dorsal flexion of the feet in a patient with 70% SCI. In A plantar flexed and in B dorsal flexed. To improve foot power, the hand grip is co-activated (clench her fists)

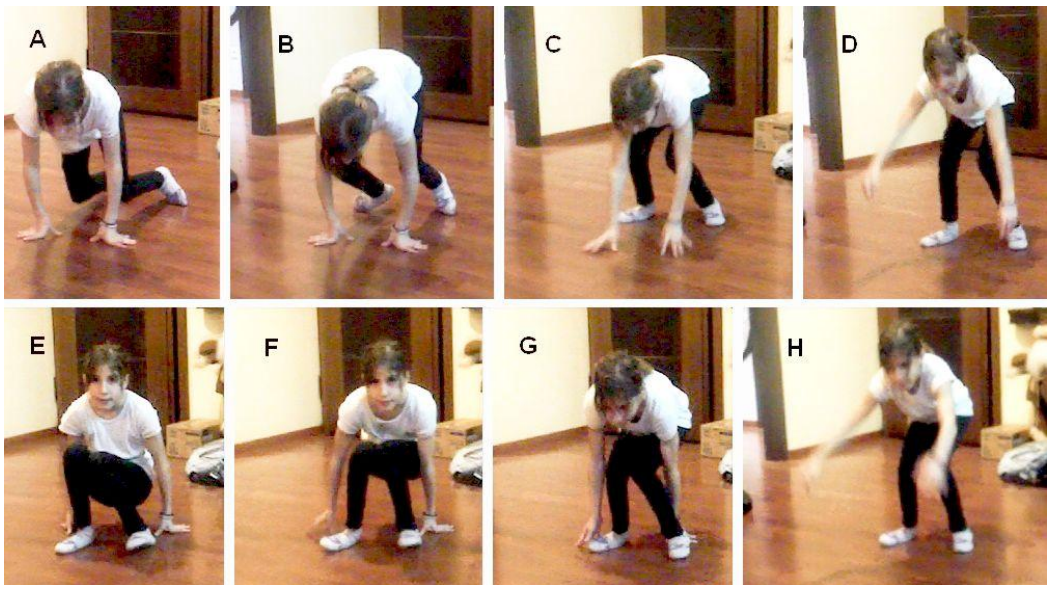


Fig. 1.55. Two ways to get up from the floor after falling. In A through D mainly the arms are used for getting up and in E through H the legs

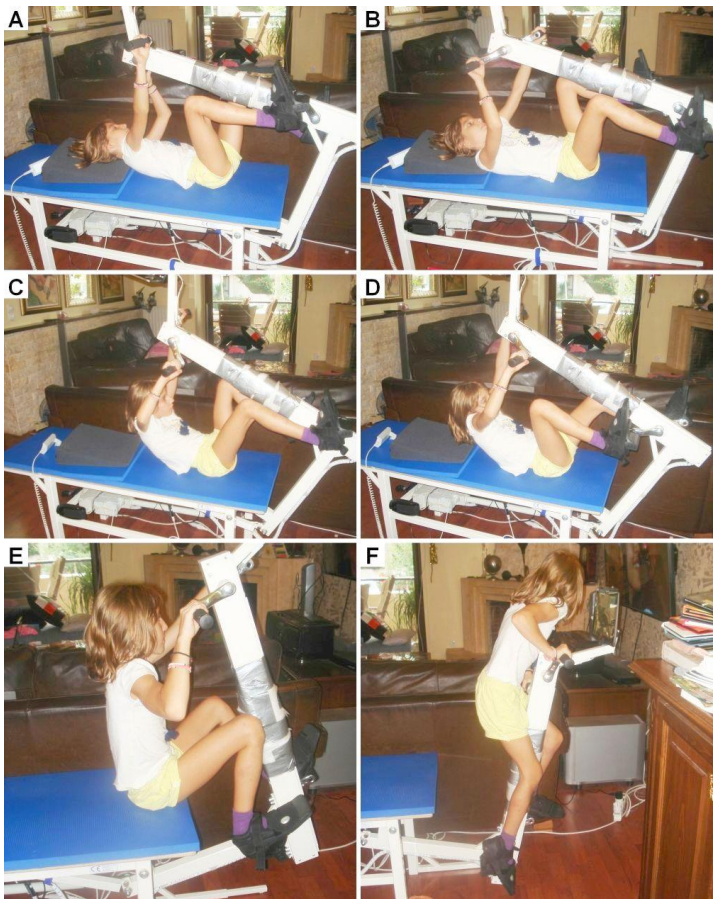


Fig. 1.56. Patient with SCI during exercising on the special CDT device different movement patterns to improve phase and frequency coordination of neuron firing. In A and B also trunk rotation is trained. When turning in the standing position (F), the performance of the right foot is pathologic (plantar flexed)

Nefeli learned to run a bit with poor performance. When falling she became able to get up from the floor by herself without support (Fig. 1.55). When she was falling, the protection automatisms worked well so that she was not afraid of falling. For getting up from the floor two patterns were used. Nefeli could mainly use the arms for getting up (Fig. 1.55A,B,C,D) or use the legs (Fig. 1.55E,F,G,H). When using the legs, she had to push herself up. This getting up with momentum was fast and made the hands in Fig. 1.55H blurred. For the repair of the CNS the getting up with the legs is more beneficial because the legs are trained more. Good balance was needed for both patterns.

Nefeli became able to regularly turn on the special CDT device against 50N and became able to use the whole repertoire of movements on a special CDT device (Fig. 1.56). The repairs of the coordinated firing of neurons deeper in the complexity of CNS neural network organization improved. Nefeli was trying out any kind of movements she was able to perform and showed them proudly to the parents (repair phase of regeneration). Since Nefeli from Greece was clever and had a good memory, she realized what functions recovered anew. She realized what hard work was necessary to get more and more functions back. The problem was that she was going to school and had not sufficient time for training. She had problems to understand that the training is more important than playing and going to school. Losing one or two years of school would not change her life. Later on, during life, the rate of learning is reduced, but since she will be more matured then, she would benefit more from the learning (second way of education). On the other hand, a not functioning bladder is a horror . One is concerned with bladder infections, catheterization and even with operations for the rest of the life. In Switzerland the school regulations are very strict; the school has always priority, what is not right.

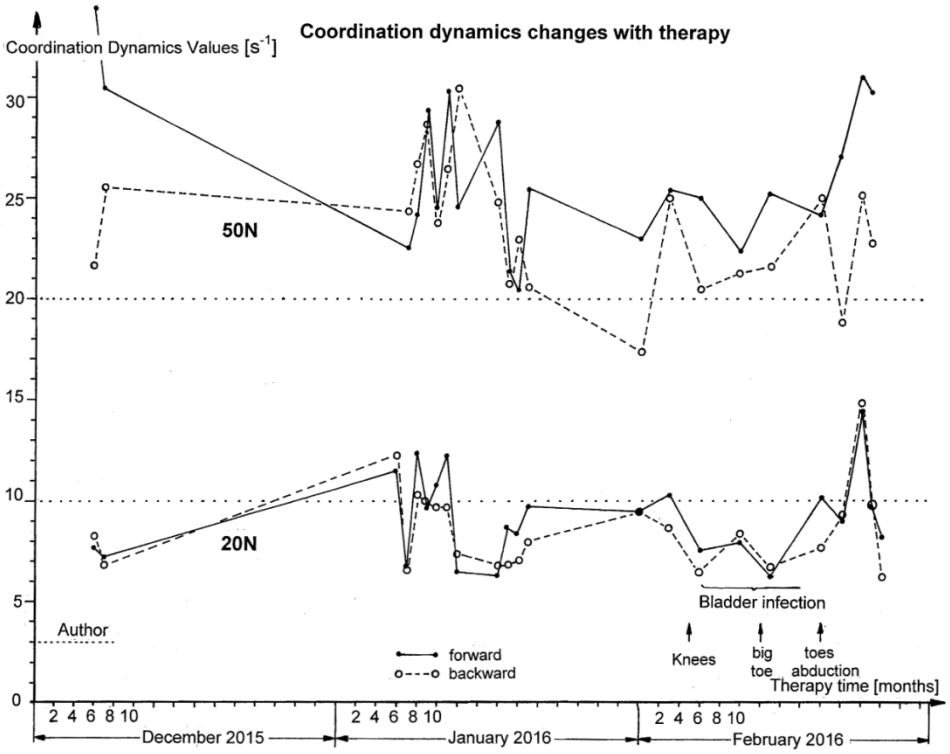


Fig. 1.57. Coordination dynamics values over time of the SCI patient Nefeli

1.3.3.4 Measuring the improvement of CNS organization non-invasively by means of coordination dynamics (CD) values

When Nefeli became able to turn continuously on a special CDT device at 20N and was accepting it also, the measuring of the improvement of CNS functioning became possible. Fig. 1.57 shows the improvement of CNS organization (lowering of CD values) when exercising at a load of 20N. A curve for best values (lowest values) over years of CDT is drawn in Fig. 1.74. One can see from Fig. 1.57

that the CD values varied strongly. There are at least three reasons for the large variation of the CD values. First, her motivation for smoothly exercising varied; she often liked to play and did not concentrate sufficiently. Second, her leg power varied, making a smooth turning more difficult, especially for the difficult coordination s between pace and trot gait. Third, with each bit of reorganization in her CNS, transiently the CNS organization gets worse till it improves again with training. In the older SCI patient Kadri it was measured that with every bit of improvement of her CNS functioning, her coordination dynamics values got transiently worse (Fig. 1.24).

1.3.3.5 Learning of deep network complexity in the short-term memory by exercising coordinated movements at high load and its problems of induction

To improve CNS functioning, the developing child or the patient has to exercise on the special CDT device in the forward and backward direction to improve symmetries of network organization. By turning fast and slow, the movement performance can be improved via the movement-improving, movement-induced afferent input which is generated by the slow, medium-fast (fast fatigue resistant) and fast contracting muscle fibres (fast fatigue) and their corresponding upstream neural networks including the premotor spinal oscillators (Fig. 1.11).

The exercising against different loads has also to be performed to enhance the integrativity (which means that many subnetworks are activated simultaneously and coordinated) and complexity of neural network organization. By increasing the load during longer periods of exercising, the slow muscle fibres (and the upstream networks) (Fig. 1.11) are trained, which, for example, a marathon runner needs. To get sufficient oxygen, to regulate the temperature and the cardiovascular performance, the vegetative nervous system is trained and improved in its functioning in general and especially because of substantial learning transfer from movements to other untrained functions in the injured and uninjured CNS.

When the CNS functioning of Nefeli had improved sufficiently she was supposed to start regularly the low (20N) and high-load (20N, 50N, 100N) testing and exercising. She was mentally prepared to start at a certain day that hard exercising. But when the day came, she did not want to do this hard training, because she was in a bad mood, had headache or bowel pain and may be some pain from the re-innervation of the S1 segment (dermatomes and sclerotomes; Fig. 1.58). She was angry with the Author because she did not want to do that test. The father pushed her and struggled with her for one hour. Nefeli s arguments were that she is exhausted and wants to play. She wants to learn for the school so that she is again one of the best ones. But the father succeeded and Nefeli started to turn 1000 times at very low load to improve her nervous system functioning in the short-term memory. Then the 20N test for 21 min was started. She was still in a bad mood. During the 20N test her mood improved and she became further cooperative. After a small brake the high-load test was started. Because of the improved nervous system functioning, she started to fight to manage 50 and a bit 100N. To manage also the 100N load is really difficult for a ten-year-old girl with a SCI, because substantial leg power is needed. But after the high-load test she was in a very good mood and had no pain any more. She was now optimistic and wanted to run, walk fast and jump. She took the stop-watch to also measure the running times for quantifying the progress in running. She became able to run first time 13m in 16s including two times falling. When running that distance a second time, she did not fall and needed now only 10.6s. To run a third time, she refused, because her legs were exhausted (70% SCI, Th10). Running backwards took much more time. When administering the low-load and high-load testing again, which is anyway a very good exercise, similar motivation problems occurred. Only with a parent present the measurements were successful at the beginning.

When Nefeli had a bladder infection, the motivation problem was bigger, because of reduced power. Bladder infections are quite a load for the body. Even though the body needs the energy to fight against the infection, the exercising at low load is helpful, because the micro-circulation improves and the exercise-dependent NK cells (immune cells) are build more, which helps to fight against the infection. A better microcirculation with more immune cells is also successful in cancer treatment [65,66].

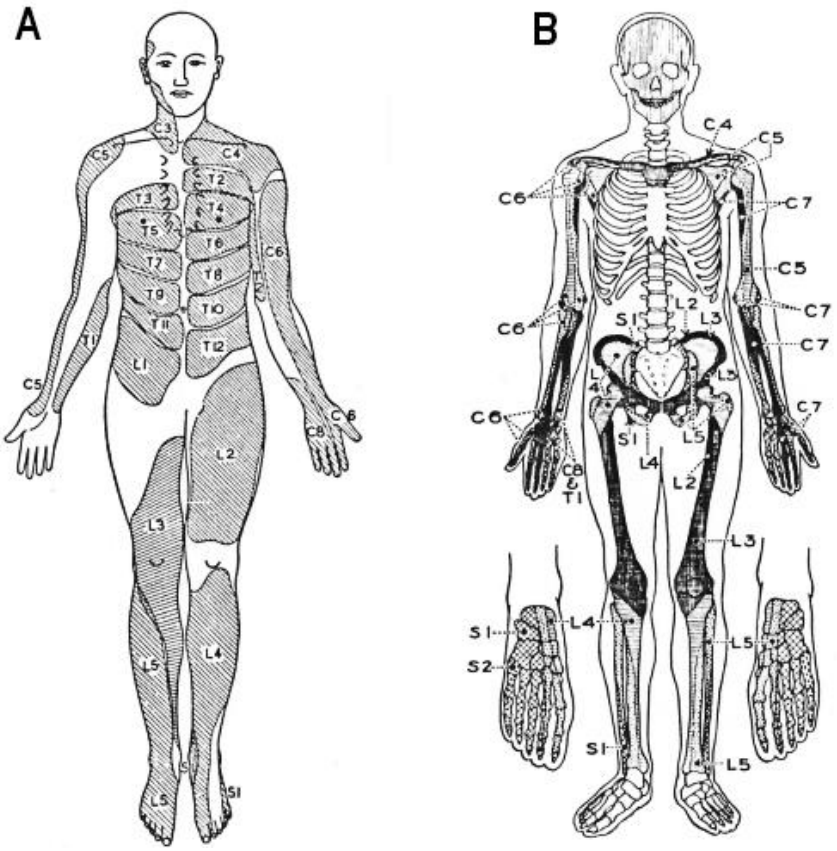


Fig. 1.58. Sclerotomes (B) and Dermatomes (A)

Interesting with these low- and high-load testing was, that firstly this exercising at low and high loads changed her feelings completely. Also, the Author feels every day much better after low-load and high-load training up to 150N or 200N. Secondly, even though being a bit exhausted, the performance of movements was much better after exercising against high load. This holds also for healthy pupils and athletes. The improvement of CNS functioning in the short-term memory has consequences for the improvement of movements and probably also for the health in general. The improvement of the health in general was important for Nefeli. After the cancer removal no chemo and radiation therapy were administered because of the SCI. There was therefore a bigger risk of a re-occurrence of the cancer. Exercising helps to inhibit a re-growing [66].

1.3.3.6 Improvement of free running

After 9 months of CDT the running was tried and sometimes Nefeli got into the running rhythm for a few steps. But after approximately 10 months she became really able to run a bit with poor performance. Nefeli was always open to run, unless the power in the legs did not allow it anymore because she wanted to run again with the other children at school and she liked the running very much. Running is a very integrative movement and trains deep neural networks complexity efficiently. Pathologic leg activation is partly compensated for by the kinetic energies which smoothen the movements. The stimulation of leg movements via arm and hand movements was limited in her because of balance problems, which made her to abduct the arms. To stop the falling due to losing the balance was solved in the way by letting her running along a floor (Fig. 1.59), where she could touch the walls for keeping the balance in similarity to the running on treadmill where she could touch the rails for keeping the balance. But she was also falling because of the low stability of the running pattern. The potential well of the running pattern was too shallow and the phase and frequency

variability too high. But as mentioned above, Nefeli was not afraid of falling and had developed a good technique to reduce the severance of falling and to get quickly up again (Fig. 1.55).

The pattern stability of free walking improved because the walking could be trained for longer distances.

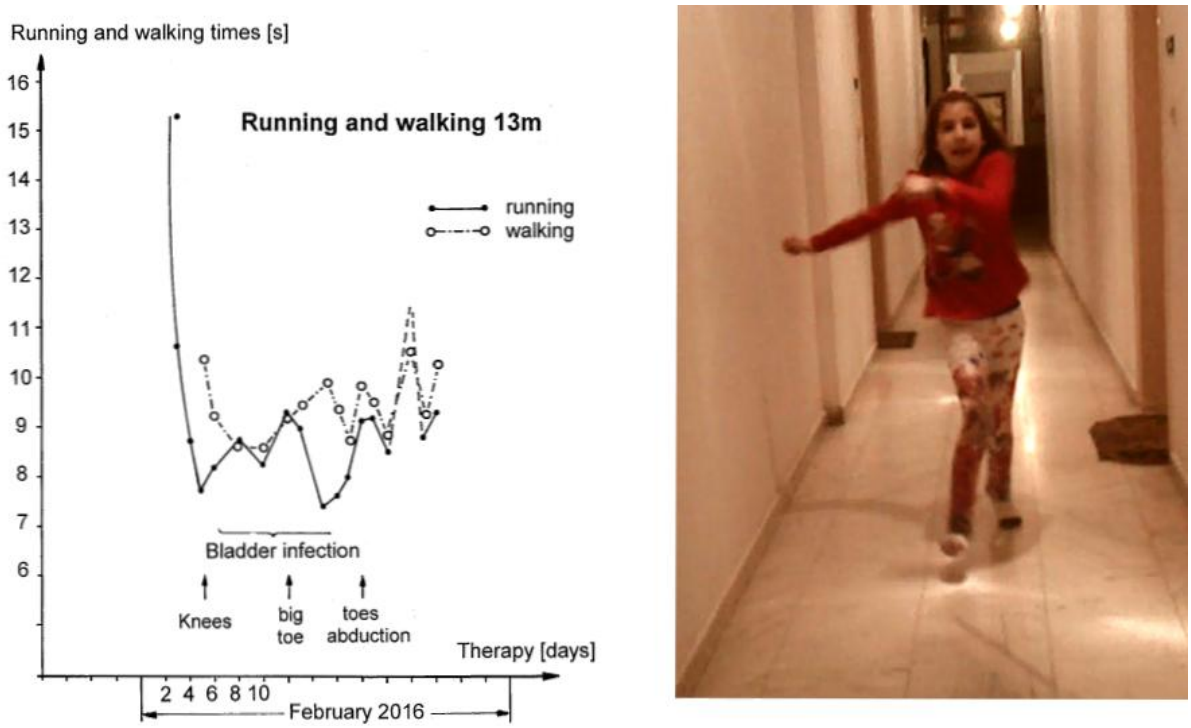


Fig. 1.59. Improvement of running and walking times when moving along a floor. The patient is using the arms also for keeping the balance

The improvement of running is shown in Fig. 1.59. The backward running also improved. At the beginning of running, she could faster walk than run. But with the improvement of the running performance she was faster with running than with walking. Measuring the running times, plotting them and showing them to her motivated her to train more. She wanted to be better than the last times.

1.3.3.7 Using the stepping automatism for improving walking and running

One problem in repair was how can Nefeli made to lift the knees and strike the ground first with the heels to improve the performance of walking.

In brain injury the brain has to be repaired. In SCI (Nefeli) the brain has to be made reorganizing the problem to compensate for the injury and mismatch of nerve/tract fiber growing. For a mainly functional repair, the remained tract fibers below the injury level have to be rewired by the brain, because there is only little plasticity in the intrinsic networks of the spinal cord. During a regeneration of the caudal spinal cord, the growing nerve/tract fibers may not find the to be re-innervated muscles/organs because of mismatch. Again, the brain has to compensate for the false growing in the periphery. The complexity of repair mechanisms is large. But through movement-based learning, the brain is able to take care of the complexity of CNS repair. In lower animals it is or was believed that the power of regeneration is very high and the growing nerve fibers know the place where to grow to. In human, the regenerative capacity is small; but the tremendous complex brain is able to solve the problem by learning. One strategy for re-learning is here the used stepping automatism.

Characteristic for the stepping automatism in babies is the high lifting of the knees (Fig. 1.53). One stimulus for inducing the stepping automatism is the heel strike. If it would be possible to (partly) stimulate the stepping automatism for repair, then, may be, the neural networks at the SCI site (around Th10) could be stimulated for functional repair and regeneration. Since the neural networks of the stepping automatism are mainly located in the intumescentia lumbosacralis and are getting only little drive from supraspinal centers, the stepping automatism pattern should be quite physiologic in a Th10 SCI and could help to improve the feet functions during walking.

After 11 months of therapy Nefeli became able to lift the knees sufficiently and became able to strike the ground first with the heels to induce the stepping automatism (Fig. 1.60). Because the sensitivity of the soles of the feet had improved, she could feel that the heel was striking the ground first (before the forefoot). To optimally use the movement-induced afferent input for walking and running, Nefeli was walking and running best without shoes.

Fig. 1.60. The patient with a SCI learned to lift the knees and strike the ground first with the heel to induce the stepping automatism for SCI repair. Note, the arch of the foot is preserved in the left foot but not in the right foot during the stance phase. With the lifting of the knees, Nefeli became able to activate the quadriceps much more; the regeneration of the spinal cord had substantially reached the L4 segment. Nefeli is walking in the usual trot gait coordination

1.3.3.8 Training of the damaged spinal cord site

The devastating consequence of a SCI is that the functions below the injury level cannot be controlled any more by supraspinal centers. But the neural networks at the injury site, in Nefeli s case Th10/11, are additionally damaged and partly lost. Nefeli trained the trunk stability including the Th10/11 spinal segments, when exercising on the special CDT device in the lying position with trunk rotation (Fig. 1.56A,B).

The teachers and pupils of the school were following up Nefeli s progress, induced by CDT, from the beginning on when she was moving with sticks (Figs. 1.32B, 1.46A). The teachers tried to contribute to the progress. The sport teacher gave Nefeli a hula hoop for training the trunk and especially the pelvis control (Fig. 1.61). The progress of trunk movements was quantified by the time she could hold the hula hoop up.

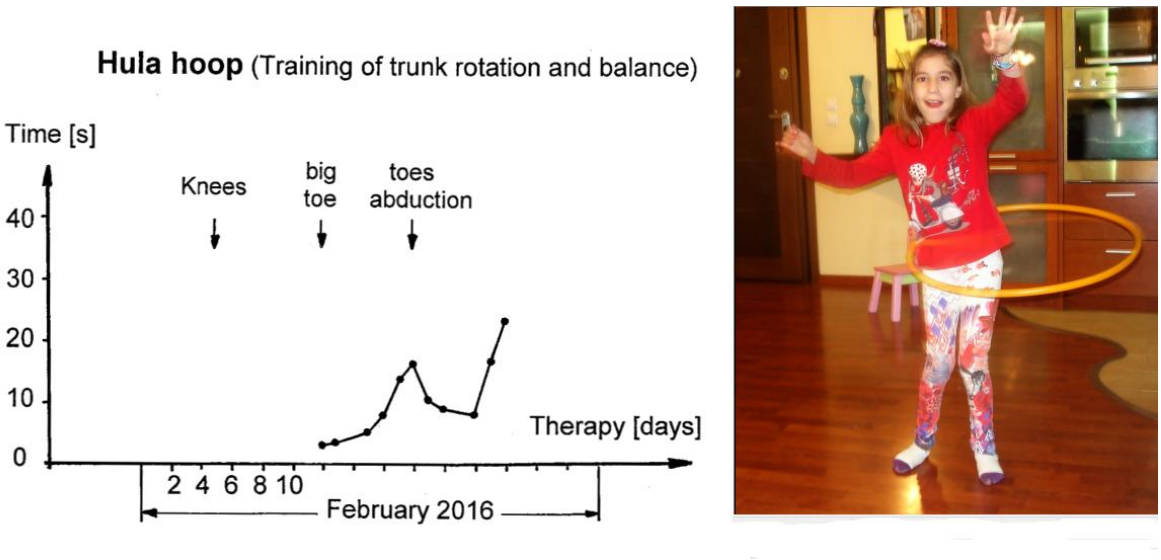


Fig. 1.61. The 10-year-old SCI patient Nefeli during training with the hula hoop to improve trunk mobility/stability and balance

1.3.3.9 Re-appearance of big toe function in relation to changes of the homunculus of the sensory-motor cortex

After 10 months of CDT, Nefeli became able to move the forefoot and a bit the toes altogether (Fig. 1.54). With 10.5 months of CDT she became able again to move a bit the big toes separately (Fig. 1.62). The dorsal flexion was easier to perform than the plantar flexion. She was glad about this new movement, because she was already afraid that she forgot that movement and could not activate it any more. The visualization of the task and movement was very important to initiate, control and continue the (slow) movement.

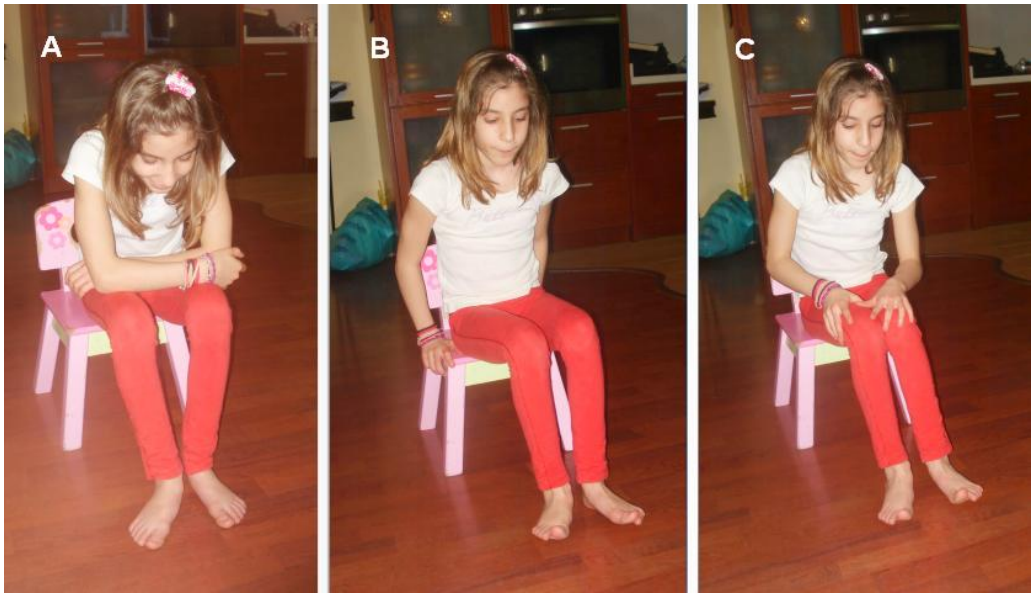


Fig. 1.62. Ten-year-old Nefeli can move again the big toe separately four years after the accident and following 10.5 months of CDT. In A she does not activate foot muscles and is relaxed. In B,C she concentrates and visualizes the task to activate the dorsal flexion of the big toe, which indicates that the spinal cord repair has reached with the activation of the halluces longus the spinal cord segment L5

Unclear is whether she only forgot the initiate that toe movement pattern or whether in the sensory-motor cortex (Fig. 1.63) the adjacent parts took these neural networks partly over and used them for other functions. Interesting is actually what changes of the homunculus take place after complete and incomplete SCI. Are these networks are partly used for the functional repair when re-wiring tract fibers in the spinal cord?

There is also localization of function in the cerebral cortex. To substitute function from one part of the CNS to another, it is important that many brain parts of a certain function are activated simultaneously and in a coordinated manner. Probably especially neighboring brain areas can take more easily functions over. Since foot, bladder and sexual functions are close together in the sensory-motor cortex (Fig. 1.63), the repair of foot functions is not only important for re-learning walking and running, but also for the repair of bladder and sexual functions.

In the patient Nefeli, spinal cord tract fibers had to be rewired by changing partly localizations of functions in the brain. Walking, bladder and bowel functions have to be repaired and colon pain stopped by shifting, enlarging, lessen and combining cortical representations of functions.

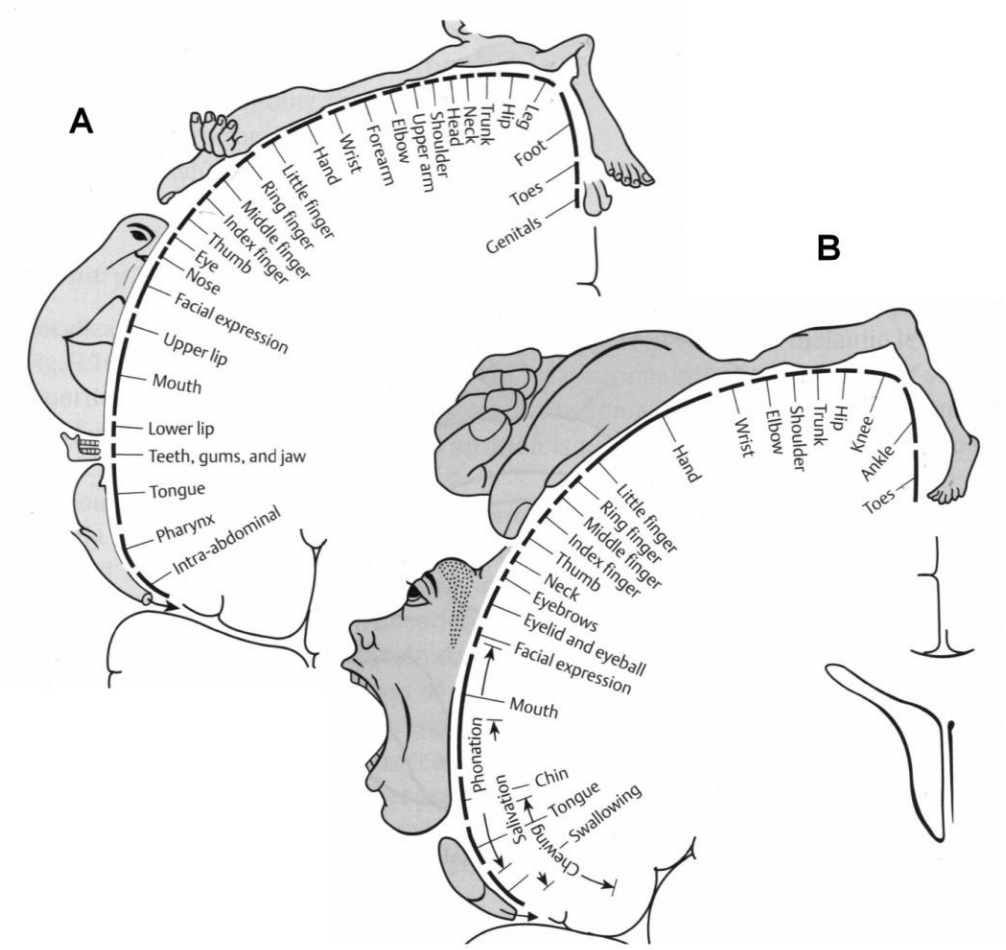


Fig. 1.63. Relative sizes of the cortical representations of different parts of the body in the human primary somatosensory (A) and motor (B) cortical fields (the so-called homunculus). (from: Penfield W and Rasmussen T: The Cerebral Cortex of Man, Macmillan, New York, 1950). Note the large representations of fingers, hand, mouth, lips, tongue and phonation. The much larger representation of the index finger than the upper trunk is in accordance with the corresponding two-point discriminations (1mm against 25mm). Following incomplete SCI and repair, these cortical representations change

1.3.3.10 Repair of rectum und colon functions

Emptying the rectum is similar to emptying the urinary bladder [17]. Filling of the rectum activates stretch, tension, mucosal and under certain circumstances pain receptors in the rectal wall (and may be some skin receptors around the anus), which transmit impulse patterns by way of the inferior hypogastric plexus and sacral roots to segments S2 through S5 of the sacral spinal cord, where probably a defecation center is located in similarity to the micturition center in the sacral spinal cord. The sacral defecation center communicates probably with a pontine defecation center in the reticular formation and the cerebral cortex.

Rectal peristalsis is induced by parasympathetic activation from the defecation center, which also induces relaxation of the internal sphincter in similarity to micturition. The sympathetic nervous system inhibits peristalsis. The external sphincter consists of striated muscle fibers of FR type, innervated by α_2-motoneurons (Fig. 1.11), and is under volitional control. The fast fatigue resistant muscle fibers secure that the sphincter can be contracted quickly and the closure can be hold for longer times. Rectal emptying is mainly accomplished voluntary by abdominal pressing.

The stretch, tension and mucosal receptors of the rectum are similar to those of the bladder and their activity was recorded when stretching the external anal sphincter by pulling the anal catheter and changing the catheter thickness from thin to thick (Fig. 1.8).

The Author had given research emphasis to the repair of the urinary bladder functions because of the bladder infections and the risk of ascending infections. Kidneys cannot be transplanted to those patients because of the necessary suppression of the immune system after transplantation. It was difficult to administer movement therapy to Nefeli when she had pain. Pain is a general problem in SCI. Even though CDT inhibits most likely cancer growing, the differential diagnoses of pain includes besides infections of kidneys and ovaries the growing of metastasis in the bowel.

Transection of the spinal cord above the lumbosacral center for defecation leads to fecal retention. Overfilling of hollow viscus is perceived as pain. In incomplete SCI, the pain can be felt. There are SCI patients which are afraid of a repair of the sensitivity because of the possibility of getting untreatable pain.

Since the middle and left abdomen was sensitive to touch and pain, Nefeli could feel the pain in the Heads zones for bladder and rectum/colon (Fig. 1.64). Nefeli felt pain in the Heads zone for the bladder with bladder/urethra problems and she nearly every day felt pain in the Heads zone for the rectum/colon in the morning and after eating. When exercising for approximately 30min on the special CDT device the pain mostly waned. Her bowel/colon/rectum pain most likely occurred due to the impaired peristalsis, caused by the impaired function of the parasympathetic nervous system, due to the SCI. The exercising on the special CDT device activated the peristalsis of the bowel by activating the parasympathetic division and the pain disappeared. The exercising on the special CDT device therefore does not only activate in the short-term memory the bladder for micturition but also the colon/rectum for defecation.

1.3.3.11 Pain perception and Zones of Head

It can be expected that Nefeli experienced pain in the lower body because of the incomplete SCI Th10. When the lower body started step by step to function again, pain occurred in the toes, knees, bowel and other parts of the lower body. To distinguish between pain she had to accept (because of mobilizing the body again due to therapy) and dangerous pain, also the heads zones (Fig. 1.64) had to be taken into consideration. An explanation of the zones of Head is the following.

The cell bodies of the afferent autonomic fibers, like those of the somatic afferent fibers, are located in the spinal ganglia. The autonomic fibers enter the spinal cord through the posterior root together with the somatic afferent fibers from the myotome and dermatome of each segmental level. Thus, each individual segment of the posterior horn receives converging afferent input, both from internal organs and from the related myotome and dermatome (Fig. 1.64A). Activation from either set of afferent

fibers (visceral or somatic) is transmitted centrally by the fibers of the anterolateral spinothalamic tract (Fig. 1.64A). It is therefore understandable that pain arising in a particular viscus (bladder, colon) is sometimes felt elsewhere, namely in the dermatome or myotome represented by the same spinal segment. This phenomenon is called referred pain. It may be accompanied by a certain degree of hypersensitivity to somatosensory stimulation in the dermatome to which the pain is referred. The abdominal wall may also become rigid. It is also possible that impulses arising from the skin can be projected (referred) to the internal organs. Clearly, the somatic afferent fibers are interconnected with visceral reflex arcs within the spinal cord. This may explain how therapeutic measures at the body surface (such as the application of warmth or heat, compresses, rubbing, etc.) often relieve pain arising from the autonomically innervated viscera.

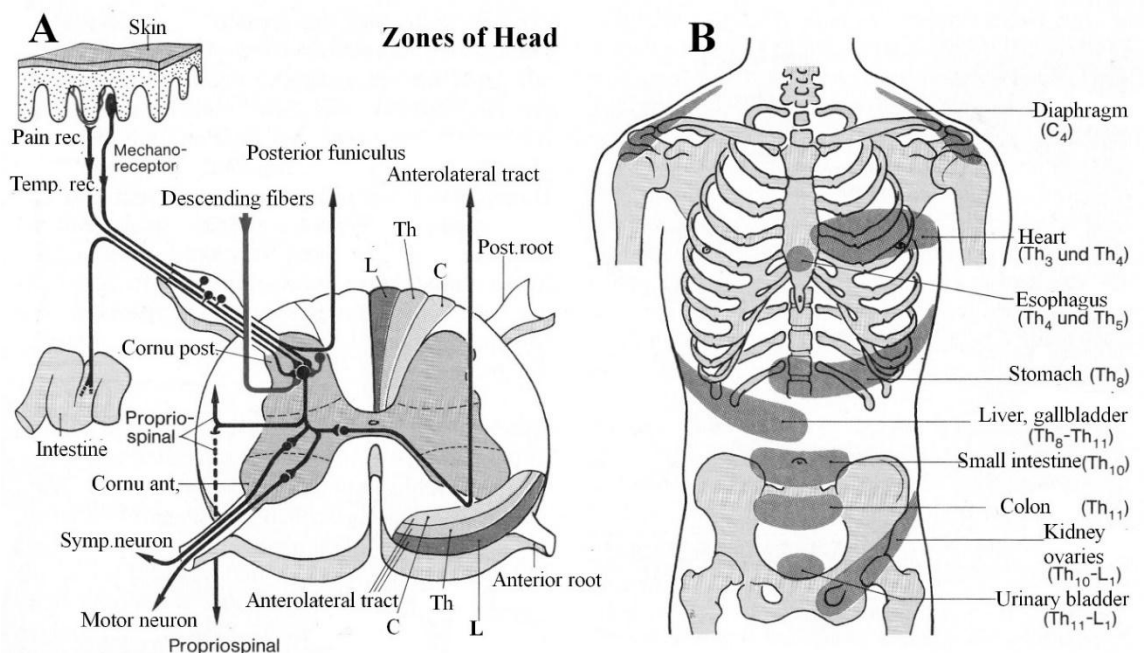


Fig. 1.64. Zones of Head and referred pain

In the patient Nefeli with an incomplete SCI at the level of Th10 we can expect pain origination in the small intestine, colon, kidney, ovaries and urinary bladder (Fig. 1.64B). Especially we have to expect pain in the colon zone of Head (Th11, Fig. 1.64B), because at this level there is the cord injury. And indeed, it seemed that she experienced pain in all of these zones of Head. Often Nefeli experienced pain in the colon zone already after sleeping in the morning. But when jumping on springboard, running or doing hula hoop after some time she often got pain in the colon zone. During jumping and running the bowel, including the colon, will move up and down and stimulate visceral receptors of the colon. On the other hand, pain in the colon zone, due to performing hula hoop, may arise because the SCI site is stimulated and may arise not so much from the mechanical stimulation of the bowel. Even though the PET showed no tumor growth, still small metastasis may escape detection and grew anywhere in the intestine and could give rise to pain later on. An important property of CDT is therefore that tumor growth will be inhibited simultaneously to a certain extent anywhere in the body. So far Nefeli refused healthy nutrition which stimulates the peristaltic of the bowel.

Additionally, Nefeli had pain in the urethra immediately following micturition. Such pain may be due to a hypersensitivity of the urethra wall and the skin around the vagina arising with the re-innervation of the urinary bladder. Hypersensitivity of the skin often occurs with re-innervation.

When pain occurred during exercising, the training of that certain movement was stopped and another movement was trained or a small break was taken intermediately till the pain was over.

1.3.3.12 Waning of the regeneration of Nefeli's spinal cord

Above it was shown that the Nefeli s spinal cord regenerated. The spinal cord regeneration was measured by the recurrence of function of segment-indicating muscles (Fig. 1.37). But the regeneration waned after one year of therapy. The important question is why did the regeneration of the spinal cord faded? One reason is that Nefeli stopped training continuously at the limit, against the advice of the Author. The chain of events for keeping certain regeneration processes going was broken with every therapy break. A continuous therapy at the limit would probably be needed for a year or more to run through the whole chain of events for continuous regeneration. Another important reason for the waning of the regeneration is that the regenerative power is probably much stronger below an age of 10 years. Also, little is known about the precise damage at the injury site. Further, the limited regeneration of her spinal cord was probably supported by recruiting ectopic pathways through root connections, sympathetic chain or plexus connections (misdirected haphazardly during development) or a re-organization of plexuses outside the spinal cord. But the regeneration speed of 1mm/day supports the direct growing of nerve fibers caudally in the spinal cord.

The first two reasons for the waning of the regeneration process have important clinical consequences. If the regenerative capacity is much stronger below an age of 10 years, then children have a much better prognosis with respect to repair than teenagers or adults. From the genetic point of view, it would be important to find out what are the differences in gene expression below 10 years of age and adults and can we change in adults the gene expression to the one below an age of 10? What are the differences of interaction of neural activity and genetic programs during development and repair?

The second possibility that one has to run through the whole chain of events to stimulate all possibilities of repair has the clinical consequence that longer therapy times are needed when administering efficient therapy. The treatment possibility that one has to run through the whole chain of events is supported by the success of bringing a permanent coma patient back to life. With four years of continuous CDT with 20 hours therapy per week, the coma patient became conscious again and with 6 years of continuous therapy he could speak again [67].

1.3.3.13 Gene expression pattern triggered by excitation in proliferating adult NPCs

For weight changes of synapses, growing of axons and dendrites, neurogenesis and building of glia cells during the process of activity induced structural repair, proteins are needed, which have to be generated by appropriate transcription from genes. It seems that natural patterned activity-dependent depolarization of the plasma membrane trigger activity-dependent gene expression programs [68]. Ca^{2+} signaling through $Ca_v1.2/1.3$ channels and NMDA receptors can activate a broad array of rapidly responsive transcription factors. Moreover, excitation could in principle induce release of autocrine factors from the NPCs themselves, leading to recruitment of a host of additional signaling pathways to nuclear transcription factors [68].

1.3.3.14 Regulation of epigenetic modification for repair by movement-based learning

To generate repair in the nervous system, it is likely that permanent changes in gene expression patterns are achieved through permanent changes in chromatin remodeling without changes in DNA sequence. The concept of chromatin remodeling addresses a key challenge of how stable changes in gene expression are induced [69] in neural networks to produce long-lasting changes in repair. DNA methylation is one of the many epigenetic modifications that can alter gene expression. Dynamic and reversible DNA methylation may be essential for learning and memory formation and could transmit repair influences onto adult neurogenesis.

If the epigenetic definition that the events are the structural adaptation of chromosomal regions so as to register, signal or perpetuate altered activity states [70], that means the nature of epigenetics is responsiveness, then epigenetic regulation for repair should be stimulated by physiologic neural network activation. Un-physiologic neural network activation like electro stimulation (which is nearly always un-physiologic apart from the heart pace maker) stimulates chromosomal changes in a

negative direction with respect to health. The DNA methylation system and the Polycomb/Trithorax systems seem to respond to previous switches in gene activity [70].

Understanding the complex epigenetic regulation of neural activity and adult neurogenesis is integral to designing therapeutic approaches to restore neurogenesis and cognitive functions. It will also give a tremendous insight into understanding how certain environmental or pathological influences, such as stress, physical activity, depression and epilepsy regulate adult neurogenesis [71]. Fig. 1.65 shows steps of epigenetic regulation induced by specific physical activity, namely movement-based learning.

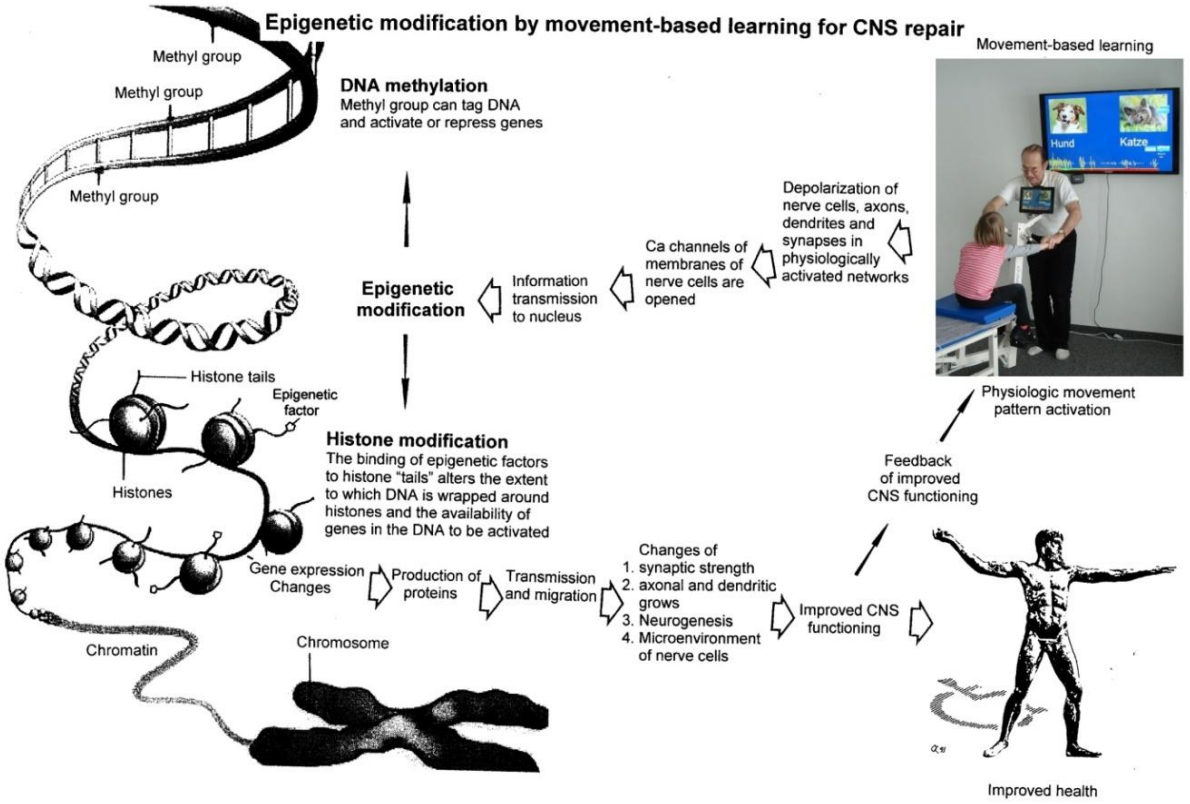


Fig. 1.65. Epigenetic regulation for repair by movement-based learning. CDT-induced stimulation of the pathways that regulate neural network repair is a proven therapeutic and preventive tool. Epigenetic mechanisms, stimulated by physiologic network activation, are likely key players within signaling networks, as DNA methylation, chromatin remodeling and small non-coding RNAs superfamily are required for the fine-tuning and coordination of gene expression during neural network repair by learning. Since the nervous system is involved in nearly all body functions, CDT will improve health

Research in movement-based learning has to identify how epigenetic mechanisms can be efficiently modified by the performance of specific, corresponding movements or learning processes to improve development (correction en route , which is particularly salient to the treatment of cerebral palsy) and repair of the human CNS and to avoid pathologic CNS changes like epilepsy and cancer. The complexity of the epigenetic regulation (Fig. 1.65) is tremendous. Already the neural network learning for repair is complex and needs human neurophysiology including new measuring methods.

1.3.3.15 Spasticity and the intrinsic neuronal apparatus of the spinal cord

Patients with a SCI or a brain injury can have little to very strong spasticity depending on the kind and severance of the injury. Here it is concentrated on the spasticity caused by a SCI.

Spinal cord spasticity is a pathologic pattern of the neuronal networks of the spinal cord. In clinics spasticity is reduced by the administration of spasmolytic drugs. The drawing back of spasmolytic drugs is that they do not only reduce the spasticity but also the power of the volitional movements. Also, there are substantial side effects.

The patient Nefeli with an incomplete spinal cord at the level of Th10 had strong extensor spasticity and some flexor spasticity besides rigor. When she was standing at the whiteboard at school and wrote there (Fig. 1.32C), here standing was not fully physiologic. Her knees were too much flexed. Probably extensor and flexor spasticity were a bit at work. On volition she could stay straight, but as she said, she would need a lot of power for that. If spasmolytic drugs would be administered to her, the spasticity would reduce, but she would have more problems with walking, because of the reduced power in the legs. The proper way to handle spasticity is to reduce the strength of the spasticity and increase the strength of physiologic movements through CDT. Within the System Theory of Pattern Formation, the potential well of spasticity has to be made shallower and the potential wells of physiologic patterns deeper (Fig. 1.66). This can be achieved to a certain extent by movement-based learning. Physiologic movement patterns are trained which are away from the pathologic spasticity patterns (extensor and flexor spasticity) so that not also the spasticity patterns are trained.

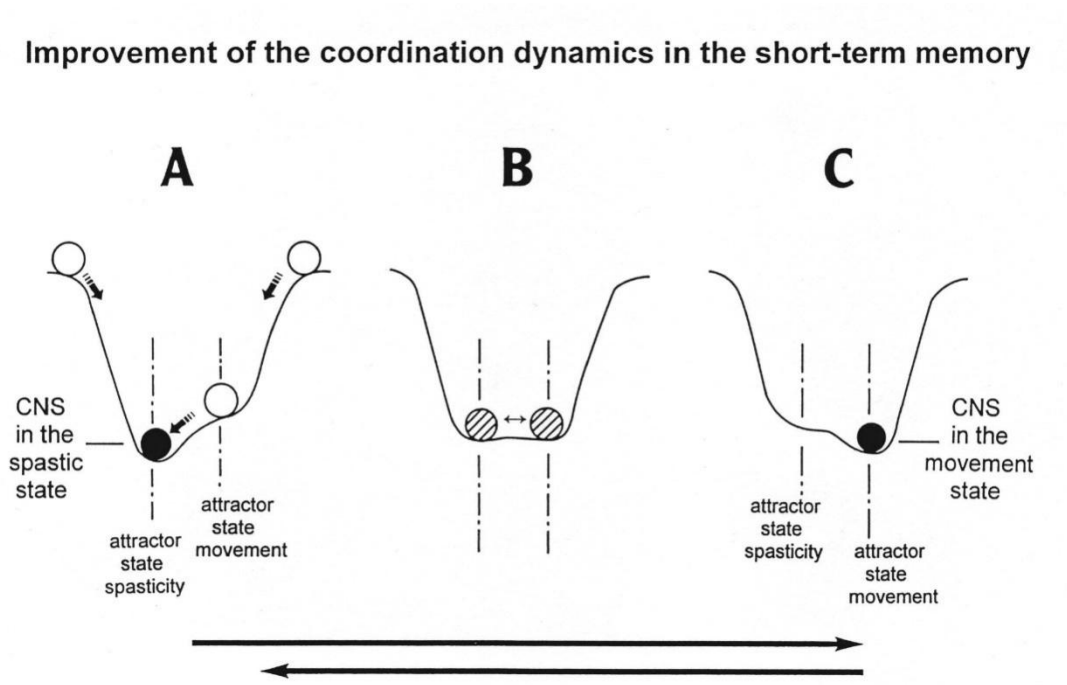


Fig. 1.66. Therapy-induced spasticity reduction in the short-term memory. The position of the ball represents the state of the system and the potential well, the attractor. The ball is attracted to the stable position in the deepness of the hole, called attractor state. The attractor layout, consisting of two attractive states of different stability, is changing upon exercising very coordinated rhythmic movements. Black ball = stable state, open ball = very unstable state, hatched ball = spasticity and movement co-exist. Variability of phase and frequency coordination not indicated

When the Author was holding Nefeli (Fig. 1.67A), she showed strong extensor spasticity. When she was lying on the special device at the beginning of training, it seemed sometimes impossible to flex her knees. But on volition she is able to flex the knees to be fixed to the special CDT device for exercising or to walk. The extensor spasticity may be mainly related to walking or running which are human specific up-righted movements. Anyway, spinal cord spasticity is generated by the damaged neural networks of the intrinsic apparatus of the spinal cord. This spinal cord apparatus can generate complex movements.

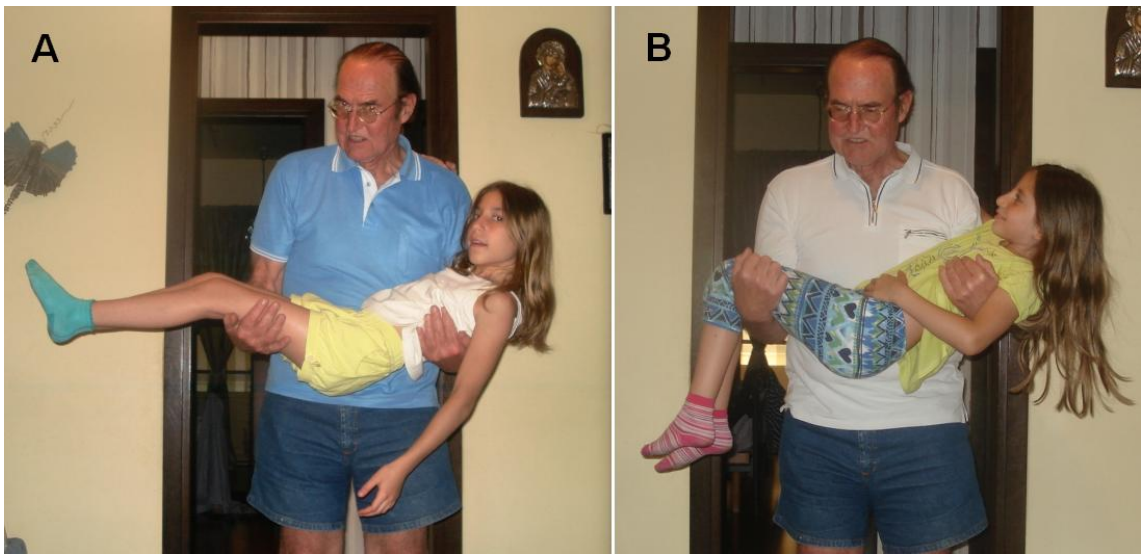


Fig. 1.67. Practical judgment of extensor spasticity. When the Author holds the patient Nefeli (SCI Th10), one can judge her extensor spasticity by the extension of her legs (A). Her present spasticity is medium strong. A physiologic leg position can be seen in B. The healthy seven-year-old sister has no spasticity and the legs are flexed

When a finger touches a hot stove, the hand is pulled back with lightning speed, before any pain is felt. The action potentials stimulated in the cutaneous touch receptors and nociceptors travel by a wave of patterns in many skin afferent fibers to the substantia gelatinosa of the spinal cord to activate this safety automatism to protect the skin. Fig. 1.10 shows such impulse patterns conducted in skin afferent fibers. The fastest pain fibers (P in Fig. 1.10F, pin-prick 1) will contribute substantially, because fast conduction of pain afferent fibers is needed for safety. According to Fig. 1.9 the fastest pain fibers conduct with 13m/s at 36°C. The distance from the finger to the spinal cord is approximately 0.8m. With $t = s/v = 0.8m/13m/s \approx 0.06s$, the conduction time in the fastest pain fibers from the finger to the spinal cord is 0.06s. Some further time is lost in the receptors to generate the pattern. Therefore, in approximately 0.1s the afferent impulse patterns reach the spinal cord for generating the pattern to pull the hand away. In Fig. 1.10F it can be seen that the fastest pain fiber reached the recording electrodes with a delay of 0.1s following pin-prick 1. Both values are compatible. The time needed to generate the protection reaction is 0.1s (page 343 of [18]). According to this approximate calculation, the hand moves away from the hot stove after 0.2s. The intrinsic neural apparatus consists of interneurons, association neurons, commissural neurons and the fasciculus proprius around the gray matter of the cord.

The stepping automatism of the newborn baby (Fig. 1.53) is also mainly generated in the neural networks of the spinal cord. One of the stimuli to activate the stepping automatism is the heel strike.

Following brain death diagnosis, the rest functions of the human body are mostly soon lost, including the functions of the spinal cord. But in exceptions in brain-dead humans, when ventilated, the spinal cord is reorganizing itself and is taking body functions over like temperature regulation. It has happened that relations visited a brain-dead human. When they touched the out of the bed hanging leg, the brain-dead human moved via a spinal cord pattern the leg into the bed. Obviously, the intrinsic apparatus of the spinal cord is really a neural network which can generate complicated movement patterns by itself.

Following SCI, the damaged networks generate pathologic movement pattern including spasticity. During CDT the brain learns to activate the damaged spinal cord in a way to generate physiologic patterns again. But the main plasticity is sited in the brain and not in the networks of the spinal cord.

1.3.3.16 Repair of the foot arch

From Fig. 1.68A it can be seen that the right foot of Nefeli had lost the arch in the stance phase. A foot arch support is only a mechanical help to stop foot arch degeneration. A causal repair, that means a reconstruction of the right foot arch, can be achieved if the nervous system is repaired. The neural network pattern, generating the foot arch, has to activate the motoneurons which drive the muscle for generating the foot arch. The muscles which have to be brought under control by the walking pattern are at least the Mm abductor halluces, flexor digitorum brevis and quadratus plantae. If the foot muscles are not properly activated, pain will occur later on and orthopedic operations are necessary.

Fig. 1.68. Foot arches during supported walking. Note the right foot has in the stance phase (A, arrow) no foot arch

The movement patterns which activate the foot arches are especially the jumping on springboard in anti-phase (Fig. 1.51) and the walking on forefoot if possible. In Fig. 1.51, the Author is trying with the small finger to reduce the outward rotation of the right foot to improve the movement-induced afferent input for better motor learning.

1.3.3.17 Participation in school sport

Following 14 months of therapy, Nefeli became able to participate in school sport (fourth class). With some help of the sport teacher, she could manage to dance with the other class maids (Fig. 1.69A). Only the fast rotation movements were difficult for her (Fig. 1.69B). The teachers made a good job to integrate her in all the activities. Nefeli would have suffered if she could not do the same things as the other ones.

Fig. 1.69. Nefeli during dancing at school. Disappointing is that 16 of the 18 pupils had over-weight

1.3.3.18 Improvement of trunk stability

Due the SCI and the removal of the cancer including the Th10 ganglion, the patient Nefeli had severe scoliosis, a lack of trunk stability and trunk spasticity. Fig. 1.70 shows the false positioning of the trunk in comparison to the healthy brother.

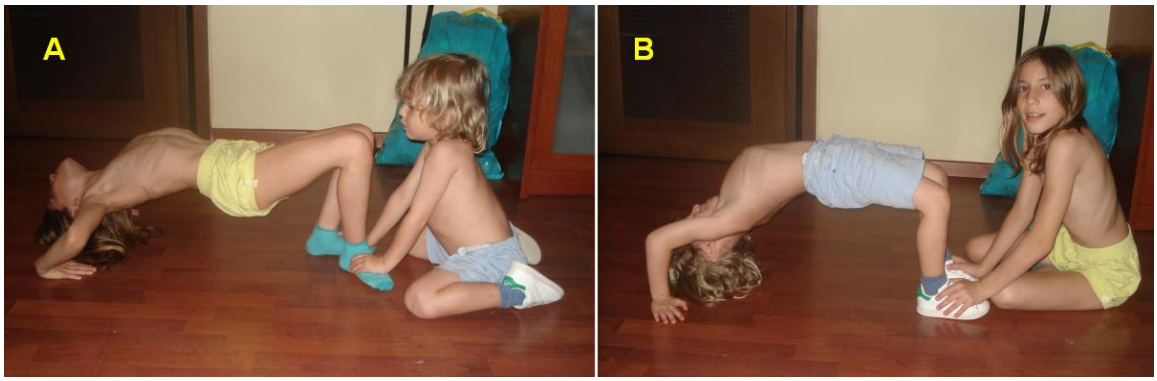


Fig. 1.70. The arching of the back is impaired in the patient Nefeli (A). In the four-year-old brother the arch of the back is physiologic (B)

The too much backward positioning of the pelvis could also be seen during walking on the knees. After about 15 knee steps, Nefeli s spasticity of the trunk pulled her pelvis backward and she fell forwardly.

To enhance the trunk repair, also the hula hoop movement was used. At the beginning the movement was difficult for her (Fig. 1.61). But then she could do the hula hoop movement much longer (Fig. 1.71). The limiting factor of the performance time was the balance of standing and bowel pain. As a consequence of the hula hoop movement and other movements like training on the special CDT device in the lying position (Fig. 1.56), her trunk functions improved so that her trunk became straighter during hula hoop (Fig. 1.72) with therapy.

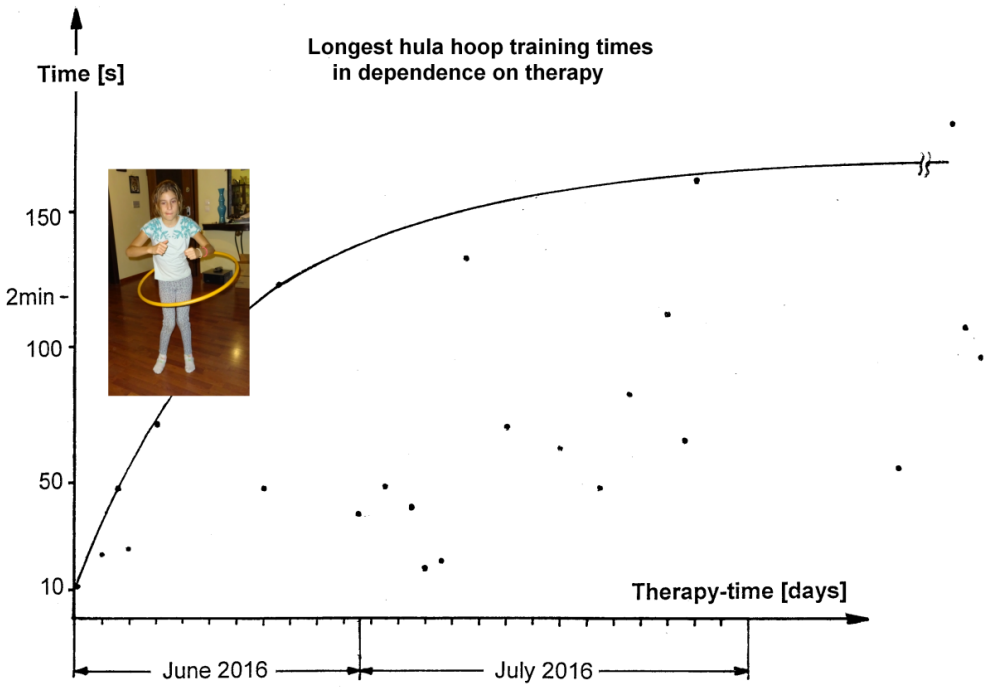


Fig. 1.71. Improvement of longest hula hoop exercising times in dependence on therapy. Note that the individual times varied much

Fig. 1.72. Improvement of the straightness of the trunk during hula hoop. The treatment time is 12 months in A, 18 in C and 22 months in D. The improvement of straightness may not be characteristic for the improvement of her scoliosis

An improvement of a straighter standing can be seen when Nefeli was working in the kitchen in comparison to a standing at the whiteboard at school (Fig. 1.73). The improvement in natural straight standing during further six months of therapy is not big but visible. On volition Nefeli could stand straighter, but that would cost her too much energy for a longer time.

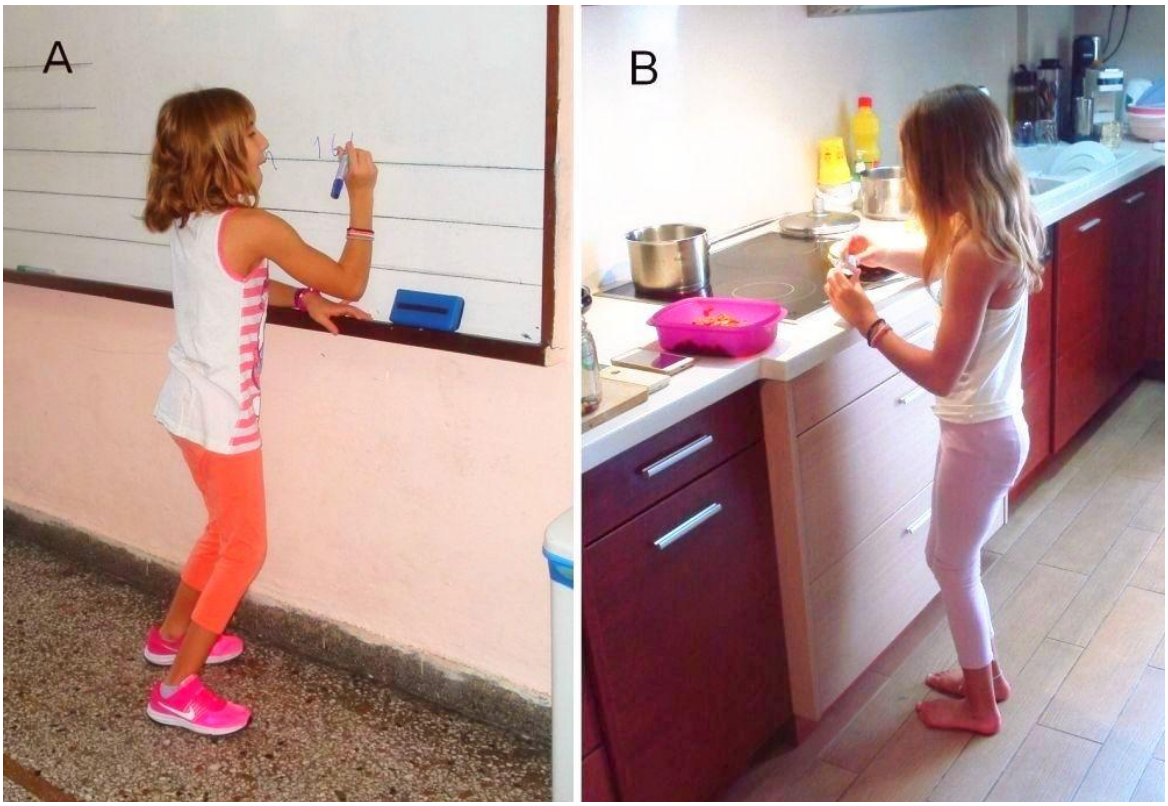


Fig. 1.73. Natural standing of the SCI patient at school following 12 months of therapy (A). After 18 months of CDT, she stands straighter during working in the kitchen (B). The patient prefers to be bare foot (B) or to wear socks to have more input from the soles of the feet for better balance because of the damage of the fasciculus gracilis

Also, other movements improved. She could crawl better in the more for her difficult pace gait coordination and during walking she could better lift the heel of the difficult right foot. During pace gait crawling, the coordination between arms and legs became better and the feet were positioned more physiologically.

The getting up from the floor after falling also improved with ongoing therapy. After 18 months of therapy Nefeli could get easier up from the floor than after 12 months of therapy, even though she still often lost the balance during getting up.

1.3.3.19 Improvement of the coordination dynamics

When the patient Nefeli with a SCI Th10 became able to turn by herself on the special CDT device, the coordination dynamics (CD) could be measured. Even though the CD varied very much, they improved with time.

Fig. 1.74 shows the overall improvement of the functioning of Nefeli s CNS quantified by the coordination dynamics (CD) values. The CD values can transiently get worse during repair due to changes of the neural networks. During CDT the nervous system learns quickly to optimize neural network functioning again after changes by improving its phase and frequency coordination among neuron firing.

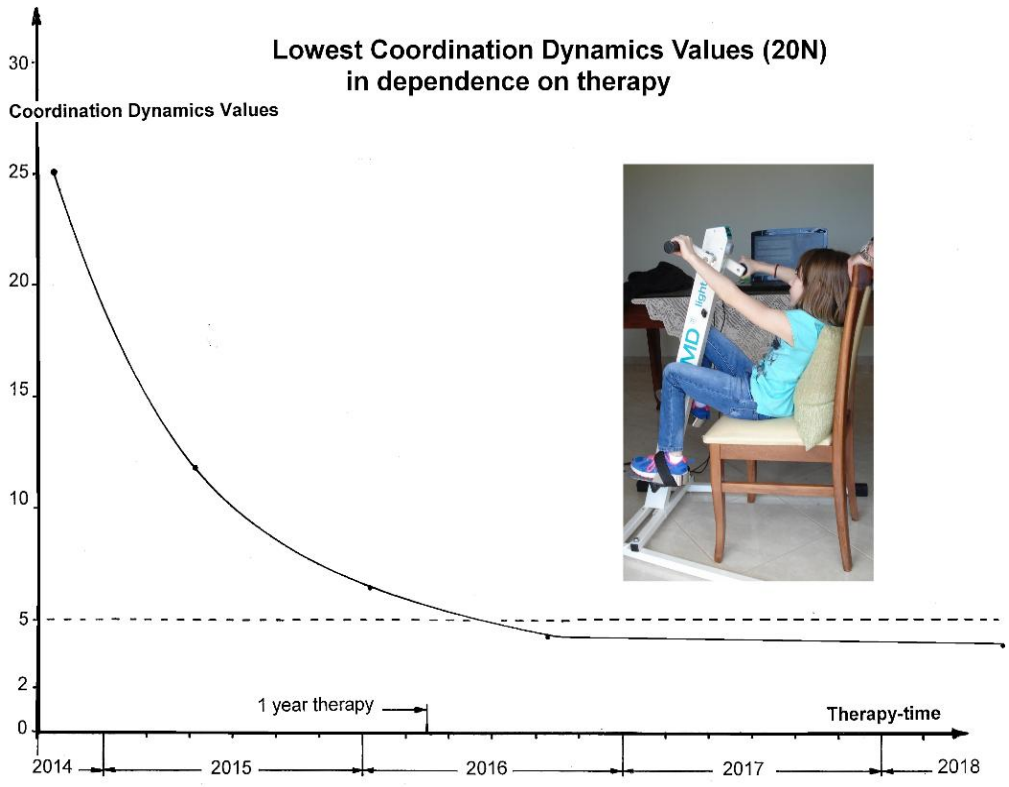


Fig. 1.74. Improvement of the low load coordination dynamics best values with therapy

But CNS functioning, quantified by CD values, can get also worse due to an illness as for example a urinary bladder infection.

1.3.3.20 Begin of repair of the sympathetic nervous system

The Author noticed the sweating below the injury level because he was supporting her training every day (Fig. 1.77). The start of the re-innervation of the lower body by the sympathetic nervous system division is of importance also for urinary bladder functioning. During the day Nefeli learned to mainly control the bladder via the somatic external sphincter (striated muscle). But at night she was sometimes getting incontinent because the internal bladder sphincter (Fig. 1.27; sited where the M is; smooth muscle), controlled most likely by the sympathetic nervous system, was not fully working again so far. Nefeli could secure the continence at night with the external sphincter. But then her sleep would be only shallow. Deep sleep is necessary to get neural network repair into the long-term memory. She was therefore wearing diapers at night for safety and a deep sleep. Since the sympathetic nervous system started to re-innervate the lower body, it is likely that in a years time the internal sphincter is functioning better, so that she will also be continent at night. The re-innervation and repair of the vegetative nervous system needs more time, probably because the autonomic efferents are thinner (Fig. 1.9) and the system is more distributed with many plexuses so that the regeneration needs more time.

1.3.3.21 Psyche and continence

With further repair of the sympathetic nervous system, also the internal bladder sphincter will improve in its functioning, that means also the patient will become continent at night and does not need diapers any more at night. But the continence at night is also affected by the psyche of patients. The stress from the cancer and the SCI may make her also incontinent at night. Healthy children at an age range between 5 and 10 years may also become transiently incontinent at night if they are exposed to strong stress as for example when they lose the parents.

1.3.4 Spinal Cord Injury Repair within 2 Years

1.3.4.1 Fading of regeneration of the spinal cord was probably caused by inefficient treatment and/or beginning of puberty

After a period of two months with nearly no exercising the above reported regeneration of the spinal cord of Nefeli seemed to have waned. The progress with exercising was only minor. To start the regeneration of the spinal cord again by exercising at the limit for approximately 3 months was not possible because her puberty seemed to have started. As she said by herself, she had no power anymore and also no motivation to train at limits. The training was now too boring for her, even though when exercising on the special CDT device she could see films on the monitor of the special CDT device. The movement support by the Author (Fig. 1.77) to increase Nefeli s motivation helped but was not sufficient to start the regeneration of the spinal cord again.

It is known in rehabilitation, that during puberty the patients with CNS injury can get much worse. Therefore, the Author was pushing the treatment as much as possible to keep the level. But how can one motivate the patient and the parents if there is only minimal progress.

1.3.4.2 Natural therapy

Hippocrates ancient wisdom that natural forces within us are the true healers of disease is in accordance with the strategy of CDT therapy to use natural means (mainly movements) for CNS repair. The question remains, how to find (identify) and stimulate the natural strategies, especially to achieve structural repair. After denervation of one leg of a rat, the rat often eats up the denervated leg, because the leg has no sensitivity and it hinders the animal s movement. If the rat knew that within a few months the leg will be re-innervated [72] and the feeling and the functions will at least partly recover, it would not eat the denervated leg. Humans, on the other hand, have the possibility to find out, understand, and use natural means of regeneration and leave destructive operations and therapies out.

1.3.4.3 Wheel devices of SCI patients for playing, competition and transportation

A psychological problem in SCI patients is that they are sitting too much in the wheelchair (Fig. 1.75A) and have to look upwards to others instead of being in eye height with partners of a conversation. Psychologically is would be very good if they could stand at least for some time in a conservation to be equal to the opponent.

In sport of SCI patients, one should therefore try to bring the patients into an upright pattern and train it for and during competitions. But what is done in sport for SCI patients, they bring the patients back into the lying position (Fig. 1.75H) instead of bringing them into a standing position. Such sport competitions for SCI patients are therefore unethical because it hinders SCI patients to reach the upright position and the equality to healthy persons.

With the improvement of the trunk stability, the patient Nefeli (Fig. 1.75A) became able to ride a bicycle with three wheels and fixed feet (Fig. 1.75B). Since also other children used that three-wheel-bicycle (not shown in Fig. 1.75) it was more a play with other healthy children than a balance training. Fig. 1.75C shows that she really liked it to be on the three-wheel bicycle. With further improvement in the short-term memory, Nefeli became able to use a four-wheel bicycle without feet fixation (Fig. 1.75G). Then Nefeli became able to use a normal bicycle with support of the father (Fig. 1.75E). During playing Nefeli trained to improve movement patterns and balance (Fig. 1.75G). Fig. 1.75F emphasizes once more that she really enjoyed the playing/riding with the different bicycles together with healthy children. In Fig. 1.75F the feet were not fixed as in Fig. 1.75C.

Fig. 1.75. Relearning to ride a bicycle (A-G) instead of riding wheel instruments in the lying position (H) of patients with SCI. In B the feet are fixed. In C Nefeli is demonstrating the improvement of trunk stability. In D through G the feet are not fixed. E. With support of the father, Nefeli can manage a bit to ride a normal bicycle

A real progress Nefeli achieved with further trunk training, approximately one year later, was, when she learned to ride a normal bicycle at an age of 12.5, seven years after the SCI, first time in her life (Fig. 1.76). The learning was supported by letting her exercising only with legs on a special CDT device during playing with the iPhone or when hearing music and moving with the music (Fig. 1.83). Such leg training improved a bit the volitional activation of leg movement patterns, necessary for walking, running and cycling.

Fig. 1.76. The SCI Nefeli just after learning to ride a normal bicycle at an age of 12.5 years (A). She manages also to ride curves (slalom) (B). She still has problems to keep the feet on the pedals, but when she slips from pedals, she has no problems to keep the balance (C). Note that she has to concentrate very much to keep the feet on the pedals (A), seven years after the SCI injury

The practical training for riding a two-wheel-bicycle was shown in Fig. 1.75 when Nefeli exercised posture, balance, leg and feet movements on different kinds of three-wheel-bicycles. Then the step was done to the normal two-wheel-bicycle. Before the first important trial she was nervous and was eating her finger nails. She wanted to ride a normal bicycle to be more normal, but she was afraid because of the SCI. Father and Author pushed her and the riding was going – she was able to ride a two-wheel-bicycle. Of course, she liked it.

She had no balance problems. But she had to fight with leg spasticity and not sufficient volitional muscle power in the legs. The power of the forefeet was too little to real push the pedals with them. She had to concentrate strongly (Fig. 1.76A) onto her feet not to slip from the pedals. When slipping with the feet from the pedals, she could still keep the balance (Fig. 1.76C). She managed also to ride slalom (Fig. 1.76B). Only with climbing and leaving the bicycle she had spasticity problems. The problem not to slip from the pedals can most likely be solved when using pedal fixations of healthy cycling athletes. In spite of all the problems, she still enjoyed it very much to be closer to the healthy children and move more quickly about. Nefeli had not learned to ride a bicycle bevor the SCI at an age of 5. Being able to ride a normal bicycle and holding the balance has consequences for her later life. Nefeli became not only able to ride a normal bicycle, but became thus also able to ride an e-bike or a suitable small motor bike in the future for being independent without a car. Being able to cover a distance with a bicycle is an independence with a small cost-benefit ratio and will improve her health.

In older patients who could ride a bicycle before the incomplete SCI, the old-learned movement cycling can be used for repair.

1.3.5 Spinal Cord Repair within 2.5 Years

1.3.5.1 Upgrading of therapy to enhance the efficiency of repair

After the cessation of the regeneration of the spinal cord and no substantial further SCI repair, a new effort was undertaken for a further repair of Nefeli s spinal cord and an improvement of walking, running and balance, bladder and bowel functioning. To achieve a further regeneration of the spinal cord, the therapy was changed and intensified in the way that Nefeli trained at least 55000 turns (up to 75000) per week on the special CDT device and trained walking, running and jumping.

In a neuro-rehabilitation center for children in Slovakia, where they also use special CDT devices, they argue that one session (21min) per week helps to improve CNS functioning. Children with minor impaired CNS functioning can turn in 21min 1000 to 1500 times. In comparison to this very low intensity, Nefeli trained now approximately 40 times more intensive. For several months she trained approximately only 13000 times per week on the special CDT device and could not fully hold the level. In relation to this low-level intensity, Nefeli trained now 5 times more intensive. Progress in repair can be expected.

To achieve at least 10 000 turns per day 5.5 times per week the strong support of a training person was needed. On one hand, such support will reduce the efficiency of repair by movement-based learning because less muscle power (motor action) of the patient is needed. On the other hand, the coordinated touch input to the hand and leg (Fig. 1.77), which means across the SCI levels Th10/11, will increase the efficiency of movement-based learning. That supported exercising on the special CDT device is also substantially improving the functioning of the neural networks of the human CNS is backed by the finding that a coma patient could be brought out of coma and re-learned to speak [67] when exercising with him mainly passively during 6 years.

When touching the skin, specific input patterns enter the CNS as shown in Fig. 1.10 for a simple pin-prick. When supporting the patients turning as in Fig. 1.77, coordinated touch input is repeatedly entering many thousand times per day the CNS and especially the intrinsic apparatus of the spinal cord in rostral and caudal directions. This coordinated touch input tells the intrinsic apparatus of the spinal cord what it has to learn for repair in addition to the input from joint, muscle (muscle spindles), tendon (Golgi tendon organs), fasciae, joint capsules and connective tissue receptors, which is mainly unconscious. The Author supported Nefeli s leg at different places to change the input to the spinal cord and to activate also those tract fibers at the SCI site (Fig. 1.44C) where neurogenesis and dendrite and axon growing are urgently needed for spinal cord regeneration. Especially tract fibers and networks at the border to the injury site, indicated in Fig. 1.44C by a bended arrow, have to be activated. Also stem cells are needed there and have to be activated for migration and proliferation. Even a massage of the triceps surae was sometimes performed in coordination to the hand input to use all possibilities to activate the critical spinal cord network site for neural repair. The patient Nefeli preferred to have support to both hands. But for neural network and tract fiber repair, the input to hands and legs is more important, because the coordinated input is over the injury site Th10. As for the unconscious receptor input, also the coordinated touch input will activate more tract fibers and networks at the injury site (Fig. 1.44C), because nerve cells are coordination receptors (Fig. 1.43) and with more coordinated input the threshold for nerve cell activation is reached earlier and more information can cross the injury site for movement-based learning. For activation changes of the intrinsic apparatus of the spinal cord, different legs, hands and touch places were used for turning support. The seemingly simple training support was also used to specifically activate certain parts of the intrinsic apparatus of the spinal cord.

The supported turning was generally performed at high frequency between 1.5 and 2Hz and additionally transiently up to 3Hz, in similarity to normal high frequency exercising during development. Such exercising was a big load for the patient and the supporting therapist (Author). But as for different sensory modality input, also with more frequent afferent and efferent input to the intrinsic apparatus of the spinal cord, thresholds for nerve cell activation are reached oftener and more communication over the SCI levels Th10/11 is possible for a higher efficiency of movement-based learning.

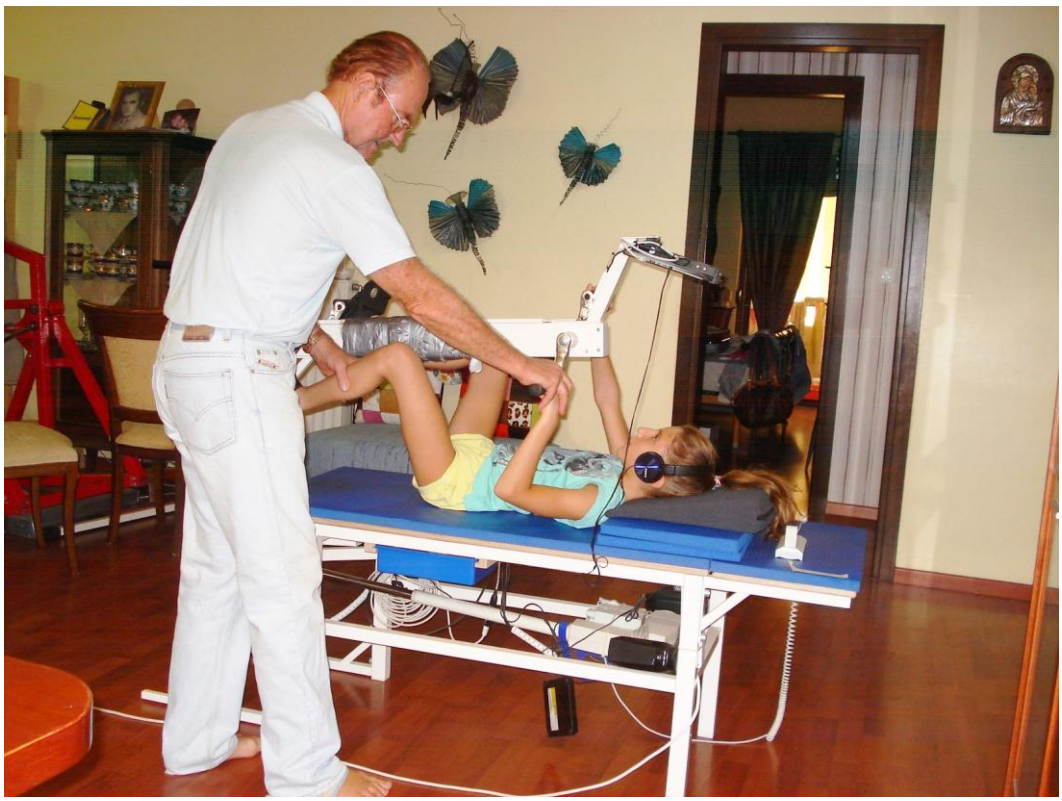


Fig. 1.77. Exercising on the special CDT device with coordinated support by the Author. The Author recognized with the left hand when Nefeli started to sweat in the leg first time after the SCI, which means that the sympathetic nervous system re-innervated the body below the injury level Th10

1.3.5.2 Further improvement of jumping and running

Fig. 1.78 shows that Nefeli learned to jump better on springboard. In Fig. 1.78A-C she jumped nicely in anti-phase by herself. The jumping in rotation (Fig. 1.78D,E) is still not symmetrical because of the scoliosis. To right (D) she can rotate more than to left (E). The jumping in abduction (F) and adduction (G) became quite good. She learned to coordinate the leg movements not to slip over the edge of the springboard (F).

The running also improved. When she became able to lift and flex more the knees, she needed not so much anymore to swing out the legs (Fig. 1.79C) and the running performance improved (Fig. 1.79A). The same holds for walking (Fig. 1.79B).

Being able to jump and run better, Nefeli became able to jump a bit during running, which was big fun to her and was good for the motivation to train further close to the limit. A lot of power for the jumping she was taking from the swinging of her arms.

An impediment of good and fast running was the spasticity of the pelvis (Figs. 1.70A, 1.80A). Partly it was exercised on the special CDT device with a more stretched pelvis, which was hard work when performed without support and also with support by the Author, because it has to be turned more against the power of spasticity.

A second exercise to reduce the flexor spasticity of the pelvis (Fig. 1.80A) became possible when she learned to run faster. With very fast running of a short distance she could mainly overcome the pelvis

spasticity (Fig. 1.80E). This shows that every little bit of performance improvement has also consequences for other movements.

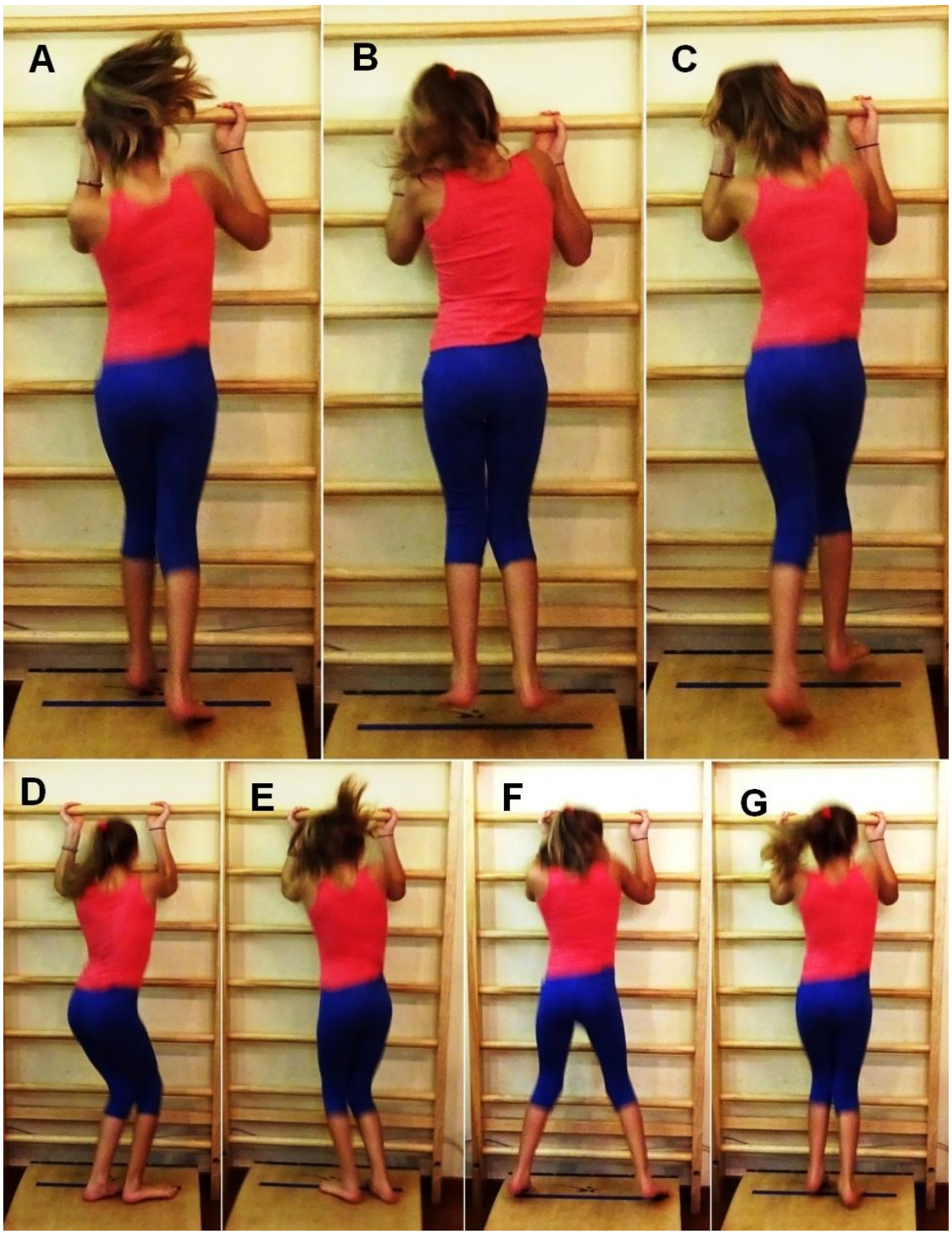


Fig. 1.78. Jumping on springboard of the 11-year-old SCI patient Nefeli after 2.5 years of CDT. Jumping in anti-phase (A-C), in rotation (D,E) and in abduction-adduction (F,G)

Fig. 1.79. Improved running performance (A) of the SCI patient because of being able to flex and lift more the knees instead of swinging the leg outwards during walking (B) and running (C)

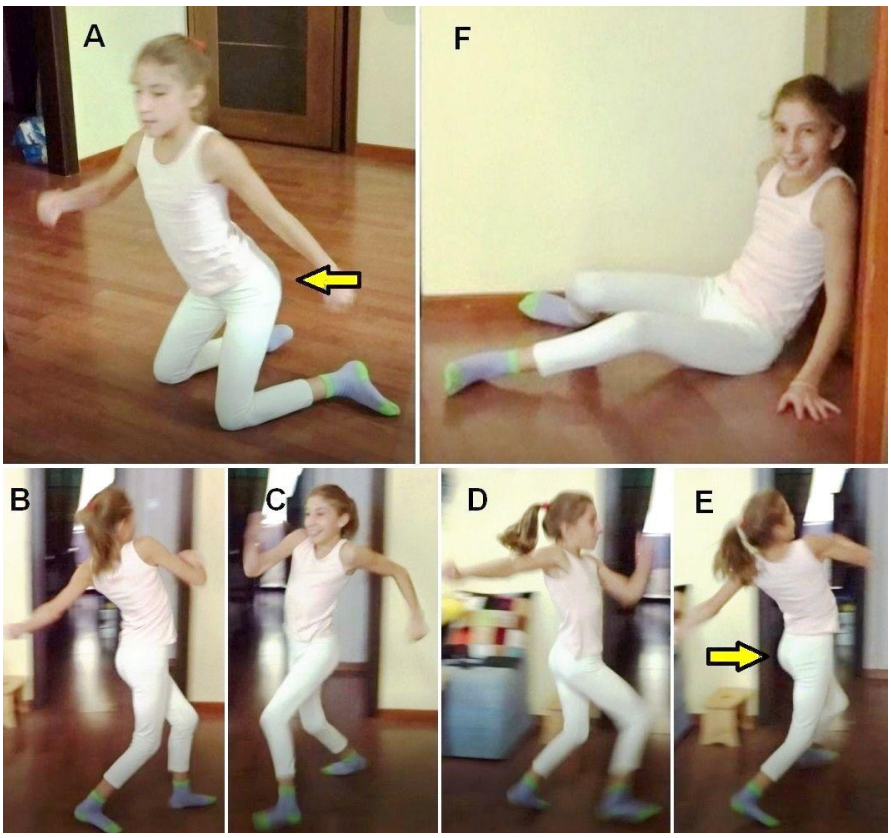


Fig. 1.80. Running to improve pelvis positioning in a patient with a SCI at the level of Th10/11. A. During walking on knees, the pelvis is too much backwards mainly because of spasticity. B-E. During running the patient is able to bring the pelvis forward, especially in E. F. After running 10 times the distance of 6m the patient was exhausted but happy. Note that the patient is strongly using her arms to increase the running speed. A high-speed camera would have been needed to improve the quality of the pictures

1.3.6 Spinal Cord Repair within 3 Years

1.3.6.1 Problems of spinal cord injury repair during puberty

After three years of CDT of varying intensity, the overall motor functions were not much better than after 2.5 years because Nefeli had trained too little in the meantime when the Author was absent and the parents did not take the therapy over. When the Author trained with her, she was getting better and when he was away, she did not get better or even got worse. Proper treatment of a handicapped infant or child consists of close cooperation between an active parent and an active therapist. The puberty seemed to have worsen the situation. It is known that during puberty the brain functions are getting worse at least in children with cerebral palsy.

Fig. 1.81. The SCI patient Nefeli during performing hula hoop and playing at the same time with the sister/Author with a balloon. B. Nefeli during hula hoop with two rings. C. With three rings, which was possible only for a few seconds. D,F,G. Nefeli during hula hoop and swinging additionally rings with the hands

In the age range between 11 and 14 years, the coordination dynamics values of healthy girls and boys got transiently worse (Fig. 1.92 of [19]), indicating transient impaired brain functioning, probably induced by the changes of hormones. In this period patients with brain or SCI may get worse. The main therapy task in that age range is therefore to keep the level of repair and if possible, to increase it. The problem of mental discipline is occurring.

Still some motor functions improved. She could do better with the hula hoop. This movement is of importance because the trunk muscles are trained and also the neural networks at the injury site (Fig. 1.44C) are activated to hopefully induce some regeneration of the spinal cord. Nefeli could manage the hula hoop for a long time with one ring and could even play a bit with the balloon with another person at the same time (Fig. 1.81A). With two rings she could do hula hoop for approximately 10 to 20 seconds (Fig. 1.81B) and with three rings up to 5 seconds (Fig. 1.81C). Then she became able to do hula hoop and swing additionally rings with the hands (Fig. 1.81E,F,G). Many school maids could not do the hula hoop because of overweight. Rotating the body with several rings probably activated more trunk muscles around and below the spinal cord segments Th10/11.

It is very unlikely that Nefeli did not get much better in her motor functions because the CDT had reached with her its limits. The coma patient Manolis, got continuously better even after 6 years of CDT and being 4 years in the coma [67]. But CDT was administered to him at the limit, that means with 20 hours per week continuously.

1.3.6.2 Improvement of urinary bladder functioning

The vegetative functions of Nefeli improved further. After three years of CDT she had no bowel pain anymore, the urinary bladder infections did not occur anymore and the storage volume of the bladder had increased. When CDT was started, she had a urinary bladder storage volume of 50ml, then 70ml and after three years of CDT the storage volume had reached 100ml. Even once a storage volume of 140ml was measured. Her normal healthy urinary bladder storage volume would be around 200ml. It seems therefore that her sacral and pontine micturition centers were still not fully repaired. Nefeli could mostly keep the fluid from the first desire to void to the second desire, which increased the storage volume. Still the detrusor seemed not to have the full power to empty the bladder, because once Nefeli could empty the bladder with 70ml (only partly) and two minutes later again with 70ml (fully).

It was shown in Fig. 1.30A how the detrusor is activated in the rather healthy case and in Fig. 1.30B following SCI. Nefeli s bladder functioning was probably somehow between the cases A and B. The detrusor activation was probably still a bit undulating (working unregularly), that means the detrusor was not getting the full-strength activation from the micturition centers and could not fully relax between the voiding s. More CDT is needed for a further repair of the micturition centers.

1.3.6.3 Treatment of iPhone mania and the coordination of fins of fish (von Holst)

The Author encountered substantial difficulties in motivating Nefeli to train close at limits. Many parents with cerebral palsy children have similar problems. The Author lost a patient for training partly because of her addiction to the iPhone. When Nefeli got a new Apple iPhone, she preferred to play more with the iPhone than exercising with the Author. The Author used two strategies to reduce this mania.

First, Nefeli was allowed more to play with her guinea pigs. But she had to care about them, which means cleaning, building simple houses for them and other things.

Second, Nefeli was motivated by the Author to work more with her fishes. She anyway liked her fishes and cared about them. But now he showed her, that the fishes move their fins in coordination (Fig. 1.82). With the Author, Nefeli took a magnifying glass and looked for the coordinated moving of the fins, even though these small fishes were not suitable for this children s research. The intention was not to start with her biology studies as von Holst did long ago, but it was the idea to make the working with the fishes more interesting and attractive.

Actually, the biologist von Holst started the research of coordinated movements and oscillators, when studying the coordinated moving of fins of fish [73]. The Author made then the step from biology to medicine that means the step from animal research to human research, analyzed movement patterns at the single-neuron level and developed treatment for patients. Von Holst s result of the interaction and struggle between Beharrungstendenz and Magnet effect create an infinite number of variable

couplings, and in essence form a state of **relative coordination** [73] which is quantified by the Author by the organization principle phase and frequency coordination in the human CNS (Fig. 1.12). Von Holst's magnet effect is quantified by the coordinated firing of oscillators and the Reafference Principle, which largely deals with the interactive processes between the CNS and the periphery by the coordinated firing of secondary muscle spindles with other CNS neurons (α and γ-motoneurons). In the framework of coordination dynamics, the coordination tendency, named Magneteffect by von Holst, can be understood as the remnant of the attractor corresponding to absolute coordination [21].

Fig. 1.82. Nefeli is watching the coordinated moving of the fins of fishes

The idea that the nervous system supplies coordination dynamics [21] rather than particular coordination patterns [74] could be viewed as an interpretation of von Holst s early work on relative coordination. Orthopedic surgeons believe more or less that the CNS supplies particular muscle function. On the basis of a gait analysis, they decide what muscles and tendons have to modulated to improve walking. This symptomatic therapy is out-of-date because there exists a causal therapy, namely CDT.

Even though Nefeli liked it very much to work with the guinea pigs and the fishes, it was still difficult to compete with the iPhone playing.

1.3.7 Spinal Cord Repair within 3.5 Years of Therapy

Following 3.5 years of CDT of changing intensity and being 12.5 years old, Nefeli did not get much better. Still the Author thinks that the limit of CDT has not been reached in her. The therapy has to be administered to Nefeli more continuously, which means that in this case the parents have to get more involved in the therapy, even though the load on a family with a disabled child is large. Hopefully the puberty changes are getting over, so that Nefeli has more motivation to train again. The efficiency of

CDT has to be enhanced and, last not least, Nefeli needs some progress/success for motivation. Even for the therapist (the Author) it is hard to work with a patient when the progress is only marginal.

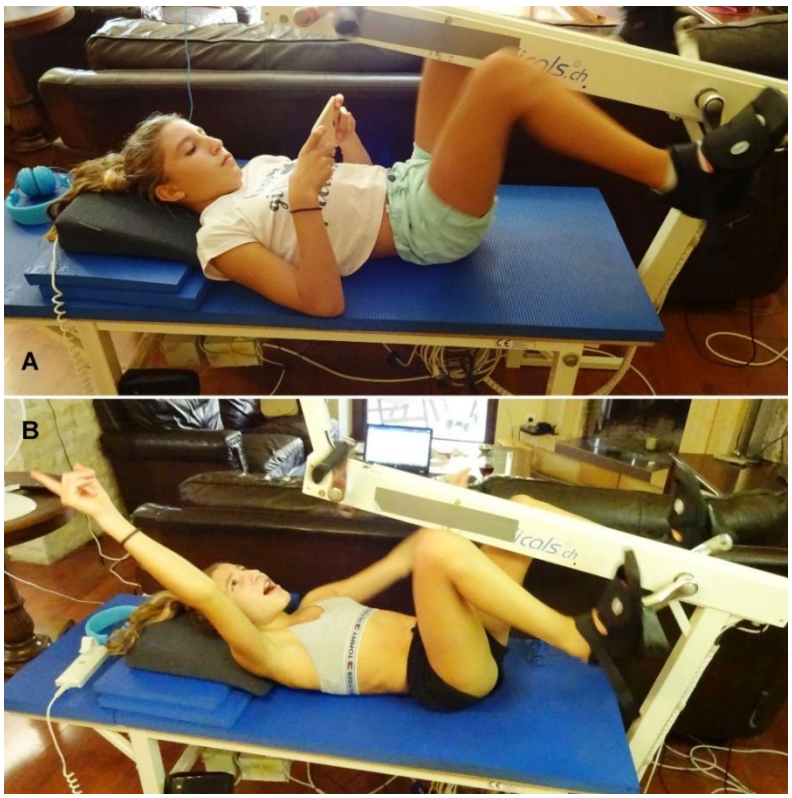


Fig. 1.83. The SCI patient Nefeli during exercising only with the legs while playing/working with the iPhone (A) or singing and moving (B). While playing a bit crazy during CDT (B) is beneficial for repair because it keeps the patient in a good mood in spite of the SCI. Being addicted to the iPhone (A) is mostly not beneficial for repair

The only real progress Nefeli achieved in the last 6 months was that she learned to ride a normal bicycle at an age of 12.5, seven years after the SCI, first time in her life (Fig. 1.76). The learning was partly prepared by let her exercising only with legs on a special CDT device during playing with the iPhone or when hearing music and moving with the music (Fig. 1.83). Such leg training improves a bit the volitional activation of leg movement patterns, necessary for walking, running and cycling. Mostly Nefeli was exercising with little clothes because of high room temperature and not fully repaired temperature regulation (sweating) below the injury level Th10/11. Also, for judging her spasticity during treatment or posture, it was beneficial to see the uncovered legs as in orthopedic.

The transient lessen of the regeneration/repair in Nefeli emphasizes the importance of continuous treatment on the long-term, especially in children during development. It would be interesting to see how animal researchers could simulate such repair over several years in rat or mice. In the patient Nefeli, the administered treatment lasted so far 3.5 years, in the former coma patient Manolis 6 years and in brain injury patient Benjamin over 18 years. It needs to be known what repair can be achieved in what time period with an efficient therapy applied aggressively and continuously.

1.4 DISCUSSION

1.4.1 Limitations of Basic Science Research

There are many inadequacies in the current research in SCI. Animal research is mainly concerned with structural repair and the regeneration of the spinal cord in animals. The aspect of functional

recovery is rarely understood and never analyzed. Even though structural repair is important in SCI, the researchers rarely discuss the difference in the potential of regeneration between animals and humans. In the goldfish, for example, the spinal cord regenerates spontaneously. But what inferences can be derived from this regeneration that can be relevant and applicable to humans? Presented gross human anatomy may make a casual reader believe that the animal data are indeed applicable to humans. However, the functional recovery is not measured thoroughly. Morphological data at the cellular level, like the degree and extent of growth and regeneration of axons across the injury site, is often not correlated with the functional recovery. The functioning of newly grown axon has to be proven in the context of neuronal network functions and not only by the improved movements of the treated animals, because in animals there exists also spontaneous recovery and functional reorganization, especially if only 50% of the cord was destroyed. Actually, fiber counts in different ascending and descending tracts would be needed to assess what percentage of tract fibers need to be regenerated for meaningful recovery in humans.

1.4.2 A Need for Scientific and Clinical Human Approach

The diagnostics at the beginning, during, and at the end of therapy is of particular importance to differentiate between spontaneous recovery and the improvement achieved by the treatment. Since spontaneous recovery may occur for up to 1 year after the injury, long-term studies are needed. In the case of a partial SCI, most of the recovery occurs between 2 to 6 months after injury and to a lesser degree up to 1 year. In the present patient Nefeli, the treatment was started 4 years after the injury and lasted for more than one year; thus, the recovery cannot be attributed to spontaneous recovery.
In the case of complete SCI (as assessed by MRI), only very limited spontaneous recovery occurs and the potential for functional reorganization is very low, since the majority of the distal cord is disconnected from the supraspinal control. In such an injury even the combination treatment of stem cell therapy and CDT did not bring about significant improvement. However, most of the spinal cord injuries are incomplete. Even in the case of a severe injury, a significant part can be salvaged by immediate removal of compression of the spinal cord by surgery (Fig. 1.5), what was not done in Nefeli and the stabilization of the spine to minimize progressive mechanical injury.

There are many unscientific reports, claiming miraculous recovery in SCI patients, which could very well be attributed to a spontaneous recovery. Most of the rehabilitation centers focus mainly on care and general maintenance of patients and administer inefficient and arbitrary treatment that does not utilize the full potential of recovery in patients with partial SCI. Patients want more choices than the no hope approach of conventional rehabilitation centers and the false hope , given by some physicians and researchers working in the field of animal research, and cell and molecular biology.

Over the last 30 years no significant conceptual or real methodical progress has occurred in the field of neuro-rehabilitation. The current science of neuro-rehabilitation is mostly outdated, as no real review of human neurophysiology has been done for many decades. The lack of any perceived need for development and in turn the absence of any efforts in that direction has perpetuated the inefficient, outdated and ineffective treatment modalities in the treatment delivery system. This is particularly relevant considering the fact that the young patients who suffered a SCI have 50 years of their remaining life span that they have to live with a very poor quality of life, while only getting care from the current rehabilitation centers. On the other hand, with optimal and intensive CDT for a few years after the injury, their quality of life can be enhanced substantially in order to achieve independence in daily activities, and most importantly physiological bladder control and may be improvement of the sexual function.

1.4.3 Animal Experiments are Removed from Human Reality

Recently it was reported on the spontaneous recovery of a SCI in rhesus monkeys and the important role for primate models in translational disease research [75]. A few comparisons will show that animal experiments are far away from human reality and normally cannot contribute to translational medicine or human disease research.

1. In human patients, as can be seen from Fig. 1.19D, the injury is often in the center of the spinal cord, and not just a half of the spinal cord is damaged as in the monkey experiment (Supplementary Fig. 1.2 of [75]). Neurons in the spared grey matter of monkeys may function as relay neurons. The blood supply is probably less impaired in the monkey.

2. Since in 50% SCI the spinal cord can mainly be repaired upon CDT [8] and the patient can be brought back to normal everyday life (Fig. 1.19D), there is not much sense of after-developments in monkeys, unless the experiments are designed to be close to the clinical human setting to obtain parameters which cannot be measured in humans. Is it actually justified to kill monkeys for an after-development? Not to cite existing qualified clinical literature for the repair of a 50% SCI is also not convincing, especially when claiming that their research is a contribution to translational medicine.

3. The biggest problems in human SCI are the urinary bladder functions [9] and the occurring pressure ulcers due to insufficient blood supply. Before World War II a majority of SCI patient mortality was due to continuing urinary bladder infections. By cutting only one half of the spinal cord in animals one is not getting urinary bladder and skin nutrition problems. The challenge of the future is to cure the 95% or complete SCI. – The neurosurgeon L.W. Freeman (USA) stated in the 1960 s after performing very many SCI repair experiments on dogs, it is difficult to find persons who do research in paraplegia and to get money for such research; probably World War II is already too far away . If one cuts the whole spinal cord in animals, then one would have to manually empty the bladder by pressing the urine out. Such work seems to be unpopular among researchers. In human patients the bladder is for example emptied approximately every 5 hours by intermitted catheterization (and other ways), introduced by Guttmann from Breslau [1] in the Second World War.

4. The improvement of hand function is also very important in cervical SCI; I have not seen animal experiments tackling the hand and finger problem. A tetra (tetraplegic patient) cannot empty his urinary bladder by intermittent catheterization without sufficient hand and finger functions. Hand functions can be improved in C5/6 SCI upon building of new motoneurons in the human spinal cord, but it needs several years of optimal CDT [32].

5. The repair of the fundamental functions such as breathing, swallowing, and speech in high cervical SCI has also not been tackled by animal research. Obviously, animal research is far removed from the human patient s real problems.

6. Humans need years for development and repair and not only a few months. Animal experimentalists are therefore working on the wrong time scale with respect to development and repair to translate their data to human reality. Again, it seems not to be popular among researchers to do experiments which last over several years.

7. Translational medicine makes only sense if the researchers have knowledge in animal and human research. A translator can only translate from German to English if he has knowledge in both languages. Also, for peer reviewed journals in translational medicine it would be important to have reviewers which are competent in animal and human research. The competence has to be documented by publications in international journals in both fields.

8. When I was for postdoc education with Sir Bernard Katz at University College London, I learned that there should be no more than 4 authors on genuine research publications. 14 authors of a publication are typical for clinical research where clinicians do not have enough time for research and putting their names as much as possible on the publications of friends and assistances to increase the number of their own publications. By avoiding real research, professors in the clinical field may have insufficient understanding of qualified research and are less open to new developments in medicine.

9. In mouse experiments, half of the spinal cord is cut and treatment success is demonstrated by the staining of neurons and nerve fibers and demonstrating that the mouse can run for example on a horizontal ladder [76]. Whether the regenerated fibers were really functioning was not measured. Something like 50 years ago, there was a treatment for thoracic SCI with which patients learned to move the legs by moving the arms. The information from the upper (arms) to the lower part of the

body (legs) took place most likely by skin traction. In a frog, I could not see from the morphology whether axons and synapses were functioning; when trying to understand regeneration, I used morphology and electrophysiology. Sir Bernard Katz, the specialist for the neuromuscular endplate, explained that sometimes denervated motor endplates survive very long and still look quite normal (as if they would really still function). In mouse treatment, success was measured by morphology and making the mouse move on a horizontal irregular ladder and arguing then that the progress is going from animal experiments to human treatment [76,77]. In the human patient with the 50% cervical SCI, treatment progress was demonstrated by letting the patient run and jump, measuring the improvement of running and jumping, measuring the coordination pattern dynamics (CD) values for different loads (Fig. 1.21) and measuring motor programs and single motor unit firing (neuron level) with surface electromyography (sEMG) (Figs. 1.12, 1.13). And the scientific basis for the repair is the understanding of CNS functioning and repair at the neuron level in human [17-19]. For the time being the progress in SCI is coming from human research and not from animal research. Human data need to be translated to animal data. Universities and research institutions world-wide seem to have an anxiety to touch human neurophysiology and qualified clinical research.

10. In severe incomplete SCI there is the problem of muscle power generation. If not sufficient motoneurons can be activated following SCI, the body tries to compensate for by axonal sprouting to innervate the (denervated) muscle fibers of not functioning motoneurons. With such collaterals the motor units increase in size. In human the motor unit can be increased by approximately 50%. One motoneuron can, for example, supply 6000 muscle fibers when it normally innervates 4000 muscle fibers. In rat the motor unit can be increased up to 400%. Therefore, frankly speaking, a rat can walk already with a few functioning motoneurons, with poor coordination. Further, the power of regeneration is much higher in animals.

11. The problem of smart-phone mania, which disturbs treatment, one is not having in rat experiments.

1.4.4 Consequences of False Hope

In Chapter I of [18] it was shown, based on frog data that exogenous stem cell therapy in its present application is not working. The main problem seems to be that the newborn cells cannot be integrated in the existing neuronal networks for various reasons. Cell communication needs to be better understood. During competition a motocross athlete suffered a clinically complete SCI at the thoracic 11/12 levels. Six weeks after the accident the subject began intensive CDT at an up-to-date therapy center. After 6 months of therapy, when further improvements were only marginal, the patient opted for hematopoietic stem cell therapy. During two years of stem cell therapy, including 4 sessions of stem cell application, and on-going CDT, improvement remained marginal – no more than what would have been achieved with continuing only CDT. This hematopoietic stem cell therapy did not have any beneficial effect on the repair of the spinal cord in this patient. When it turned out that the costly stem cell therapy had no beneficial effect on the regeneration of his spinal cord, the patient lost the belief in SCI treatments and stopped also CDT. He only continued with some training, according to his opinion, to reduce spasticity. Another patient with a probably complete thoracic SCI was sent by a physiotherapist to the Author to get advice concerning a stem cell therapy in addition to the administered movement therapy. The patient did not consult the Author, because he wanted to have the stem cell therapy administered, whatever the arguments of the Author would have been. He even raised the argument that the Author may be against progress in SCI. Up until two years after the start of the stem cell therapy there was no real progress in repair. The patient stopped the therapy in the physiotherapy place and was doing then his own treatment at home. It seems that he had lost the belief in any treatment. During the treatment at the physiotherapy place no MRI was performed in this patient (messy treatment and diagnostic situation (Switzerland)). It was argued that this is not possible because of the metal fixation. But with a Titan fixation, which is nowadays mostly used, an MRI is often giving quite a good anatomical information about the severance of the injury of the spinal cord. This can be seen if one compares the MRI s of a patient with Titan fixation (Fig. 1.19C) and after its removal (Fig. 1.19B).

Instead of raising false hope that the animal data can be easily used to cure diseases of the human CNS, the universities and research institutions should first do their duty, namely organizing qualified human neurophysiologic research, especially treatment research, and also support such research.

1.4.5 Ethics of SCI Research, Treatment, and Clinical Trials – False Hope from Animal Treatment Research

Transplantation of both embryonic stem cells and embryonic stem cell-derived neural (neural or glial) progenitors is able to efficiently promote CNS regeneration in preclinical models of stroke, myelin deficiency, acute SCI [78,80] and Parkinson s disease [79]. This sentence of an article makes the reader believe that the research made already the step from the animal research to the human research and treatment is already administered to humans. Looking up the references one finds the title: Human embryonic stem cell-derived oligodendrocyte progenitor cell transplants remyelinate and restore locomotion after spinal cord injury. Patients with SCI or journalists think immediately that the SCI problem has been already solved! I have learned that it has to be written in the title on what species the research has been performed. In this case it was the rat. Animal researchers often deliberately choose the words in a way to make the reader believe that this research has already solved the SCI problem in humans. A well-known journal in medicine is even redefining medicine. It makes the reader believe that measurements in mouse are a part of medicine [81]. I have learned in my medical study that medicine has something to do with the cure of diseases in human. Specialist journals and general audience media need to set reasonable expectations of the safety and efficacy of potential therapies to avoid raising and then dashing the hopes of those living with SCI or those in government, those carrying out research, or the general public [81]. High ethical standards are required by researchers, clinicians and journalists to ensure that results are communicated to the general public in a manner that honestly reflects the safety and efficacy of a potential therapy [81].

Medicine is very successful if natural existing repair mechanisms are supported like in surgery or immunology. But if repair mechanisms do not exist, then medicine is not very successful. The repair of the nervous system is very limited and depends on the site of the injury. An exogenous stem cell therapy must be very sophisticated to be better than nature with respect to repair. The integration of new-born cells into the existing neuronal networks is by far not solved. Further, the scientific basis for doing neurobiology is out-of-date. The understanding of the functioning of the CNS in animals and humans has to be upgraded. In physics, for example, the basis is continuously upgraded. In Chapter I of [18] it was shown how complicated the innervation of two kinds of muscle cells by two kinds of motoneurons is (4-cell communication). The innervation and innervation changes during development and repair are probably much more complicated in the human CNS. It is too simple thinking to believe that an addition of cells can repair the CNS what the CNS cannot do by itself. CDT, on the other hand, rests on learning which is natural for humans. Academically accepted articles are generating false hope by allowing authors to state that stem cells can potentially be used in different CNS diseases including SCI. The authors are stating it to get funding for their animal research, by making believe that their research has direct consequences for the treatment of human patients. No wonder that practitioners also want to participate in getting money. Instead of warning that some clinics in Asia may look more for profit than for qualified stem cell therapy, the editorials should first think over their own research policies which are giving rise to such unqualified medical treatment. It is not enough to state that the medical promise of stem cells remains real, but largely unrealized for now. The excitement must not be left to dissolve into a muddle of disappointment, frustration and fear because of the practices of a few irresponsible profiteers [4]. There are principal problems to be solved for stem cell therapy in humans. A few years ago, there was a big propaganda in the TV and other mass media in Switzerland about the suppression of grow-inhibiting properties for the regeneration [76,77] of the spinal cord. It was stated that SCI could be cured in a year’s time. It seems to be popular among neurobiologists to raise false hope in society concerning treatment in human patients, as if they have not understood much about treatment of human patients.

If we want to repair function, we also have to measure function in a qualified way and one powerful tool is the electrophysiology, because the nervous system is mainly functioning by electric currents and potentials. It is difficult to understand why electrophysiology has mainly been destroyed world-wide, even though this tool was very successful in neurophysiology in the past. One reason could be

that although the younger generations are capable of handling computers or electronic equipment very good, they do not have the manual skill any more to perform complicated electrophysiology. Statistics are needed concerning treatment success beyond the placebo effect, including the occurrences of cancer and CNS instabilities (seizure disorders). But more is needed in medical research than just statistics. Hopefully the globalization does not give rise to the coordination in thinking (in German: Gleichschaltung der Denkweise).

It is depressing for a qualified therapist that there is an abundance of patients desperate for miracle cures, and one stem cell treatment can bring in tens of thousands of US dollars [4]. Western scientists and clinicians would argue that controls are necessary to identify unambiguously whether a therapy is safe and effective, some clinicians have claimed that withholding a potential therapy from a patient with SCI is in itself unethical [5]. Many SCI units know about CDT. But the patients are not informed that such a therapy exists! A real change from care to cure seems not to be in the interests of the neuro-rehabilitation centers. More money can be earned with care.

There is too much false hope generated by animal physiologists, neurobiologists, and researchers working in the field of genetics. Without detailed knowledge of the human physiology and pathophysiology, the animal knowledge is only of limited help to cure diseases in humans. False hope also stops the patient from fighting for improvements which are needed for everyday life. Why should a patient fight for three years or more with a movement-based learning therapy to get urinary bladder and some motor functions repaired, if in a few years' time walking can be returned with miracle cells or pills? Such false hope is coming from qualified researchers, when they make believe that the animal data can be easily used to repair the human CNS. Qualified human research is needed and has to be organized. Only if there is an overlap between animal and human research, there is the possibility of rather safe transfer of knowledge from animals to humans. As long as human research is not organized properly, the patients have to suffer or even to die (for example Christopher Reeve). Even monkey experiments are far away from human reality. A monkey cannot speak, write or read, and will never be able to solve differential equations (mathematics). The power of the human CNS is its learning capacity, which is outstanding among different species. A fly demonstrates with how little brain matter sophisticated fly tasks are possible. Qualified human CNS research, including at the single-neuron level, is needed for understanding the functioning and repair of its neuronal networks.

Authors of recent review articles presented approximately 1000 citations on the repair of the human spinal cord following injury [5,6,79,82]. Less than 10% of the citations were from human research. Interestingly, the author was not cited, even though his work is widely available online. I learned a lot from these brilliant research articles with respect to animal research. But with respect to human research and applicability to human patients they were out of date by 20 years.

Miracle treatments are not the only dangerous for patients and the freedom in research. It is the worldwide research, treatment, and teaching system, that does not allow qualified human research, which is urgently needed to cure diseases and make humans live longer with a better quality of life [19,83]. And if there are really operations with unbelievable success, then the treatment before those operations was wrong.

For example, a paraplegic patient came by wheelchair from a well-known German rehabilitation center to a neurosurgery department, was operated and walked 2 weeks later out of the neurosurgery department. A second patient was cured in the same way. The reason for this progress was caused by a mistake of the rehabilitation center. Bones from the spinal canal caused pressure on the spinal cord (in some similarity to Fig. 1.5A). The spinal cord stopped working but was damaged only little. A laminectomy freed the spinal cord and the spinal cord started to work again. Follow up MRI s are needed which are normally not performed in rehabilitation centers. The argument is that it has no clinical consequence, because the patient is staying anyway in the wheelchair for the rest of his or her life. This argument is wrong since for example cysts can build up in the injured spinal cord which enlarges the spinal cord and pressure symptoms will occur and the patient loses further functions. The injury level may then rise for example from C6 to C5. And, of course, SCI can partly be repaired.

1.4.6 Out-of-date of the Clinical Treatment System

On the clinical side the human research situation is not better. The diagnostic in clinics is good till sophisticated, because it is organized and money can be earned. Sometimes too much diagnostic is performed. But the cervical SCI patient Kadri (Fig. 1.17) said, why should I go to the neurologist. He is telling me what is wrong in my body, but he is not telling me how to repair the lost or impaired functions. Apart from exceptions, one cannot repair the human nervous system with drugs or operations. Movement-based learning, on the other hand, is a causal therapy which repairs the neural networks. But the physiotherapy to repair the nervous system is mainly out-of-date and inefficient. When in Switzerland the physiotherapy education was upgraded from school to academy, only the names were upgraded, not the education. Physiotherapists do not learn, for example, to perform electromyography (EMG) on patients. When the Author demonstrated surface EMG to physiotherapists in a course, they all liked it, because one could really see pathologic motor programs and spasticity on the screen of the scope. When seeing their own volitional muscle activation, physiotherapists were impressed.

Being at the international conference for pediatric acquired brain injury (IPBIS2018), really interest was only coming from one physiotherapy student who wanted to do research, a physician who was interested in neural network learning and two lawyers, who were supporting and supervising the families of brain injured children. But all the physiotherapists, rehabilitation physicians, neurologists or neuropediatric did not want to get informed about new developments in CNS repair. Robotics were of interest to them. When the Author is seeing a picture where a child with a nervous system injury is in the wheelchair (Fig. 1.32A), he is getting angry and depressive. When the Author asked neuropediatric from New Zeeland whether they are not getting depressed when they diagnose all the deficits of a brain-injured child but cannot offer treatment, he did not get an answer and next day they did not come to the Authors poster (Fig. 1.84) to get informed and discuss problems. The members of the conference seem to be afraid to see that the nervous system of children can partly be repaired. A physician, who treated Nefeli and Sophie (pictured on the lower part of the poster, Fig. 1.84) in a rehabilitation center, did not want to see the outcome of his former patients on the long-term. Interesting is further that no member of the conference wanted to try out the special CDT device placed besides the poster (Fig. 1.84). And no physician wanted to get a reprint or wanted to look in some publications or books (Fig. 1.84). When the Author exercised at the entrance of the conference building on the special CDT device, after some time he was pushed away by the administration (the organizer of the conference) so that nobody can see his exercising on the device (out of view – out of mind). Students and stuff of the nearby School for Management, who were passing the Author during exercising on the special CDT device, were more interested what the Author is trying to demonstrate than the members of the conference. When the Author gave long ago a talk at a Nobel institute for Neuroscience in Stockholm (Prof. Grillner [83], pattern generator), he was not allowed to discuss with all the assistances, even though at that time they were thinking of a rat experiment to repair the spinal cord. They were planning at that time a rat experiment what the Author had mainly done already on human.

When really some junior physicians get motivated to try new repair strategies of the brain, they are punished by the establishment. Why to develop new treatment to repair the human brain, when it is impossible to bring it to the patient? Moderators in TV are often open to new developments. But first, explanations have to be that simple that a differentiation between qualified research and hocus-pocus is not possible and secondly, the neuro-rehabilitation is still going on with their out-of-date treatment whatever the progress is in their field.

New organizations and predatory organizations organize journals and conferences without sufficient knowledge. For both knowledge and money is needed. They screen the market and choose what sounds nice. But they are not blocking new developments. Researcher can now choose between not publishing or publishing in a new journal which may be predatory. But a real research worker has to publish because it is part of the profession and secondly, in human neurophysiology and clinical research, apart from statistics, many patients are suffering and dying and that puts load on the clinical researcher. It was estimated that by shifting the new Berlin airport from the South of Berlin to the periphery of Berlin, approximately 11 inhabitants will die per year caused by aircraft noise. By not

using CDT, which improves health of patients in general, there may die a million people on earth every year.

Fig. 1.84. Poster of the Author Schalow G (Number 38) at the international conference IPBIS2018 in Belfast 2018: Pediatric acquired brain injury repair. The poster is not especially good because of lack of money. But the repair progress of the nervous system in children can clearly be seen It is also shown that human anatomy and physiology is needed for repair

Movement therapies are not popular because mental discipline is needed. Probably more than half of the population on earth has overweight. Especially young ones, who alternate between fast food and smart phone, have massive overweight. On Kriti (Greece), there are many children between 5 and 10 years which have already very much overweight and move therefore very little. In the class of Nefeli (Fig. 1.69) there were 2 of the 18 children who had no overweight! But movements like walking, running and jumping are necessary for a healthy development. Many new diseases will therefore occur in the future due to the too little movements performed by children. Patients and healthy people only enjoy movements, if they have no overweight. Also, the elegance of walking is lost with overweight.

Universities and rehabilitation centers are with respect to human neurophysiology approximately 30 years out-of-date. Just now an internet organization (academia.edu) tells what papers of the Author are read most. These papers are the ones which the Author published 10 to 20 years ago (Classification scheme of human peripheral nerve fibers). That the neuro-rehabilitation is out-of-date

is generally known. The Author was even told that for bringing progress to the rehabilitation an agreement with the devil is justified. But how is it, most likely, with the so-called progressive institutions? Astronauts are brought into space and because of missing gravity it has to be looked for their health. Astronauts get for example osteoporosis from which they do not recover again on earth. Their physical exercise in space is for the time being the walking on treadmill. Exercising on a special CDT device would at least also be needed. One could measure then additionally the organization of their CNS first on earth, then in space and afterwards on earth again and see what had changed of CNS functioning and health in space. By measuring at the same time heart rate variability and split it by Fourier analysis into sympathetic and parasympathetic contributions, one could see whether the astronauts have stress and reduce it, if possible, by exercising. Further, because CDT improves also coordinated finger movements, astronauts could better perform complicated experiments, in which coordination is needed.

Plenty of money is given to enhance artificial intelligence and necessary infrastructure is built. The highest intelligence is still by far generated in the human brain. Why the researchers in the field of artificial intelligence are not trying to learn from the organization of the human neural networks for their artificial neural networks? The human brain is very fast and is most likely not using iteration processes for network changes. It seems that not only disabled children have a tunnel-view.

Aging men are worried to get prostate cancer. It is likely that prostate cancer growth can be inhibited by CDT in similarity to breast cancer [66]. In TV it was recently analyzed what operational strategy is better, to operate only with the hands or using additionally a robot. But on prevention of prostate cancer, namely to reduce the probability of prostate cancer occurrence by physical activity (including CDT), it was not reported of.

1.4.7 Children with SCI are Hoping for Better Treatment to Become Like the Other Children Again

The patient Nefeli was saying to the Author: Giselher, I want to be again like the other children. The Author answered: Nefeli, then we have to train very much at the limit. And Nefeli answered: Giselher, but I also want to play now. When I am grown up, I cannot play anymore.

The girl in Fig. 1.85 is looking at the reader with the hope that she/he is helping to get treatment for children to make them healthy again.

Fig. 1.85. The girl looks at you in the hope that you will help to cure SCI (and other diseases) in children. The picture was taken from the fairy tale film Till Eulenspiegel. In the film she (Jule Hermann) is hoping that her father wants her

1.4.8 Ethics to Use the Patients Name

The patient Nefeli and her parents agreed to have pictures and Nefeli s name in the book. By demonstrating in detail through movements how Nefeli became better, she wants to help also other children. Children with a CNS injury have psychological stress and need hope. Once, when Nefelis stress with the SCI was very large, she drew a picture of the surgeon, who made her paraparetic, cut it out and threw it into the fire to reduce her stress in similarity to the fairy tale Hänsel und Gretel, where Gretel pushed the witch into the fire.

To have real names in the medical research publications emphasizes its importance. Qualified medical research is connected to real human life and is not just a more or less theoretical game.

Chapter 2
Print ISBN: 978-93-5547-205-2, eBook ISBN: 978-93-5547-216-8

CNS Repair in a Girl with a Spinal Cord Injury Which was Caused by a Children Physician and Worsened by an Orthopedic Surgeon

DOI: 10.9734/bpi/mono/978-93-5547-205-2/CH2

ABSTRACT

By medical malpractice, the 5.5-years-old Nefeli suffered an incomplete spinal cord injury (SCI) at Th10/11 levels. At an age of 9, through 4 years of Coordination Dynamics Therapy (CDT), she re-learned walking, running, jumping and became continent again. At an age of 14, an orthopedic surgeon made the family believe that the walking performance could substantially be improved by a leg operation. Against the strong advice of the Author 'to avoid the operation', because such operations in SCI reduce the plasticity, necessary for repair, the parents decided for the operation. Till 6 weeks after the operation, the patient could not move the legs anymore because of extreme flexor spasticity, rigor and cramps. 3.5 months after the operation, including 8 weeks of intensive CDT with the Author, she could move the legs a bit again, but could not walk freely. 6 months after the operation, she became able to walk a bit with orthoses and after 8 months she re-learned to walk a bit without orthoses. Through the operation, the patient lost approximately 2 years of movement-based learning therapy. It will be analyzed in detail that the orthopedic surgeon operated without sufficient knowledge in human repair-neurophysiology, necessary especially in SCI. The operation-induced extreme flexor spasticity made the standing and upright movements impossible. Only the Author was able, through administering CDT, to slowly reduce the extreme flexor spasticity and to make the SCI patient Nefeli walk again.

Keywords: Human repair-neurophysiology; Electrophysiology; Single-nerve fiber action potentials; Surface EMG; Oscillatory firing; Phase and frequency coordination; Coordination dynamics therapy; Spinal cord injury repair.

2.1 INTRODUCTION

It is known for something like 70 years that the plasticity of the nervous system is highest if no operation is performed in nervous system-injured patients. Especially in critical patients, like the SCI patient Nefeli, in whom only approximately 30% of the spinal cord was remained, operations are contra-indicated. A four-year CDT made her walking, running, jumping and continent [1]. Through movement-based learning, the CNS just succeeded to generate everyday functions again. Because of the limited variability of the injured CNS (SCI), the movement performance was not optimal.

Through an operation of tendons and bones, the inputs, from the different receptors of the periphery to the CNS, will change and reduce. The achieved movement performance will be ruined. Only tremendous movement-based learning therapy for years could compensate for such an operation. But patients, who have trained already for years, are worn out to train further for years. Only few patients have the mental discipline to train at limits for years as Wilma Rudolf. She got poliomyelitis and could win gold medals in running in 1956.

Further, during puberty, patients with CNS injury loose functions due to the puberty-induced changes of the CNS. Only intensive therapy can compensate for these changes. Therefore, the timing of the operation was also wrong, because the patient Nefeli was already in the phase of puberty. The surgeon disregarded that the patient Nefeli had a critical incomplete SCI (approximately 30% of the

cord were left) and was in the phase of puberty. He seemed not to know that CNS plasticity reduces with an operation.

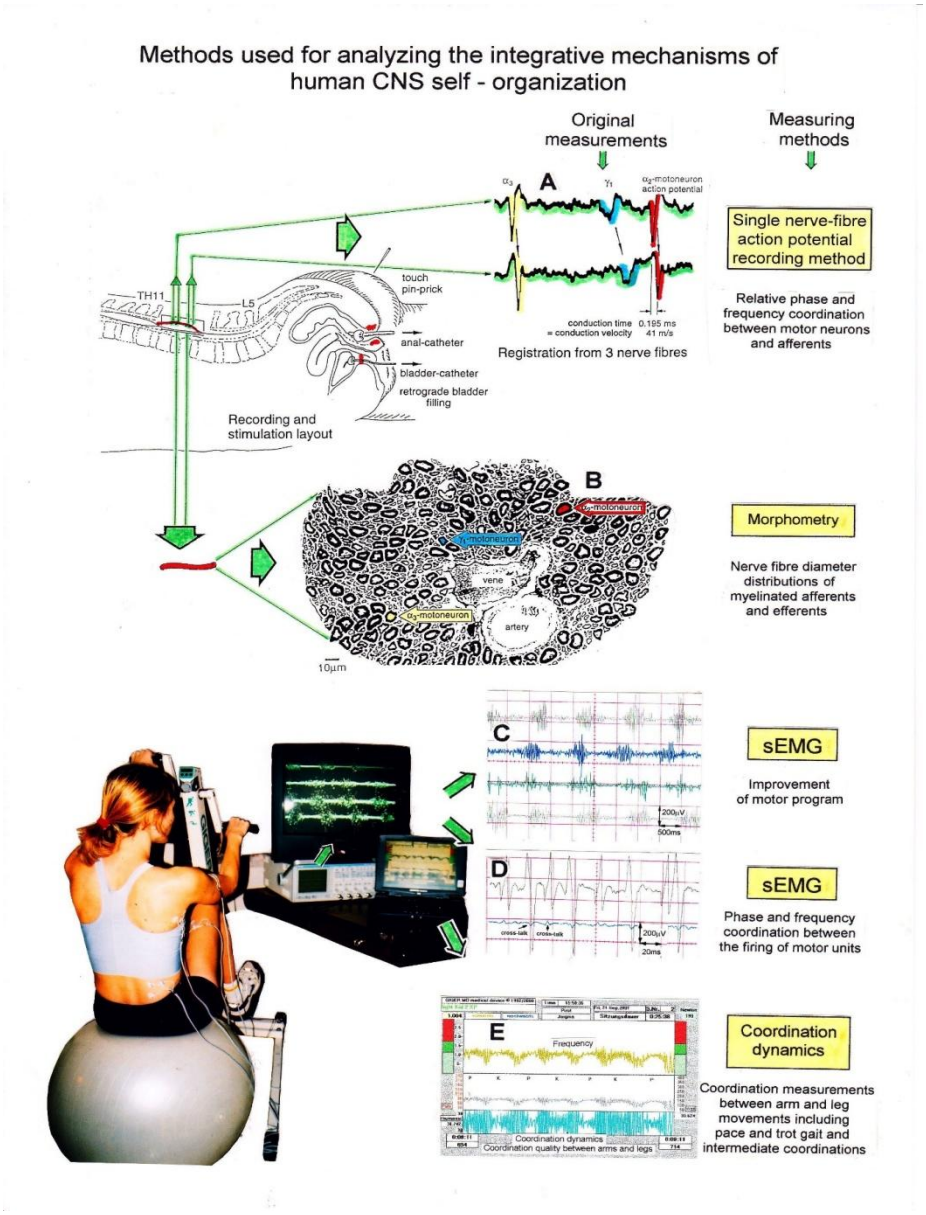


Fig. 2.1. Schematic layout of the methods used to study the self-organization and repair of neuronal networks of the human CNS. A. Single-nerve fiber action potential (AP) recording method to measure with wire electrodes simultaneously from a set of single afferent (AP phase upward) and efferent (AP phase downward) nerve fibers to analyze the simultaneous impulse traffic running in and out of the spinal cord. B. Morphometry of nerve roots and nerves to identify groups of nerve fibers. C, D. By performing surface electromyography (sEMG) with up to 4 electrode pairs (2 indifferent electrodes, 1 earth electrode; pre-amplification x1000, 4-channel oscilloscope) the changes of motor programs were measured (C). When recording from appropriate patients, natural activation patterns of several single-motor units were obtained (D) and coordination between motor unit firing could be studied. E. Coordination between arms and leg movements was quantified by the single integrative parameter, arrhythmicity of turning (df/dt or df/dt/f; f = frequency) during exercising on a special coordination dynamics therapy device

But where is such miss-knowledge coming from? In patients with no CNS injury, the plasticity is enormous. Every operation-induced change in the periphery is compensated for, especially through movement-based learning, by the complexity of the CNS, mainly located in the brain. After an operation, in minutes to hours, the human brain learns to generate physiologic movements again. Poliomyelitis patients relearned in minutes, when tendons were transposed. Surprisingly few trials were required for poliomyelitis patients to use transposed tendons successfully [2]. Animals on the other hand have a less complex CNS with less variability and plasticity. Approximately 75 years ago, Sperry transposed the nerve supplies of flexor and extensor muscles in rats [3] and monkeys [4]: the monkey relearned the task after some time; the rat did not.

Nearly all patients with an SCI have different kinds of spasticity according to the injury. Due to the injury, the CNS is not able anymore to generate certain automatisms in a physiologic way. These patterns become pathologic and are called spasticity or spastic patterns. Of interest here are especially the extensor and the flexor spasticity of the legs. The extensor spasticity seems to originate from the anti-gravity muscle activation pattern and the flexor spasticity of the legs from the protection automatisms.

When stepping on a sharp stone, the leg is lifted automatically to protect the foot against injury. The protection automatism of hand and fingers is well-known. When touching with fingers a hot plate, the hand is moved quickly away, before it is realized that the plate was very hot, which means, before the brain (thalamus) realized that there is danger to the fingers. The protection automatism is organized at the spinal cord level for being fast. The conduction time of the painful information, from pain receptors to reach the brain, would be too long for protection. Hands or feet would have been already damaged.
It has been shown that coordination dynamics therapy (CDT) can improve or repair central nervous system (CNS) functioning after stroke [5], traumatic brain injury [6, 7], spinal cord injury [1, 8-11], cerebellar injury [12], cerebral palsy [13], hypoxic brain injury [14], in Parkinson's disease [15], spina bifida (myelomeningocele) [16] and scoliosis [17]. Speech had been induced and improved in a patient with severe cerebral palsy [18]. A permanent coma patient could be brought out-of-coma and relearned to speak [19] and cancer grows could be inhibited through CDT [20, 21]. Cardio-vascular performance could be improved.

There is indication that the general health can be improved via CDT to live longer with a better quality of life.

2.2 METHOD

With the development of new electrophysiologic recording methods [22] (Fig. 2.1), it became possible to analyze CNS functioning at the single-neuron level under rather natural conditions. With the single-nerve fiber action potential recording method, single-nerve fiber action potentials can be recorded from sacral nerve roots, running in and out of the spinal cord and CNS functions can be analyzed. By comparing CNS functioning in brain-dead humans (where the spinal cord is functioning rather physiologically) and patients with spinal cord injury, injury-induced changes of CNS functioning can be measured and partly repaired. Mainly the phase and frequency coordination [23] of neuron firing becomes impaired following injury. This impaired coordination among neuron firing can efficiently be repaired through exercising on the special CDT device (Fig. 2.2).

The special CDT device has three important properties. First, the patient performs coordinated arm, leg and trunk movements when exercising on it. The training of integrative patterns take care of that the pathologic organization cannot escape from repair by shifting to another part of the CNS and the whole CNS, including the injured parts, is reorganized so that other CNS parts can take function over through plasticity. Second, the device is extremely exact, so that the endplate potentials in the neural networks (approximately 5ms long) overlap, to improve the efficiency of organization. In spinal cord injury, for example, the transmission over the injury site is increased. Third, the coordination between arm and leg movements changes from pace to trot gait, imposed by the device. The intermediate coordination patterns between pace and trot gait are difficult to generate for the CNS networks. If the patients CNS learned to generate these intermediate patterns, imposed by the device, then the networks have learned to function better in the deep complexity of CNS organization. The neural

networks are repaired in the deep complexity of CNS organization. The patient's nervous system learned by turning from the device, to function more physiologic through improving especially the phase and frequency coordination of neuron firing. This phase and frequency coordination can be measured by the single-nerve fiber action potential recording method invasively and by single-motor unit surface electromyography non-invasively (Fig. 2.1) [24].

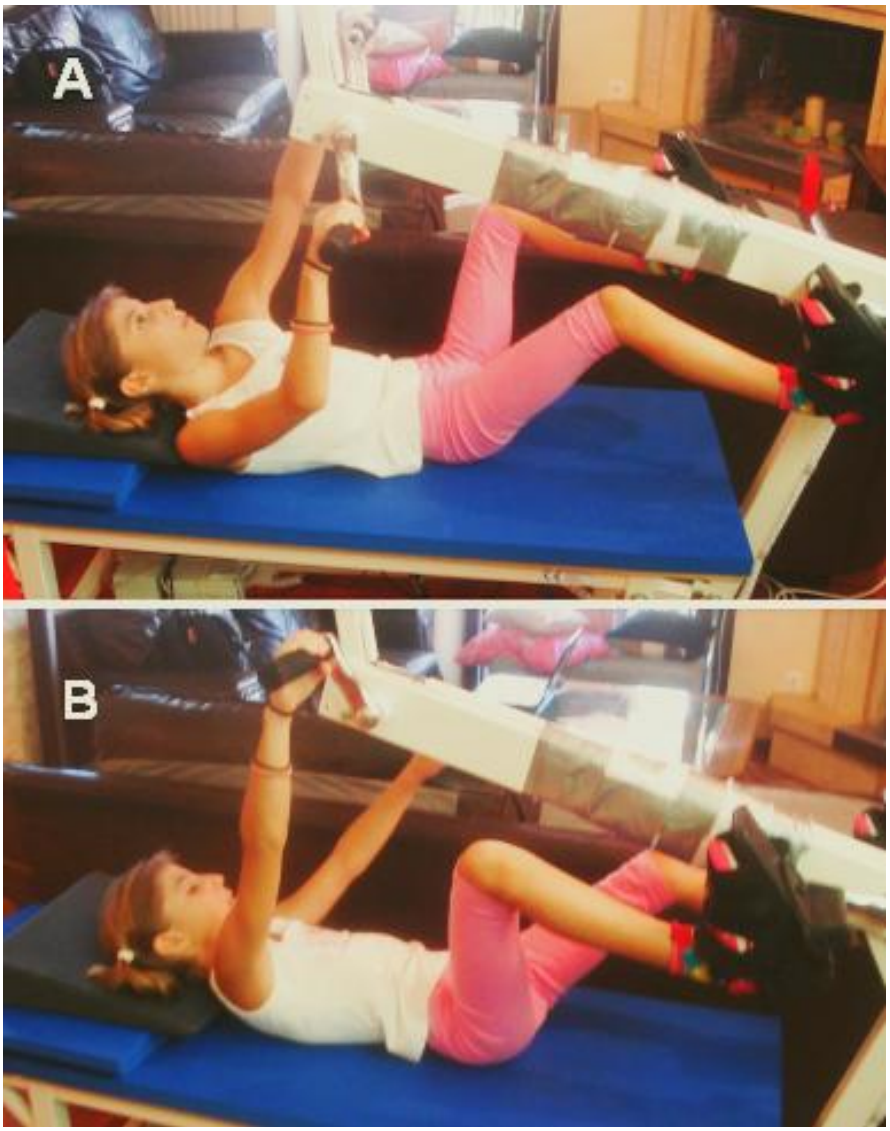


Fig. 2.2. Training of neck, trunk and pelvis control, besides the training of arm and leg movements, of a patient with SCI (Th10) during exercising trunk rotational movements on the special CDT device in the lying position. Due to the coordination changes of arms and legs between pace and trot gait all vertebra segments are trained

During exercising coordinated arm, leg and trunk movements, the coordinated firing of neurons and sub-neural networks are improved. This special CDT device for measuring and therapy (int.pat.) is produced by the firm: Giger Engineering, Martin Giger dipl.Ing. ETH/SIA, Herrenweg 1, 4500 Solothurn, Switzerland, www.g-medicals.ch.

Since through the damage of the spinal cord or brain also nervous tissue is lost, certain movements have to be trained so that other parts of the CNS can take function over through plasticity. Efficient training patterns are the automatisms creeping, crawling, up-righting, walking, sky-walking (Fig. 2.3C)

and running. The jumping on springboard (Fig. 2.3B) improves especially the functioning of premotor spinal oscillators [25], activating the muscle fibers. Also the balance has to be trained (Fig. 2.3A) during pattern performance.

Further, through learning transfer [26] other CNS functions improve, which cannot be trained or are difficult to train. Urinary bladder functions, for example, can be repaired especially when exercising on the special CDT device and jumping on springboard (Fig. 2.3) [18]. Only those functions can be trained which the patient is able to train with or without support.

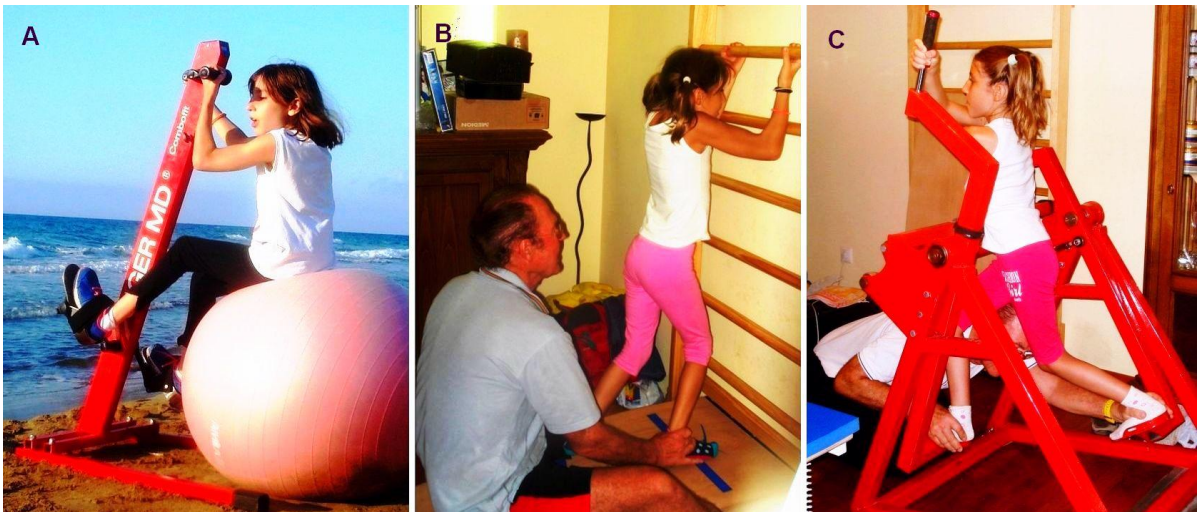


Fig. 2.3. A. SCI patient Nefeli during exercising on a special CDT device on a ball at the beach, to train apart from phase and frequency coordination also balance. B. By the Author supported jumping on springboard in antiphase. C. Nefeli during sky-walking. To achieve a large stride length, the Author is supporting the feet to avoid the slipping of the feet from the pedals

2.3 RESULTS

2.3.1 Improvement of Walking and Continence Following Spinal Cord Injury

In the 5.5-years-old Nefeli a neuroblastoma was found to grow from the Th10 ganglion. With the surgery to remove the cancer, she suffered an incomplete SCI at Th10/11 levels by medical malpractice (Figs. 2.4-2.6). An 8-months-rehabilitation in Switzerland brought only little progress. Most of the repair was probably due to spontaneous recovery. When Nefeli started school, she was incontinent and could not walk. An assistance helped her to manage at school (Fig. 2.7B).

At an age of 9, Nefeli started CDT with the Author. Spasmolytic drug and urinary bladder medications were stopped. Following four years of CDT, Nefeli became continent and she learned to walk again (Fig. 2.7D) with some balance problems. She learned to creep and crawl. Even a bit of running and jumping became possible. At an age of 13 years, Nefeli learned a bit to ride a normal two-wheel bicycle (Fig. 2.8) [1].

With increasing age, the scoliosis got worse, because one or two intercostals were cut when removing the neuroblastoma. But scoliosis can be reduced, when exercising on the special CDT device in the lying position with trunk rotation (Fig. 2.1) [17]. Because the orthopedic gave the instruction that Nefeli should not move too much, because the scoliosis will increase, Nefeli trained very little and the CNS repair did not progress any more. At an age of 14 a rod was implanted to keep the spine straighter. This operation was probably justified, even though not all training possibilities were used so far.

The orthopedic promised Nefeli and the parents that an operational correction of the legs will improve her walking performance strongly, not knowing that in such a critical incomplete SCI an operation is

contraindicated (Introduction), because the plasticity will reduce and her movements will get worse. Against the strong advice of the Author to avoid surgery, an operation of both feet bones was performed (Fig. 2.9) and a tendon of the left leg elongated.

In the next section, the reduction of movement functions following the operation will be tackled in detail. To say it clearly, one cannot improve CNS functioning through operations and also not by administering drugs. Movement-based learning is the only causal therapy.

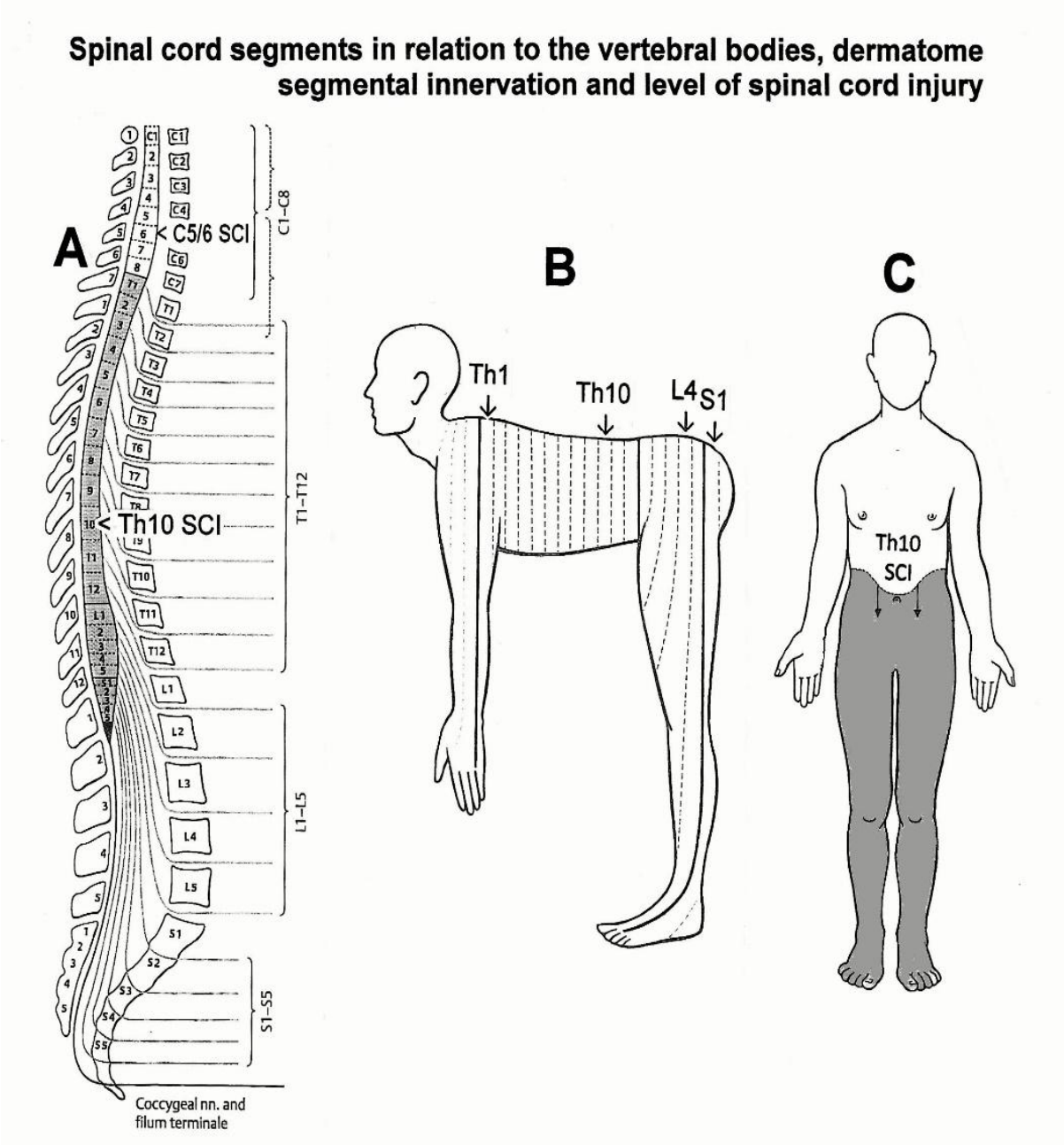


Fig. 2.4. A. Spinal cord segments and their relation to the vertebral bodies. Note the Ascensus of the spinal cord, giving rise to the long cauda equina nerve roots. B. Approximate segmental innervation of the skin. C. Below the SCI level there is loss of sensitivity and loss of connectivity to muscle and other organs

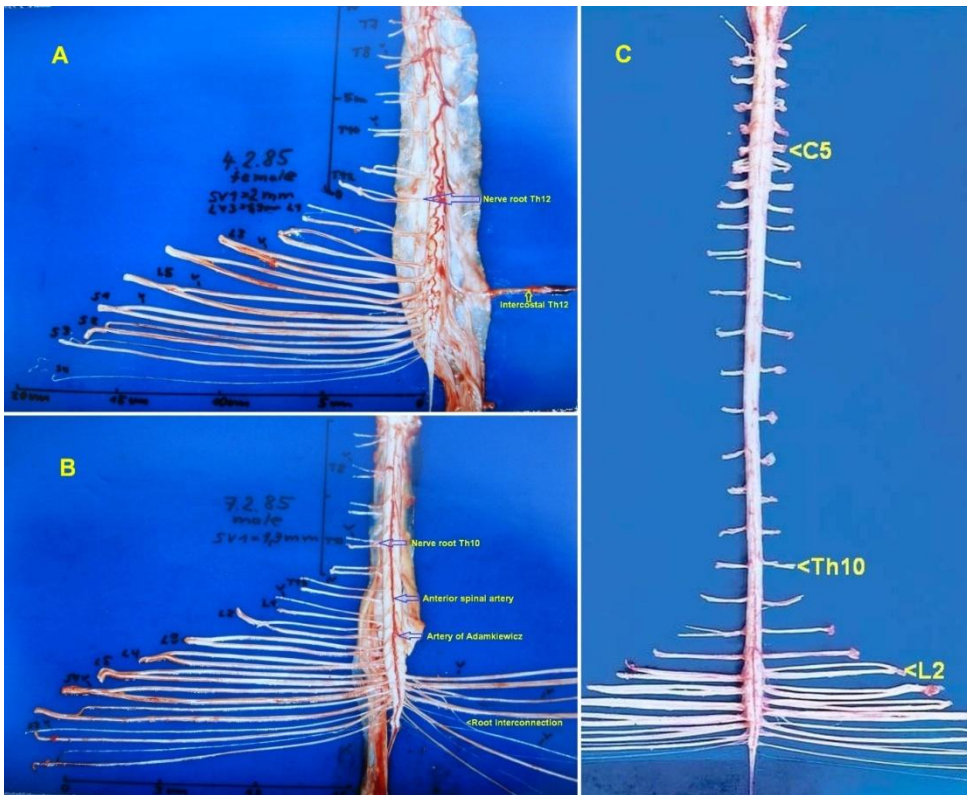


Fig. 2.5. Human spinal cord from dorsal (A) and ventral (B, C). Intumescentia cervicalis and lumbosacralis are visible in C. The caudal ventral roots are thinner than the dorsal roots. The passage of the artery spinalis magna (Artery of Adamkiewicz) and the anterior spinal artery are indicated. The C5, Th10 and L2 roots and the intercostal nerve Th12 are indicated. Dissection by the Author

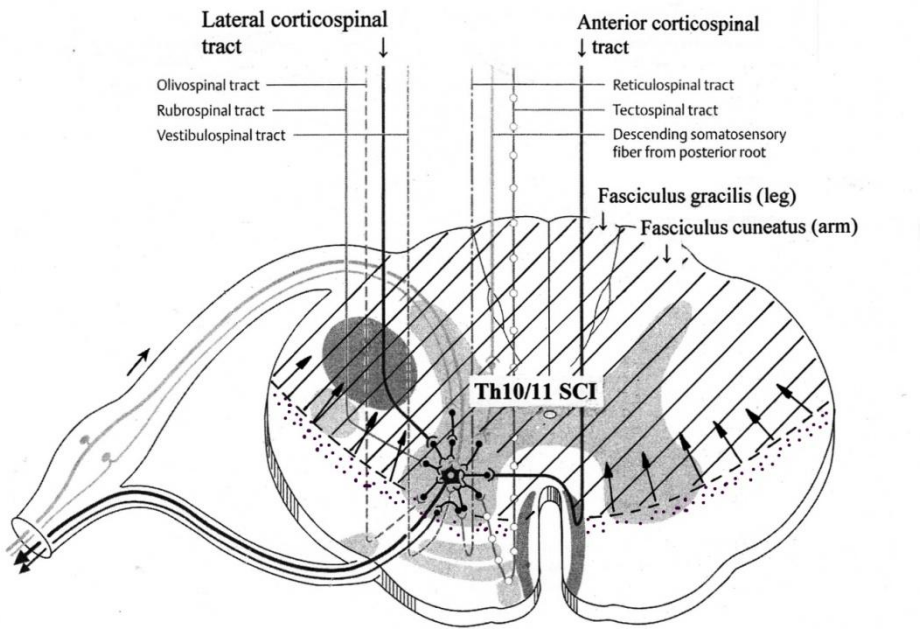


Fig. 2.6. Spinal cord cross section with indicated approximate injury (cross-hatched) and loss of interneuron (dotted area) of the patient Nefeli. Synapses of descending motor tracts onto anterior horn neurons are shown

Fig. 2.7. A. The 5.5-year-old Nefeli after suffering an incomplete SCI at Th10 by medical malpractice. B. Nefeli after eight months of conventional children rehabilitation in Switzerland (Affoltern). Sticks and orthosis were needed. C, D. Ten-year-old patient Nefeli after six months of CDT. At school she can walk again and can write at the white board

Fig. 2.8. The SCI patient Nefeli just after learning to ride a normal bicycle at an age of 12.5 years (A). She manages also to ride curves (slalom) (B). She still has problems to keep the feet on the pedals, but when she slips from pedals, she has no problems to keep the balance (C). Note that she has to concentrate very much to keep the feet on the pedals (A), seven years after the SCI injury

2.3.2 Dramatic Loss of Repaired CNS Functions Due to the Orthopedic Operation

After the bone operation of the feet (Fig. 2.9) and a tendon elongation of the left leg, the patient had the legs in plaster up to the knees and should stretch and flex the legs according to the instructions of the surgeon. But a few days after the operation, slowly the stretching became more difficult till the patient became unable to stretch the legs. Extreme strong flexor spasticity, cramps and rigor had appeared and the patient had not sufficient volitional power anymore to stretch the legs. Nefeli

struggled with the father for 10 days, because he thought that she was able to move the legs by herself, according to the instructions of the surgeon. The patient Nefeli had to stay in bed and she had to be carried to the toilet because she could not move the legs anymore. They were always in an extreme flexed position (Fig. 2.10).

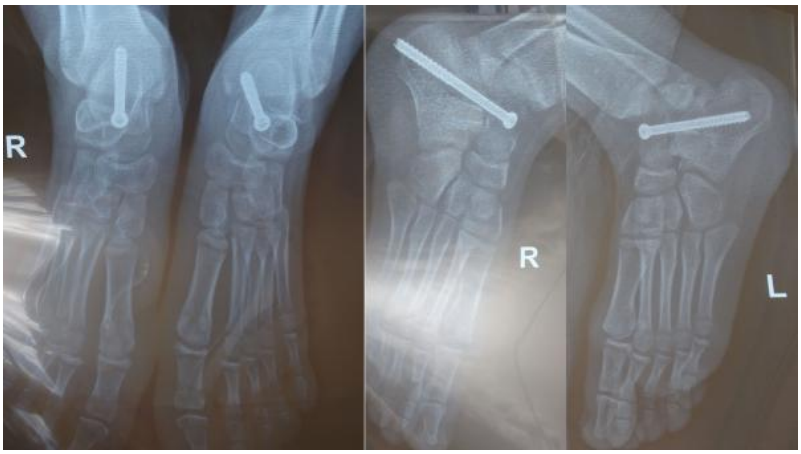


Fig. 2.9. Performed foot operation, which threw the spinal cord injury patient Nefeli two years of movement-based learning therapy backwards. A transposed piece of bone cannot be seen. The seemingly simple operation had tremendous consequences for the patients CNS functioning and her everyday life

When the Author saw her the first time, 6 weeks after the operation, she was in bed and could not move the legs (Fig. 2.10). The legs were always in an extreme flexed position. When it became possible with tricks to extend the legs a bit (Fig. 2.11A), they went immediately into the flexed position when touched (Fig. 2.11B), independently where the leg was touched. When trying to put her on the feet, the feet flexed (Fig. 2.11C), so that a standing was impossible. This flexor spasticity could also be seen when holding her with the arms. Fig. 2.12B shows the physiological positioning of the legs of the healthy sister. Before the second operation, after three years of CDT, Nefeli had some extensor spasticity (Fig. 2.12A), which helped her to stand straight. After the second operation, the legs were clearly in a strong flexed position (Fig. 2.12C).

Fig. 2.10. Six weeks after the operation, the SCI patient cannot move the legs any more, because of extreme flexor spasticity, which developed one to two weeks after the operation

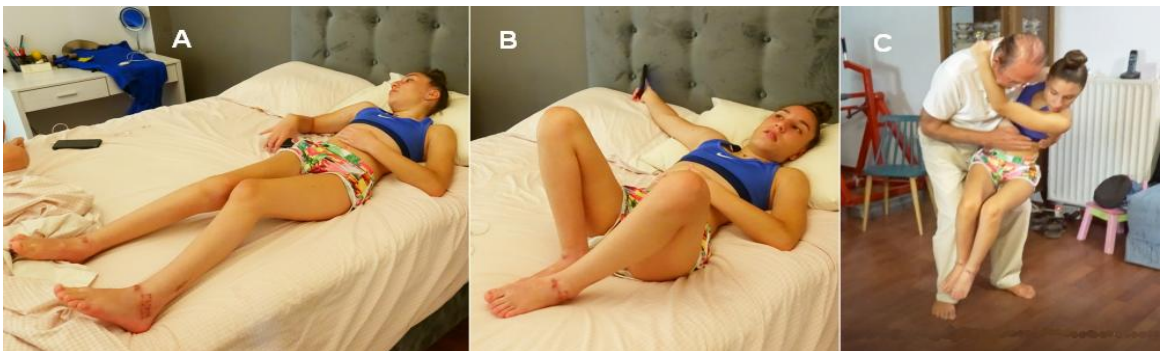


Fig. 2.11. When it became possible by some tricks to get the legs somehow stretched (A) and one touched the legs, they went immediately into flexor spasticity position (B). When the Author tried to put the SCI patient onto the legs for standing, the legs flexed immediately (C)

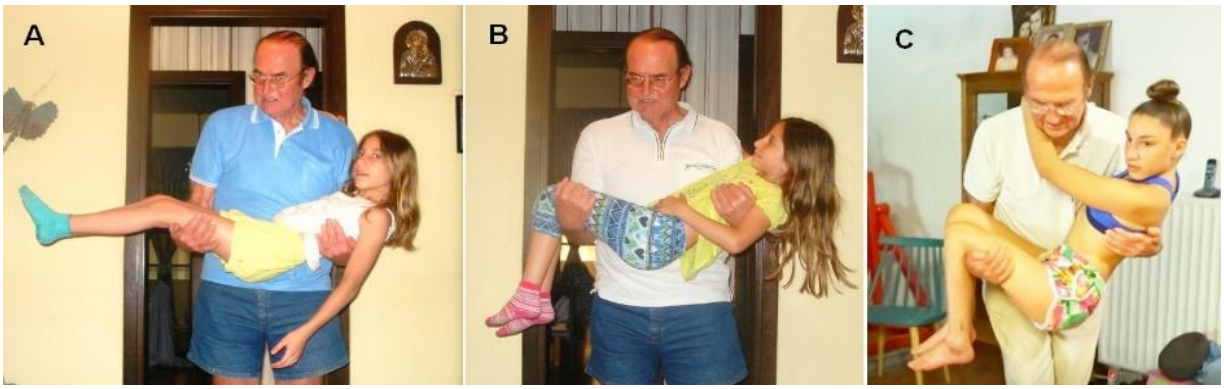


Fig. 2.12. The extreme flexor spasticity of the SCI patient was also visible when holding her. The physiologic holding position can be seen when the Author was holding the patient's sister (B). Before the second operation, the patient's legs were more stretched because of the mild extensor spasticity (A), which can be helpful for standing and walking. After the second operation, the legs were strongly flexed, due to the extreme flexor spasticity (C)

The question was now, how can the by the operation damaged CNS repaired, to make the patient move again to the toilet. Wherever touching the legs, they went by strong flexor spasticity into the flexed position. No movement training seemed to be possible. The Author tried with the patient many movement possibilities, which could be used for training to reduce the extreme flexor spasticity. Luckily, they found a movement. When putting on the orthoses (Fig. 2.13A), the flexor spasticity was not that strong, probably because the input was more general and unspecific. A bit of turning on the special CDT device in the sitting position became possible (Fig. 2.13B). Even though that sitting position was unphysiological and not good for the scoliosis, the patient trained in that position. With ongoing training, the flexor spasticity reduced. Following two months of therapy, Nefeli became able to exercise also a bit in the lying position which was a physiologic patterns for her (Fig. 2.13C). At the beginning, this turning in the lying position was not possible, because Nefeli did not have sufficient power to train against spasticity and rigor. Touching the legs for support made it harder for her to turn. Also, at the beginning it was nearly impossible for the Author to fix her legs in the lying position, because the legs were too stiff. The Author and also the patient could not understand why the turning in the sitting position became possible and why not in the lying position.

The Author had also no idea how he could have treated the patient without the special CDT device. Anyhow, a training became possible, spasticity reduced and leg movements became slowly possible again. Spasmolytic drugs for 5 days were tried by the surgeon without success. Apart from the side effects, spasmolytic drugs are not helpful in incomplete SCI, because they do not only reduce the spasticity, but also reduce the remained volitional muscle power.

Fig. 2.13. To be able to exercise on the special CDT device, the SCI patient Nefeli had to wear orthoses up to the knees. The for the back healthy lying position (C) was only possible 3 months after the operation because of spasticity and rigidity

Fig. 2.14. The walking performance of the SCI patient before (A, B) and 3 months after the second operation (C)

2.3.3 Repair Achieved 3.5 Months after the Operation through 2 Months of CDT

The spinal cord injury was the result of a mistake of the first operation. When removing the cancer starting from the Th10 ganglion, the hemostasis was wrongly performed in the way that blood went into the spinal canal and caused in during 3 days through pressure an incomplete spinal cord injury. The pain of the crying child after the operation was ignored by the operating team. When the SCI manifested itself, after 3 days, in the way that the patient could not stand anymore and became incontinent, the parents just took Nefeli to another hospital.

Different movement performances will now be compared before and after the second (feet) operation to see the results of the feet operation, to show how much repair was destroyed by the operation.

2.3.4 Walking

Before the second operation, 9 years after the first operation, the patient Nefeli was able to walk with and without crutches (Fig. 2.14A, B) up to 1000m; 3.5 months after the second operation she could

walk only with crutches up to 10m (Fig. 2.14C). She needed shoes and the arms were just strong enough to keep her up.

2.3.5 Running, Jumping and Getting Up from the Floor

Before the second operation Nefeli could run and jump a bit (Fig. 2.15A, B) and could get up from the floor (Fig. 2.15C) without support (Fig. 2.16). After the operation she could not get up from the floor anymore without support and could not run and jump anymore.

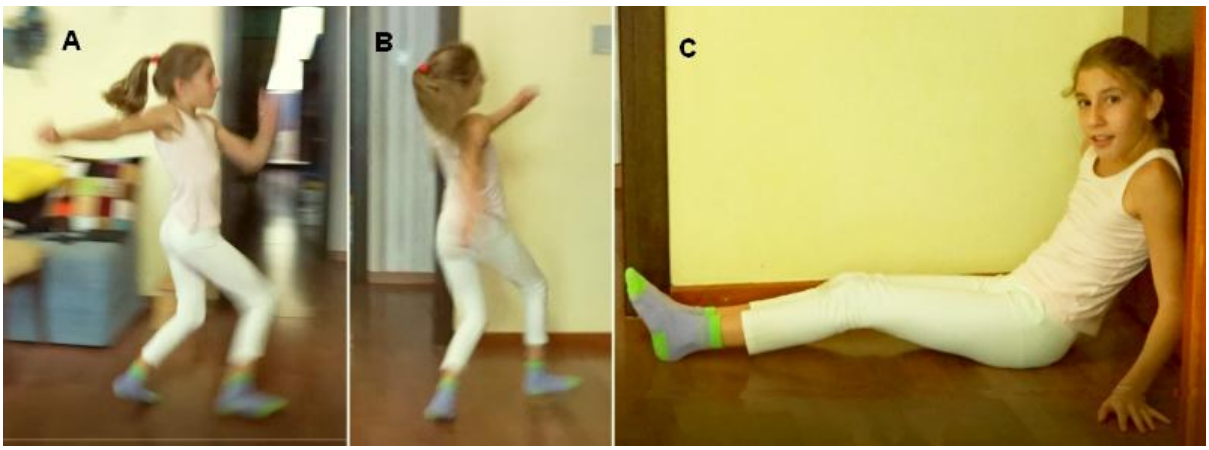


Fig. 2.15. Before the second operation the SCI patient Nefeli was able to run and jump a bit (A, B) and she enjoyed it very much. She was very relaxed and happy afterwards (C)

Fig. 2.16. Before the second operation, the spinal cord injury patient Nefeli was able to get up from the floor in two ways. Even when having balance problems during getting up, she managed well (lower A-D). When really falling, there was no risk of damage, because all protection mechanisms walked well. After the operation she could only get up from the floor with substantial support

2.3.6 Staying Straight

Before the second operation, Nefeli could nearly stay straight (Fig. 2.17A, B); 3.5 months after the operation she could only stay less straight (Fig. 2.17C, D).

Fig. 2.17. Free standing of the SCI patient before the second operation (A, B) and after (C, D). In spite of pushing herself up with crutches (D), the flexion of the legs was stronger than before the operation

2.3.7 Foot Arch

Before the operation, the right foot had no arch if full body weight was on it (Fig. 2.18A), which could not be repaired so far. Such foot arch repair needs long-time training on the forefoot. After the operation the right foot arch was not much better (Fig. 2.18D) and could not trained sufficiently because of the necessary orthoses. Before the operation no orthoses were needed and the foot arch could be trained.

Fig. 2.18. Bar foot walking of the patient Nefeli with a spinal cord injury begore the second operation (A-C). Three months after the operation she could not walk freely any more (D)

A physiologic foot arch is important, otherwise pain may occur later during walking. The patients left foot had a physiologic arch (Fig. 2.18B). The right foot arch was lost when putting weight on it (Fig. 2.18A). The foot arch muscles (Fig. 2.19) could not be activated sufficient strong by her because of the SCI. On the long term, the foot bones may rearrange (Fig.2.20). But a training on the forefoot can repair the foot arch in cerebral palsy and probably also in incomplete SCI.

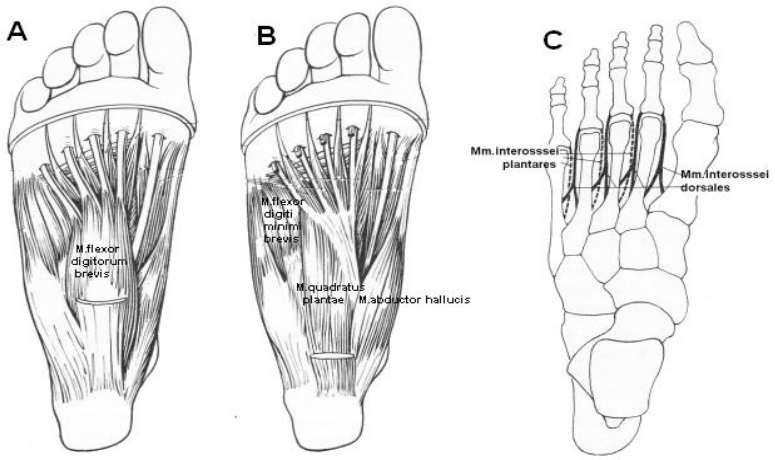


Fig. 2.19. Superficial (A) and deep (B) plantar muscles of the foot to support the arch of the foot. C. Mm. interossei plantares and dorsalis

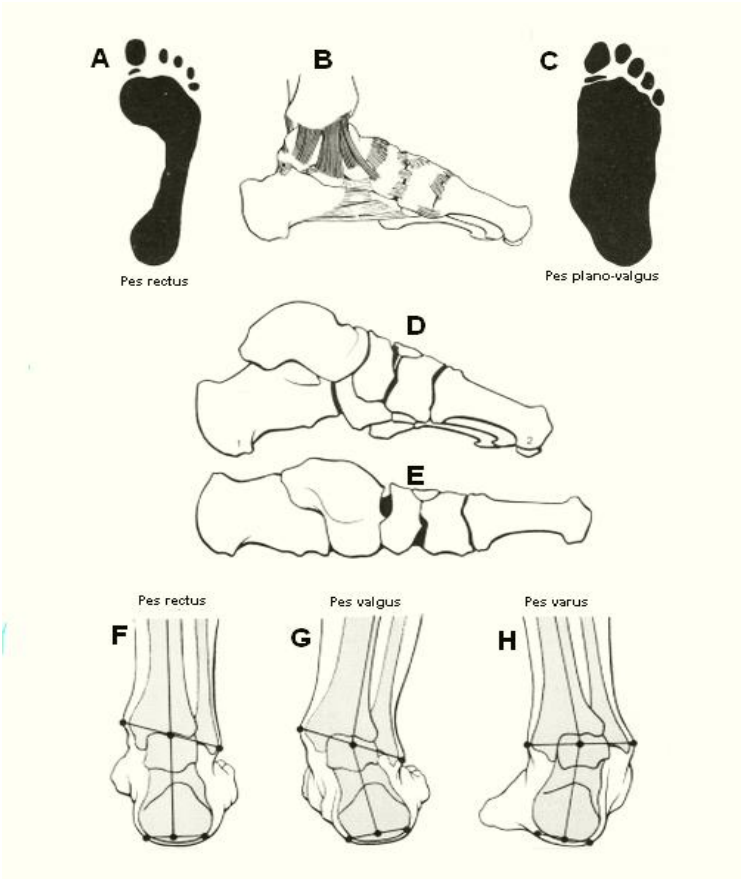


Fig. 2.20. A. Healthy foot print (pes rectus). B. Foot ligaments. C. Pes plano-valgus. D. Bones of the healthy foot arch from medial. E. Broken foot arch from medial

2.3.8 Walking on Sky Walker and Training Symmetries

Before the second operation Nefeli could walk on the sky walker easily (Fig. 2.21A). When exercising with crossed arms or legs, even the right-left symmetry via the corpus callosum could be trained (Fig. 2.21B, C). Also, some stretching was possible on the sky walker (Fig. 2.22A). After the second operation, the right leg went into the flexed position due to flexor spasticity (Fig. 2.22B). After 3.5 months, a bit of exercising on the sky walker became possible if Nefeli was wearing shoes and the feet were fixed.

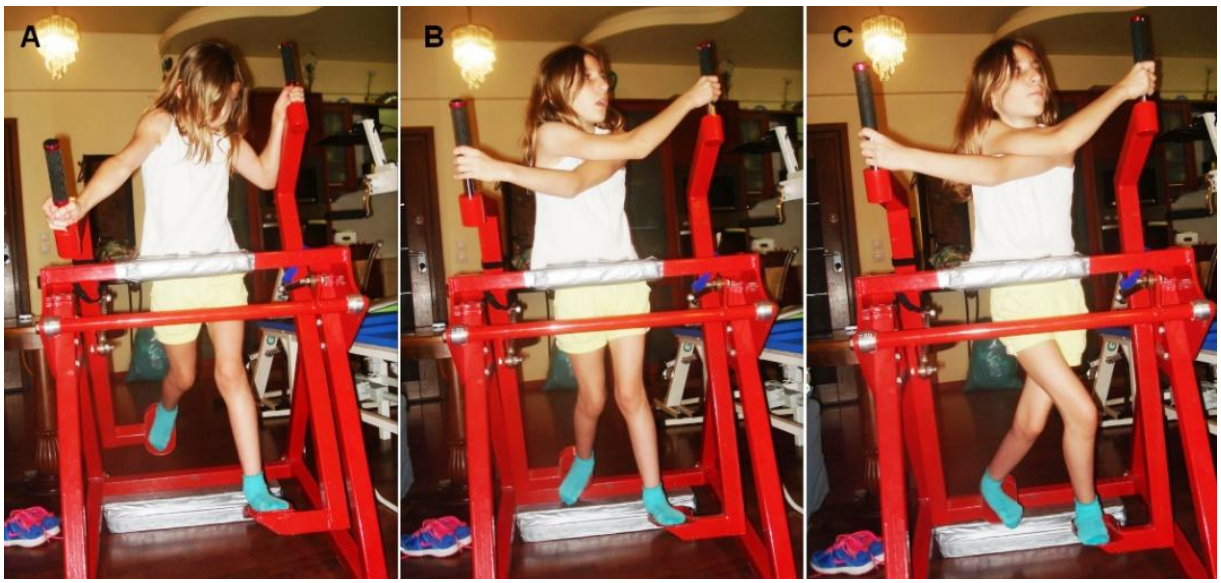


Fig. 2.21. Different movement patterns on the sky-walker. A. trot gait. B, C. Combinations of pace and trot gait to activate commissural fibers (Fig. 2.23D)

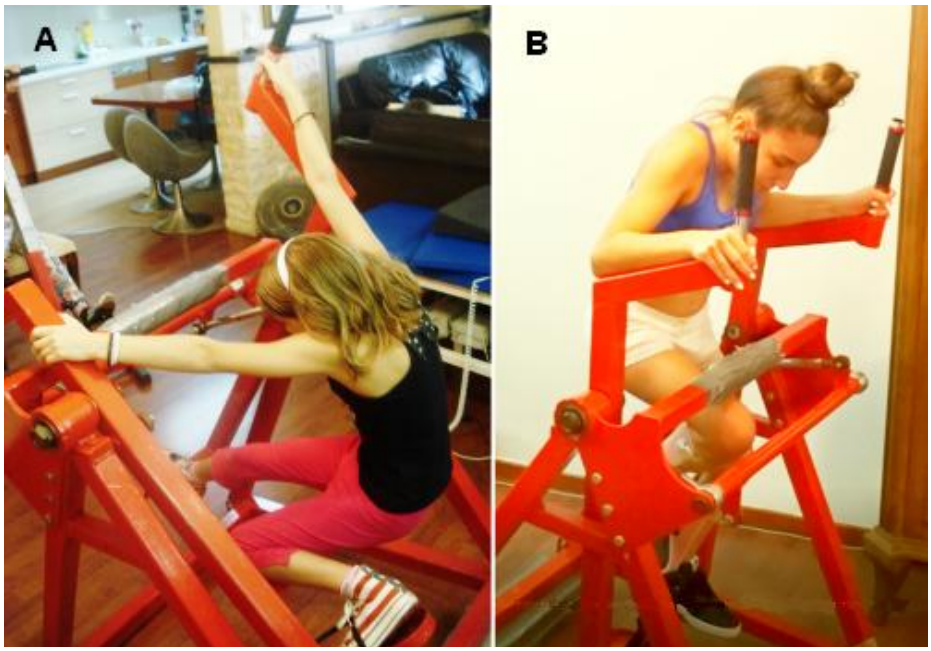


Fig. 2.22. A. Sky-walker used for stretching in the ten-year-old Nefeli with a spinal cord injury (before the second operation). B. Two months after the second operation, the 14-year-old Nefeli is trying the sky-walker, but the right leg went into the extreme flexor spasticity pattern

In CNS injuries, malformations, degenerations and brain cancer operations, the improvement of right-left symmetries is important. It can be trained on the sky walker (Fig. 2.21), on the special CDT device (Fig. 2.23C) and on the floor (Fig. 2.23A, B). The corpus callosum and other right-left connecting tracts (Fig. 2.23D) allow that functions of one hemisphere to be partly taken over by the other hemisphere through plasticity, especially for children under 10 years. Scoliosis can also be improved through such movements. 3.5 months after the second operation, these movements could not be trained. The scoliosis became worse (Fig. 2.13A, B) in spite of a fixation of the spine by a rod.

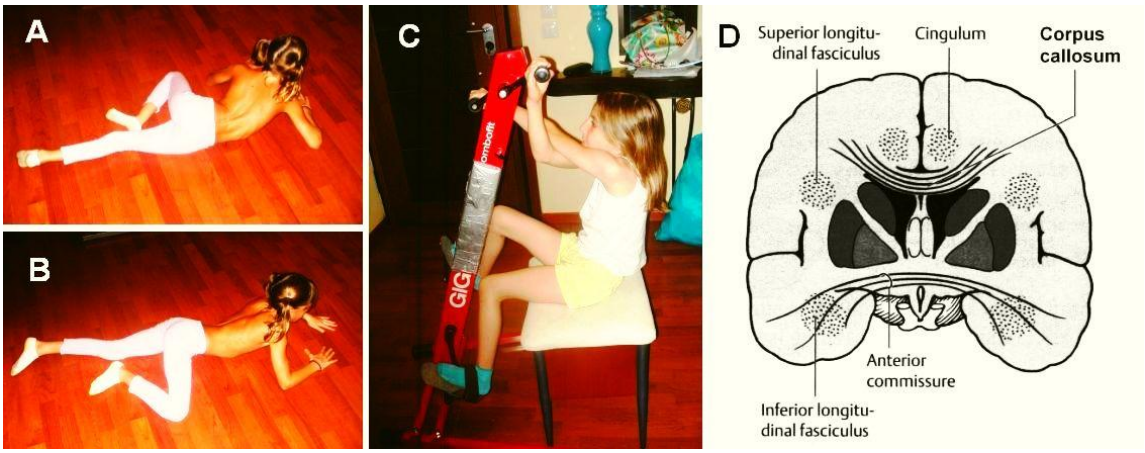


Fig. 2.23. A, B. Ten-year-old patient with an incomplete SCI at the Th10 level during creeping. Note, because of the severe scoliosis, the creeping is not symmetrical. The rotation to the left is limited because of the scoliosis. C. Training of right-left symmetry via the corpus callosum (D) when exercising on the special CDT device with crossed arms

2.3.9 Repair Achieved 6 Months after the Second Operation

Six months after the operation, there was some improvement in CNS functioning. The patient relearned a bit to walk without support when using orthosis (Fig. 2.24). But the performance of the walking was not better than before the operation. Nefeli still had to swing the legs during walking (Fig. 2.24B, C). For the walking without orthoses, she needed substantial support (Fig. 2.25A, B). The dorsal flexion of the right big toe was strong (Fig. 2.25C). Spasticity of toes hinder to put on shoes.

Fig. 2.24. Free walking of the 14-year-old Nefeli after the second operation when wearing shoes. She is still swinging the right leg because of no proper walking performance (B, C). The balance during walking did not improve; it got worse

Before the operation, the patient could walk with and without shoes (Fig. 2.18A-C) with some balance problems. Relaxed walking of long distances she managed easily when touching another person and getting in this way additional stability.

Six months after the second operation, the balance problem had not improved. It was worse. When walking without shoes, there was a risk of foot damage when falling, especially the right 'bad' foot was at danger. Before the operation there was no risk when falling. Altogether, the walking after the second operation was by far not as good as before the operation.

Fig. 2.25. 14-year-old Nefeli after the second operation. She was able to walk bar foot only with strong support (A, B). The right big toe was strongly dorsal flexed during walking

The surgeon had promised Nefeli and her parents a much better performance of the walking after the operation, which did not take place. The surgeon only raised false hope and made her movement performance worse.

2.3.10 No Substantial Further Walking Improvement 8 Months after the Operation

Not much further walking pattern performance following eight months after the operation. Luckily, urinary bladder functioning did not get worse with the second operation.

2.4 DISCUSSION

2.4.1 Comparison between an Operation and a Movement-based Learning Therapy in CNS Injury or Malformation

It has been shown that the SCI patient Nefeli lost something like two years of movement-based learning therapy (CDT) through an operation of the feet. This loss of repair of the CNS was mainly due to the missing knowledge of that orthopedic surgeon in repair-neurophysiology. Damage or disturbances of the nervous system, including the vegetative divisions, have to be attacked through movement-based learning and not through an operation. Of course, if the patient has not the mental discipline to train, then a drug therapy or an operation is the only choice. Patients and parents complain that they are not informed by physicians about other treatments.

The question is now, how would the repair of Nefeli been, if she would not have been operated. Some kind of comparison is given here, even though there are differences between the repair in SCI and cerebral palsy.

Nefeli trained often together with the cerebral palsy girl Sophie who had an atrophy of the cerebellum and pons. At the beginning of CDT, Sophie could not stand and walk (Fig. 2.26A, B), was incontinent

and had no protection automatisms. When falling, she would hurt herself because of missing protection automatisms, located mainly in the cerebellum. With training, the functioning of the cerebellum improved and she learned the protection automatisms. Now standing and walking could be trained, because the danger of damage was over, since the protection automatisms worked now in her. Through 4 years of CDT, Sophie learned to stand freely and walk without falling (Fig. 26C). She became continent and her higher mental functions improved.

Fig. 2.26. A, B. At the beginning of coordination dynamics therapy, the cerebral palsy girl Sophie could not stand and walk and was incontinent. C. After 4 years of CDT she can train together with Nefeli the walking in interpersonal coordination

Also Sophie had no foot arches and surgeons said that she will get pain in the future because of the missing foot arches. When the parents saw the operation results of Nefeli, they decided against an operation and used CDT for further progress. For building up a foot arch, Sophie trained walking on the forefoot and climbing staircases in the proper way. Via the forefoot the patient has to feel the edges of the staircases for proper climbing. The building up of foot arches may take a few years of training, but the malformed CNS is not injured by an additional operation. Anyway, Sophie has to learn to walk better and to run and has to climb the staircases in the physiologic way for safety.

Fig. 2.27. A. The SCI patient Nefeli needed after the feet operation again support when going at home to the WC. B-D. The cerebral palsy girl learned in the meantime the running. Note from the expression of the face of Sophie, how hard she is fighting to run. She liked the running, even though being very hard

Five months after the feet operation, Nefeli could just walk a bit with orthosis and needed support when moving to the WC at home (Fig. 2.27A), whereas the not feet operated Sophie learned in the meantime the running (Fig. 2.27B, C, D). Nefeli and her parents were getting depressed when seeing the improvement in Sophie and the loss of repair in Nefeli.

It is the duty of surgeons not just to see only their own operational repair strategy. They have to tell patients and parents about alternatives. Such behavior of some surgeons ruins the reputation of medicine.

2.4.2 CDT is a Healthy Non-invasive Neurotherapy with Nearly no Alternatives

Figs. 2.28 and 2.29 show that when exercising on a special CDT device, nearly the whole brain (CNS, Fig. 2.28A) is activated for repair. If one includes coordinated speech in the movement training by giving coordinated instructions 'right-left' or 'one-two-three', the efficiency of repair can further be increased. Even cognitive visual input can be included to enhance the repair.

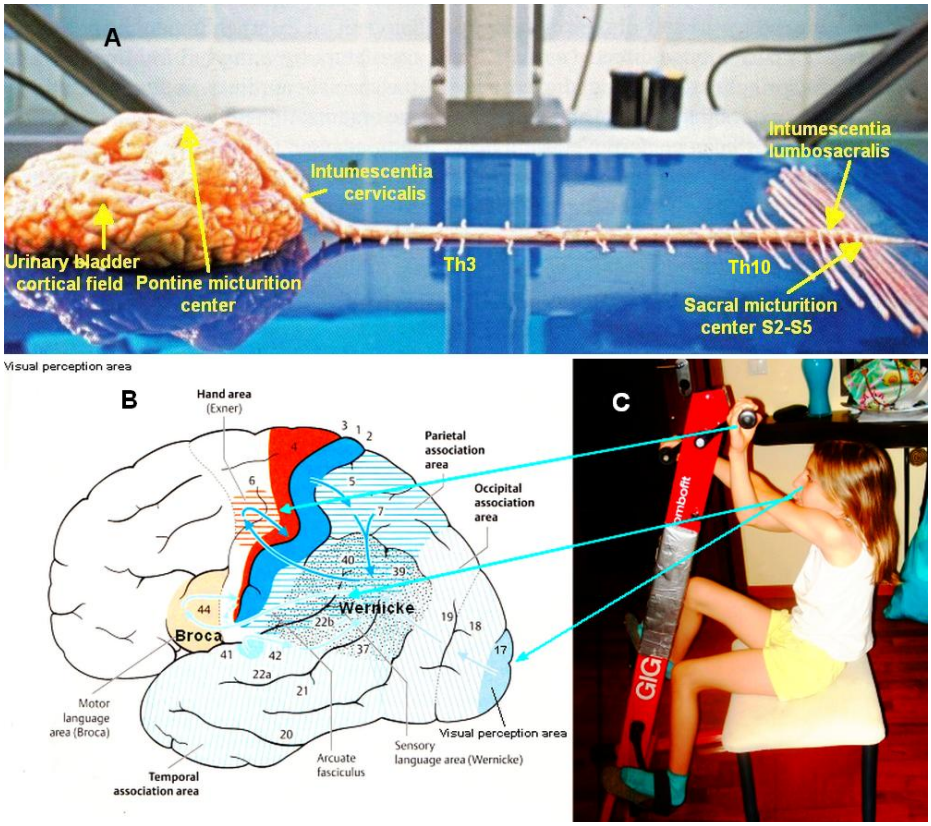


Fig. 2.28. A: Unfixed human CNS dissected by the Author. Lumbosacral and cervical enlargements of the spinal cord (intumescentia lumbosacralis and cervicalis) are indicated. The S1 root is the last thick nerve root. The urinary bladder cortical field is inside and cannot to be seen. Such a dissection of the human CNS is not simple. To take the brain out during an autopsy in the Pathology department is standard. Following 50 to 100 cadaver dissection, the Author was quite experienced to remove the spinal cord. But to remove the brain in connection with the spinal cord from a cadaver is difficult, if one does not want to damage the outside of the cadaver too much, so that relations of the dead loved person can say in peace goodbye. B, C. Efficient coordination dynamics therapy through including the coordination of vision, speech and coordinated arm and leg movements (C) for brain and spinal cord injury repair. Especially the multimodal association areas (B), in the deep complexity of CNS organization, are activated for repair. This neurotherapy is also efficient for a language repair of the Wernicke area of the brain cancer patients.

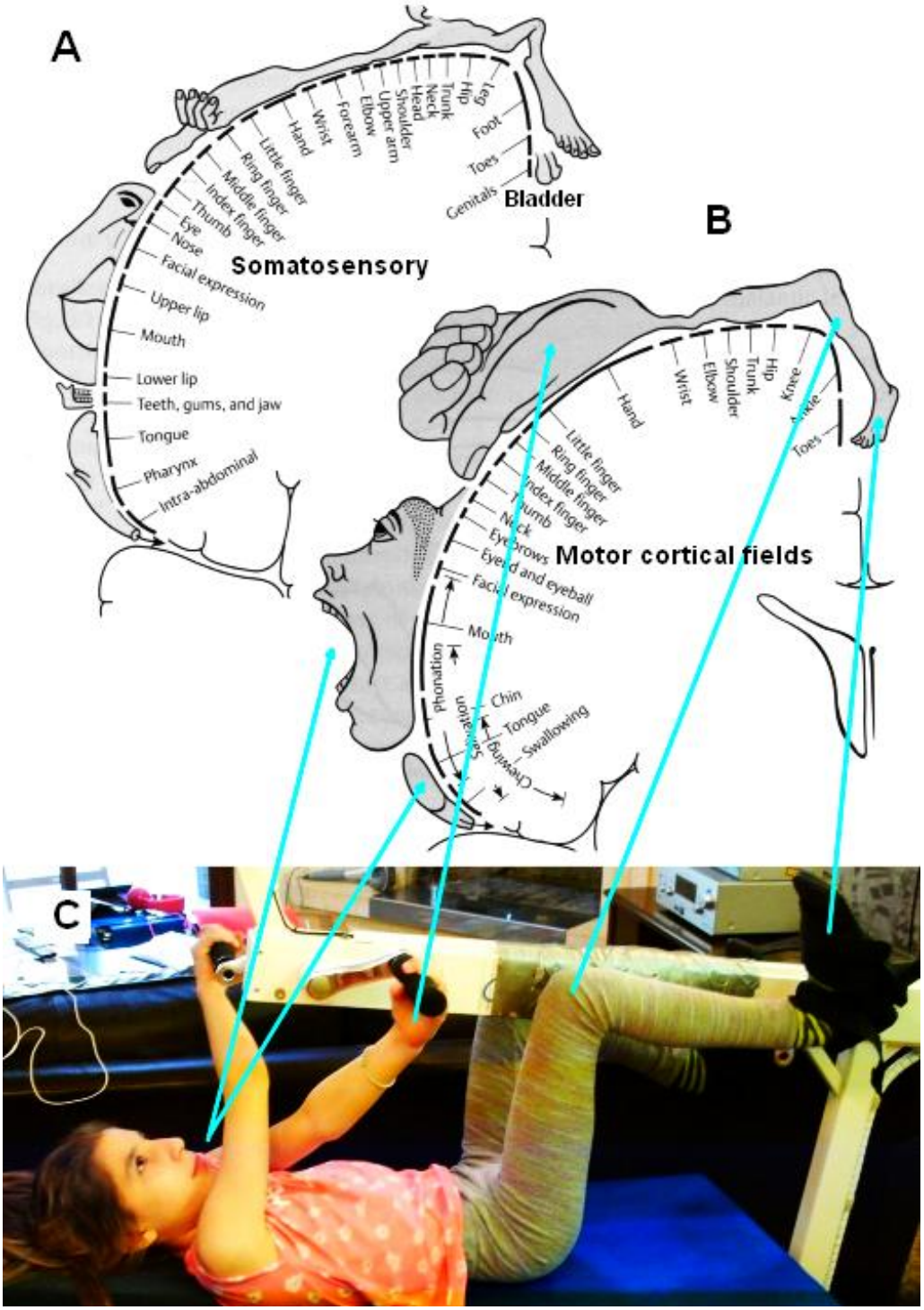


Fig. 2.29. Relative sizes of cortical representations of different parts of the body which are activated when exercising on special CDT devices in coordination with instructions. Nearly the whole somatosensory (A) and motor cortical fields (B) are activated. When moving only the legs, as in case of a fitness bicycle, the activated areas are relatively small. Note, the cortical representation of the urinary bladder is close to the representation of the toes, and during jumping the forefoot and the toes are activated. The patient Nefeli in 'C' suffered a spinal cord injury during a cancer removal by medical malpractice and had also the urinary bladder to be repaired

2.4.3 Progress in Human CNS Repair Achieved Through Basic Medical Research Which is Not Organized Worldwide

The progress in human CNS repair was achieved through basic medical research. Based on a new recording method (the single-nerve fiber action potential recording method, Fig. 2.1A), a classification scheme of human peripheral nerve fibers [28] could be developed. Through measuring at the single-neuron level the impulse traffic of identified neurons which runs into and out of the spinal cord, premotor spinal oscillators could be found and the important 'phase and frequency coordination' [23] among neuron firings for the self-organization of human neural networks measured (Fig. 2.30). Out of the difference between physiologic and pathologic functioning, a neural repair method, the CDT, was developed with which it became possible to repair the injured or malformed human CNS or improve its functioning in the healthy case. Since the nervous system is involved in nearly all body functions, the general health of humans can be improved to live longer with a better quality of life by 10 to 20 years.

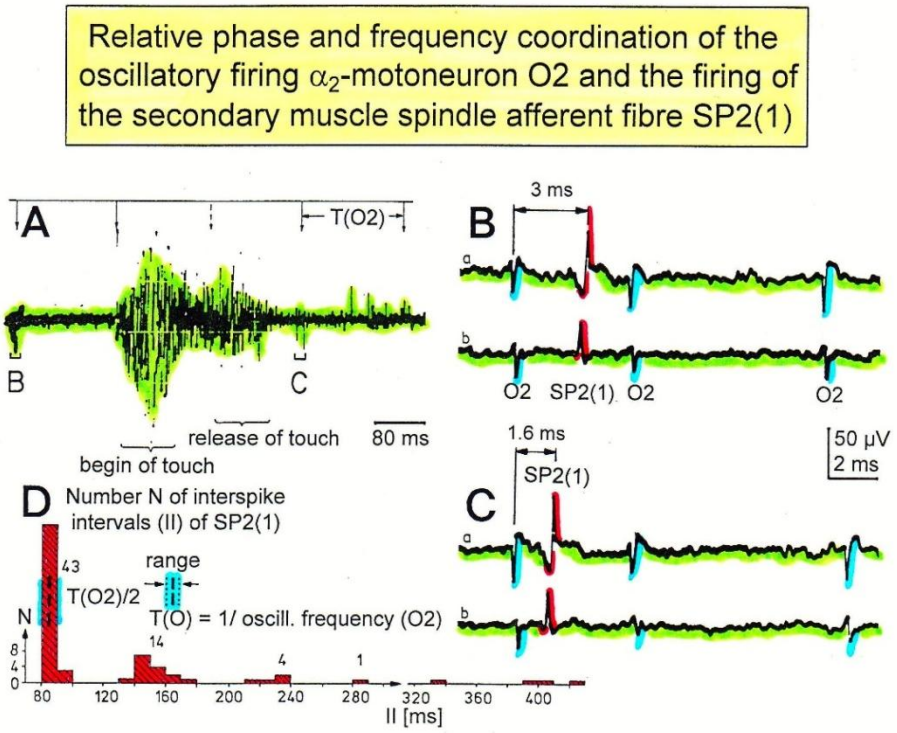


Fig. 2.30. Time relation between the occurrence of the action potentials (APs) of oscillatory firing α_2-motoneuron O2 and the firing of the secondary muscle spindle afferent fiber SP2(1). Brain-dead human HT6. S4 dorsal root recording. A. Overall view of the used sweep piece; only trace "a" shown. Four oscillation cycle periods of motoneuron O2 are indicated (T(O2)). The APs of the impulse trains can be recognized only partly, because of the slow time base and poor digitalization. One impulse train (dashed arrow) is lost in the touch stimulated activity, which consists of a touch (large overall activity) and a release part (lower overall amplitude). B, C. Sweep pieces from A, time stretched. In B, motoneuron impulse train APs are marked O2, spindle afferent APs are marked SP2(1). Note that the APs of the spindle afferent fiber are not time-locked to the first AP of the impulse train of the rhythmically firing motoneuron (relative phase coordination). Digitalization four times better than in A, but still rather poor, as can be seen from the low amplitudes of the motoneuron APs on trace "b" in C. D. Occurrence of interspike intervals of the secondary muscle spindle afferent fiber SP2(1). The numbers give the amount of IIs in each distribution peak. The oscillation period of motoneuron O2 (and the range of variation) and the half period are indicated by short dashed lines. Note that the IIs of fiber SP2(1) are very similar to the oscillation period (or the half of it) of α_2-motoneuron O_2 (relative frequency coordination)

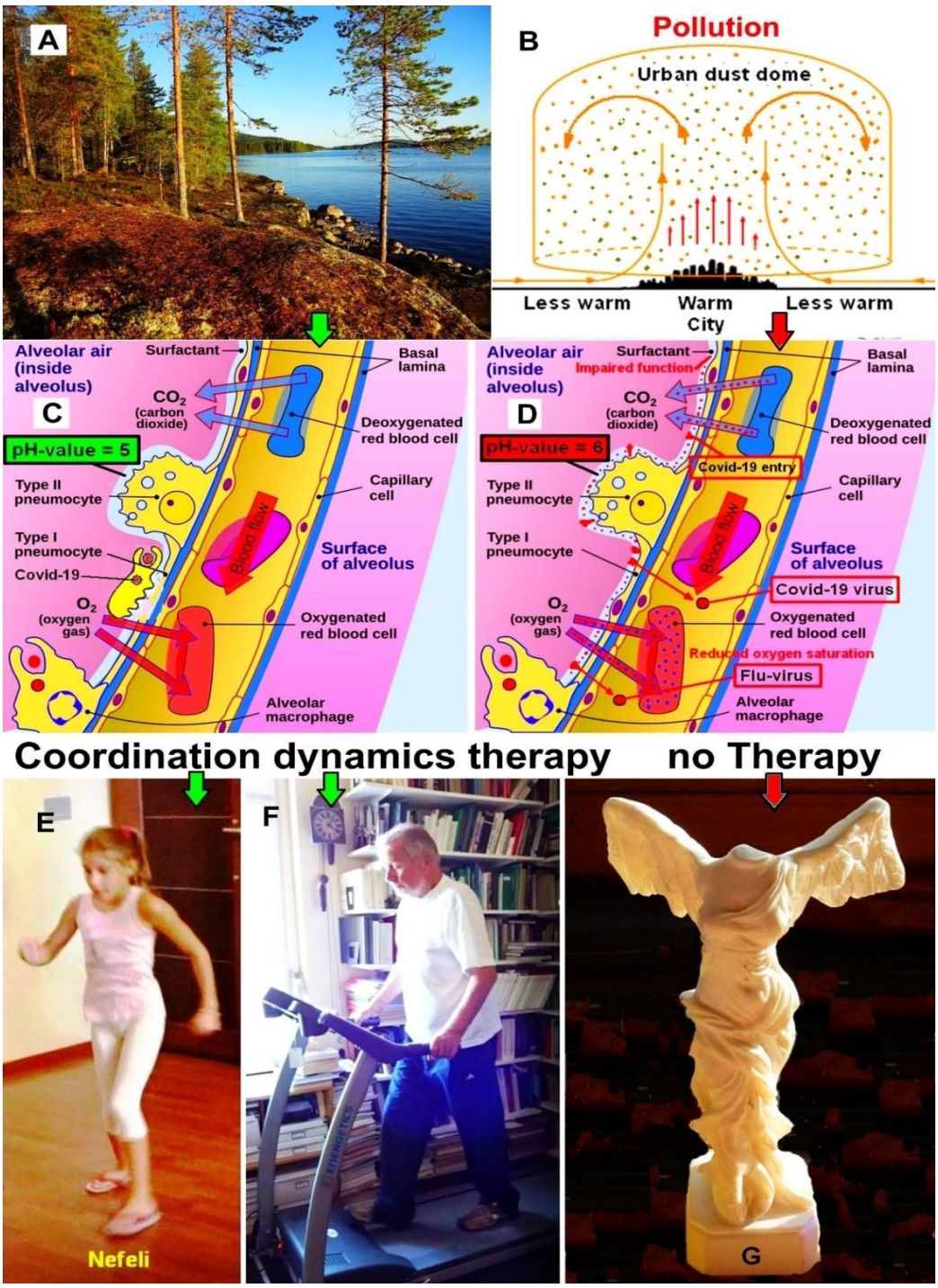


Fig. 2.31. Physiologic and pathologic pulmonary epithelial functions to impede virus and bacterial infections. When living in a healthy surrounding (A) and exercising (E, F), the lung epithelia is in a healthy condition (C) and can partially protect against infections to a certain extent; the surfactant has a pH of 5 and is liquid so that macrophages can move about and engulf viruses, bacteria and particulates. The lung protection shield against infections is working. When living in a polluted surrounding with wrong air ionization (B), the surfactant gets a wrong pH value (pH value = 6) and becomes more rigid so that macrophages cannot move easily about and attack and engulf viruses and bacteria (D). Viruses can also invade the body through cracks. The pulmonary surfactant cannot protect any more against infections. Viruses and bacteria get into the body. Critical patients may die (G)

The treatment of the patients Nefeli and Sophie can be followed up on a video film with the heading 'From brain repair to Covid-19 treatment via Coordination Dynamics Therapy' [27].

No sign of long-term treatment of covid-19 infections around the world and the lack of basic medical (human) research

It has been published that more has to be done than just to develop a vaccine against covid-19 viruses [21, 27, 28]. The vaccine efficiency will be much less than 100% and the side effects of the drugs will only be known in the future. The side effect of the pain killer Contergan was that babies were born only with fingers instead of arms. Sometimes Contergan adults come to conferences or exhibitions to warn of drug side effects.

For a long-term treatment of covid-19 infections, especially the functions of the lung have to be improved to partly protect against covid-19 and other infections. The lung is the first protective shield against infections (Fig. 2.31). Already 15% of the covid-19 infections are due to environmental pollution. Forests have to be planted around the world for improving the breathing air. Pollution and wrong ionization of the breathing air change the pH value of the surfactant of the lung from 5 in the direction of 6 and ruins the first protective shield against covid-19 infections (Fig. 2.31) with the consequence that the immune system of the surfactant is not working anymore and that the surfactant becomes crackly to allow viruses to penetrate the lung epithelia (Fig. 2.31D). Ventilation systems must offer breathing air with negative ionization to keep the pH at 5. Fresh clean air with the natural negative ionization is the best for breathing. Climatization systems are the breading places for viruses and bacteria. To stop the climatization system is insufficient, also the outlets have to be covered to stop viruses and bacteria to come out. Trees have to be planted around schools to improve the breathing air for pupils at school. Generally, the hygiene has to be improved. Handles and hand rails have to be, for example, made of brass which is bacteriostatic. Also viruses will have problems to survive on clean brass. In Germany and Switzerland, the Author has not seen any yellow-looking handles so far. For cleaning the hands, soap is best because the soap ruins the lipid membrane of viruses so that they cannot attach to cells anymore and washing the hands with soap does not ruin the healthy bacteria of the skin for protection. Whereas disinfections kill pathologic and healthy microbes of the skin. Specific knowledge seems not to be of interest to the world society. Research progress is ignored.

Apart from the lockdowns, nothing seriously has been done so far to stop infections on the long-term. Patients suffer or die because they are afraid to go to physicians. The Author cannot look sufficiently for his patients, because they are afraid to see him or the lockdown is blocking the consultation. His patient with the brain tumor (oligodendroglioma WHO III) is at high risk to die, because the Author cannot supervise him for an optimal therapy to inhibit cancer regrowing [21]. Supervising the patient Nefeli via telephone is also not working. She needs direct training with the Author.

The lack of qualified human (medical) research for a few decades, apart from statistics and a few exceptions, is one reason for the covid-19 pandemic. The pandemic is therefore self-made. Only qualified medical research opens new possibilities of treatment.

The restrictions of basic human right are ethically only justified, if the mistakes of medical research of the past are uncovered and investments in infrastructure and implementation of the clinical research, apart from statistic, are executed. Biological research is no substitute for human research. With respect to spinal cord injury, in goldfish the spinal cord is regenerating by itself.

REFERENCES

1. Schalow, G. (2019). Regeneration of the human spinal cord via coordination dynamics therapy. Peertechz Publications, 97 pp. eBook.
2. Weiss P and Brown PF (1941) Electromyographic study on recoordination of leg movements in poliomyolitis patients with transposed tendons. Proceedings of the Society for Exper. *Biology and Medicine*, 48, 384-387.

3. Sperry RW (1945) The problem of central nervous reorganosation after nerve regeneration and muscle transposition. *Quart. Rev. Biol.,* 20, 311-369.
4. Sperry RW (1947) Effect of crossing nerves to antagonistic limb muscles in the monkey. *Arch. Neurol. Psychiat.* Chicago, 58, 452-473.
5. Schalow, G. (2002). Stroke recovery induced by coordination dynamic therapy and quantified by the coordination dynamic recording method. Electromyogr. Clin. Neurophysiol. 42, 85-104.
6. Schalow, G. (2002). Improvement after traumatic brain injury achieved by coordination dynamic therapy. Electromyogr. Clin. Neurophysiol. 42, 195-203.
7. Schalow, G. and Jaigma, P. (2006). Improvement in severe traumatic brain injury induced by coordination dynamics therapy in comparison to physiologic CNS development. Electromyogr. Clin. Neurophysiol. 46, 195-209.
8. Schalow, G. (2002). Recovery from spinal cord injury achieved by 3 months of coordination dynamic therapy. Electromyogr. Clin. Neurophysiol. 42, 367-376.
9. Schalow, G. (2003). Partial cure of spinal cord injury achieved by 6 to 13 months of coordination dynamic therapy. Electromyogr. Clin. Neurophysiol. 43, 281-292.
10. Schalow, G., Jaigma, P. and Belle, V.K. (2009). Near-total functional recovery achieved in partial spinal cord injury (50% injury) after 3 years of coordination dynamics therapy. Electromyogr. Clin. Neurophysiol. 49, 67-91.
11. Schalow, G. (2010). Cure of urinary bladder functions in severe (95%) motoric complete cervical spinal cord injury in human. Electromyogr. Clin. Neurophysiol. 50, 155-179.
12. Schalow, G. (2006). Cerebellar injury improvement achieved by coordination dynamics therapy. Electromyogr. Clin. Neurophysiol. 46, 433-439.
13. Schalow, G., Jaigma, P. (2005). Cerebral palsy improvement achieved by coordination dynamics therapy. Electromyogr. Clin. Neurophysiol. 45, 433-445.
14. Schalow, G. (2006). Hypoxic brain injury improvement induced by coordination dynamics therapy in comparison to CNS development. Electromyogr. Clin. Neurophysiol. 46, 171-183.
15. Schalow, G., Pääsuke, M., Ereline, J. and Gapeyeva, H. (2004). Improvement in Parkinson's disease patients achieved by coordination dynamics therapy. Electromyogr. Clin. Neurophysiol. 44, 67-73.
16. Schalow, G. and Nyffeler, T. (2001). Koordinationsdynamik-Therapie: Myelomeningozele (Spina bifida). Physiotherapie.
17. Schalow, G. and Nyffeler, T. (2000). Koordinatiosdynamik-Therapie: Skoliose. Physiotherapy.
18. Schalow, G. (2013). Human Neurophysiology: Development and Repair of the Human Central Nervous System. Nova Science Publishers, Inc, Hauppauge NY, USA, 734 pp.
19. Schalow, G. (2019). Permanent coma patient re-learned to speak via Coordination Dynamics Therapy. Arch. Clin. Med. Case Rep. 3(2), 33-50.
20. [20] Schalow, G. (2017) Breast cancer growth inhibition via Coordination Dynamics Therapy. In: "Horizons in Cancer Research. Volume 68". Editor: Hiroto S. Watanabe. Nova Science Publishers, Inc, Hauppauge NY, USA, pp. 125-151.
21. Schalow, G. (2020). Anaplastic oligodendroglioma WHO III brain cancer-patient recovered following operation, radiation and chemotherapy through Coordination Dynamics Therapy, which is also a Covid-19 treatment without ventilator. Int. J. Med. Clin. Imaging 5(2): 165-210.
22. Schalow, G. and Lang, G. (1987). Recording of Single Unit Potentials in Human Spinal Nerve Roots: a New Diagnostic Tool. Acta Neurochir. 86, 25-29.
23. Schalow, G. (2005). Phase and frequency coordination between neuron firing as an integrative mechanism of human CNS self-organization. Electromyogr. Clin. Neurophysiol., 45: 369-383.
24. Schalow, G. (2006). Surface EMG- and coordination dynamics measurements-assisted cerebellar diagnosis in a patient with cerebellar injury. Electromyogr. Clin. Neurophysiol. 46: 371-384.
25. Schalow, G. (1993). Spinal oscillators in man under normal and pathologic conditions. Electromyogr. Clin. Neurophysiol. 33: 409-426.
26. Schalow, G. (2010). Scientific basis for learning transfer from movements to urinary bladder functions for bladder repair in patients with spinal cord injury. Electromyogr. Clin. Neurophysiol. 50, 339-395.

27. Schalow, G. (2020). From brain repair to Covid-19 treatment via Coordination Dynamics Therapy. (Video film contains therapy movements of patients' recent publications). Video conference August 19, 2020. (Download from www.coordination-dynamics-therapy.com).
28. Schalow, G. (2020). Classification and Identification of Human Peripheral Nerve Fibers by Conduction Velocity, Nerve Fiber Diameter and Natural Firing Patterns with Consequences for CNS Repair and Covid-19 Infection Treatment. Int. J. Med. Clin. Imaging 5(3): 231-314.

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This chapter is an extended version of the article published by the same author(s) in the following journal.
Advances in Public Health, Community and Tropical Medicine, 2011(01), 2021.

Chapter 3
Print ISBN: 978-93-5547-205-2, eBook ISBN: 978-93-5547-216-8

Cure-like Brain-repair in a Girl with Atrophied Cerebellum and Pons through Coordination Dynamics Therapy

DOI: 10.9734/bpi/mono/978-93-5547-205-2/CH3

ABSTRACT

The cerebral palsy girl Sophie had from birth an atrophy of the cerebellum and ponds. At an age of 5.5, Coordination Dynamics Therapy was started. At the beginning, Sophie was incontinent and her speech was very poor. She could not stand, walk, run or jump. When falling, her protection automatism patterns were not working. The first fundamental progress in repair was achieved when the protection automatisms appeared in Sophie at an age of 6.5 years. The parents were not so much afraid anymore when trying to make her walking and Sophie tried now to walk by herself. The protection automatisms became operational at a time when she became able to exercise by herself on a special coordination dynamics therapy device. When the protection automatism occurred, the learning to walk became much easier and less risky. Sophie was not afraid anymore to fall and she tried herself now to walk without falling and she liked it. At an age of 8 she was able to walk without falling. Sophie's trot gait crawling improved. The pace gait crawling became possible with poor performance. At an age of 9, Sophie could creep, crawl, upright, walk, jump and play with a ball. She was fully continent. Her speech had improved, so that the Author started to understand her. Her writing got better and her higher mental functions improved. She still had some problems with the balance, but she managed without falling. She was not able to run. The mother, teacher by herself, taught her at home. Through 6 years of CDT, at an age of 12 years, Sophie could fully manage the balance. She became able to run and jump freely and walk to a 1km distant supermarket for shopping.
Sophies cerebellar and pons repair is compared with the repair of a traumatic cerebellar and pons injury and her repair-stimulated development is compared with the development of healthy children in the age range between 3 and 18 years, quantified by coordination dynamics values and the ontogenetic landscape for locomotion, based on the System Theory of Pattern formation. Sophie could not fully catch-up so far with the normal development. Further therapy is needed. The health of normal pupils could be enhanced if the training on the special coordination dynamics therapy device would be included in school sport.

Keywords: Human repair-neurophysiology; Electrophysiology; Single-nerve fiber action potentials; Surface EMG; Oscillatory firing; Phase and frequency coordination; Coordination dynamics therapy; Cerebellum repair; Ontogenetic landscape for locomotion.

3.1 INTRODUCTION

It has been shown that Coordination Dynamics Therapy (CDT) can improve or repair central nervous system (CNS) functioning after stroke [1], traumatic brain injury [2, 3], spinal cord injury (SCI) [4-8], cerebellar injury [9], cerebral palsy [10], hypoxic brain injury [11], in Parkinson's disease [12], spina bifida (myelomeningocele) [13] and scoliosis [14]. Speech had been induced and improved in a patient with severe cerebral palsy [15]. A permanent coma patient could be brought out-of-coma and relearned to speak [16]. Cancer grows could be inhibited through CDT [17, 18]. Cardio-vascular performance could be improved. There is indication that the general health can be improved via CDT to live longer with a better quality of life for 10 to 20 years.

I this case report, it will be shown that, based on human repair-neurophysiology, the cerebral palsy girl Sophie with an atrophied cerebellum and pons could nearly be cured from her malformation through the movement-based learning therapy called CDT. Such great repair of a malformation became possible through on an efficient human science-based CNS repair method, administered aggressively with up to 20 hours therapy per week for 6 years.

This powerful repair in cerebral palsy indicates that disabilities are diseases, which can partly be cured through movement-based learning, especially in children under 10 years of age. The problem with such learning therapy is that there is a lot of mental discipline necessary for the family and the patient. No real help is coming from the mainstream medicine. With respect to the repair of the CNS, mainstream medicine is something like 30 years out-of-date. Too much research and health insurance money is wasted in inefficient treatments. Human repair-neurophysiology is not organized and real expert knowledge is not of interest to the society. Medical faculties of universities are not trying to get up to date for teaching and medical research. Movement-based learning is besides drug therapy and operations a third leg of medicine. Since the nervous system is involved in nearly all body functions, an improvement of nervous system functioning will improve the health in general.

In the Method, the human-science-based CDT is shortly introduced and applied to the repair of the CNS, including the cerebellum and pons. It will be shown that Sophie got a senseful life through human neuroscience. In the Results, the improvement of CNS functioning through CDT is displayed step by step. In the Discussion, the repair of the atrophy of cerebellum, pons, and may be some other malformed CNS structures, is compared with the repair of a traumatic cerebellum and cerebrum injury. The repair-induced development of Sophie is compared with the development of the healthy brother and healthy girls and boys, quantified by the low-load coordination dynamics values.

3.2 METHOD

3.2.1 Human Neurophysiology

With the single-nerve fiber action potential recording method, single-nerve fiber action potentials can be recorded from sacral nerve roots, running in and out of the spinal cord (Fig. 3.1) [19].

By measuring the conduction times and with the known electrode pair distance of 10 mm, conduction velocity distribution histograms were constructed in which the myelinated nerve fiber groups larger than 4μm could be characterized by group conduction velocity values (Fig. 3.2). After the recording, morphometry was performed. Distributions of nerve fiber diameters were constructed and nerve fiber groups were characterized by the peak values of asymmetrical distributions (Fig. 3.2). By correlating the peak values of the conduction velocity distributions with those of the diameter distributions, obtained for the same root, a classification scheme was constructed of the human peripheral nervous system (Fig. 3.3) [20, 21]; the only existing one for human peripheral nerve fibers.

This classification and identification scheme represents a solid basis for classifying and identifying nerve fiber groups in the human peripheral nervous system (PNS) and analyzing central nervous system (CNS) functions at the single-neuron level. It became thus possible to record natural impulse patterns simultaneously from identified single afferent and efferent nerve fibers and to analyze self-organizing mechanisms of the human CNS under physiologic and pathologic conditions.

The most important finding with the single-nerve fiber action potential recording method was that nerve cells in the human CNS are organizing themselves through “Phase and Frequency coordination” [22, 40] (Figs. 3.6, 3.50). In nerve fibers, this phase and frequency coordination can easily be measured, because the three motoneuron types fire for high activation oscillatory [23] and offer in this way a structure to which the timed firing of neurons can be related to. Since the α_2-motoneuron oscillations are most stable, firing phases of neurons can be related best to the α_2-motoneuron firings.

Fig. 3.4 shows schematically the oscillatory firing patterns of the three kinds of motoneurons and the muscle fiber types they innervate.

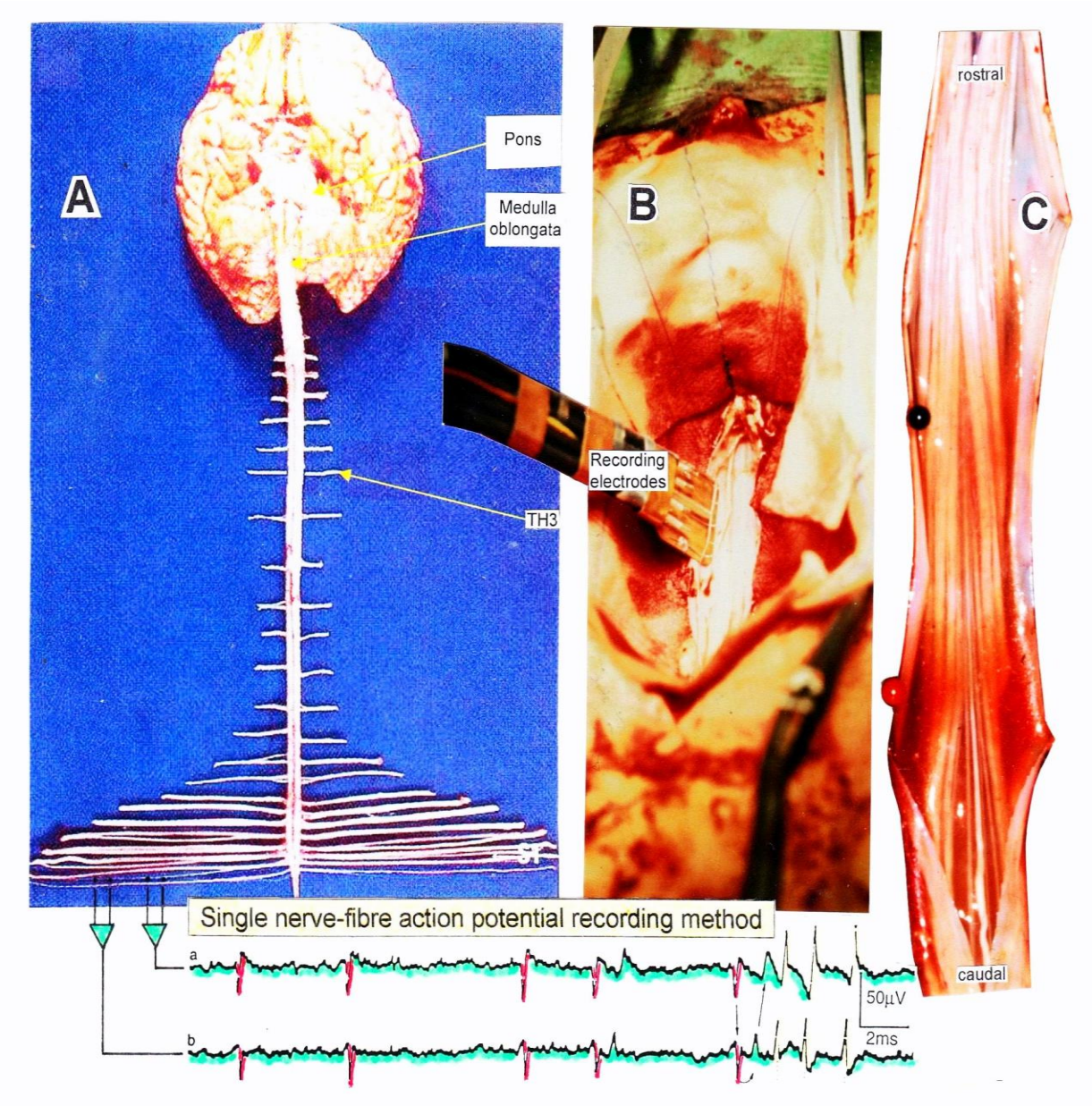

Fig. 3.1. Layout of the recording of single-nerve fiber action potentials to analyze the self-organization of neuronal networks of the human CNS under physiologic and pathophysiologic conditions. A, B, C. By recording with two pairs of platinum wire electrodes (B) from sacral nerve roots (cauda equina, C) containing between 200 and 500 myelinated nerve fibers, records were obtained in which single nerve-fiber action potentials (APs) were identified from motoneurons (main AP phase downwards) and afferents (main AP phase upwards). A. Human CNS with the schematic illustration of the recording layout and an original record of single nerve-fiber action potentials. Note the time calibration of 2ms. B. Intraoperative recording layout (when implanting a bladder stimulator) with two pairs of wire electrodes and one temperature sensor. A thin nerve root is positioned over the platinum wire electrodes. C. Dissection of the human cauda equina. At the caudal end, the filum terminalia and thin nerve roots can be seen. Dissections of the Author apart from the laminectomy in B

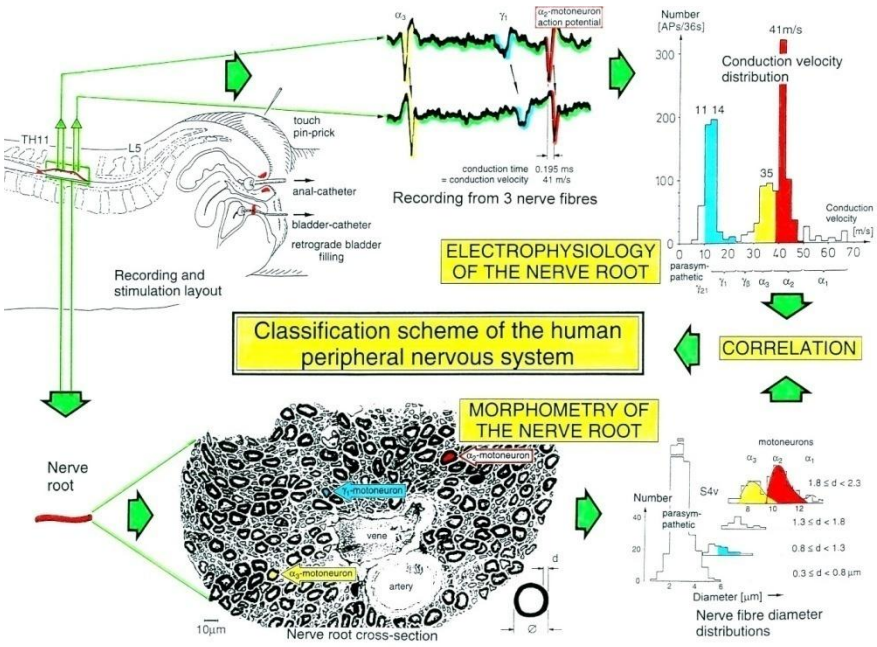

Fig. 3.2. Development of a classification scheme for human peripheral nerve fibers. Conduction velocities (V) and nerve fiber diameters (∅) of afferent (from receptors) and efferent (motor) nerve fiber groups in normal humans and in patients with a traumatic SCI for 0.5 to 6 years

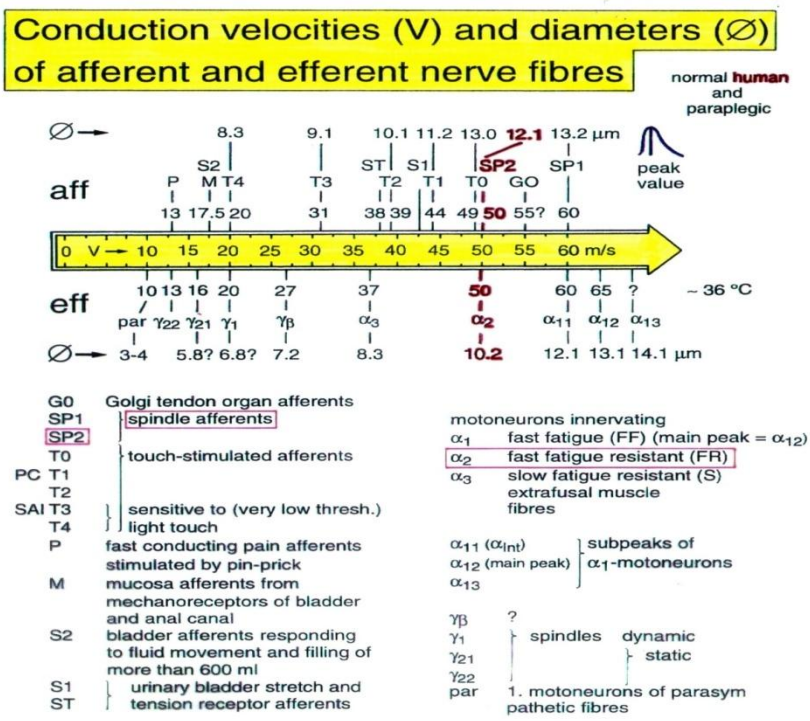

Fig. 3.3. Classification scheme for human peripheral nerve fibers. Conduction velocities (V) and nerve fiber diameters (∅) of afferent and efferent nerve fiber groups in normal humans and in patients with a traumatic spinal cord injury for 0.5 to 6 years. The splitting of the α_1-motoneurons into the 3 subgroups, α_{11}, α_{12}, α_{13}, has not yet been confirmed. This is the only existing classification scheme for human peripheral nerve fibers!

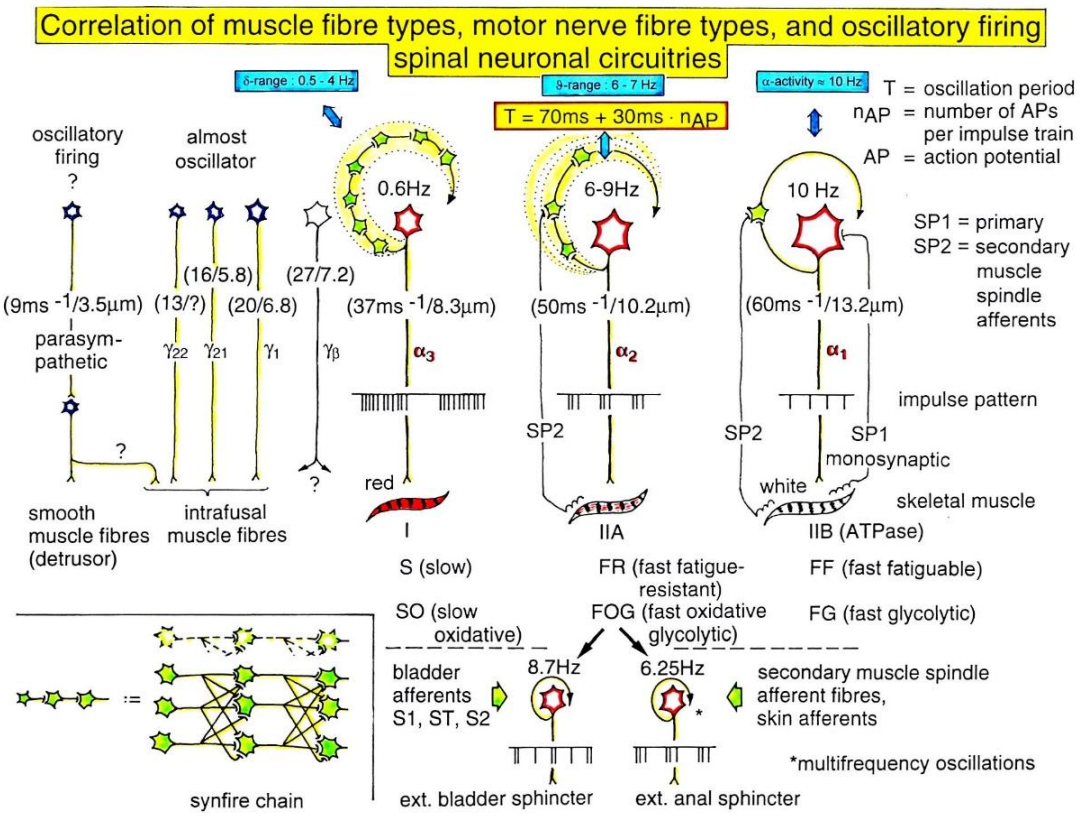

Fig. 3.4. Correlation of muscle fiber types, motor nerve fiber types, and oscillatory firing spinal neuronal networks (oscillators), based on histochemical, morphological and neurophysiological properties. This figure provides a simplified correlation between muscle fiber, motoneuron and sacral oscillator types. No additional subtypes have been included. The existence of α_1-motoneuron (FF) oscillators firing at 10 Hz has been predicted and they have been identified in paraplegics. α = motoneuron, γ_1, γ_2 = dynamic and static fusimotors, parasympathetic = parasympathetic preganglionic motoneuron. S1, ST, S2 = stretch, tension and flow receptor afferents.

By comparing CNS functioning in brain-dead humans (where the spinal cord is functioning rather physiologically) and patients with spinal cord injury, injury-induced changes of CNS functioning can be measured and partly repaired. Mainly the phase and frequency coordination of neuron firing becomes impaired following injury. This impaired coordination among neuron firings can efficiently be repaired through exercising on the special CDT device (Figs. 3.19-3.21).

The drawing back of the single-nerve fiber action potential recording method is that it is an invasive recording method. But with the surface electromyography (sEMG) [24] one can record non-invasively coordinated firing among motoneurons via their motor units if one records from suitable patients, like incomplete spinal cord injury patients, when a certain muscle is only innervated by a few motoneurons.

In Fig. 3.5, the recordings from motoneurons and motor units are compared. The firing patterns of α_1, α_2 and α_3-motoneurons can easily recorded with the single-nerve fiber action potential recording method but not with the sEMG (Fig. 3.5). From spinal cord injury patients, on the other hand, single-motor unit APs can be easily recorded from α_1 motor units but not from α_2 and α_3 motor units (Fig. 3.5), because their AP amplitude seems to be too small. Clinical sEMG recordings therefore show mainly the activity of α_1 motor units. The generation of motor patterns of α_1-motoneuron firings with increasing load and the phase and frequency coordination among single-motor unit firings can be recorded with sEMG (Fig. 3.6).

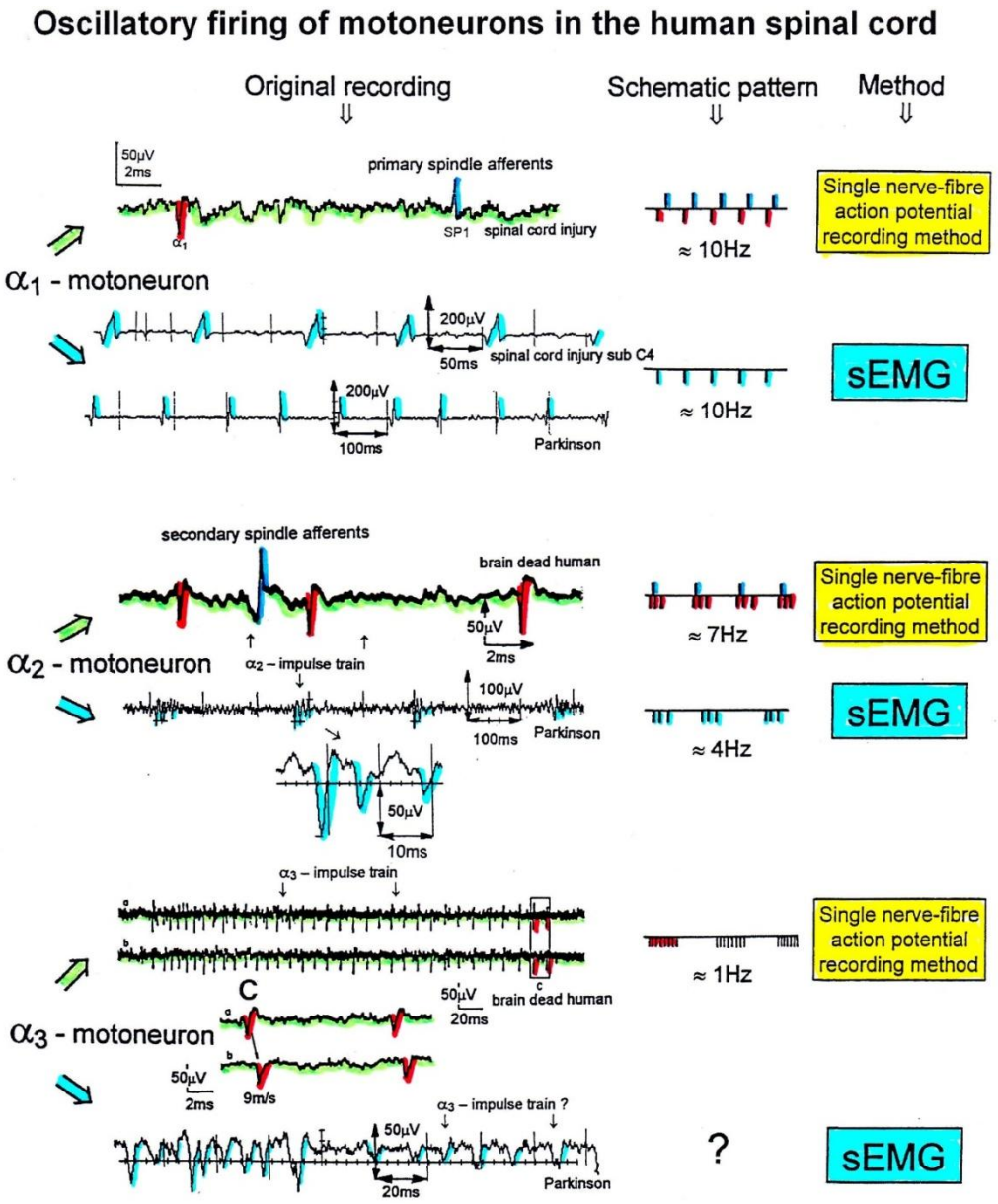

Fig. 3.5. Oscillatory firing patterns of α_1, α_2, and α_3-motoneurons recorded from motoneuron axons with the single-nerve fiber action potential recording method and by surface electromyography (sEMG) from FF, FR, and S-type motor units. The left panel shows original recordings, the middle panel the schematic patterns; the recording methods are indicated on the right side. The recordings were taken from patients with spinal cord injury and Parkinson's disease and from brain-dead humans

The neural networks of the human brain, including the cerebellum, organize themselves by phase and frequency coordination among neuron firings and neural subnetworks as for example the network oscillators of which the motoneuron is a part. This coordination is achieved by the organization tendencies of the network, the descending impulse patterns from the brain and the spatiotemporal afferent impulse patterns from the periphery.

If the premotor spinal oscillators would not coordinate their firing and synchronize their firing for longer periods of time, tremor would occur. Such pathologic synchronization can be observed in patients with Parkinson's disease [25, 40]. If the neural networks are damaged by trauma, degeneration or

malformation, the coordination between neuron firings becomes impaired and has to be repaired by movement-based learning (CDT). Drugs and operations cannot repair neural network functioning.

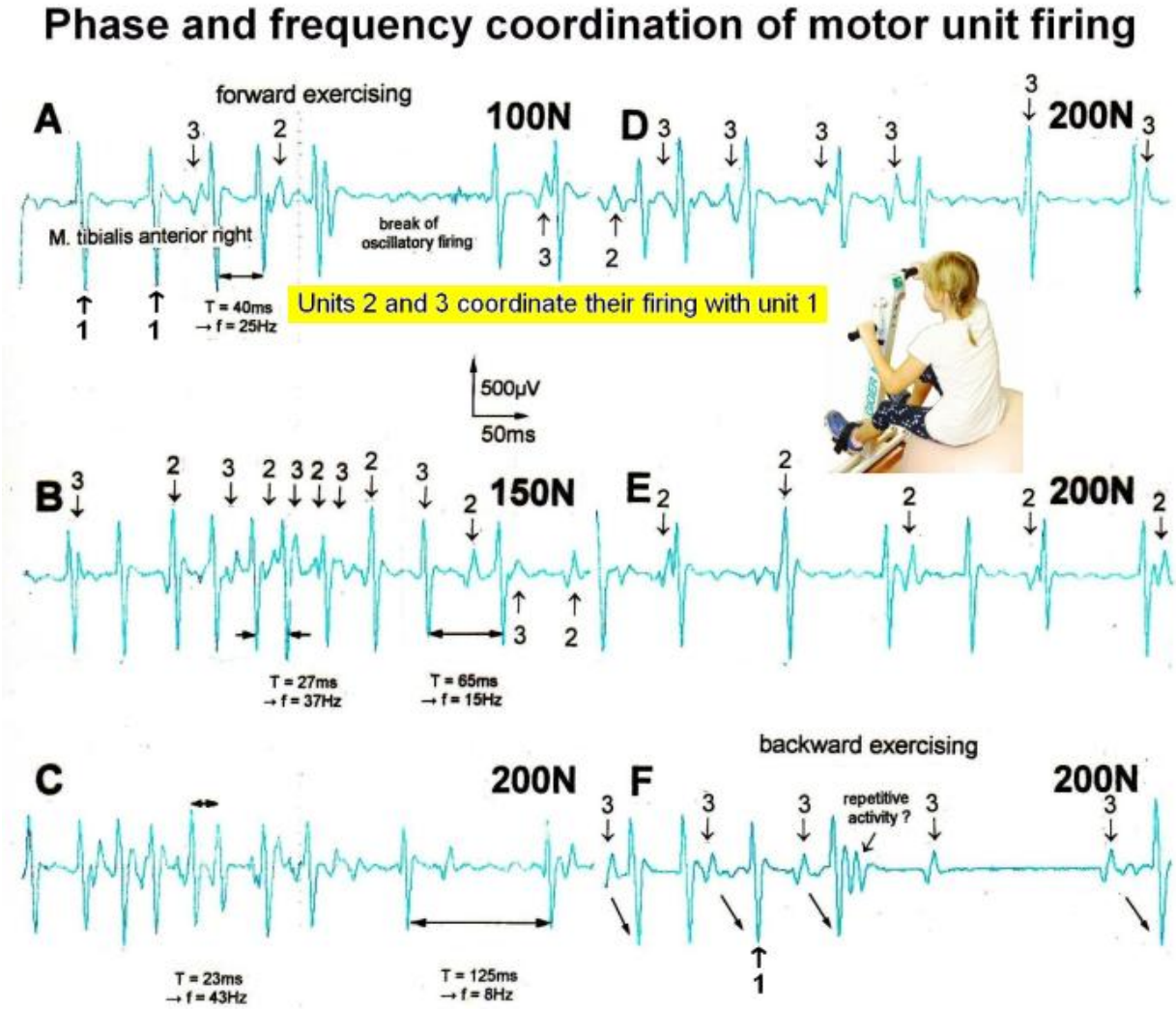

Fig. 3.6. Phase and frequency coordination between oscillatory firing of 3 motor units (FF-type, motor units '2' and '3' are partly marked) during the generation of a motor program when exercising on the special coordination dynamics therapy device at loads increasing from 100 to 200N. Oscillation periods (T) and oscillation frequencies (f [Hz]) of oscillatory firing motor unit 1 (largest motor unit) are partly indicated. 'C, F' soleus electrodes shifted to gluteus muscles. In 'F', some coordination's between motor unit '3' and '1' are marked

Improvement of the stability and exactness of phase and frequency coordination to allow specific patterns formation and learning transfer (System Theory of Pattern Formation)

The importance of stable and exact phase and frequency coordination, to allow specific pattern formation and in consequence **learning transfer** [26] to other patterns, can be understood at the collective variable level (System Theory of Pattern formation [27-29]) and at the neuron level. The behavioural information F_{inf} of the coordination pattern dynamics, characterized by equations of motion of collective variables, $dX/dt = F_{intr}(X) + \sum c_{inf}F_{inf}(X,t)$, affect the whole coordination pattern dynamics, including stability, rather than only certain coordination patterns. If the behavioural information includes the exercising of extremely coordinated, integrative movements, like exercising on the special CDT device for turning, then the quality of CNS self-organization can be enhanced by improving the exactness of self-organization, namely the precision of phase and frequency

coordination between neuron and neural assembly firings. By improving the precision of organization of the intrinsic dynamics $F_{intr}(X)$, that is, the specific variability of the injured networks, certain patterns do then already reappear. In the patient Sophie, the protection automatisms appeared with the improvement of CNS functioning, first time in her life.

Neurons often serve more than one network pattern at the same time by time sharing of neuron firing and, in this way, give rise to learning transfer among the activated patterns. If subnetworks are improved in the organization of one pattern, the organization of the other pattern will also improve. Neurons involved in the organization of breathing and activating intercostal muscles, for example, are also involved in the organization of trunk stability. By reducing the spasticity of the trunk (in patients with Parkinson's disease), the breathing will also improve. Similarly, sphincteric motoneurons are involved in continence and pelvic floor weight bearing. If during pregnancy the pelvic floor is not trained, sometimes incontinence occurs. This stress incontinence after birth can be repaired by learning transfer from coordinated movements. By mainly exercising on the special CDT device and jumping on springboard, urinary bladder functions can be repaired by learning transfer in healthy women. Also the girl Sophie became continent in this way.

3.2.2 Measuring CNS Functioning by the Arrhythmicity of Exercising (Coordination Dynamics Value)

The impaired phase and frequency coordination at the single neuron level, the assembly level and the macroscopic level can be measured macroscopically when the patient is exercising on a special coordination dynamic therapy device (Figs. 3.19-3.21) on which arms and legs turn with a slightly different frequency (transmission 19 (arms) : 18 (legs)). The phase coordination between arms and legs is imposed by the device. The loss of phase and frequency coordination between arm and leg movements becomes visible and measurable by the arrhythmicity of turning. During a turning cycle the coordination between arms and legs changes between pace and trot gait and according to the difficulty of the coordination, the turning frequency increases and decreases. This frequency variation (df/dt; f = frequency) can be recorded, quantified and displayed on a computer screen (Fig. 3.27) and is called coordination dynamics value. CNS functioning is therefore measured though pattern change (continuous change from trot gait to pace gait) according to the System Theory of Pattern Formation.
During the functional reorganization of the injured CNS of patients, the relative phase and frequency coordination of neuron firing has to be entrained as exactly as possible by the movement induced afferent impulse patterns from the receptors (learning through feedback information) to restore coordination in the range between 3 and 5 milliseconds (approximate lengths of postsynaptic potentials). The device has therefore to impose the exercising patient a coordination in the millisecond range for the different coordination's of arm and leg movements between pace gait and trot gait. The easy pace and trot gait coordination's, but not the difficult intermediate coordination's, can often be performed by the patient easily. Therefore, the continuous change from the easy to the difficult coordination's and backwards diagnoses the capability of the CNS to organize easy and difficult organizational states. If the movement states can be easily generated by the neuronal networks of the CNS, then the frequency variation of turning is small during the turning cycle, and if the movement state is difficult to be organized by the CNS, then the frequency variation is large (the coordination dynamics value is large).

3.2.3 Unique Properties of Special CDT Devices

The special CDT device has three important properties. First, the patient performs coordinated arm, leg and trunk movements when exercising on it. The training of integrative patterns take care of that the pathologic organization cannot escape from repair by shifting to another part of the CNS and the whole CNS, including the injured parts, is reorganized so that other CNS parts can take function over through plasticity. Second, the device is extremely exact, so that the endplate potentials in the neural networks (approximately 5ms long) overlap, to improve the efficiency of organization. In spinal cord injury, for example, the transmission over the injury site will increase. Third, the coordination between arm and leg movements changes from pace to trot gait, imposed by the device. The intermediate coordination patterns between pace and trot gait are difficult to generate for the CNS neural networks.

If the patients CNS learns to generate these intermediate patterns, imposed by the device, then the neural networks have learned to function better in the deep complexity of CNS organization. The patient's nervous system learns by turning from the device, to function more physiologic through improving especially the phase and frequency coordination among neuron firings. This phase and frequency coordination can be measured by the single-nerve fiber action potential recording method (Fig. 3.50) invasively and by single-motor unit surface electromyography non-invasively (Fig. 3.6).

3.2.4 Motor Learning and Problem-solving Therapy

Because of atrophied cerebellum and pons in a patient, there are retarded, accelerated or deviant development of motor and other functions. Some functions may not develop at all, while others show only a decrease in variability. Both impaired and healthy parts of the brain mature over time and thus lead to increased complexity, which has direct repercussions on the quality of the learning (trial-and-error-elimination [30]) processes. Processes that in themselves are normal cannot bring about good results because some areas of the brain which are also necessary for the accomplishment of the particular motor function are deficient.

The well-known symptoms and signs of cerebral palsy in the first year of life (poverty of movements, stereotypy of posture and motility, inability to "discover" new motor possibilities, neglect of one extremity, stereotyped extension of the legs during vertical suspension, head-lag during the traction test or during sitting) can all be traced back to a lack of trial-and-error-elimination processes (learning) as a consequence of deficient brain structure. In the case of an inability to "discover" new motor possibilities, there may be a disturbance in the chain of events because errors are not recognized (or not eliminated), with the result that the processes stop prematurely [31]; the learning therapy has therefore to be administered continuously over longer times to run through the whole chain of events.
The System Theory of Pattern Formation of CNS development encompasses all areas of development and is derived from mathematics, physics, human neurophysiology, clinical research, and developmental psychology. The CNS is considered as one neuronal network. A new behavior is generated, which is dependent on the input of all subsystems. This behavior may have a characteristic that could not have been determined by evaluating the contributing behaviors individually [32].

The system repair approach is a "feed-forward system" that is self-correcting 'en route' rather than hardwired from the cerebral cortex. It also implies that all factors, subsystems, or structures contributing to the motor behavior (or patterns in general) are important and exert an influence on the outcome [32]. If the cerebellum and pons are atrophied in an infant, then many patterns become abnormal or do not exist. The higher centers can no longer control movements or other patterns sufficiently. But through movement-based learning, a self-correction 'en route' may partly compensate for the missing contribution of a subsystem in the way that other subsystems take functions over and/or the cerebellum and pons are partly repaired.

The problem-solving learning tries to repair sub-networks that are necessary for functioning and learning. By inducing trial–and-error-elimination processes in subunits of the normal developing nervous system, an optimal development is achieved [30]. To teach the injured CNS to repair itself by trial–and-error-elimination processes, the CNS has to recognize upon CDT which sub-networks, regulation units or sub loops are not functioning properly (or are missing) and to repair them by error elimination, including the possibility that other brain parts partly take functions over, and sub-networks build anew to a limited extent.

3.2.5 Functional Anatomy Pons and Cerebellum

The patient Sophie had the diagnosis of cerebral palsy with ataxia and speech developmental retardation. Because of a prolonged postnatal icterus, the basal ganglia may have been damaged. At an age of 4.5 years an MRI was performed to update the diagnosis. A severe cerebellar atrophy with accompanied atrophy of the ponds was found. Especially the cerebellar hemispheres and the vermis were atrophied. No pathology of the basal ganglia, no myelin sheath disturbance and no signs of postnatal ischemia were found. The CNS repair strategy of Sophie was therefore to concentrate on

the repair of the cerebellar and pons atrophy, even though other mild atrophies/injuries of other brain parts cannot be excluded.

The cerebellum (Fig. 3.7) is the central organ for fine motor control and modulates the activity of motor nuclear areas in the brain and spinal cord. Cerebellar injuries manifest themselves clinically with disturbance of movement, balance, speech and urinary bladder functioning.

Functionally and phylogenetically, the cerebellum is anatomically divided into three components: the vestibulocerebellum (flocculonodular lobe), the spinocerebellum (vermis and paravermian zone, it receives most of its afferent input from the spinal cord) and the cerebrocerebellum (the two cerebellar hemispheres). The cerebrocerebellum (youngest portion of the cerebellum) occurred during phylogenetic development with the expansion of the cerebrum and the transition to an upright stance and gait. The two cerebellar hemispheres have an intimate functional connection to the cerebral cortex, which projects to it by way of the pontine nuclei (Fig. 3.8).

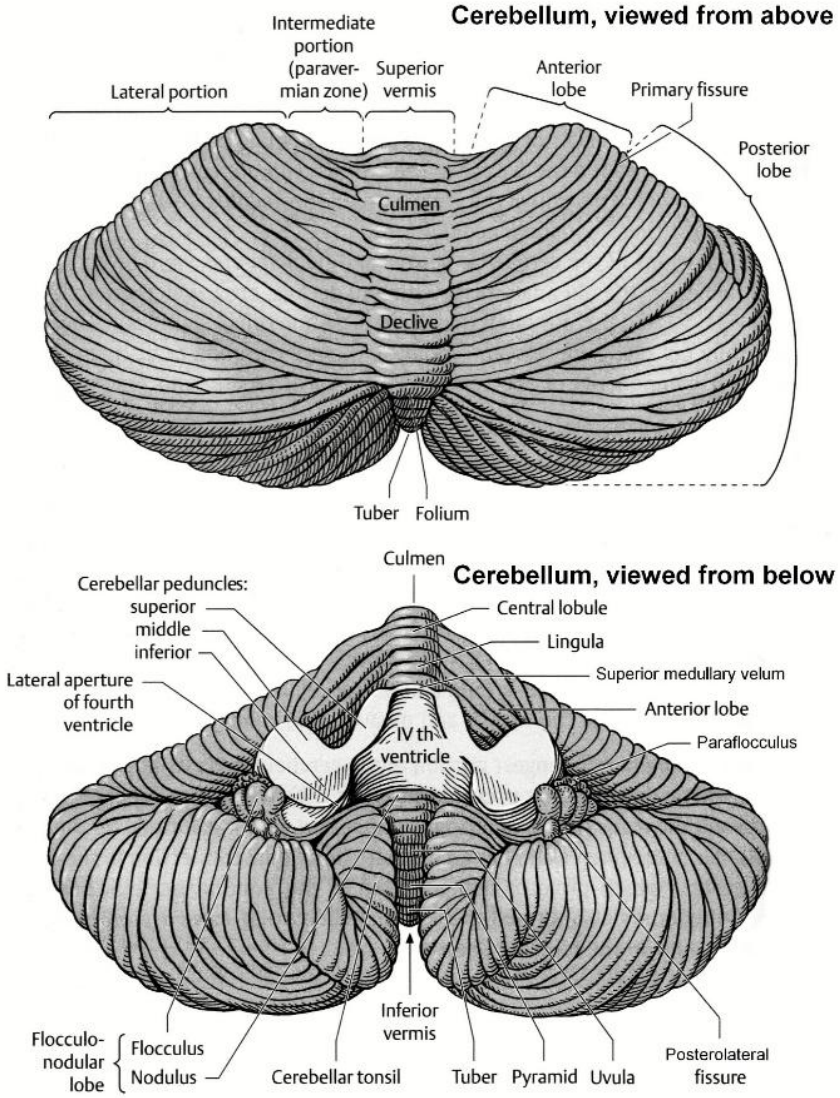

Fig. 3.7. Cerebellum. Above left side: division into vermis, pars intermedialis, and pars lateralis. Right side: division into vermis, anterior lobe, and posterior lobe. The anterior and posterior lobes are separated by the primary fissure. (from Duus [34])

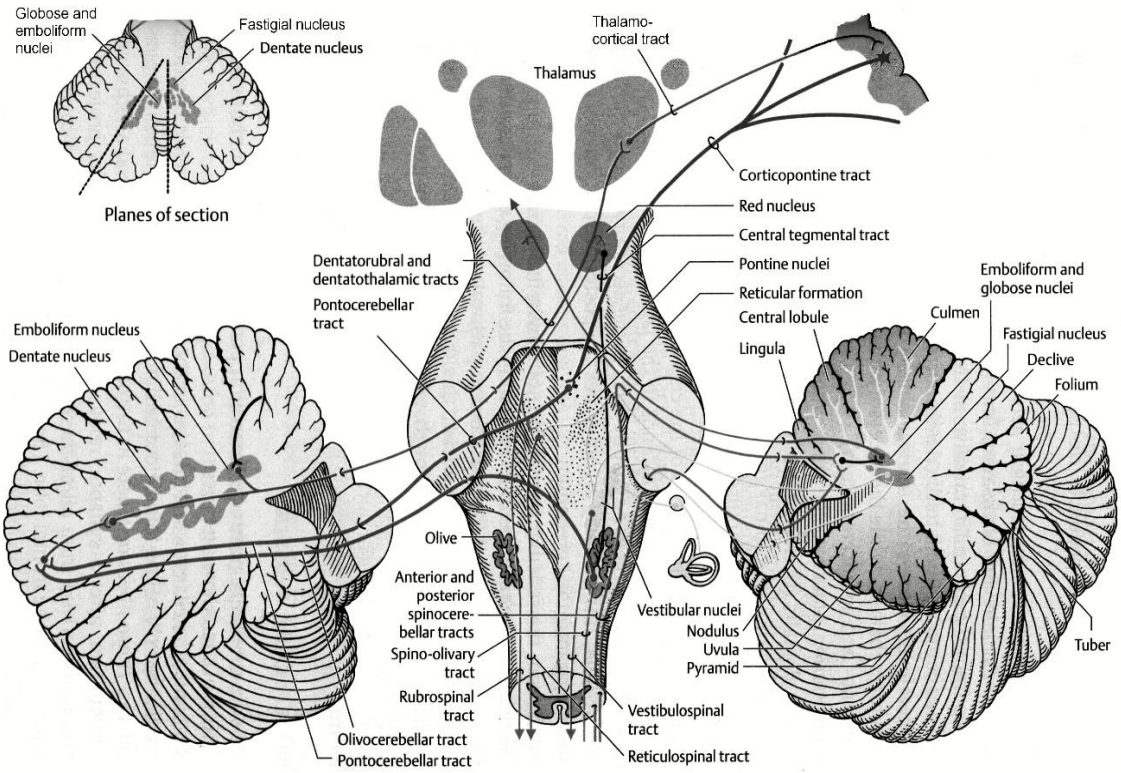

Fig. 3.8. Afferent and efferent connections of the cerebellum with other parts of the nervous system (from Duus [34])

The cerebellum may not only be responsible for fine motor control but may also store important movement automatisms. It processes information from multiple sensory channels (particularly vestibular sense, touch, proprioception, bladder fullness sense, vision and hearing), together with motor impulses, and modulates the activity of motor nuclear areas in the brain and spinal cord. Cerebellar injuries (and atrophy) manifest themselves clinically with disturbances of movement, balance, bladder functioning and loss of protection automatisms. The cerebellum plays a major role in motor learning and memory. The disturbance of movement and balance includes the disturbance of cerebellar regulatory circuits which have to be repaired.

Important regulatory circuits do exist. A long regulatory loop is created, travelling from the cerebral cortex to the pontine nuclei, cerebellar cortex, dentate nucleus, thalamus, and finally back to the cortex (Fig. 3.9A, D). The cerebellum gets an efference copy of motor activity for processing. A further regulatory circuit comprises the triangle of Guillain and Mollaret, travelling from the red nucleus by way of the central tegmental tract to the olive, then to the cerebellum and back to the red nucleus (Fig. 3.9B). The cerebellum influences spinal motor function by many descending tracts (Fig. 3.10) including the rubrospinal and the reticulospinal tract (Fig. 3.9C).

The repair of the impaired phase and frequency coordination of neuron firing (Fig. 3.6) in the neural networks, when exercising on a special CDT device (Fig. 3.9D), means that also the coordinated firing of neurons in the regulatory circuits has to be repaired. Otherwise, the regulatory circuits cannot sufficiently regulate movement and other functions. Furthermore, the organization in the nuclei has also to be repaired with respect to the coordinated firing of their neurons. As will be shown below in the patient Sophie, the improvement of phase and frequency coordination of neuron firing had tremendous consequences for the improvement of her movements.

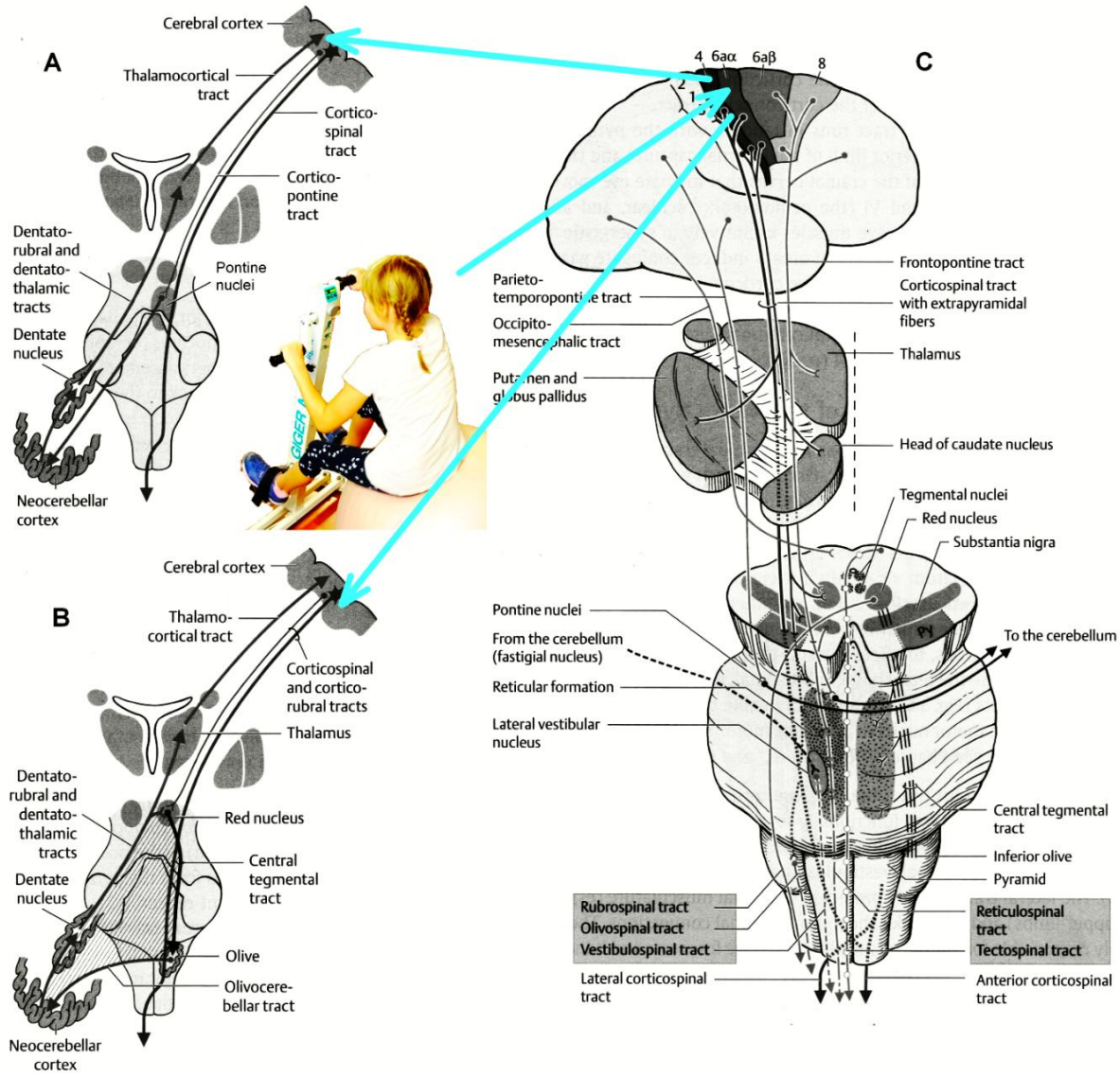

Fig. 3.9. Cerebellar regulatory circuits involving the pontine nuclei (A) and the olive (B, triangle of Guillain and Mollaret). The cerebellum influences spinal motor functions by way of fibers traveling from the red nucleus, reticular formation, olive, tegmental nuclei and vestibulocerebellum (C). A damage or atrophy of the cerebellum and ponds must have tremendous consequences for balance and walking performance. (from Duus [34]).

The **vestibulocerebellum**, the spinocerebellum and the cerebrocerebellum have different functions in the coordination of movement which become apparent in cerebellar injuries. It seems that if the cerebellar cortex is injured, other portions of the brain can assume some of the functions. If the deep cerebellar nuclei are impaired minimal recovery is likely to occur.

The vestibulocerebellum receives impulses from the vestibular apparatus carrying information about the position and movements of the head. Its efferent output influences the motor function of the eyes and body in such a way that equilibrium can be maintained in all positions and with any movement.

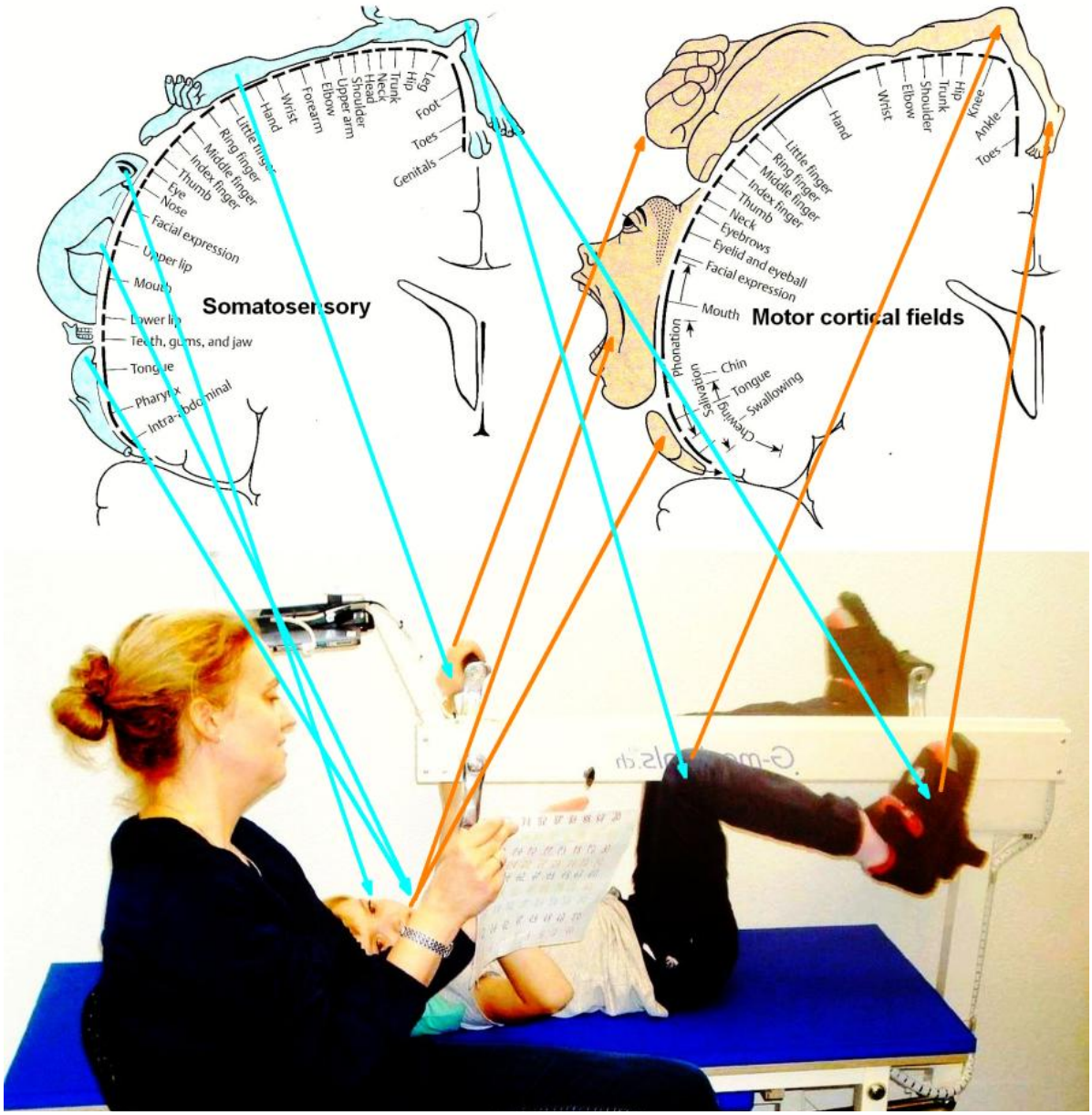

Fig. 3.9D. The cerebral palsy girl Sophie during exercising on a special CDT device. At the same time, the mother (teacher herself) is administering speech therapy to her. If Sophie would stop turning, because she has problems to perform two patterns at the same time, the mother could support the turning movement of Sophie with one hand (not doing in this moment). In such very integrative training setting, nearly the whole somatosensory and motor cortical fields are activated with their associated fields. Of course, the important cerebellar regulatory circuits (Fig. 3.9A, B) get also the integrative coordinated input for regulation. Such combination of movement and speech therapy is therefore very efficient for repair. Because the hand leavers pass through the field of vision of Sophie, speech, movement and vision are activated in coordination. - Cortical fields are taken from Penfield W and Rasmussen T, New York, 1950). - This special CDT device for measuring and therapy (int.pat.) is produced by the firm: Giger Engineering, Martin Giger dipl.Ing. ETH/SIA, Herrenweg 1, 4500 Solothurn, Switzerland, www.g-medicals.ch

The **spinocerebellum** controls muscle tone and coordinates the actions of antagonistic muscle groups that participate in stance and gait. Its efferent output affects the activity of the anti-gravity muscles and controls the strength of forces induced by movement (e.g., inertia and centrifugal force). Injuries of the anterior lobe and of the superior portion of the vermis in and near the midline produce ataxia of stance and gait. The gait ataxia (abasia) produced by such injuries is worse than the ataxia of stance (astasia). During the process of repair by learning, Sophie with an atrophy of the vermis, had more problems to learn to walk and run than to stand freely.

The **cerebrocerebellum** receives most of its neural input indirectly from extensive portions of the cerebral cortex, mainly Brodmann areas 4 and 6 (the motor and premotor cortex) via the corticopontine tract (Fig. 3.9A, C) but also, to a lesser extent, from the olivocerebellar tract (Fig. 3.9B). The cerebellum receives advance notice of any planned voluntary movement initiated in the cerebral cortex, so that it can immediately send modulating and corrective impulses to the motor cortex through the dentatothalamocortical pathway (Figs. 3.8, 3.9A). The dentate nucleus also projects to the parvocellular portion of the red nucleus. This dentate-rubro-olivo-cerebellar feedback loop (Fig. 3.9A) plays an important role in neocerebellar impulse processing.

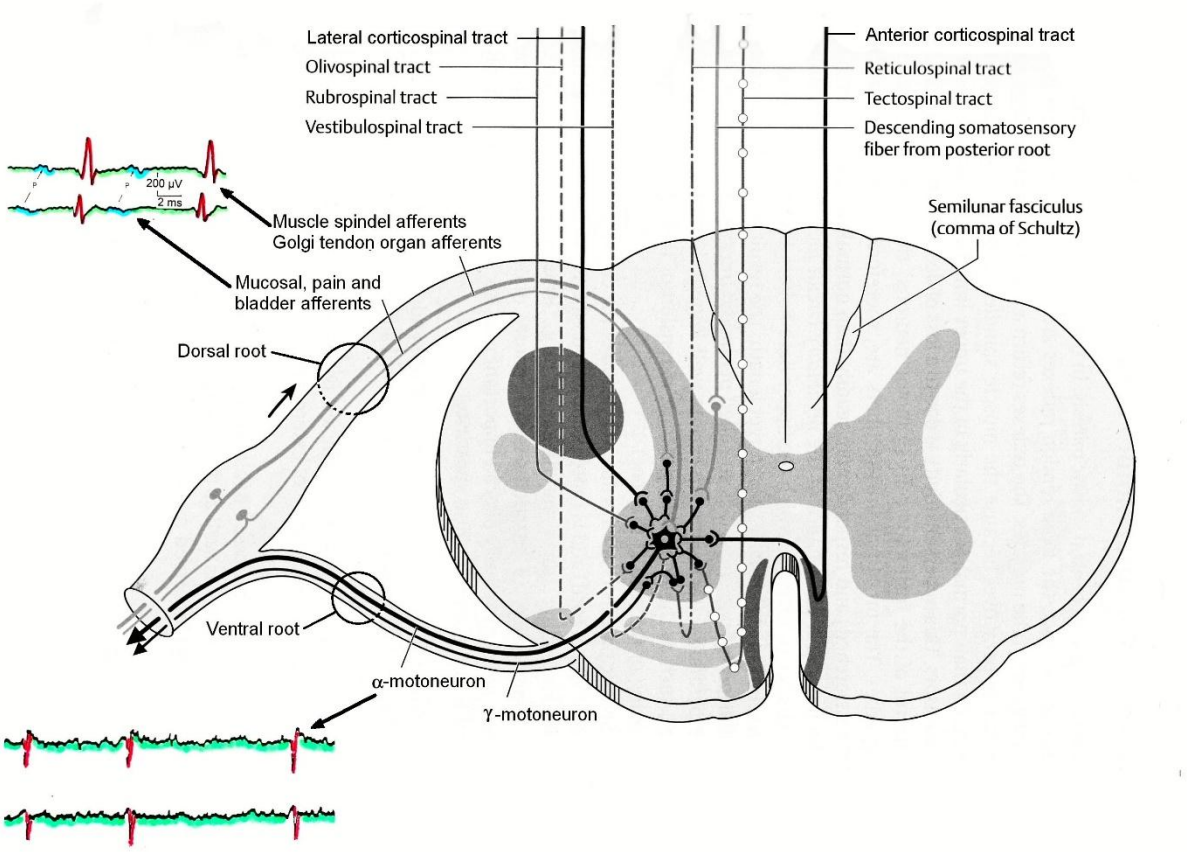

Fig. 3.10. Synapses of the descending motor tracts onto anterior horn motoneurons. The motoneuron is a summing point. It is getting many inputs including those from the periphery (reflexes) and from many descending tracts. The simultaneous input from the reticulospinal tract could give rise to α- and γ-motoneuron co-activation. In difference to the picture, dorsal and ventral nerve roots fuse before the ganglion (see Fig. 3.1A)

The complex connections of the cerebellum enable it to regulate all directed movements smoothly and precisely. By way of the very rapidly conducting afferent spinocerebellar pathways (Fig. 3.11), it continuously receives real-time information about the activity in the periphery. It can thus take action

to correct any errors in the course of voluntary movement to ensure that they are executed smoothly and accurately.

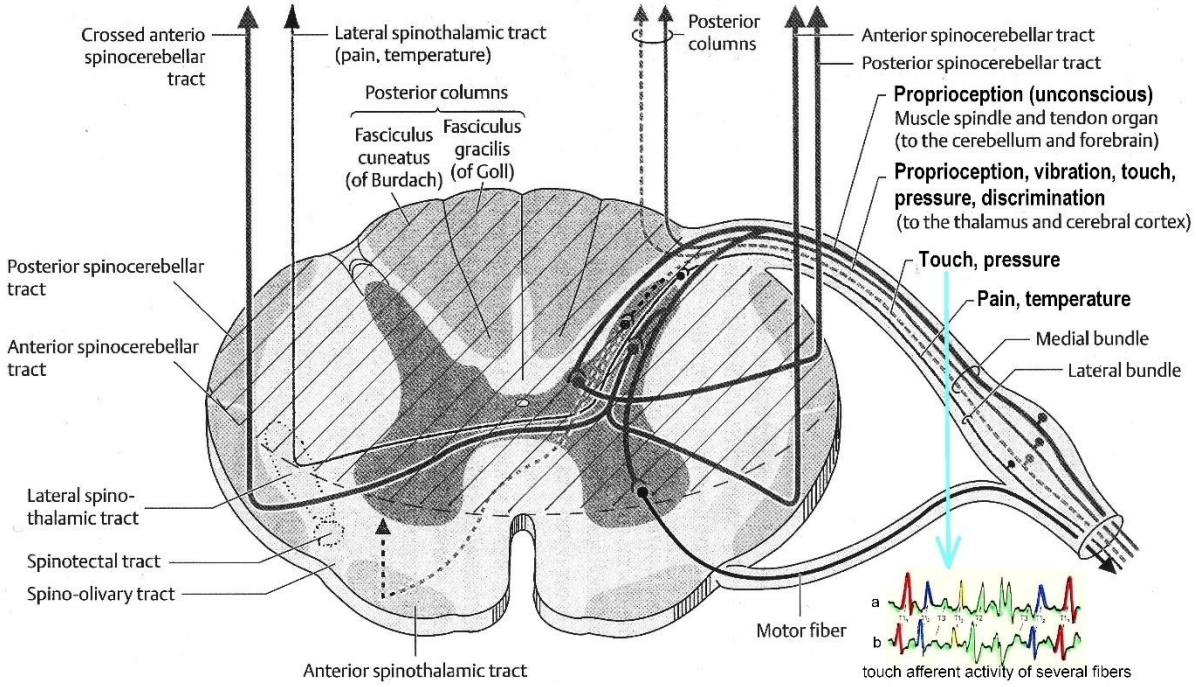

Fig. 3.11. Anterior and posterior spinocerebellar tracts (from Duus [34]). Single-nerve fiber activity of several touch fibers (conduction velocity ≈ 44m/s (Fig. 3.3)) are indicated, which may contribute to the spinocerebellar tracts because the conduction velocity is high. Primary spindle afferents (and α_1-motoneurons) conduct at a velocity of 60m/s (Fig. 3.3))

It was argued above that the phase and frequency coordination among neuron firing in the neural networks is efficiently improved when exercising on the special CDT device. More precisely with respect to cerebellum injury, the phase and frequency coordination between neuron firing is improved in regulation units like in Figs. 3.9A, B and in the organization patterns in the nuclei as for example in the dentate nucleus. The cerebellum obtains an efference copy of the performed movements via the pontine nuclei (Fig. 3.9A) and receives at the same time real time information about the motor activity in the periphery (muscles, tendons, joints; spinocerebellar tracts (Fig. 3.11)). Volitional movements and automatic movements can thus be performed smoothly and precisely.

With injury or atrophy of the cerebellum, the movements cannot any more performed smoothly and accurately. The impairment depends on the actual injuries of the cerebellum and pons nuclei/tracts.

Automatisms are absolute necessary for everyday life and make life easier. The automatisms creeping, crawling, up-righting, walking and running are used in CDT for nervous system repair. It is believed that inborn automatisms and learned automatisms are stored in the cerebellum and can be recalled from it at any time precisely, rapidly and relatively effortless. In cerebellum injury these inborn and learned automatisms are impaired or lost. In difference to the computer, the automatisms can be repaired by learning. In the language of computer, the automatisms can be re-learned by improving software and hardware as will be shown in the cerebral palsy girl Sophie.

Some theory of Coordination Dynamics Therapy, including original recordings of single-nerve fiber action potentials from human, and treatment of the patient Sophie can be followed up on a video film with the heading ‘From brain repair to Covid-19 treatment via Coordination Dynamics Therapy’ [33]. Actually, the new method of recording single-nerve fiber action potentials from human peripheral

nerve fibers was the main step to develop Coordination Dynamics Therapy for repairing the human CNS.

3.2.6 Repair Strategies at the Neuron Membrane and Genetic Level

The building of functions/patterns in the young cerebral palsy patient, first time in life, make it likely that excitation-neurogenesis coupling [35] contributed, stimulated through CDT.

1. Repair depends on learning and memory formation, mediated or supported by epigenetic mechanisms. Epigenetics is the interplay between genes and the environment resulting in phenotype and epigenetic landscape.

2. Epigenetic mechanisms, like DNA methylation, are probably sensors for movement-based learning and memory formation and fine modulators of neurogenesis though CDT (Fig. 3.12).

3. The epigenome consists of non-coding RNA and chromatin, a proteinaceous matrix surrounding DNA. The dynamic interactions of post-translationally modified chromatin proteins, covalently modified cytosines inside DNA and non-coding RNA define the complex pattern of gene expression beyond the four bases of DNA.

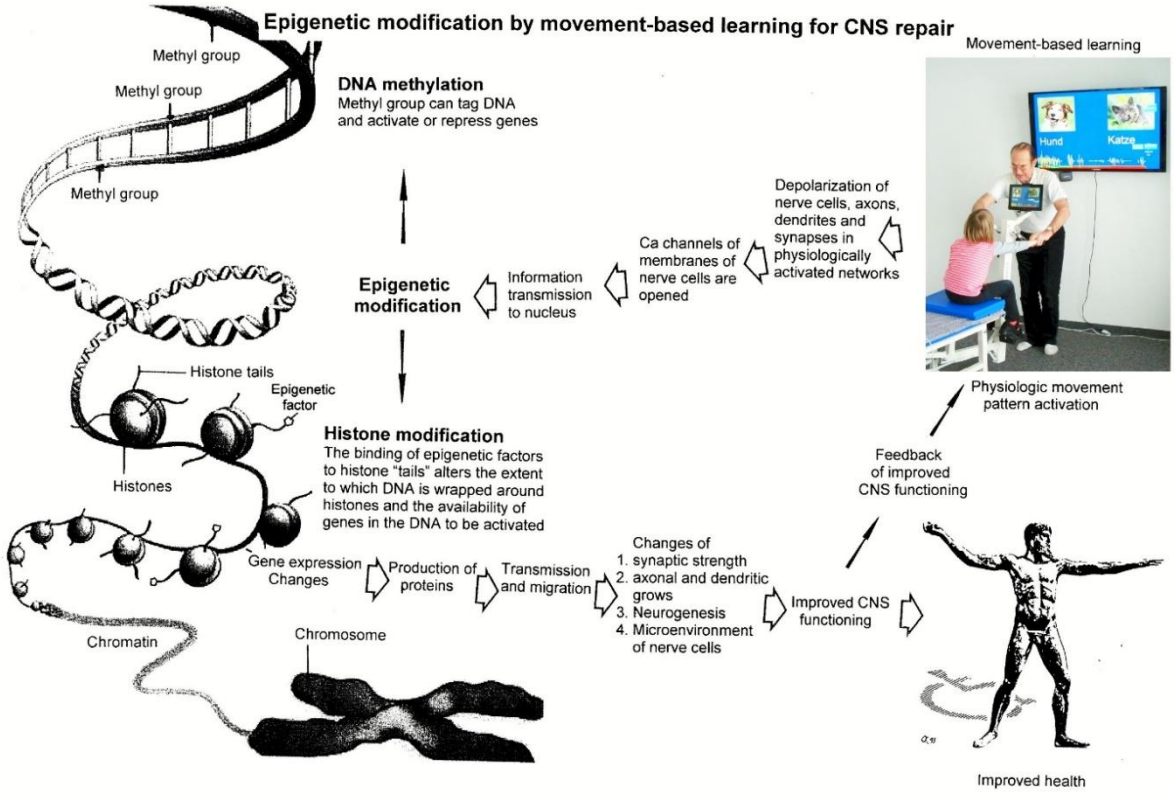

Fig. 3.12. Epigenetic regulation for repair by movement-based learning. CDT-induced stimulation of the pathways that regulate neural network repair is a proven therapeutic and preventive tool. Epigenetic mechanisms, stimulated by physiologic network activation, are likely key players within signaling networks, as DNA methylation, chromatin remodeling and small non-coding RNAs superfamilies' are required for the fine-tuning and coordination of gene expression during neural network repair by learning

4. The hippocampus plays an essential role in learning and memory. In the hippocampus there exists a specialized form of neural plasticity, which is, the generation of new functional neurons from stem

cells occurring throughout life. Adult hippocampal neurogenesis contributes to learning and memory formation.

5. New neurons are important for learning and memory formation (besides functional reorganization), i.e., for increasing the rate of repair, for the following reasons:

a. The insertion of new neurons helps to store the memory of the same activity that led to the creation of the neuron.

b. Activity-dependent neurogenesis enhances the learning of new memories and degradation and clearance of previously stored unwanted memories like spasticity, because the synapses, dendrites and axons can be devoted more fully to the newer memories. The old neurons with large and complex axon and dendritic trees are difficult to change. They can only be changed with sustained effort.

c. New neurons seem to improve the accuracy of relearned patterns (from model study [35]). This means that new neurons help to improve phase and frequency coordination of neuron firing and pattern stability.

d. The advantage of new neurons seems to be dramatically greater in networks that had been more active and had been required to store more memories [35]. The advantage of neurogenesis for memory storage in heavily active networks is that it provides an increased rate of repair if movement-based learning is administered aggressively and if different movements are trained.

6. Specific natural network activity is required for multiple aspects of repair. Specific activity is essential for correct migration of interneurons and it also controls the development and repair of their axons and dendrites. During repair there is a specific requirement of network activity in shaping the cortical integration of specific neural subtypes. Newly build neurons are likely electrically active shortly after their birth and participate in the early network activity that contribute to circuit maturation during repair by CDT.

7. Specific activity is required for migration and maturation at several stages of repair. A break in CDT may invalidate the whole chain of repair events. Specific interneuron subtypes require activity for migration and morphological maturation at two distinct stages of development [35]. Newly built neurons may even require specific activity for migration and maturation at several distinct stages of repair. **During a break in CDT, the specific activity, required for neuron migration, maturation and network integration may not be supplied at one of these stages so that the chain of repair events is severed and the whole repair chain has to be started anew.**

8. Drug application may undermine repair. Altering the level of neuronal excitability within genetically targeted neurons from drug application, for example antiepileptic drugs may have profound consequences on multiple aspects of the repair of select types of neurons within a population of neurons, as well as their associated gene expression. The pain-killer ‘Contergan’, taken during pregnancy, changed gene expression and the babies were born without arms.

9. Excitation-neurogenesis coupling [35]:

a. Excitation increases or decreases neuron production directly by excitation-neurogenesis coupling.

b. The excitation acts indirectly on the surrounding mature (hippocampal) cells through depolarization-induced release of growth factors.

c. Adult neurogenesis is enhanced by excitatory stimuli and involves Ca^{2+} channels and NMDA receptors.

d. The Ca^{2+} influx pathways are located on the proliferating stem/progenitor cells (NPCs), allowing them to directly sense and process excitatory stimuli. The Ca^{2+} signal in NPCs leads to rapid induction of a proneural gene expression pattern.

10. Integrative coordinated movements have to be trained to allow functional reorganization and new nerve cell integration across very large distances. CDT has to activate injured and uninjured networks to enhance physiologic CNS functioning and learning transfer.

11. Conclusion for optimal therapy according to the present stage of knowledge. If there is similarity between development and repair, animal (mice) data also hold in humans and the principles of neurogenesis of the hippocampus also hold in other parts of the brain, albeit to a much lesser extent, then the patient has to be trained at his limits (1) to induce substantial building of new nerve cells [36]. The treatment has to be continuously administered (2) to support all stages of repair at the progenitor level as migration, maturation and integration. The networks requiring repair have to be activated specifically (3) to generate repair-friendly, micro-environmental properties in the networks. No drugs should be administered that change neuron excitability (4). The exercises have to include coordinated arm, leg and trunk movements (if possible) to improve the impaired phase and frequency coordination for CNS self-organization (5). The performed movements have to be as integrative as possible to reconnect distant brain parts and to induce learning transfer.

This very short introduction to the theory of coordination dynamics therapy may help to understand the substantial progress achieved in the cerebral palsy girl.

3.3 RESULTS

3.3.1 Cerebellum Repair within 12 Months of CDT

Fig. 3.13. The cerebral palsy Sophie when trying to walk with her mother before CDT was started. She could not generate a walking pattern. Knees were overstretching (A) which blocks the walking pattern and she was immediately falling (B)

At the beginning of CDT, the 5.5-year-old Sophie could not perform any movement accurately. She was incontinent and her speech was poor. The Author could not understand her. She could crawl on the floor in trot gait coordination with poor performance. Pace gait crawling was not possible.

Of course, Sophie could not walk. When the mother tried to walk with her, she was more hanging in her hand than walking (Fig. 3.13). There was no real walking pattern and no balance. She could not

really learn it, because she had no protection automatism when falling, which are probably normally stored in the cerebellum. If she would fall, she would injure herself, of what the parents were very afraid of.

Fig. 3.14. The CP girl Sophie during jumping on a trampoline (A), during supported jumping on springboard with the mother (B) and during free jumping on springboard (C, D)

Sophie could not jump because she did not have that pattern learned and stored in her CNS and jumping is no automatism. She learned the jumping slowly and hated it. First, she could jump a little bit by herself on a trampoline (Fig. 3.14A). The jumping on springboard was harder to learn. The supported jumping was a big load for the parents, because Sophie contributed only little (Fig. 3.14B).

Slowly she contributed more and more and at the end she could jump by herself on springboard, but with poor performance (Fig. 3.14C). When she had learned the jumping, she liked it.

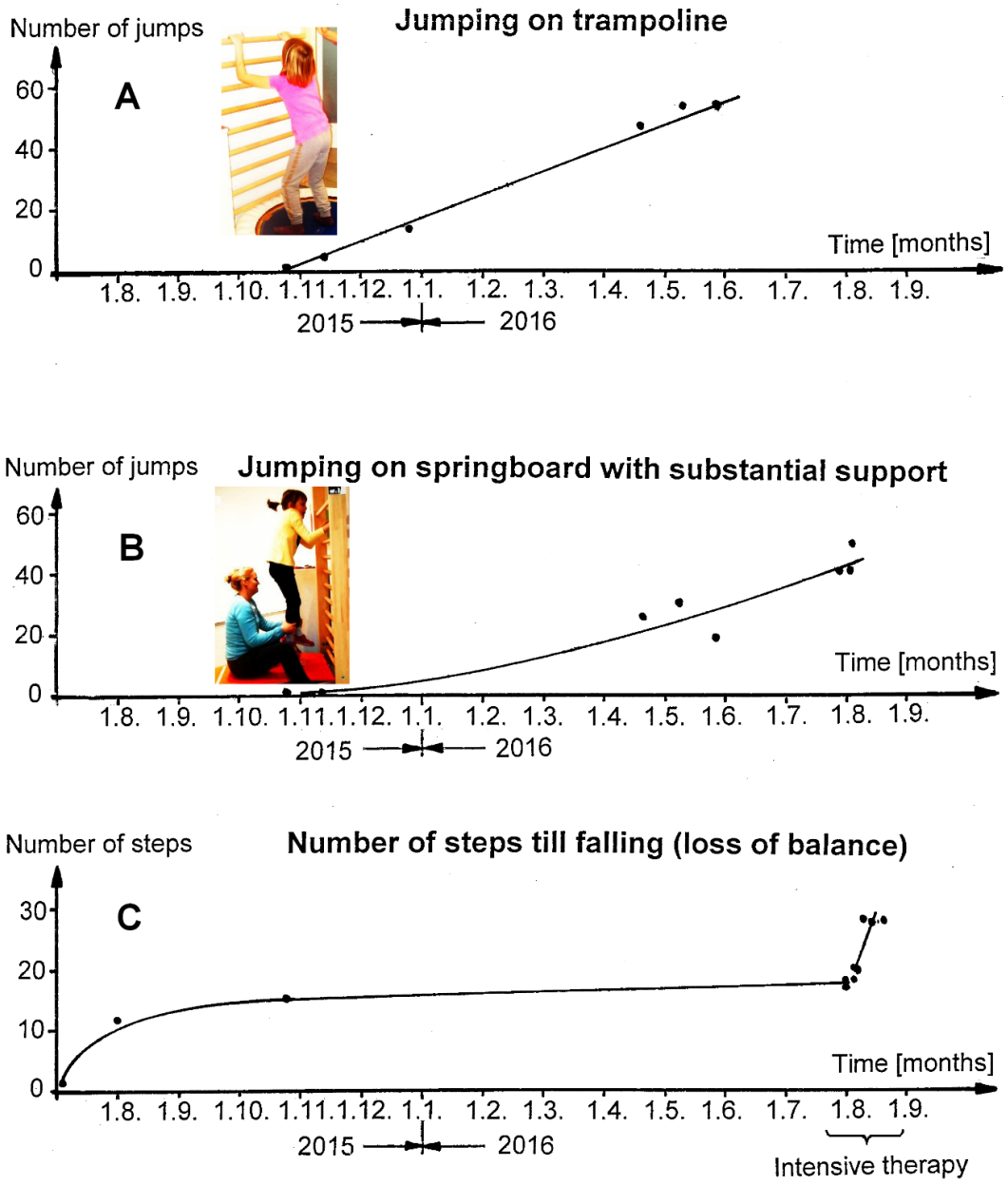

Fig. 3.15. Improvement of CNS functioning of the CP girl Sophie, quantified by jumping on trampoline (A), jumping on springboard (B) and walking without falling (C)

The first improvement in movements is shown in Fig. 3.15. She started the continuous jumping with one jump (Fig. 3.15A, B) and the walking with two steps (Fig. 3.15C). The progress of learning was slowly. With a second intensive training (Fig. 3.15C), the learning process speeded up.

The first fundamental progress in repair was achieved when the protection automatisms appeared in Sophie at an age of 6.5 years (Fig. 3.17A). The parents were not so much afraid anymore when trying to make her walking and Sophie tried now also by herself to walk. The protection automatisms

became operational at a time when she became able to exercise by herself on the special CDT device (Fig. 3.21). Also, the assessment of low-load CD values became possible (Figs. 3.27, 3.28).

When she became able to perform the automatism creeping, some malformations of the cerebellum became visible. When Sophie crept in interpersonal coordination with the patient Nefeli (SCI), and she liked it very much to copy Nefeli's movements, her inaccurate performance became apparent (Fig. 3.16). Nefeli crept physiologically, apart from the wrong positioning of the right foot and the dorsal flexion of the pelvis due to trunk spasticity. Since Nefeli and Sophie were creeping, balance was not needed and the vestibulocerebellum was not or only little activated.

Fig. 3.16 shows, in comparison to the performance of Nefeli, that Sophie's legs were moving uncoordinated about (Fig. 3.16K) even though Sophie was crawling in interpersonal coordination with Nefeli. The leg functions were more impaired than the arm functions. She could also better stand (Fig. 3.16L) than walk (see below). This indicates an injury of the anterior lobe and the superior portion of the vermis in and near the midline of the spinocerebellum [34]. Such injury produces ataxia of stance and gait and the gait ataxia (abasia) is worse than the ataxia of stance (astasia). A broad-based, unsteady gait was not observed in Sophie (Figs. 3.17H, 3.18C) with her cerebellum atrophy, but was observed in an adult patient with a severe traumatic cerebellum injury (Fig. 3.18D).

Fig. 3.16. Creeping in interpersonal coordination of the CP girl Sophie with an atrophy of the cerebellum and pons with the patient Nefeli, who had suffered an incomplete SCI at the level of Th10. Note the partly uncoordinated leg movements of Sophie in spite of no balance problems. Nefeli was crawling rather physiologically. When Nefeli was lying relaxed on the floor, trunk spasticity did not occur (M) and pulling the pelvis dorsally

From Fig. 3.16B it can be seen that Sophie was overstretching the left leg during creeping. The inability to stop the leg movement on time is called dysmetria (past-pointing, overshoot; hypermetria [34]). For sure Sophie had also dyssynergia; the loss of the precise cooperation of multiple muscle groups in the execution of a particular movement (creeping). Each muscle group contracts, but the individual groups fail to work together correctly. This severe impairment of the execution of voluntary movement is due to the atrophy of her cerebrocerebellum (Fig. 3.7).

The learning to walk was extremely difficult. The parents tried hard to have Sophie not in the wheelchair for the rest of her life. When the protection automatism occurred (Fig. 3.17A), the learning of walking became much easier and less risky. Sophie was not afraid to fall and tried herself to walk without falling and she liked the walking. Fig. 3.17 shows how Sophie was getting up (Fig. 3.17B-G) after falling (Fig. 3.17A). Interesting is that Sophie started to walk (Fig. 3.17F) before she was fully in the upright position (Fig. 3.17G). She was able to combine the movement 'getting up' and 'walking'. This indicates that certain functions in her cerebellum were working physiologically. At the beginning, the rather physiologic walking pattern as in Fig. 3.17H, with a too large stride length, was achieved only sometimes. The stability of the walking pattern was low and also the stability of the balance was low. Probably there was also some atrophy in the vestibulocerebellum. Her nervous system had to achieve three goals: First to have a higher stability of the walking pattern, second to improve the stability of the balance pattern and third to combine both patterns. The fundamental hope for Sophie was, that it becomes possible, with further therapy, to correct 'en route' the atrophy during the further development of the CNS so that her cerebellum would function rather physiologic at the end.

Fig. 3.17. Cerebral palsy girl Sophie (7.5 years old) during getting up after falling and starting walking. In "A" her arms protect her when falling completely. Before being fully upright, Sophie started to walk (F)

Astonishing is that Sophie's walking pattern was rather physiologic. The typical walking pattern of a patient with a severe cerebellum injury is completely different. Fig. 3.18D shows the typical walking pattern of a 57-year-old patient with the loss of approximately 80% of the cerebellum and damage of the frontal (Fig. 3.45B, C) and parietal lobe in a traumatic brain injury.

Sophie's trot gait crawling improved. The pace gait crawling became possible with poor performance (Fig. 3.18A). The positioning of the legs was still pathologic. The malformation was not symmetrical. To improve the walking pattern, Sophie and Nefeli exercised the walking on the knees (Fig. 3.18B) and they liked it. Sophie's pattern was quite physiologic apart from the abducted hands because of the balance problem. Nefeli's arms were working fine (SCI, Th10), but her pelvis was too much backwards positioned because of trunk spasticity. After approximately 15 knee-walking steps, Sophie and Nefeli were both falling forwardly. Sophie was falling because of the loss of balance and Nefeli was falling because the spasticity which pulled her pelvic too much backward so that she was falling forwardly. But for both, the walking on knees was fun and they enjoyed the discovery of a new motor movement. Sophie could perform this movement first time in her life and Nefeli first time again after the SCI. From the therapeutic point of view this walking on knees is beneficial because it improves the walking on feet. By training parts of the walking pattern, the brain can better realize what processes are deficient in the chain of pattern events to generate the walking pattern and can correct them by learning.

Fig. 3.18. The SCI patient Nefeli and the CP girl Sophie during crawling (A), walking on knees (B) and walking (C) in interpersonal coordination. The walking in interpersonal coordination with Nefeli helped Sophie to walk longer distances before losing balance. Note that the walking pattern of Sophie with an atrophied cerebellum and ponds was completely different to the walking of an adult patient with a severe traumatic cerebrum, cerebellum and pons injury (D)

The walking in interpersonal coordination with Nefeli (Fig. 3.18C) helped Sophie to stay longer in the walking pattern. The stability of walking pattern improved in the short-term memory and improved in this way the learning process and contributed to the improvement of walking in general. The walking distances, quantified by the continuous steps, improved (Fig. 3.15C). At home Sophie could now cover distances by walking instead of crawling, because with a walking distance of 5 to 10m, there was sufficient support when losing the balance. The walking pattern could therefore be used now in everyday life. As can be seen from Fig. 3.15C, the walking improved especially with an intensive therapy of four weeks.

3.3.2 Cerebellum and Pons Repair through 3 Years of CDT

3.3.2.1 Upgrading of the therapy

Most of the time (11 months) Sophie exercised 8000 to 9000 turns per week on the special CDT device in the lying position (Fig. 3.19) and trained jumping, sky walking, walking and balance (Fig. 3.21). Mainly the balance and the higher mental functions, including the speech, improved. In the last month of therapy, the intensity was strongly increased. She exercised now approximately 50000 turns per week (9000 times per day); most of the turns were supported (Fig. 3.19). Additionally, she trained jumping, walking and running. Real running was not possible. She could not get into the running pattern. The intensity of the therapy was therefore approximately increased by a factor of 5 to see whether more substantial repairs were possible! She trained again together with the patient Nefeli as a year before, which seemed to be beneficial for both of them. In Fig. 3.20 she supported the training of Nefeli for fun and was improving at the same time her right-left symmetry of the arms, which is important for improving her hand and finger functions as for example the writing.

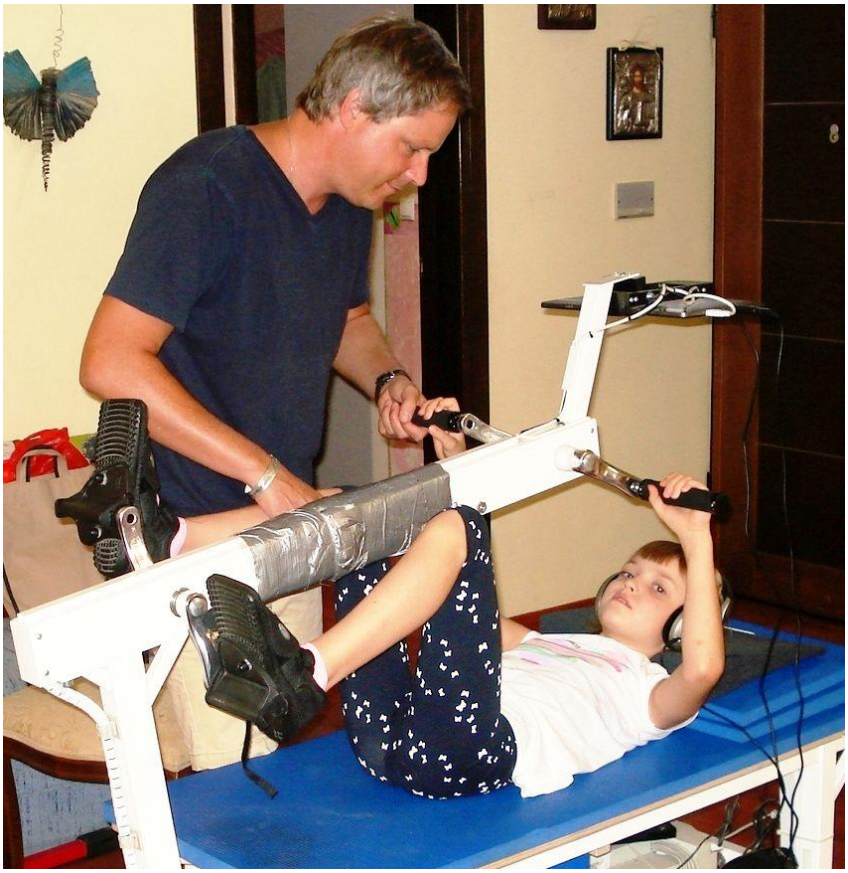

Fig. 3.19. Sophie (cerebral palsy, malformation of cerebellum and pons) is exercising on the special CDT device, supported by her father. The father makes a small supporting mistake: his left hand has to touch Sophie's right hand for improved input to pons and cerebellum.

Fig. 3.20. Training of right-left coordination of arm, hand and finger functions of the cerebral palsy girl Sophie. For fun Sophie helped Nefeli with turning; but because of the coordination changes between foot paddles and handles, Sophie improved her arm and hand functions

Fig. 3.21. The 8-year-old girl Sophie during exercising on a special CDT device when sitting on a ball. Also balance and trunk stability were trained in this way. The younger brother Lukas was training in the background

3.3.2.2 Improvements achieved when exercising at her limits

After two weeks of intensive therapy, Sophie could better perform the poor pace gait crawling and she learned to walk freely on the forefoot. After 23 days of treatment a substantial repair progress occurred. The evening before she was that exhausted that she had problems to walk even with very poor performance and she slept very long. The mother was worried that Sophie may have become overloaded. But next day, Sophie wanted to jump, what she hated before, and she performed the in-phase jumping very well (Fig. 3.22A). The performance of jumping in rotation (Fig. 3.22AB) was good, first time in her life.

Fig. 3.22. Sophie during jumping in in-phase (A) and in rotation (B, C)

This sudden improvement of CNS functioning can be explained by the System Theory of Pattern Formation. According to this theory, there are smooth changes with movement-based learning. But sudden changes may also occur when intrinsic (present inner CNS organization) and informational requirements (CDT) conflict, while behavioral information is changing smoothly. Such abrupt change may have taken place in Sophie in the short-term memory after approximately 6000 supported fast turns. Other movements as knee walking (Fig. 3.23) and walking with sandals (Fig. 3.24), which activates the forefoot, may have contributed.

Fig. 3.23. Sophie (front) during walking on knees. A part of the pattern walking is trained in this way

Disappointing is that the running pattern could not be learned so far. Sophie was not able to get into the high frequency pattern, even though she was able to step a bit on the forefoot.

Fig. 3.24. Sophie (left) during walking with sandals to train forefoot functions. When Sophie and Nefeli were training together they motivated each other to fight more

The achieved progress of the intensive CDT for 23 days was that she could jump better in-phase and learned to jump in rotation (Fig. 3.22). Rotational movements are important to increase trunk stability and balance. It became thus possible that Sophie started by herself to perform hula hoop (Fig. 3.25), for which trunk stability and balance is needed. The improvement of trunk stability made it possible that Sophie became able to exercise on a special CDT device when sitting on a ball (Fig. 3.21). The activation of the forefoot could be trained now when walking with sandals (Fig. 3.24).

Fig. 3.25. Sophie during trying to learn hula hoop. Note the sudden rotational movements of the upper body. Trunk stability and balance are trained in this way. Astonishing is that she did not lose balance

The most important progress achieved in the last two year was the improvement of the higher mental functions. She became able to speak more clearly, write better (Fig. 3.40) and showed beginning of creativity, entrepreneurship and sense of initiative. She started for example to learn hula hoop by herself (Fig. 3.25), which is no simple movement: a lot of trunk stability and balance is needed. To appreciate the progress, one has to remember that at an age of 5.5 years she was not able to walk even with support by the mother (Fig. 3.13).

The efficiency of the treatment can sometimes also be improved if the children compete with one another and can have fun together. For playing, Nefeli (11.5 years old at that time) was supporting Sophie (8 years old) and Sophie was supporting Nefeli (Fig. 3.26). As Nefeli said afterwards, Sophie was not able to give her good rhythmic support as the Author did when he was supporting the jumping.

Fig. 3.26. During jumping on springboard Nefeli supports Sophie (A) and Sophie supports Nefeli (B) for fun and treatment motivation

3.3.2.3 Improvement of coordination dynamics values with therapy

A part of CNS repair is to quantify the progress. Besides clinical judgements, objective measurements are needed. The improvement of Sophie's brain functioning by therapy was measured objectively when exercising on a special CDT device.

Fig. 3.27 shows the improvement of the coordination dynamics at the beginning of therapy (A) and later on (B). The arrhythmicity (coordination dynamics (CD) values) reduced from 38.2 to 8.3. At the beginning of therapy (A), she got stuck with the difficult coordination's between pace (P) and trot gait (K). Later on, she also managed well with the intermediate difficult coordination's between pace and trot gait and could exercise rather smoothly.

Fig. 3.28 shows the improvement of CNS functioning with ongoing therapy, quantified via the low-load CD values as measured in Fig. 3.27. Even though children are not always trying to be good in a test, in Sophie characteristic changes were observed. When she trained intensively with up to 20 hours per

week for approximately 4 weeks, the CD values got better (lower) and when she trained only 5 to10 hours per week, the values got worse. This clearly shows that an intensive therapy is much more efficient.

But why did her CD values got worse when training only with half of the load? When during development the neural networks become more complex with an enhanced connectivity, the phase and frequency coordination becomes worse. Healthy children train continuously their networks by running, jumping and other movements. The injured CNS needs not less but even more movements for holding the exactness level of phase and frequency with increasing neural network connectivity. If Sophie would have trained continuously at her limits, the CD values would vary but would not get worse.

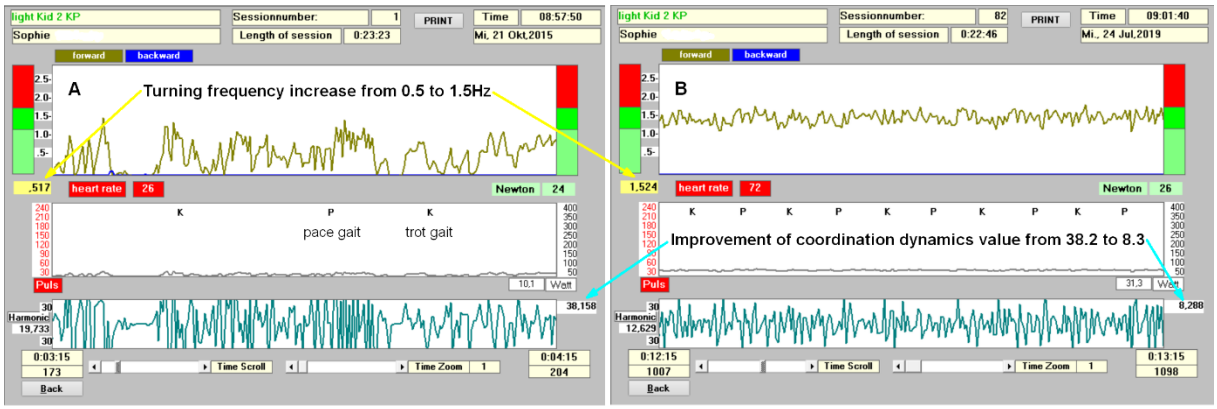

Fig. 3.27. Coordination dynamics (CD) measurements at the beginning (A) and later on during therapy (B). The turning frequency on the special CDT device increased from 0.5 to 1.5 and the CD values reduced (improved) from 38.2 to 8.3. The cerebral palsy patient learned to exercise much better with therapy, that means more smoothly and faster

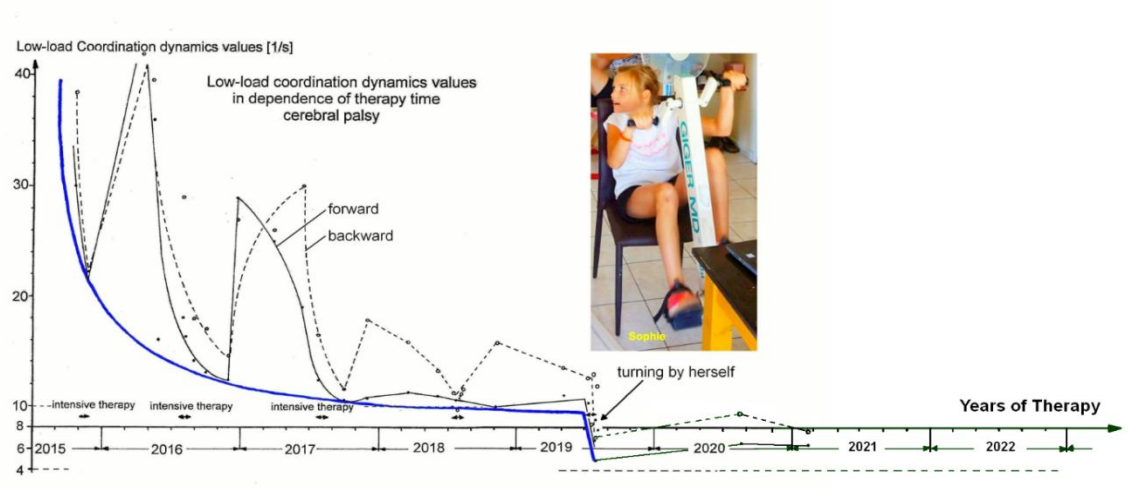

Fig. 3.28. Low-load coordination dynamics (CD) values in dependence of therapy time in years. Forward exercising = continuous line; backward exercising = dashed line. Note, with intensive therapy periods the CD values got at each time period strongly lower (better) and successively lower. The measuring of the low-load CD values became possible, one year after the beginning of the CDT (2014), when she became able to exercise by herself on the special CDT device. The solid thick line connects the best values, which reached nearly a plateau of no further progress. When using a special CDT device with more complicated coordination's between arms and legs, the CDT values substantially improved (lowered) further (2019). With this improvement of brain functioning, the cerebral palsy girl Sophie started to turn by herself without mental support

Interesting is that the movements, vegetative and higher mental functions continuously improved. Most likely, if CDT would have been administered continuously at her limits, let's say for 12 months instead of only 1 month repeatedly, then her repair would have been faster and Sophie (from Switzerland) would have had a better chance to catch-up in a few years' time with the other healthy children of the same age. But the load on a family with a disabled child is already very high. Training then additionally at the child's limit, in which a lot of patience is needed, may overload the family, especially when getting no help from the educational and rehabilitation systems, which are working according to duty. In Switzerland a proposal from the invalid insurance (IV) that the parents can chose the kind and place of rehabilitation was not accepted by the parliament in 2018. In the coma patient Manolis [16], who had lost approximately 50% of the brain tissue in a car accident, a miracle-like progress was achieved, when CDT was administered to him for 6 years with 20 hours therapy per week. But nearly 10 persons were contributing to the brain repair, including 2 sisters, 2 brothers and the mother. No financial support was coming from the state.

3.3.3 Cerebellum and Pons Repair within 4 Years of CDT

With low-level therapy of approximately 10 hours CDT per week, Sophie improved but only little. Her handwriting improved (Fig. 3.40, 02.06.2018) and, very importantly, her balance improved substantially. She became able to play with the father with the ball. When the balance further improved, Sophie became able to walk on the forefoot and she became able to balance the posture during ball-playing with a cousin by also going on the forefoot (Fig. 3.29).

Fig. 3.29. Sophie (left) with an atrophy of the cerebellum and pons during ball-playing with a healthy cousin. She trains the balance when going on the forefoot (arrow)

3.3.3.1 Still insufficient repair of the vermis (spinocerebellum)

Because of an insufficient repair of the genetical old vermis, Sophie could still not control sufficiently inertia and centrifugal forces during fast moving with the consequence that during fast creeping, she was still overstretching the legs (Fig. 3.30a) and swinging them too much (Fig. 3.30b) (creeping ataxia). This inability to stop leg movement on time did not improve much to the repair stage of one year ago (Fig. 3.16B, A).

Fig. 3.30. Sophie during creeping in interpersonal coordination in antiphase with Nefeli (SCI). Sophie is overstretching (a) and overswinging the legs (b) in comparison to Nefeli. She had not fully learned to control the inertia and centrifugal forces of leg movement. She cannot stop leg movement in time. The spinocerebellum (vermis) had not been repaired sufficiently so far

The walking performance improved further. The overshoot of leg movement became more one-sided (Fig. 3.31D). In the swing phase of the right leg, the stride length was not so large any more, the balance was quite good and the arms moved in coordination (Fig. 3.31b). But in the swing phase of the left leg, the stride length was too large and Sophie had balance problems; the arms did not move in good coordination with the legs because they were used for keeping balance (Fig. 3.31a).

Fig. 3.31. a. During walking the left leg is over-swinging and the balance is poor; Sophie is using the arms for keeping balance. b. During the swing phase of the right leg the control of inertia and centrifugal forces is better already; she can keep balance without using the arms

Hopefully Sophie does not have a severe atrophy of the deep cerebellar nuclei, in which case only minimal recovery is believed to occur [34]. Since the vermis is phylogenetical an older part of the cerebellum, may be some genetical old movements (as for example from the Tiktaalik's (Fig. 3.32)) have to be trained additionally.

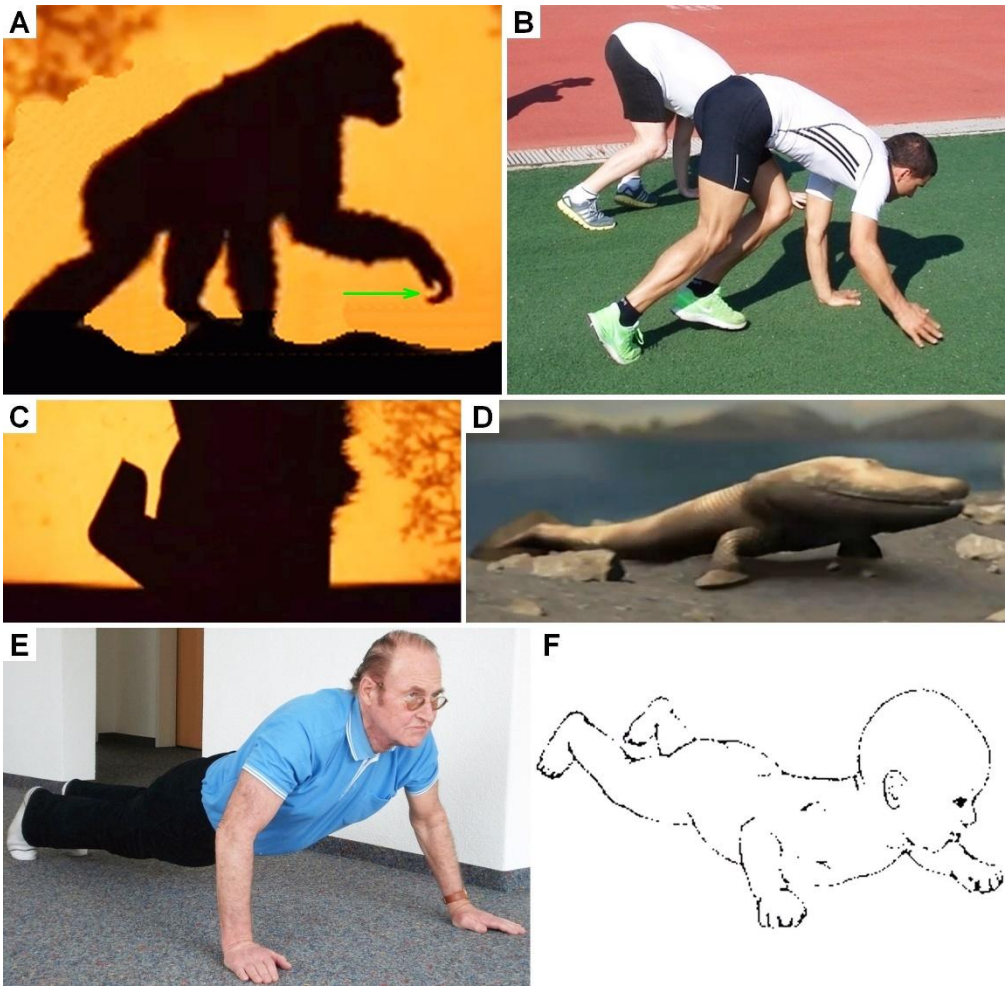

Fig. 3.32. A. Four limb walking of the monkey. Because the palm of the hand is not touching the ground, this movement is not suitable for training. B. Bear-walking of patients with brain injuries (suitable for training). C. Only the fingers and finger bones of the hands of the monkey are touching the ground. D. Tiktaalik (phylogeny between fish and Ichthyostega): the fish which is leaving the sea. Its movement on land bears similarity to push-up. E, F. Author and baby during push-up

3.3.3.2 Upgrading of the therapy

Fig. 3.33 shows some movements performed with Sophie to hopefully include more efficiently the repair of the vermis (spinocerebellum). If the argument with the possible Tiktaalik's movements is wrong, the performed movements train anyway the trunk stability, which was still deficient in Sophie. Even though Sophie could crawl very fast in trot gait coordination, the coordination of the pace gait crawling (Fig. 3.33b) was still poor. During hopping overshoot of the right leg (Fig. 3.33c) did occur.

To train deeper in the complexity of CNS organization, further complicated coordination's were trained on a certain special CDT device. Sophies CNS has to recognize where there are pathologic neural network organizations and has to repair them by trial–and-error-elimination processes.

Fig. 3.33. a. Author and Sophie during push-up. b. Pace gait crawling with Nefeli (SCI) in interpersonal coordination. As indicated, the arm of Sophie moves to late or the leg too early. c, d. Hopping movement performed with the brother Lukas. As marked, there is also dysmetria of the right foot (c) during this hopping movement

3.3.3.3 Beginning of running

Because of the inability to sufficiently control inertia and centrifugal forces, Sophie had problems in performing small steps. She also had problems to increase the stepping frequency. By training the increase of the stepping frequency (Fig. 3.34a) and training volitionally to perform smaller steps (Fig. 3.34b), she became able to learn a bit running. When moving fast with the father, she became able to run for few meters in spite of the overshoot of leg movement (Fig. 3.34c). The training of the integrative and high frequency moving 'running' will, most likely, bring further repairs in Sophies CNS.

For learning running, she has to learn firstly to move with high frequency for which a precise high-speed communication between the cerebellum and the periphery is needed. Secondly, she has to learn to reduce the overshoot of leg movement. Thirdly, she has to learn to increase the pattern stability, that means to stay longer in the running pattern than just for a few running steps. Fourthly, she needs to learn running pattern variability to adapt to uneven ground. Sophie, therefore, needed to learn variability and stability of motor performance. And fifthly, she has to learn to keep balance during running. At that time, she could only get into the running pattern when she was running with the father (Fig. 3.34c), to have support. The improvement of walking and running was in accordance with the improvement (reduction) of the low-load coordination dynamics values (Figs. 3.27, 3.28).

There was still a long way of treatment to go to fully learn running. Luckily, parents, grandparents, the brother and other relations were substantially contributing to the repair of Sophies CNS.

3.3.3.4 Improvement of speech

The speech improved further, but it was still far away from normal. The coordination of the speaking with coordinated movements is helpful (Fig. 3.35), since deficient speech is mainly caused by insufficient speech muscle coordination caused by cerebellum and pons atrophy.

Fig. 3.34. a. Sophie during training high frequency stepping with the father. b. Training to reduce the stride length during walking to reduce the overshoot of leg movement (with grandparents). c. Sophie during running with the father. Note her laughing during running (c)

Fig. 3.35. Sophie during speech therapy when exercising on a special CDT device with father and mother

3.3.4 Cerebellum and Pons Repair through 6 Years of CDT

Through 5.5 years of CDT, Sophie learned the running. It was hard training for her, but she liked it (Fig. 3.36B-D). By use of volitional power and intention, she got into the running pattern and could keep it for some time. The running is very efficient for repair, because the movement-induced afferent input is high (behavioral information $\sum c_{inf}\mathbf{F}_{inf}$) in comparison to (pathologic) internal neural network organization (intrinsic dynamics $\mathbf{F}_{intr}$). The only problem was that she got quickly exhausted.

Fig. 3.36. B-D. The cerebral palsy girl Sophie learned through 5.5 years CDT the running. Note from the expression of the face, how hard she is fighting to run. She liked the running, even though being very hard for her. A. The SCI patient Nefeli, with whom Sophie trained partly together, lost functions with orthopedic surgery [8]

To motivate Sophie, parents and grandparents trained sometimes together with her (Fig. 3.37). Simultaneously, they improved their own general health.

Fig. 3.37. The patient Sophie with cerebellum and pons atrophy, during training together with the mother and the grandparents

To further improve the running pattern performance, Sophie trained with the grandmother the forefoot activation (Fig. 3.38). She became also able to walk and run a bit on the forefoot (Fig. 3.38). The movements on the forefoot are important for building up the foot arc and seem to improve cerebellar functioning. When Sophie just learned to walk, the walking with sandals went astonishing well (Fig. 3.24), probably because the toes and the forefoot were activated.

Fig. 3.38. Forefoot training of Sophie with the grandmother during walking and running

Through 6 years of CDT, the running performance improved and she could run longer distances with better performance. She became able to run on uneven ground (Fig. 3.39A, B). This means that she learned to a certain degree running pattern variability to adapt to the uneven ground When the ground was too uneven, she used the arms for keeping balance (Fig. 3.39B).

Fig. 3.39. Cerebral palsy girl Sophie during running on uneven ground and free jumping. A. Running in normal trot gait coordination. B. When the ground was too uneven, she used the arms for keeping balance. C, D. Free jumping in pace gait coordination in front of the farther. From her face (A, B) it can be seen that she was fighting for performing running and jumping well. She liked to perform both learned movement patterns

Also, the jumping improved. She became able to freely jump in-phase (Fig. 3.39C, D). The jumping in anti-phase, in which she has to swing also the arms in coordination with the legs, in similarity to running (Fig. 3.39A), she had not learned so far. Altogether, the locomotion had improved substantially. At the beginning of therapy, the farther asked the Author whether it is possible that her daughter could learn to walk up to 5m to be able to walk at home instead of covering distances by crawling. Now, Sophie walks with her cousin to a 1km distant supermarket for shopping.

In spite of the tremendous progress in movements, the cognitive functions and the fine control need further improvement through intensive CDT. The speech is still poor. The writing of Sophie improved. She became able to write better and smaller letters (Fig. 3.40). But she did not catch-up with healthy boys and girls to visit a normal school. The integration at school may be difficult, even if Sophie would

have an assistant. The spinal cord injury patient Nefeli (Fig. 3.18) had problems with the integration at school. Pupils can be quite hard in critic. And the schools for disabled are out-of-date.

Fig. 3.40. The cerebral palsy girl Sophie learned to combine letters to words (left) and to write at an age of 8 (13.12.2016). The writing improved when she was 9 and 9.5 years old (21.9.2017, 2.06.2018). During 6 years of CDT at an age of 12, she learned to write better and smaller letters (13.03.2021). The language is German

The only real solution for Sophie to catch-up with healthy pupils is to further repair her CNS. But because the mainstream medicine is 30 years out-of-date, the load on the parents is high and they get worn-out with ongoing years of therapy.

3.4 DISCUSSION

It was shown that the CNS of a young patient with an atrophy of the cerebellum and pons and may be a mild injury of the basal ganglia could substantially be repaired through coordination dynamics therapy (CDT). The girl Sophie started CDT at an age of 5.5 years and could 6 years later walk run, jump and hold balance. She became continent, learned writing and her cognitive functions improved strongly.

3.4.1 Comparison of Therapy-induced Improvement of CNS Functioning between Cerebellum and Pons Atrophy and Cerebellum Traumatic Injury

The improvement of CNS functioning of Sophie will be compared with that of the patient Dr. Cwienk who suffered a severe traumatic brain injury at an age of 55. The frontal and parietal lobe of the cerebrum and pons were injured and 80% of the cerebellum lost. Sophie was at the beginning of therapy a severe disabled child and Dr. Cwienk was given up by school medicine. To Sophie, CDT was administered with changing intensity and Dr. Cwienk performed CDT continuously for more than 20 years with rather high intensity. Even though these two patients are quite different, still some important similarities and differences in repair will turn out.

1. The most important difference between the now 12-year-old Sophie and the 80-year-old Dr. Cwienk was the speed of learning, when CDT was administered. What Sophie learned in 12 months, Dr. Cwienk needed up to 20 years.

2. Sophie learned the protection automatisms when falling (Fig. 3.17A) within 6 months and it was easy to walk with her when holding her hand. Already the walking in interpersonal coordination with Nefeli (SCI) improved her walking performance (Fig. 3.18C). Her left arm was abducted to keep balance.

Dr. Cwienk did only re-learn the protection automatisms, when falling, after 20 years of therapy. With a lot of concentration, he could move step by step without falling (Fig. 3.18D). But when he was really falling, it was nearly impossible to support him, because his reactions were un-physiologic and unexpected for the supporting person. It was therefore stress to support him during walking. Even the Author thought that the patient will never re-learn the protection automatisms because of the loss of 80% of the cerebellum. But he did. Therefore, what Sophie learned in 6 months Dr. Cwienk needed 20 years.

3. The performance of the walking pattern was smoothly and physiologic in Sophie (Fig. 3.17H) apart from the balance problem (Fig. 3.18C) and the inability to stop the leg movement on time. But not in Dr. Cwienk (Fig. 3.18D).

4. Sophie could combine the getting up movement and the walking (Fig. 3.17E-G), whereas Dr. Cwienk could not combine the two movement patterns. He first had to get up, concentrate and then start to walk very slowly step by step with support.

5. Sophie could do sky-walking (Fig. 3.41A), including sky-walking with crossed arms (Fig. 3.41B), to activate commissural fibers (Fig. 3.41B inset) for improving right-left communication. Quite often she overstretched the knees, what she was not doing during normal walking. This means that sky-walking is not an inborn automatism like walking. Later on, Sophie learned the sky-walking without overstretching the knees.

Sky-walking was not administered to Dr. Cwienk. But since he could walk on treadmill with both hands and one hand (Fig. 3.41D), he could most likely also perform sky-walking because no balance is needed. Walking with sticks (Fig. 3.41C) was already difficult for him.

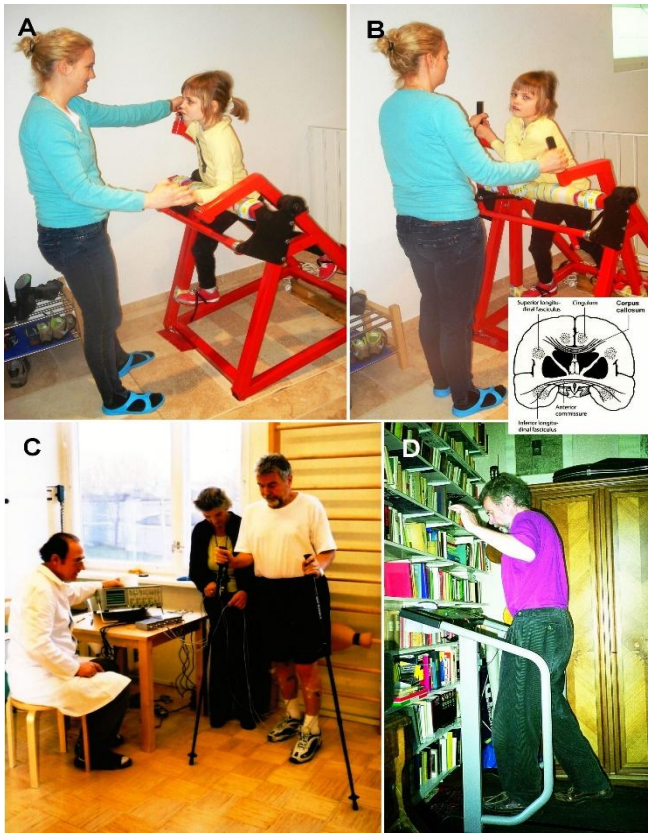

Fig. 3.41. A, B. Sky-walking of the 7-year-old Sophie with atrophied cerebellum and ponds. C, D. Walking with sticks and walking on treadmill of the 70-year-old patient with traumatic cerebellum and ponds injury. B, inset = commissural fibers of the cerebrum

6. Within 6 months, Sophie learned a bit the jumping on springboard with poor performance (Fig. 3.14) and later on with good performance (Fig. 3.22). The free jumping was achieved through 6 years of CDT (Fig. 3.39). Dr. Cwienk re-learned the jumping on springboard, but the smoothness was missing. Because of extensor spasticity and missing elasticity, there was the danger of damaging the knee joints. He had no chance to learn the free jumping.

7. Sophie and Dr. Cwienk re-learned the trot gait crawling, even though the performance in Sophie was better. But the pace gait crawling (Fig. 3.18A) was difficult for both of them. The problem of Dr. Cwienk with the pace gait crawling is understandable because of his one-sided cerebellum injury (Fig. 3.45) in some similarity to stroke. But Sophie had an atrophy of the cerebellum and not a one-sided injury. Also, the 10-year-old Nefeli (SCI) had more problems to re-learn the pace gait crawling (Fig. 3.18A), even though during development the pace gait crawling is learned first because it is easier for the CNS to generate it.

8. When being able to exercise on the special CDT device, both, Sophie and Dr. Cwienk could exercise on it in the standing position (Fig. 3.42), because only little balance is needed.

Fig. 3.42. Exercising on the special CDT device in the standing position of the 7-year-old Sophie with cerebellum and pons atrophy and a 60-year-old patient with traumatic cerebellum, pons and cerebrum injury. Note that when no balance is needed, both can perform this coordinated arm and leg movement, but the girl with more elegance

9. Sophie had to learn to become fully continent. Dr. Cwienk had no problems with urinary bladder functioning.

10. Sophie and Dr. Cwienk had scanning dysarthria and dysarthrophonia. Both patients had also a paravermian injury/atrophy and an impaired coordination of the musculature of speech. Both patients were speaking slowly and haltingly with poor articulation. In both patients the speech improved with therapy but was still far away from physiologic after 6 years and 20 years of CDT respectively. To enhance the rate of learning/re-learning of speaking, speech therapy was partly performed when the patients were simultaneously exercising on the special CDT device (Fig.3.43) to improve CDT functioning in the short-term memory in general and speech performance in specific.

Fig. 3.43. Speech therapy during exercising on the special CDT device in a girl with cerebellum and pons atrophy by the mother (A, teacher herself) and an adult patient with traumatic cerebellum and brain injury by a speech therapist (B).

11. The improvement of CNS functioning in the long-term memory improved the face expression strongly in Dr. Cwienk within 10 years (Fig. 3.43C). In Sophie the expression of the face became livelier.

12. Dr. Cwienk, being 80 years old, was performing 10 hours CDT per week to keep the achieved level of repair. He had no recurrence of a colon carcinoma. Sophie was performing therapy with changing intensity. It seems that her prognosis to recover further from the atrophy of the cerebellum and pons is good, may be, in similarity to children with hydrocephalus in whom the prognosis of

recovery is surprisingly good. With further therapy, further correction 'en route' of the development to repair the cerebellum atrophy is possible in Sophie.

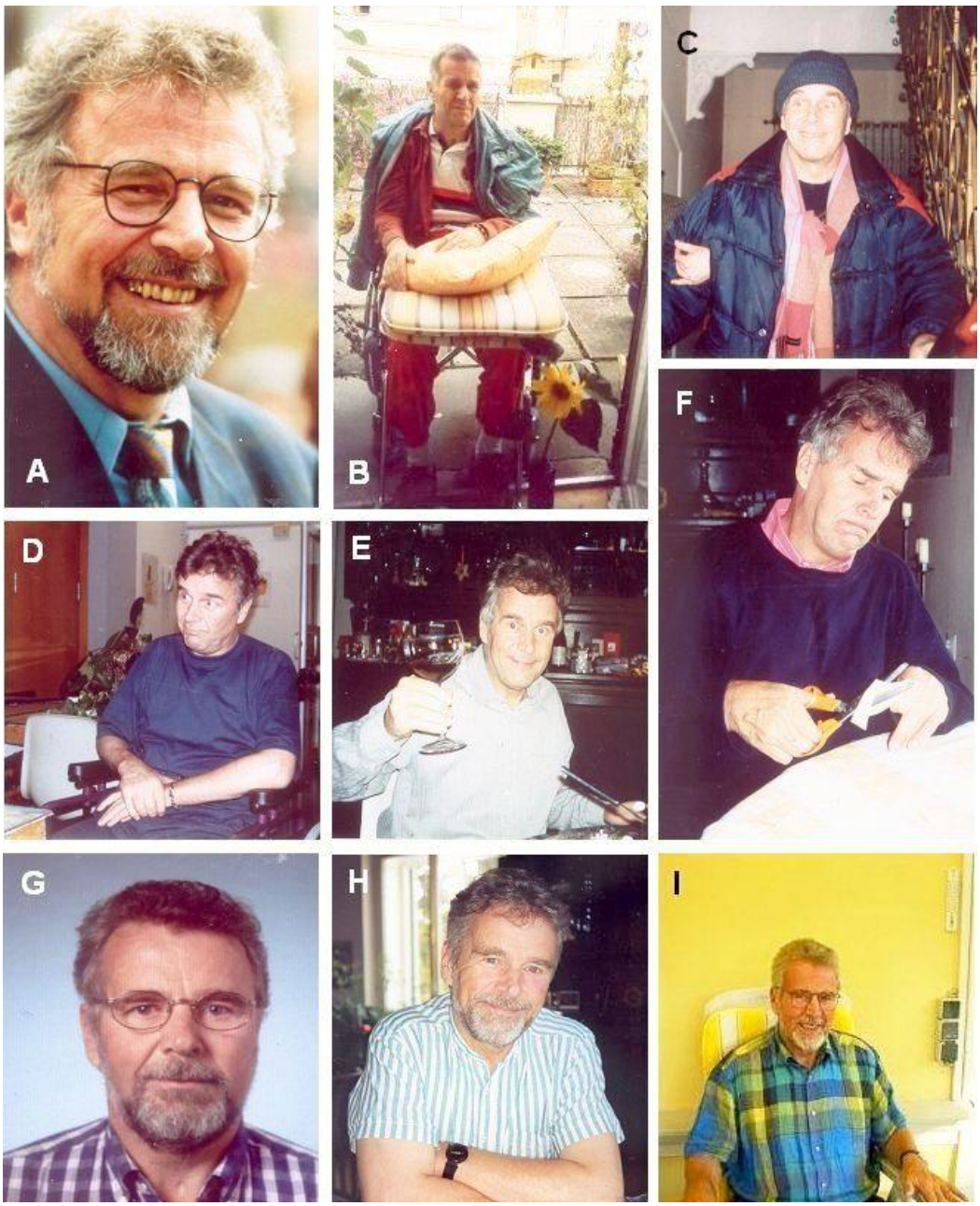

Fig. 3.43C. Coordination dynamics therapy-induced improvement of the face expression of the patient Dr. Cwienk, who suffered severe cerebellar and cerebrum injuries. A. before the accident; B-I. after the accident in 1995 till 2006. After the injury the patient was able to move one finger. At the stage of 'B', his wife struggled with the physicians, because they wanted to put him to a place till he dies there. But the wife took him home and started therapy with him. Note the pathologic face expression from 'B' to 'F'

13. In spite of the tremendous progress of the very intelligent Dr. Cwienk with CDT, he could not reach the high intelligence level of before the injury. As he said himself, before the injury he could listen to somebody and generate arguments against the opponent at the same time. Now, after the recovery from the severe brain and cerebellum injury, he can do only one thing at a time. This means,

he first has to store the information and then develop a strategy against the arguments of the opponent. The intelligence of Sophie improved with therapy.

14. Dr. Cwienk was an extremely cooperative patient, which helped him to recover partly from the severe cerebellum and frontal lobe injuries. The cooperation of Sophie was poor but improved. Her parents had to be very patient to administer therapy successfully. But when she learned a new movement, first time in her life, she used it immediately like crawling, walking on knees (Fig. 3.18B), walking, jumping and running (Fig. 3.39).

15. The writing and drawing was poor in both patients, but improved (Figs. 3.40, 3.44). For some improvement of hand coordination, Sophie needed 9 months and Dr. Cwienk a few years. After 2006 the handwriting of Dr. Cwienk got worse again due to aging, reduced therapy and not writing with the hand anymore (using a keyboard for writing). The handwriting of Sophie improved continuously with further therapy (Fig. 3.40), including writing exercises.

The learning of continuous hand writing at school is given up in several countries. The coordination in continuous hand writing (Fig. 3.44) between movement and cognitive functions is important for specific neural network learning and structuring the human brain and should not be given up. In aging fewer spelling mistakes are done with the continuous hand writing than with the keyboard writing. An experience made also by the Author. An interchange of letters in a word does not take place in continuous hand writing.

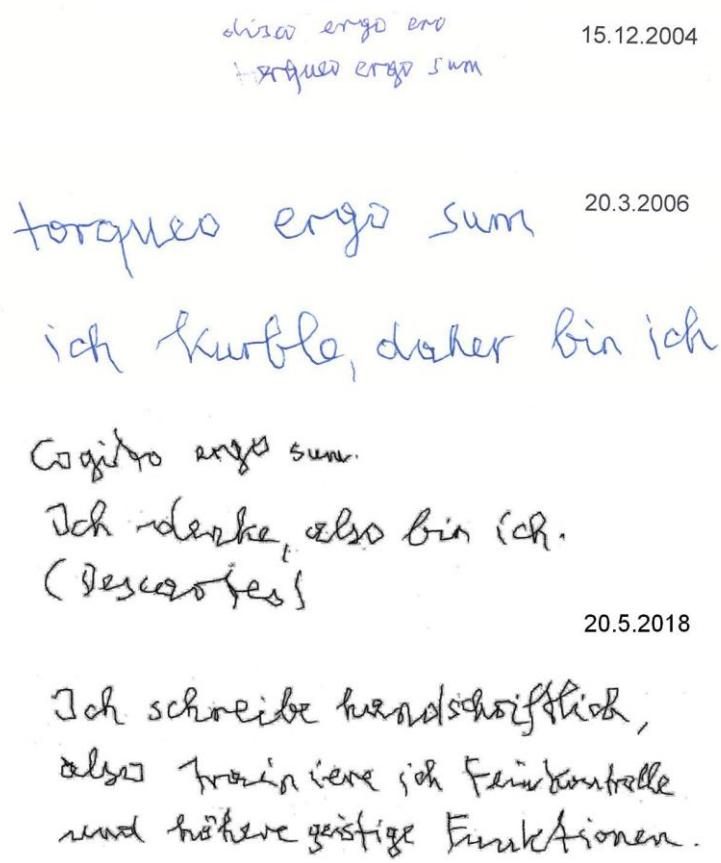

Fig. 3.44. The writing of Dr. Cwienk. It improved within two years of CDT from 2004 to 2006. In 2018 his handwriting got worse again due to aging, reduced therapy and using only the keyboard of the computer for writing instead of performing continuous hand writing

16. No changes in the MRI with therapy could be seen for the atrophied cerebellum of Sophie (Fig. 3.45A) and the injured cerebellum of Dr. Cwienk (Fig. 3.45C). Repairs were mainly due to functional reorganizations. In Sophie, we can expect that some neurogenesis contributed to the repair, because CDT was started when she was 5.5 years old. In Dr. Cwienk, excitation-induced neurogenesis [35, 36] will have contributed only little because of much higher age. The building of some new nerve cells is not visible in standard MRI's.

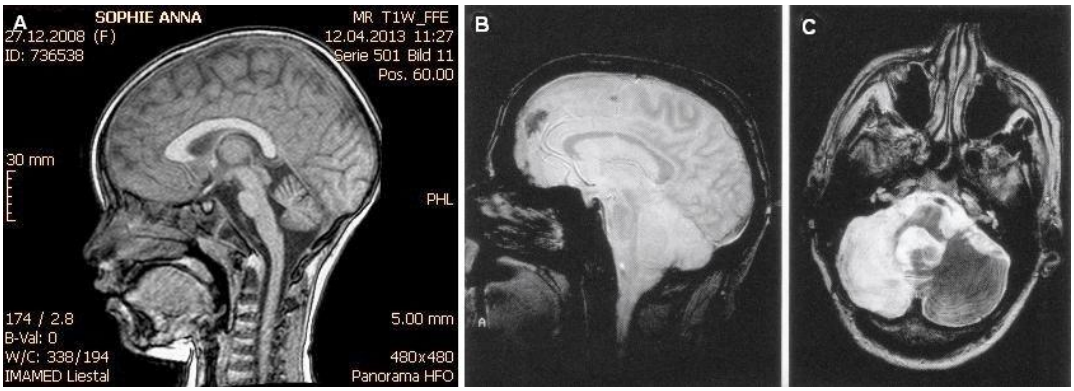

Fig. 3.45. A. Magnetic resonance imaging of Sophie in 2013. In 2016, the cerebellum and ponds had approximately the same size, but they did not atrophy further. B, C. MRI's of the 63-year-old patient Dr. Cwienk who suffered a severe cerebellar and cerebral injury. The cerebellum was lost/destroyed to approximately 80% (C, light parts of the cerebellum). There was also loss of brain tissue in the frontal lobe (B, dark areas) and parietal lobe (not shown). No loss of nervous tissue in the following years

17. At an age of 11 years, Sophie learned running through 5.5 years of CDT (Fig. 3.36). Dr. Cwienk had never a chance to re-learn the free running.

18. Dysmetria was very much observed in Sophie, but not in Dr. Cwienk. During crawling in trot gait coordination and walking on treadmill (Fig. 3.41D), the Author did not see in Dr. Cwienk overshoot of leg movements due to uncontrolled centrifugal forces. But he could walk on treadmill only up to 2km and at such low-speed centrifugal forces and kinetic energies are generated only little.

Due to a prolonged postnatal icterus in Sophie, a mild damage of the basal ganglia cannot be excluded and could have contributed to her dysmetria, because a 12-year-old boy with a damage of the basal ganglia, caused by hypoxia, showed overshoot of leg movements during walking and creeping (Fig. 3.45A). But through CDT and 'error-elimination processes' (learning), also an injury of the basal ganglia can be repaired simultaneously.

Fig. 3.45A. A boy with injured basal ganglia, caused by hypoxia, during creeping. The performance of the pattern is very pathologic (compare with Fig. 3.30). Strong overshoot (dysmetria) of the left leg can be seen (marked). The left marked hand is also activated pathologically

3.4.2 Training on the Forefoot

Some mothers of cerebral palsy patients experience that, besides the exercising on the special CDT device, the jumping on the springboard is effective for repair.

First, when jumping on springboard, the forefoot is activated. Second, the springboard has an eigenfrequency of approximately 1Hz, which is the eigenfrequency of α_3-motoneurons (Fig. 3.4). Therefore, when jumping on springboard, the neural network of α_3-oscillators are entrained to function better. The α_3-oscillators, of which the α_3-motoneurons are a part, get repaired, which can be called oscillator formation training. These α_3-oscillators are self-organized through continuous jumping and building up an external loop to the periphery (Fig. 3.46) for repair and coordination with other α_3-oscillators. Third, the jumping on springboard trains dynamicity.

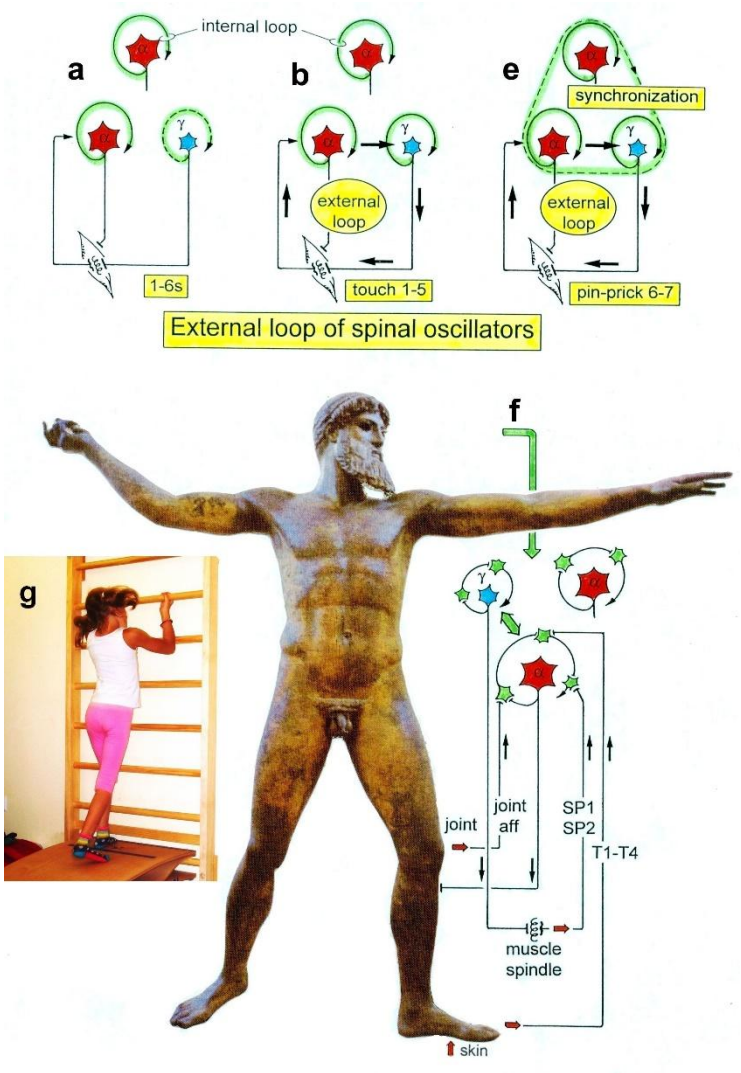

Fig. 3.46. Spreading of oscillatory firing from α-motoneuron neuronal network to include muscle spindles (periphery) and synchronization of different α and γ-motoneuron neuronal networks caused by touch and pin-prick stimulation

(a) α-motoneuron neuronal networks fired oscillatory (solid line loop), γ-motoneuron neuronal network did not or did only partly (dashed line loop), upon no additional stimulation.

(b) Oscillatory firing α and γ-motoneuron neuronal networks built up a phase relation with muscle spindle afferents and efferents (external loop to the periphery, indicated by thick arrows) upon touch 1-5.

(e) Oscillatory firing α (internal circuitry loop) and γ-motoneuron neuronal networks (external loop) synchronized (broad peak phase relation) upon pin-pricks 6-7. The dashed line loop represents synchronization.

(f) Oscillatory firing α (internal circuitry loop) and γ-motoneuron neuronal networks (external loop) are extended by analogy from the continence muscles to muscles for locomotion. The open arrows indicate that it may be possible to synchronize spinal oscillators by rhythmic afferent input, generated by rhythmic movements (such as jumping on a springboard or running), and to re-preformat the neuronal circuitry by synapse remodeling to fire more physiologically oscillatory to reduce spasticity and improve locomotion. Extensive pathologic movement like tremor may entrain neuronal circuitry to increase tremor movement. (g) when jumping on springboard, the forefoot touches the board first. The Greek good is a bronze statue of Zeus found close to the cape of Artemision 460 BC.

3.4.3 Cerebellum and Pons Repair with Respect to the Ontogenetic Landscape for Locomotion

A physiologic landscape for locomotion [37] is shown in Fig. 3.47. Because of cerebellum and pons atrophy, Sophie's landscape for locomotion had changed.

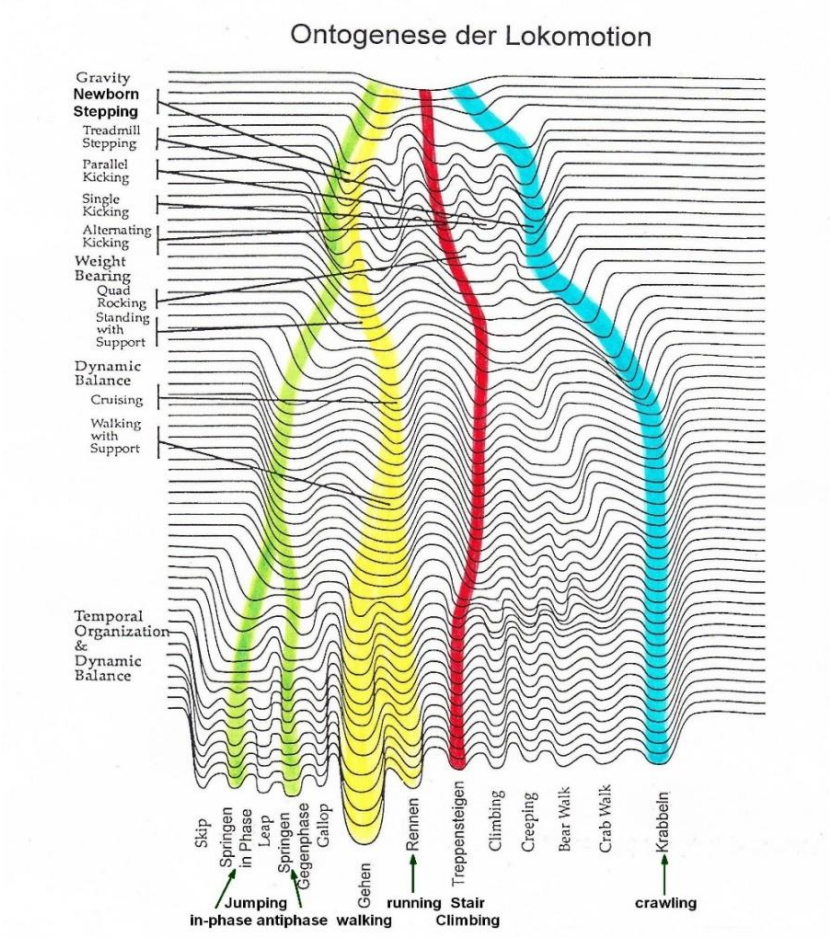

Fig. 3.47. Ontogenetic landscape for locomotion. The evolution of the attractor layout (System Theory of Pattern Formation) for the different movements. Permission of Esther Thelen (†) [37]

CDT partly recapitulates the development. But the learning process is hampered by the deficiency of the cerebellum and pons, on which the learning process also depends. To teach the injured CNS to repair itself by trial-and-error elimination processes, the CNS has, in similarity to the development, to recognize through CDT, which subnetworks, regulation units, subloops or tracts are not functioning properly (or are missing) and to repair them by error elimination, including the possibility that other brain parts take functions partly over and subnetworks and tract fibers built anew to a limited extent.

At the beginning of CDT, at an age of 5.5 years, Sophie could only crawl in antiphase to cover distances at home by herself, whereas healthy children at that age can creep, crawl, upright, walk, run and jump. Because of missing dynamic balance, she relearned the jumping on springboard late and the running very late. The functioning of the cerebellum and pons was pathologic and too slow to be able to generate in time the patterns jumping and running, according to the ontogenetic landscape. When she eventually learned the running, her dynamic balance had improved strongly.

3.4.4 Ontogenetic Landscape for CNS Functioning, Quantified by the Coordination Dynamics Values, between Healthy Children and Sophie with Cerebellum and Pons Atrophy

The learning for repair in the girl Sophie was something like 10 times faster than in the aging Dr. Cwienk.

But how was the speed of learning to improve CNS functioning of Sophie in comparison to healthy children? Probably, healthy children learn much faster than the formally disabled Sophie, even though through CDT Sophie's learning, to improve CNS functioning, speeded up. To quantify the improvement of CNS functioning in relation to healthy children, the low-load coordination dynamics values of Sophie is compared with those of healthy children.

Fig. 3.48 shown the low-load coordination dynamics values of healthy children in the age range between 3 and 18 years when being measured the first time [15, 38]. The CD values for girls and boys were the same (Fig. 3.49) and lumped together to have large groups, because the CNS functioning depends on many factors.

At an age range between 3 and 6 years, the healthy children had very high (poor) CD values. With ongoing development, the CD values became lower (better) and reached a plateau at an age of 18 (Fig. 3.48, solid and dashed line). When a child was measured again, the CD values got better (dotted line), because the CNS learned to function better through the repeated measurements. If a healthy child would perform CDT, CNS functioning would improve strongly and the low-load CD values would become much lower as is shown in Fig. 3.48 with Sophie's brother Lukas.

Lukas, the younger brother of Sophie, was squint eyed and physicians offered spectacles. But instead of wearing spectacles, he performed for a few years CDT and the mild strabismus disappeared. Anyhow, Lukas performed for a few years low-intensity CDT and his low-load CD values became much lower than those of healthy children, not exercising on special CDT devices. If healthy pupils, therefore, would also exercise on special CDT devices during school sport, their CNS functioning would get better and they would learn faster. The female director of that gymnasium, where the pupil's measurements were mainly done, exercised several times on a special CDT device and she liked it, because she was feeling better afterwards. She had better low and high-load CD values than the sport teacher. The sport teacher was disappointed and angry about that and blocked the use of CDT devices in school sport. At another gymnasium, the sport teacher had no problems to also use special CDT devices. In both schools (Tallinn, Estonia) also disabled pupils were attending.

The patient Sophie with cerebellum and pons atrophy had at the beginning of CDT much worse (higher) CD values than healthy pupils, measured one time (Fig. 3.48). But with ongoing therapy, her low-load CD values became better than those of the healthy children. But, as explained with her brother Lukas, if the healthy pupils would also have trained additionally on special CDT devices for example in school sport, their low-load CD values would have become better, because of improved

CNS functioning. But since Sophie's brother Lukas could turn much better than Sophie, she had not reached the CNS functioning of the healthy girls and boys.

Some pupils of that gymnasium had less good CD values than others of same age and got depressed. The Author told them that they should not be depressed because they can improve their nervous system functioning by learning. As is shown, even Sophie could improve her nervous system functioning tremendously, quantified by CD values, through learning (Fig. 3.48).

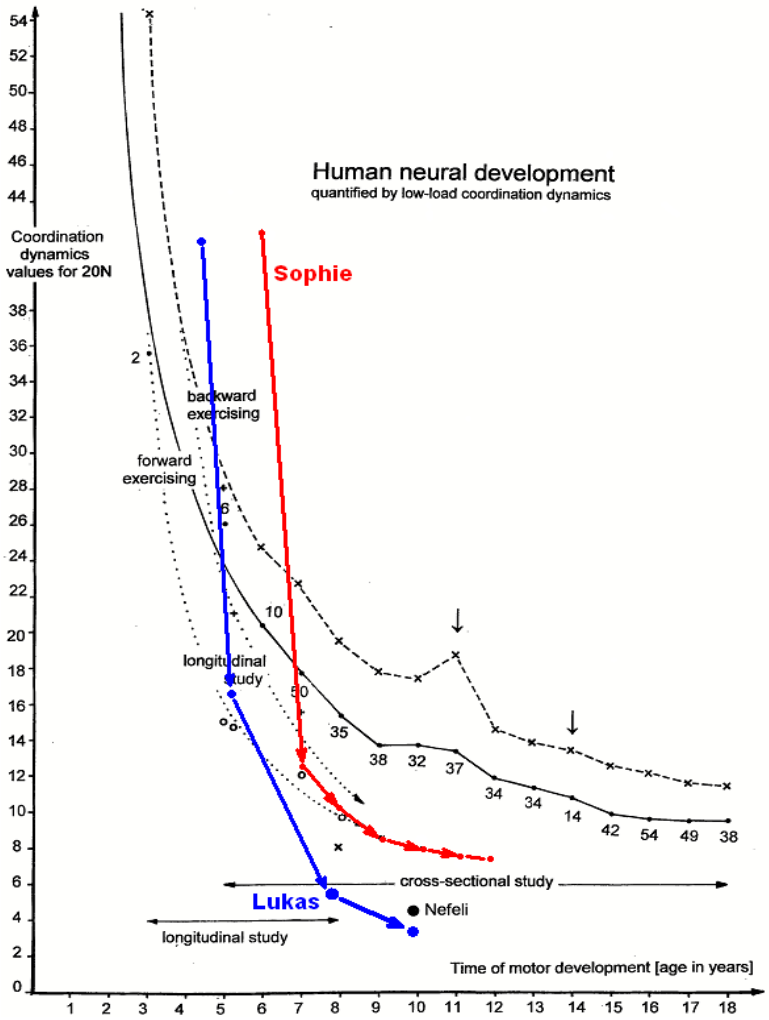

Fig. 3.48. Coordination dynamics (CD) values of boys and girls (lumped together) to quantify human neural development in relation to those of the patient Sophie. The CD values, of mainly healthy pupils from a gymnasium, transiently increase at 11 years and the group size number is small at an age of 14 (puberty, missing motivation to get measured), as is indicated by arrows. The CD values for backward exercising during the whole developmental period are worse (higher). In the longitudinal study (dotted lines) CD values become smaller (better) than the average ones of the cross-sectional study due to the repeated assessment. The patient Nefeli with SCI at the level of Th10/11 has a much better (smaller) CD value because of the CDT. Approximate good CD values from Sophie and her healthy brother Lukas (mean of forward and backward exercising) are inserted according to the age. At the beginning of CDT, the CD values of Sophie are worse than the ones from healthy children. Later on, they are better. Lukas, the younger brother of Sophie, performing CDT at a low level, has much better (lower) values than Sophie and the healthy children. A value of 1.8 is the approximately the best one, one can achieve

3.4.5 Frequency of Turning during Development and Repair

The frequency of turning, when exercising on the special CDT device, gives further information how much Sophie could catch up with healthy peoples. Those frequencies values were taken when the subject had the best CD value during a session. The pupils turned with their own inner frequency.

Healthy children improve their CNS functioning by movement-based learning. Such movements include running, jumping and training balance. When exercising on a special CDT device, these for the development necessary movements can be partly made visible. As can be seen from Fig. 3.49, the children were turning generally very fast up to a frequency of 2 Hz around the age range of 9 years. Before 9 years they could not turn that fast, even though they wanted, because their neural networks were not sufficient complex to generate the complicated coordination's between pace and trot gait. The children got stuck during turning. When being older than 9 years, they probably turned not so fast anymore, because the neural networks of the CNS did not need so much anymore the input from the fast movements. For further details of the human development with respect to CD see [1, 2, 39].

At the beginning of CDT, Sophie was not able to exercise on a special device. When she became able to turn by herself, she got often stuck, especially at the difficult coordination's (Fig. 3.27A), and the overall frequency of turning was low (0.5Hz). With ongoing therapy, she turned much faster (1.5Hz, Fig. 3.27B) and nearly reached the turning frequency of the healthy pupils (Fig. 3.49). But again, if the healthy pupils would have turned quite often, their frequency would have been even higher, because the healthy brother Lukas turned faster than all the girls and boys (Fig. 3.49). Sophie had therefore not reached the level of CNS functioning of the healthy pupils.

In conclusion, through CDT Sophie's CNS functioning improved very much, but she did not cache-up with healthy girls and boys.

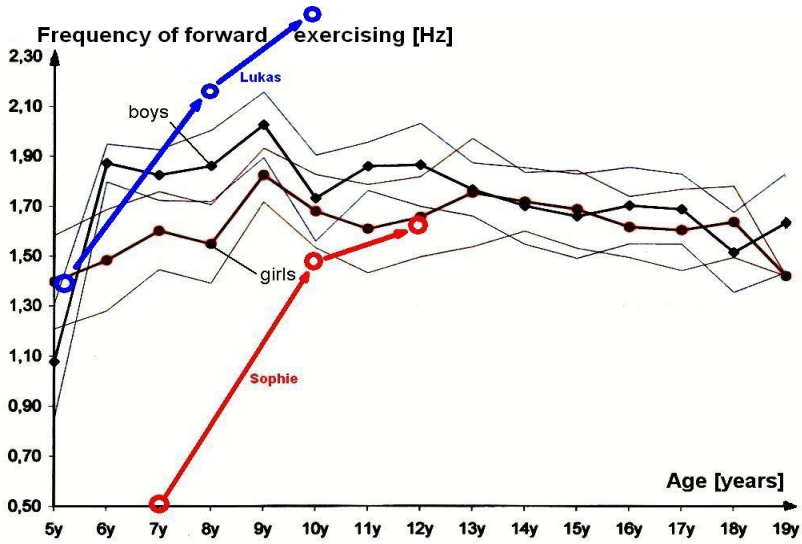

Fig. 3.49. Frequency of forward exercising (average) of boys and girls in dependence on age. "■" are boys and "●" are girls. Note that the average group values of boys and girls are very similar. The standard deviations overlap much. The frequency of turning first increased strongly and then decreased slowly. Turning frequencies of the cerebral palsy girl Sophie and her healthy brother Lukas during their development are inserted for comparison

Even though Sophies learning was very slow at the beginning of CDT, it speeded up with ongoing therapy. Her improved nervous system functioning will hold forever, as can be measured with low-load and high-load CD values in ageing. At an age of over 80, top athletes can still have very good low and high-load CD values! In a cerebral palsy patient like Sophie, priority has given first to the

repair of the CNS through movement-based learning than the learning at school, because with the improved CNS functioning, they will learn faster afterwards.

3.4.6 Reasons for the Tremendous Cerebral Palsy Repair through CDT

Without CDT, the cerebellum and pons injured/malformed Sophie and Dr. Cwienk would not have improved much. Both would have lived as disabled subjects at home and may have ruined the social life of the family. In severe cerebral palsy, often fathers cannot manage the life with the disabled child and leave the family. The big load is then on the mothers with additional money problems.

But why is such great repair in cerebral palsy possible and the mainstream medicine is mainly concerned with care? The reason is that coordination dynamics therapy was developed on the grounds of human repair-neurophysiology (Method). Especially the new single-nerve fiber action potential recording method brought the progress, because it became possible to record from an ensemble of identified single afferent and efferent fibers simultaneously and analyze human nervous system functioning at the single neuron level under physiologic and pathologic conditions. Especially the phase and frequency coordination among neuron firings and its impairment could be measure with the single-nerve fiber action potential recording method (Fig. 3.50) and the single-motor unit surface EMG (Fig. 3.6). The human repair-neurophysiology mainly brought the progress.

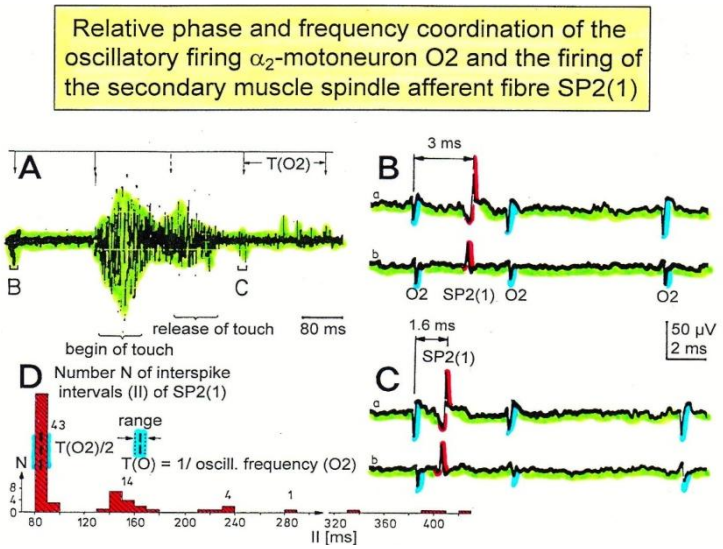

Fig. 3.50. Time relation between the occurrence of the action potentials (APs) of the oscillatory firing α_2-motoneuron O2 and the firing of the secondary muscle spindle afferent fiber SP2(1). Brain-dead human HT6. S4 dorsal root recording. A. Overall view of the used sweep piece; only trace "a" shown. Four oscillation cycle periods of the motoneuron O2 are indicated (T(O2)). The APs of the impulse trains can be recognized only partly, because of the slow time base and poor digitalization. One impulse train (dashed arrow) is lost in the touch stimulated activity, which consists of a touch (large overall activity) and a release part (lower overall amplitude). B, C. Sweep pieces from A, time stretched. In B, motoneuron impulse train APs are marked O2, spindle afferent APs are marked SP2(1). Note that the APs of the spindle afferent fiber are not time-locked to the first AP of the impulse train of the rhythmically firing motoneuron (relative phase coordination). D. Occurrence of interspike intervals of the secondary muscle spindle afferent fiber SP2(1). The numbers give the amount of IIs in each distribution peak. The oscillation period of motoneuron O2 (and the range of variation) and the half period are indicated by short dashed lines. Note that the IIs of fiber SP2(1) are very similar to the oscillation period (or the half of it) of α_2-motoneuron O_2 (relative frequency coordination)

In Switzerland, insurance companies pay for care, but not for cure, even though care is on the long term more expensive. At an international conference for pediatric acquired brain injury (IPBIS2018),

physiotherapists, rehabilitation physicians, neurologists and neuropediatric did not want to get informed about new developments in brain repair for children. Expert knowledge (in German: Fachwissen, Sachverstand) is not of interest anymore to the world society. No wonder that we have a Covid-19 pandemic [41]. CDT for example reduces the blood pressure [42] and improves cardio-vascular performance, so that the risk of thrombosis is reduced. Thrombosis is one side effect of Covid-19 infection/treatment.

REFERENCES

1. Schalow G (2002) Stroke recovery induced by coordination dynamic therapy and quantified by the coordination dynamic recording method. Electromyogr. Clin. Neurophysiol. 42: 85-104.
2. Schalow G (2002) Improvement after traumatic brain injury achieved by coordination dynamic therapy. Electromyogr. Clin. Neurophysiol. 42: 195-203.
3. Schalow G and Jaigma P (2006) Improvement in severe traumatic brain injury induced by coordination dynamics therapy in comparison to physiologic CNS development. Electromyogr. Clin. Neurophysiol. 46: 195-209.
4. Schalow G (2003) Partial cure of spinal cord injury achieved by 6 to 13 months of coordination dynamic therapy. Electromyogr. Clin. Neurophysiol. 43: 281-292.
5. Schalow G, Jaigma P and Belle VK (2009) Near-total functional recovery achieved in partial spinal cord injury (50% injury) after 3 years of coordination dynamics therapy. Electromyogr. Clin. Neurophysiol. 49: 67-91.
6. Schalow G (2010) Cure of urinary bladder functions in severe (95%) motoric complete cervical spinal cord injury in human. Electromyogr. Clin. Neurophysiol. 50: 155-179.
7. Schalow G (2019) Regeneration of the human spinal cord via coordination dynamics therapy. Peertechz Publications, 97 pp. eBook.
8. Schalow G (2021) CNS repair in a girl with a spinal cord injury. Adv Pub Health Com Trop Med: APCTM – 121.
9. Schalow G (2006) Cerebellar injury improvement achieved by coordination dynamics therapy. Electromyogr. Clin. Neurophysiol. 46: 433-439.
10. Schalow G, Jaigma P (2005) Cerebral palsy improvement achieved by coordination dynamics therapy. Electromyogr. Clin. Neurophysiol. 45: 433-445.
11. Schalow G (2006) Hypoxic brain injury improvement induced by coordination dynamics therapy in comparison to CNS development. Electromyogr. Clin. Neurophysiol. 46: 171-183.
12. Schalow G, Pääsuke M, Ereline J and Gapeyeva H (2004) Improvement in Parkinson's disease patients achieved by coordination dynamics therapy. Electromyogr. Clin. Neurophysiol. 44: 67-73.
13. Schalow G and Nyffeler T (2001) Koordinationsdynamik-Therapie: Myelomeningozele (Spina bifida). Physiotherapie.
14. Schalow G and Nyffeler T (2000). Koordinatiosdynamik-Therapie: Skoliose. Physiotherapy.
15. Schalow G (2013) Human Neurophysiology: Development and Repair of the Human Central Nervous System. Nova Science Publishers, Inc, Hauppauge NY, USA, 734 pp.
16. Schalow G (2019) Permanent coma patient re-learned to speak via Coordination Dynamics Therapy. Arch. Clin. Med. Case Rep. 3(2), 33-50.
17. Schalow G (2017) Breast cancer growth inhibition via Coordination Dynamics Therapy. In: "Horizons in Cancer Research. Volume 68". Editor: Hiroto S. Watanabe. Nova Science Publishers, Inc, Hauppauge NY, USA, pp. 125-151.
18. Schalow G (2020) Anaplastic oligodendroglioma WHO III brain cancer-patient recovered following operation, radiation and chemotherapy through Coordination Dynamics Therapy, which is also a Covid-19 treatment without ventilator. Int. J. Med. Clin. Imaging 5(2): 165-210.
19. Schalow G and Lang G (1987) Recording of Single Unit Potentials in Human Spinal Nerve Roots: a New Diagnostic Tool. Acta Neurochir. 86: 25-29.
20. Schalow G (2009) The classification and identification of human somatic and parasympathetic nerve fibres including urinary bladder afferents is preserved following spinal cord injury. Electromyogr. Clin. Neurophysiol. 49: 263-286.
21. Schalow G (2020) Classification and Identification of Human Peripheral Nerve Fibers by Conduction Velocity, Nerve Fiber Diameter and Natural Firing Patterns with Consequences for CNS Repair and Covid-19 Infection Treatment. Int. J. Med. Clin. Imaging 5(3): 231-314.

22. Schalow G (2005) Phase and frequency coordination between neuron firing as an integrative mechanism of human CNS self-organization. Electromyogr. Clin. Neurophysiol., 45: 369-383.
23. Schalow G (1993) Spinal oscillators in man under normal and pathologic conditions. Electromyogr. Clin. Neurophysiol. 33: 409-426.
24. Schalow G (2006) Surface EMG- and coordination dynamics measurements-assisted cerebellar diagnosis in a patient with cerebellar injury. Electromyogr. Clin. Neurophysiol. 46: 371-384.
25. Schalow G (2005) Tremor in Parkinson's disease patients can be induced by uncontrolled activation and uninhibited synchronization of α_2-motoneuron firing to which α_1-motoneuron firing synchronizes. Electromyogr. Clin. Neurophysiol. 45: 393-406.
26. Schalow G (2010) Scientific basis for learning transfer from movements to urinary bladder functions for bladder repair in patients with spinal cord injury. Electromyogr. Clin. Neurophysiol. 50: 339-395.
27. Kelso JAS (1995) Dynamic Patterns. The Self-Organization of Brain and Behavior. MIT Press, Cambridge.
28. Schöner G, Zanone PG and Kelso JAS (1992) Learning as change of coordination dynamics: Theory and experiment. Journal of Motor Behavior 24: 29-48.
29. Zanone PG and Kelso JAS (1992) Evolution of behavioral attractors with learning: Nonequilibrium phase transition. Journal of Experimental Psychology: Human perception and Performance, 18 (2): 403-421.
30. Popper KR (1972). Objective knowledge: An evolutionary approach. London: O.U.P.
31. Touwen B (1987) Variability and stereotypy in normal and deviant development. In: Care of handicapped child. Apley, J. (Ed.). Clinics in Developmental Medicine No. 67. Philadelphia, pp. 99-110.
32. Thelen E (1987) The role of motor development in developmental psychology: a view of the past and an agenda for the future. In: Eisenberg, N. (ed.): Contemporary Topics in Developmental Psychology. New York, Wiley, pp 3-33.
33. Schalow G (2020) From brain repair to Covid-19 treatment via Coordination Dynamics Therapy. (Video film contains therapy movements of patients' recent publications). Video conference August 19, 2020. (Download from www.coordination-dynamics-therapy.com).
34. Baehr M and Frotscher M (2005) Duus' Topical Diagnosis in Neurology. Thieme Verlag, Stuttgart. (a very good book for medical neuroscience since it correlates structure and function in human nervous system injuries; only human neurophysiology is missing).
35. Deisseroth K, Singla S, Toda H et al (2004) Excitation-neurogenesis coupling in adult neural stem/progenitor cells. Neuron 42: 535-552.
36. Schalow G (2009) Building of New Motoneurons in the Human Spinal Cord upon Coordination Dynamics Therapy to Improve Finger Functions in Motoric Complete Cervical Spinal Cord Injury. In: Berkovsky, T.C. (Ed.), Handbook of Spinal Cord Injuries, Chapter 4. pp. 231-264, Nova Science Publishers.
37. Thelen E and Smith LB (1994) A dynamic approach to the development of cognition and action. MIT Press, Cambridge.
38. Schalow G (2015) Repair of the Human Brain and Spinal Cord. Nova Science Publishers, Inc, Hauppauge NY, USA, 525 pp.
39. Schalow G (2015) Neural network learning in human. Nova Science Publishers, Inc, Hauppauge NY, USA, 324 pp.
40. [40] Schalow G (2021) Phase and frequency coordination improvement among neuron firing for improved CNS self-organization and neural repair in Parkinson and spinal cord injury. Int J Med Clin Imaging 6(1): 350-425.
41. Schalow G (2020) Covid-19 infection improvement through the movement-based learning therapy 'Coordination Dynamics Therapy'. Int. J. Med. Clin. Imaging 5(2): 157-164.
42. Schalow G (2020) To live longer with a better quality of life through coordination dynamics therapy especially in patients with severe brain injury and brain-cancer. Int. J. Med. Clin. Imaging 5(2): 118-155.

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This chapter is an extended version of the article published by the same author(s) in the following journal.
Advances in Public Health, Community and Tropical Medicine, 2021(1), 2021.

Chapter 4
Print ISBN: 978-93-5547-205-2, eBook ISBN: 978-93-5547-216-8

Basal Ganglia and Cortex Repair through Human Repair-Neurophysiology 12 Years after Hypoxia during Birth

DOI: 10.9734/bpi/mono/978-93-5547-205-2/CH4

ABSTRACT

The patient Alen suffered at birth an insult and an asphyxia with the consequence of a sustained cerebral hemiplegia on the left side, a parenchyma defect of the basal ganglia and a degeneration of a pyramidal tract. At an age of 12 years coordination dynamics therapy was started.
Most functions were impaired in Alen. He could not use the left hand, which is a disability of 50%. But he could walk and run with deficits. Through 6 months of coordination dynamics therapy, creeping, crawling, walking and running became nearly normal. He learned to jump in-phase and in anti-phase. Most importantly, he learned left hand functions, including the power and precision grip, and could use them for everyday life. His cognitive functions improved. He could better learn at school. What main stream medicine did not achieve in 12 years; coordination dynamics therapy succeeded in 6 months.

Keywords: Human repair-neurophysiology; Electrophysiology; Single-nerve fiber action potentials; Oscillatory firing; Phase and frequency coordination; Coordination dynamics therapy; Basal ganglia repair; Ontogenetic landscape for locomotion.

4.1 INTRODUCTION

Fig. 4.1. The spinal cord injury patient Nefeli relearned to walk and became continent again (A-D) [7,13]. The cerebral palsy girl Sophie with atrophied cerebellum and pons could not stand, walk, run (E, F) or jump and was incontinent. She learned to walk, run (G, H) and jump, became continent and her higher mental functions improved [15]

Based on human repair-neurophysiology [1, 2], a movement-based learning therapy was developed, called Coordination Dynamics Therapy (CDT) [3], with which it is possible to improve or repair central nervous system (CNS) functioning after stroke [4], traumatic brain injury [5, 6], spinal cord injury [7, 8, 9, 10, 11, 12, 13] (Fig. 4.1, Nefeli), cerebellar injury/atrophy [14, 15] (Fig. 4.1, Sophie), cerebral palsy [16], hypoxic brain injury [17], in Parkinson's disease [18], spina bifida (myelomeningocele) [19] and scoliosis [20]. Speech had been induced and improved in a patient with severe cerebral palsy [1]. A permanent coma patient could be brought out-of-coma and relearned to speak and move [21, 57] and cancer grows could be inhibited through CDT [22, 23] by improving cardio-vascular performance [1, 21] and building of natural killer cells [24]. Urinary bladder functions [1] could be cured in cerebral palsy [1] and spinal cord injury [7, 12, 13]. There is indication that the general health can be improved via CDT to live longer with a better quality of life [25].

A further repair step through human repair-neurophysiology is to repair an injury of the basal ganglia. With the 12-year-old boy Alen it will be shown on what level of medical research the cerebral cortex and the basal ganglia can be repaired. Alen had suffered a perinatal insult and an asphyxia with the result of a sustained cerebral hemiplegia, a parenchyma defect of the basal ganglia and a degeneration of the pyramidal tract to the left side. Basal ganglia injuries are supposed to be difficult to repair. But by using probable movements of phylogenetical older species, phylogenetical old motor centers can also be repaired, as will be shown.

In the Method, on the basis of functional anatomy, the deficits of movements and other patterns due to the injury of the basal ganglia and the cortex are explained. It will be shown how CDT is adapted to the repair of these injuries. In the Results, the CNS disorders will be shown at the beginning of therapy. With ongoing CDT, the improvements of CNS functioning are quantified clinically by the repair of movements and other patterns and theoretically with the improvement (lowering) of the coordination dynamics value. In the Discussion, the basal ganglia repair of Alen will be compared with the cerebellum repair of Sophie (Fig. 4.1E-H).

4.2 METHOD

4.2.1 Movement-based Learning Strategies to Repair the Human CNS

To repair the human CNS, several strategies are used. First, to repair the always impaired phase and frequency coordination (a principle of CNS organization) through exercising on a special coordination dynamics therapy (CDT) device. Second, to train important automatisms during ontogenetic development like, creeping, crawling, up-righting, walking, running and breezing, because genetic support can be expected and repair shows similarities to ontogenetic development. Third, to repair the especially phylogenetic old CNS structures like the spinal cord, the vermis of the cerebellum and the paleostriatum (globus pallidus) of the basal ganglia, movements have to be trained, which phylogenetic ancestors like Tiktaalik, may have used for locomotion. Such movements are creeping, salamander crawling, hopping and others. Fourth, to activate and train important regulation circuits, which, for example, are activated during jumping. Jumping helps to repair urinary bladder and other functions. Fifth, those patterns have to be trained which activate the CNS most integrative, because only then the whole complexity of the regulation units/circuits are entrained and pathologic neural network organizations cannot shift to another CNS part and escape repair.

The nervous system has to recognize which structures or regulation units are deficient, to repair them by error elimination processes. Movement-based learning in combination with instructive training (1-2-3-..), visual (mirror) and auditive (music) feed-back increases the efficiency of treatment.

4.2.2 Basal Ganglia and Cortex Injury Due to Hypoxia

Alen suffered a brain injury through the complications during birth (vasa previa?). After the caesarean delivery he had fluid mixed with blood in the lung and did not breath. When the fluid was removed, he started to breath, but he had suffered hypoxia. Hypoxia is a condition in which the brain or a region of the brain is deprived of adequate oxygen at the brain parenchyma level. Since Alen suffered a tissue

loss of the basal ganglia, an injury of the primary cortices and an atrophy of a pyramidal tract, probably the middle cerebral artery transported blood with too little oxygen (Fig. 4.2), because it supplies, among other parts, the primary and sensory cortices, the language areas of Broca and Wernicke (Alen had speech problems), the primary auditory cortex and the basal ganglia. Other nuclei could be slidably damaged, as for example the thalamus, which was not diagnosed by the MRI. Anyhow, those brain tissue parts are most injured, which get the littlest oxygen. The most far away rami striati may lack most oxygen. Since the delivery was a caesarean, a mechanical brain damage is unlikely.

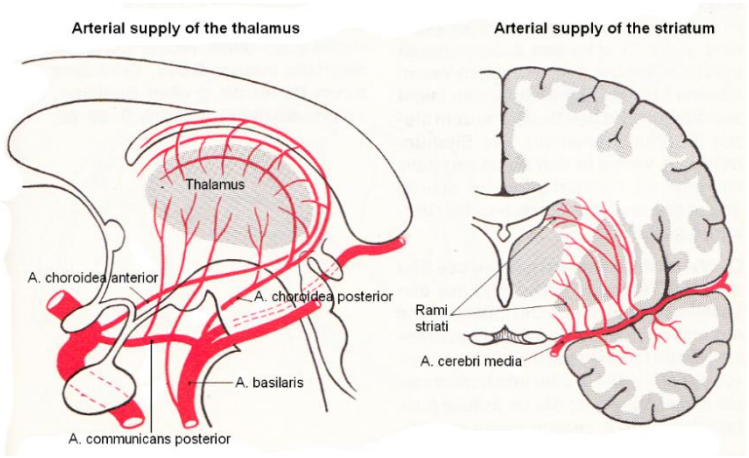


Fig. 4.2. Arterial blood supply of the striatum (and thalamus). The middle cerebral artery supplies with its branches, among other parts, the primary and sensory cortices, the language areas of Broca and Wernicke, the primary auditory cortex and the basal ganglia. (Van den Berg and Vander Eeken)

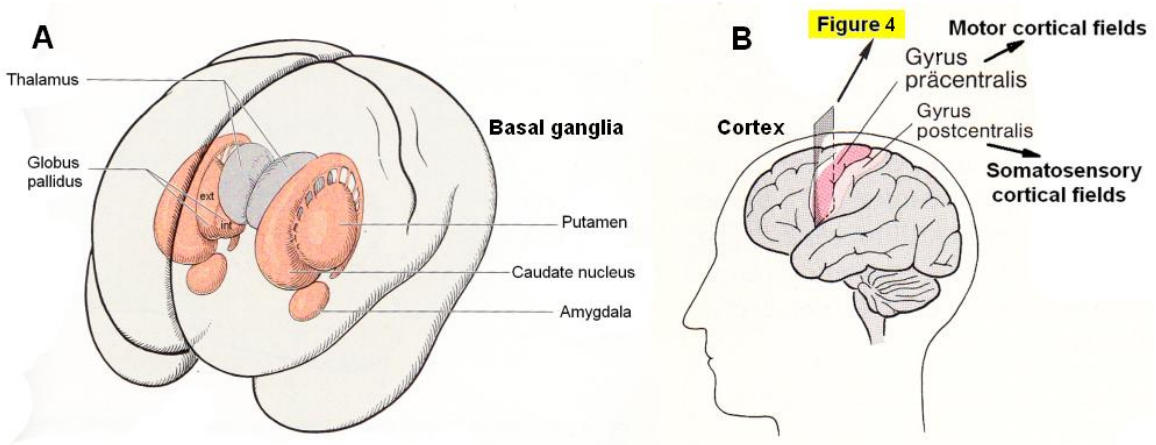


Fig. 4.3. A. Topographical relationship of the basal ganglia (in red) [26]. B. Position of motor and somatosensory cortical fields, displayed in Fig. 4.4

4.2.3 Functional Anatomy of the Cerebral Cortex and Basal Ganglia for Understanding the Repair

Figs. 4.3 and 4.4 show the gross anatomy of the basal ganglia and the cortex. A loss of parenchyma of the basal ganglia and an injury of the sensory-motor cortex was diagnosed in Alen and had to be repaired. The basal ganglia are a part of the motor system. The principal nuclei of the basal ganglia are the caudate nucleus, the putamen, and the globus pallidus (Fig. 4.3A). These nuclei are connected to each other and to the motor cortex (Fig. 4.5A) in complex regulatory circuits (Fig. 4.5B).

They exert both excitatory and inhibitory effects on the motor cortex. They play an important role in the **initiation, maintenance** and **modulation** of movement patterns. In phylogenetically older species, the older neural centers are primarily responsible for the maintenance of movement patterns and the automatic control of locomotion. Injuries of the basal ganglia, and of other, functionally related nuclei, such as the substantia nigra and the subthalamic nucleus, can produce either an excess or the deficiency of movement-related impulses (the left hand of Alen was not activated), and/or pathological alterations of movement and other patterns.

The hierarchically uppermost center for the control of movement is the cerebral cortex, whose signals are transmitted by the pyramidal pathway (in Alen atrophied to the left body part) to the motor cranial nerve nuclei and to the anterior horn cells of the spinal cord (pyramidal system). The pyramidal and extrapyramidal systems are subunits of a single integrated motor system and, as such, are closely linked to each other, both structurally and functionally (Fig. 4.5) and have to repaired integrative.

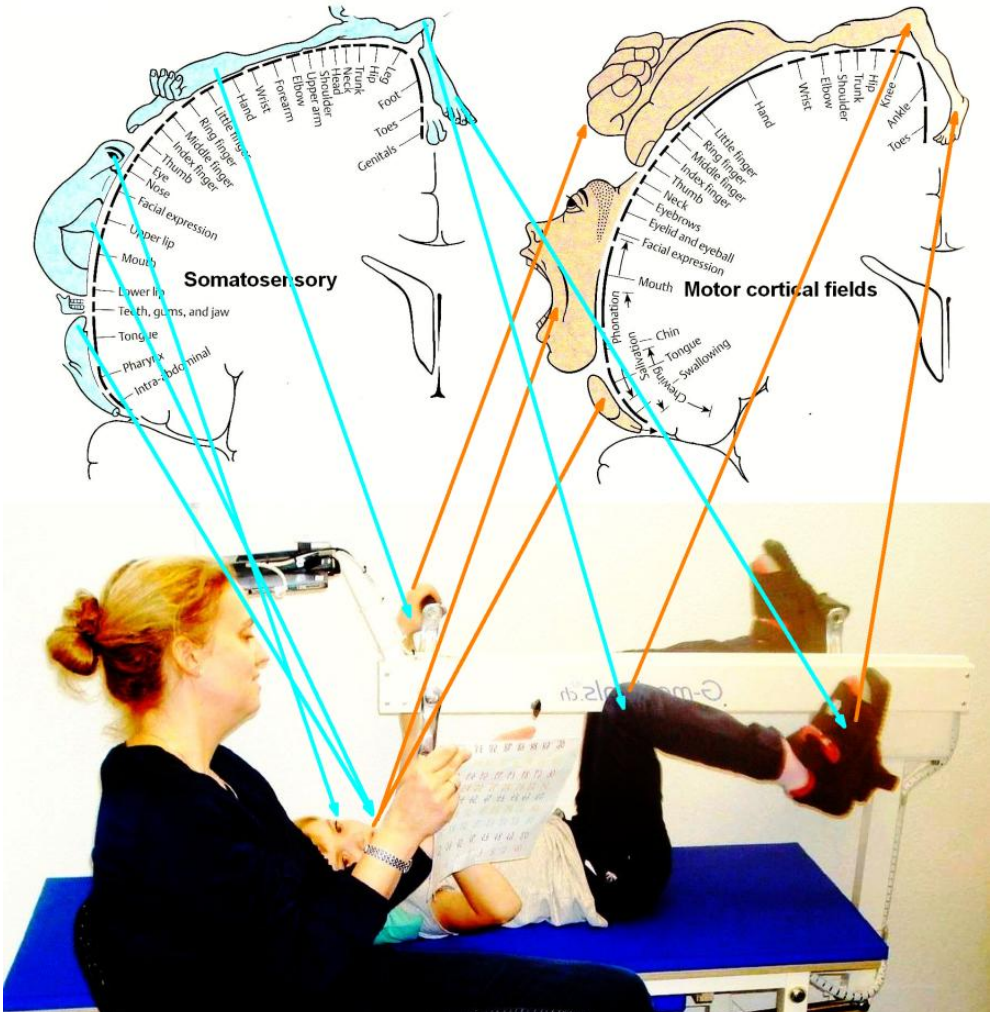


Fig. 4.4. The cerebral palsy girl Sophie during exercising on a special CDT device. At the same time, the mother (teacher herself) is administering speech therapy to her. In such a very integrative training setting, nearly the whole somatosensory and motor cortical fields (Fig. 4.3B) are activated with their associated fields for repair. - Cortical fields are taken from Penfield W and Rasmussen T, New York, 1950. - This special CDT device for measuring and therapy (int.pat.) is produced by the firm: Giger Engineering, Martin Giger dipl.Ing.ETH/SIA, Herrenweg 1, 4500 Solothurn, Switzerland, www.g-medicals.ch

As the cerebral cortex developed, the phylogenetically older motor centers (paleostriatum (globus pallidus) and neostriatum (caudate nucleus and putamen)) came increasingly under the control of the new motor system, i.e., the pyramidal system. The cat can still walk without much difficulty after the removal of the cerebral cortex, whereas humans are entirely dependent on an intact pyramidal system. As will be shown in the Results, Alen could not activate on volition the fingers of the left hand. But through co-movement from the rather healthy right hand, he learned within 6 weeks the power grip and the precision grip of the left hand (plegic side), mainly generated by the older motor centers.

When exercising on the special CDT device, including speech therapy (Fig. 4.4), the whole sensory-motor cortex is activated and entrained, including the premotor areas and the association field, and also the basal ganglia and other nuclei or structures. But to repair more specifically the basal ganglia, also probable movements of phylogenetic ancestors have to be trained. Such movements are creeping, salamander crawling, hopping and similar movements (see below).

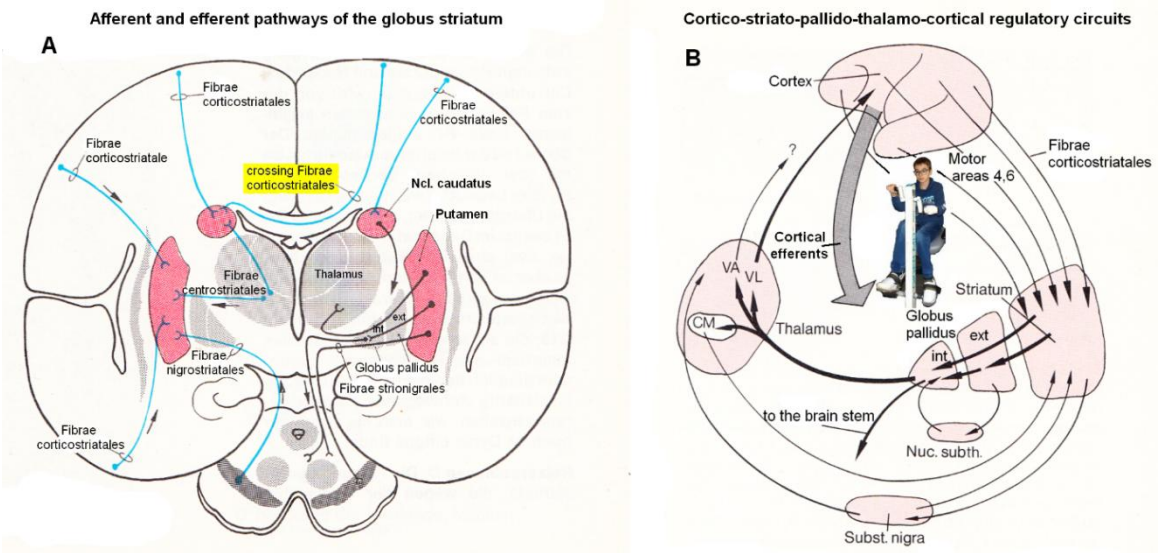


Fig. 4.5. A. Afferent and efferent pathways of the striatum (Ncl. caudatus and Putamen) [27]. B. Cortico-striato-pallido-thalamo-cortical regulatory circuits. CM Centrum medianum, VA Ncl. Ventralis anterior, VL Ncl. Ventralis lateralis [28]

4.2.4 Probable Movements to Activate, Train and Repair More Specifically the Basal Ganglia

Tiktaalik and other animals may have used creeping, salamander crawling, hopping and similar kinds of movements for locomotion.

Why is it important to look for repair movements which originate in phylogeny? First, anyway further movements are needed to find and repair the deficiencies of neural structures in different injuries. Second, it seems difficult to repair functions when old CNS structures, including the spinal cord and basal ganglia, are injured and contribute to complex pathologic movement patterns. If, for example, the basal ganglia or the thalamus are damaged, a repair is difficult to achieve by movement-based learning. But maybe if movements of animals of the phylogeny are trained, we may reach more efficiently the injured old brain structures for repair. Gene expression changes may be activated then for further repair of the deficient neural structures.

Tiktaalik roseae is a lobe-finned fish from the late Devonian period, about 375 million years ago, having features akin to those of four-legged animals (tetrapods) (Fig. 4.6) [29-31]. Tiktaalik (Fig. 4.6B) has a possibility of being a representative of the evolutionary transition from fish to amphibians. It and similar animals (Fig. 4.6A) may possibly be the common ancestors of amphibians, reptiles, birds, and mammals. Tiktaalik was gaining structures that could allow it to support itself on solid ground and

breath air, a key intermediate step in the transformation of the skull that accompanied the shift to life on land by our distant ancestors.

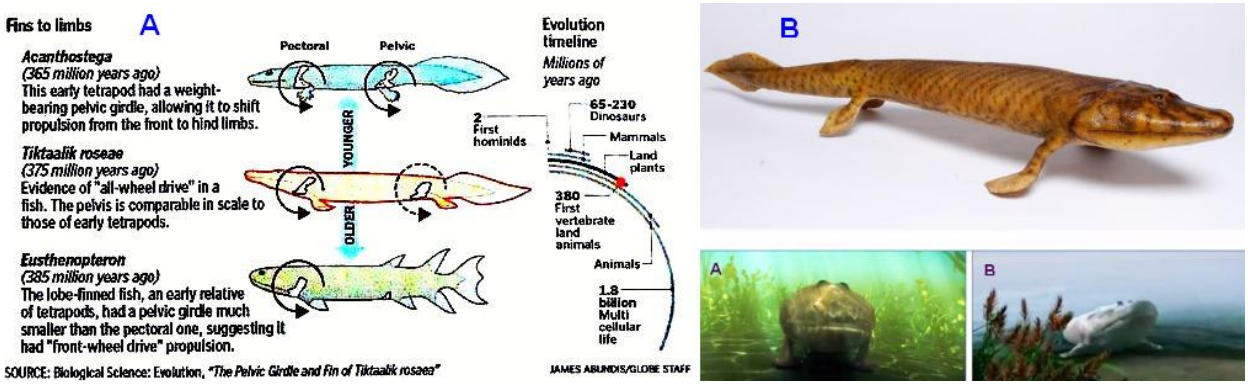


Fig. 4.6. A. Evolutionary transition from fish to tetrapod's. B. Tiktaalik roseae. Possible movements in shallow water (A) and when coming out of water (B)

The patient Nefeli with an incomplete spinal cord injury at Th10 could simulate with the arms the symmetrical front fin movements of Tiktaalik (Fig. 4.7C, D) and also the alternating fin movements (Fig. 4.7C, D) and trained in this way trunk stability. Still these movements are not suitable for trunk stability repair, because firstly, the patients do not like those movements, secondly, the movements are not very integrative and thirdly arm and leg movements have to be integrated in the movement to activate neural networks across the injury site. The creeping (Fig. 4.10), the propulsion from the arms to the legs (hopping, Fig. 4.8) and the salamander crawling (Fig. 4.10) are more suitable for the repair of spinal cord and brain injuries. May be, also Tiktaalik, Acanthostega or similar animals used these movements for locomotion.

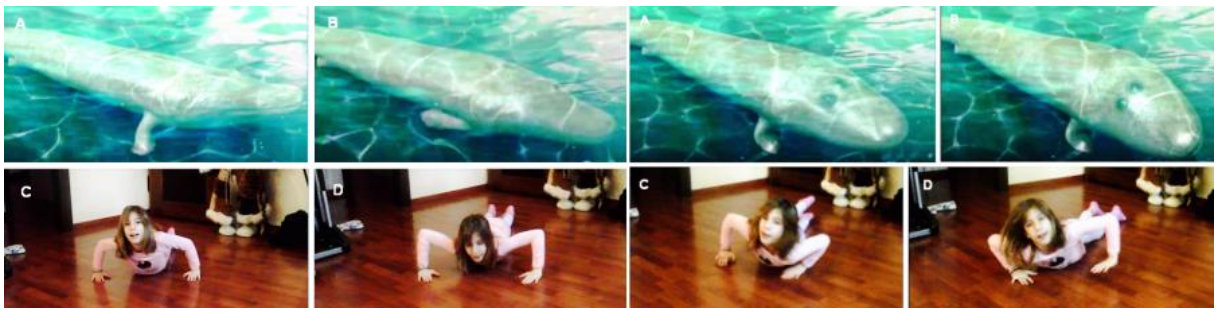


Fig. 7. Left. Possible symmetrical front limb movement of Tiktaalik (A, B), simulated for repair by the 10-year-old Nefeli with an incomplete spinal cord injury at the level of Th10 (C, D). Right. Possible rotational body movement of Tiktaalik (A, B), caused by alternately using one front limb for forward locomotion. This front limb movement is simulated by a patient with a spinal cord injury by using alternately the right and left arm (C, D)

Many scientists regard Tiktaalik as the crucial animal between fish and the first tetrapod's. But numerous track ways seem to show that first tetrapod's appeared long before Tiktaalik. Track ways were reflecting quadrupedal gait and diagonal walk (Fig. 4.9). A model of Tiktaalik's skeleton could also produce a print much like the one published (Fig. 4.9) if it's mushed into sand. Different consistencies or angles could produce an even closer match. There is nothing in Tiktaalik's described anatomy that suggests it didn't have a stride.

The salamander-crawling (Fig. 4.10) may be a pattern from phylogeny which helps to repair the CNS. How much such salamander-walking is helpful has to be seen. This movement pattern includes the trot gait crawling combined with a bending of the trunk and will be anyway helpful to reduce scoliosis and improve trunk performance. As can be seen from Fig. 4.10, the spinal cord injury patient Nefeli

could bend the trunk well to one side (Fig. 4.10C) but only little to the other side (Fig. 4.10D) because of scoliosis and spasticity. Emphasizing the bending to the difficult side will reduce the scoliosis. A more efficient reduction of the scoliosis will be achieved when exercising the trunk rotation on the special CDT device in the lying position (Fig. 4.4).

Fig. 4.8. Propulsion forward movement from the front to the hind limbs, performed by a patient with an incomplete spinal cord injury Th10 (Nefeli)

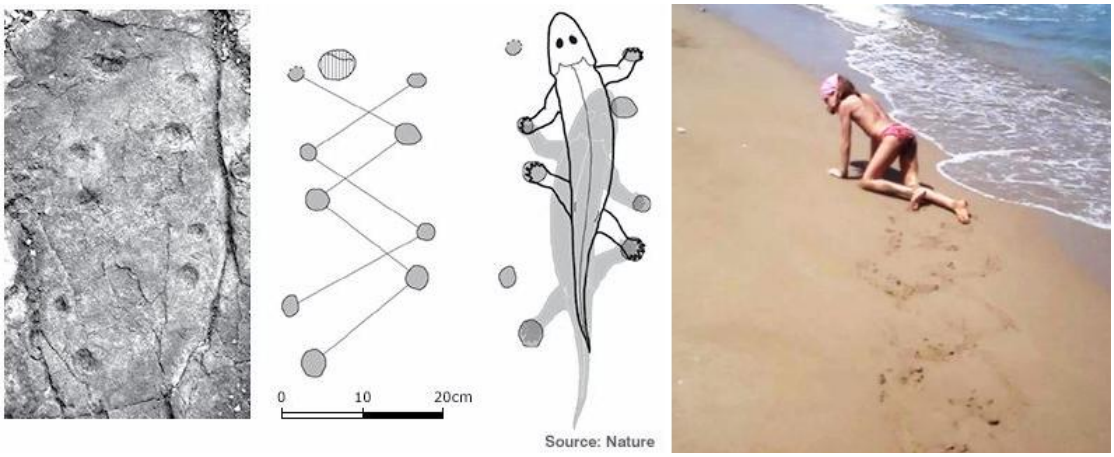


Fig. 4.9. Footprints of tetrapod's and track way of crawling of a patient with incomplete SCI Th10

Fig. 4.10. A, B. Moving of the salamander (Salamander-walking). C, D. Salamander-walking (salamander-crawling) of the 10-year-old Nefeli with a spinal cord injury (Th10). In D the bending is disturbed because of the scoliosis and spasticity

With respect to the repair of the basal ganglia by movement-based learning, it is unimportant when tetrapod's appeared. Important is whether there are movements which can repair old brain structures efficiently. When a patient or healthy person moves at beach (Fig. 4.9), different track ways can be mashed into the sand, depending on what movement pattern is performed. The patient Nefeli could creep, crawl, salamander-crawl, bear walk, spider-walk, walk and could run a tiny bit and can mush into sand many very different track ways. The movement pattern of Fig. 4.10 is the here named salamander-crawling. Crawling in pace or trot gait in the forward or backward direction can generate already many different track ways. What movements a nervous system can generate, we only know when the nervous system is available and we can measure it up with basic methods.

The cerebral palsy girl Sophie (Fig. 4.1E-H) was not able to creep. When she learned to exercise by herself on the special CDT device (Fig. 4.4) she suddenly could creep with quite a good performance (Fig. 4.16 of [15]). Obviously, the creeping (Fig. 4.30 of [15]) is an automatism. Interesting is, why does the pelvis rotate during the creeping movement? Is there an animal with a similar moving pattern? One possibility is that rotational movements occurred already in the Tiktaalik, Acanthostega or similar animals. Tiktaalik may moved symmetrical with the front fins, moved alternately with one front fin or moved with front and hind fins at different patterns. A repair of trunk stability/performance is necessary in most CNS injuries. But especially in spinal cord injuries between the intumescentia cervicalis and lumbosacralis, the repair/improvement of the trunk stability is important. The possible different trunk movements of Tiktaalik or similar animals may contribute to the repair of the trunk.

In Alen the improvement of trunk movement performance is also important, because he is growing and because of the hemiplegia, his trunk is already deformed and may get further deformed.

4.2.5 Repair of Phase and Frequency Coordination through Exercising on Special CDT Devices

The first and most important movement, to be trained during repair, is the exercising on a special CDT device to repair the coordinated firing of neurons, namely, the phase and frequency coordination. This new repair strategy is based on a new development in human neurophysiology with which it is possible to record the impulse traffic among neurons at the single-neuron level.

4.2.6 Human Neurophysiology

With the single-nerve fiber action potential recording method, single-nerve fiber action potentials can be recorded from sacral nerve roots, running in and out of the spinal cord (Figs. 4.11, 4.67) [32].

By measuring the conduction times and with the known electrode pair distance of 10 mm, conduction velocity distribution histograms were constructed in which the myelinated nerve fiber groups larger than 4μm could be characterized by group conduction velocity values (Fig. 4.12). After the recording, morphometry was performed. Distributions of nerve fiber diameters were constructed and nerve fiber groups were characterized by the peak values of asymmetrical distributions (Fig. 4.12). By correlating the peak values of the conduction velocity distributions with those of the diameter distributions, obtained for the same root, a classification scheme was constructed of the human peripheral nervous system (Fig. 4.13) [33,34]; the only existing one for human peripheral nerve fibers.

This classification and identification scheme represents a solid basis for classifying and identifying nerve fiber groups in the human peripheral nervous system and analyzing CNS functions at the single-neuron level. It became thus possible to record natural impulse patterns simultaneously from identified single afferent and efferent nerve fibers and analyze self-organizing mechanisms of the human CNS under physiologic and pathologic conditions.

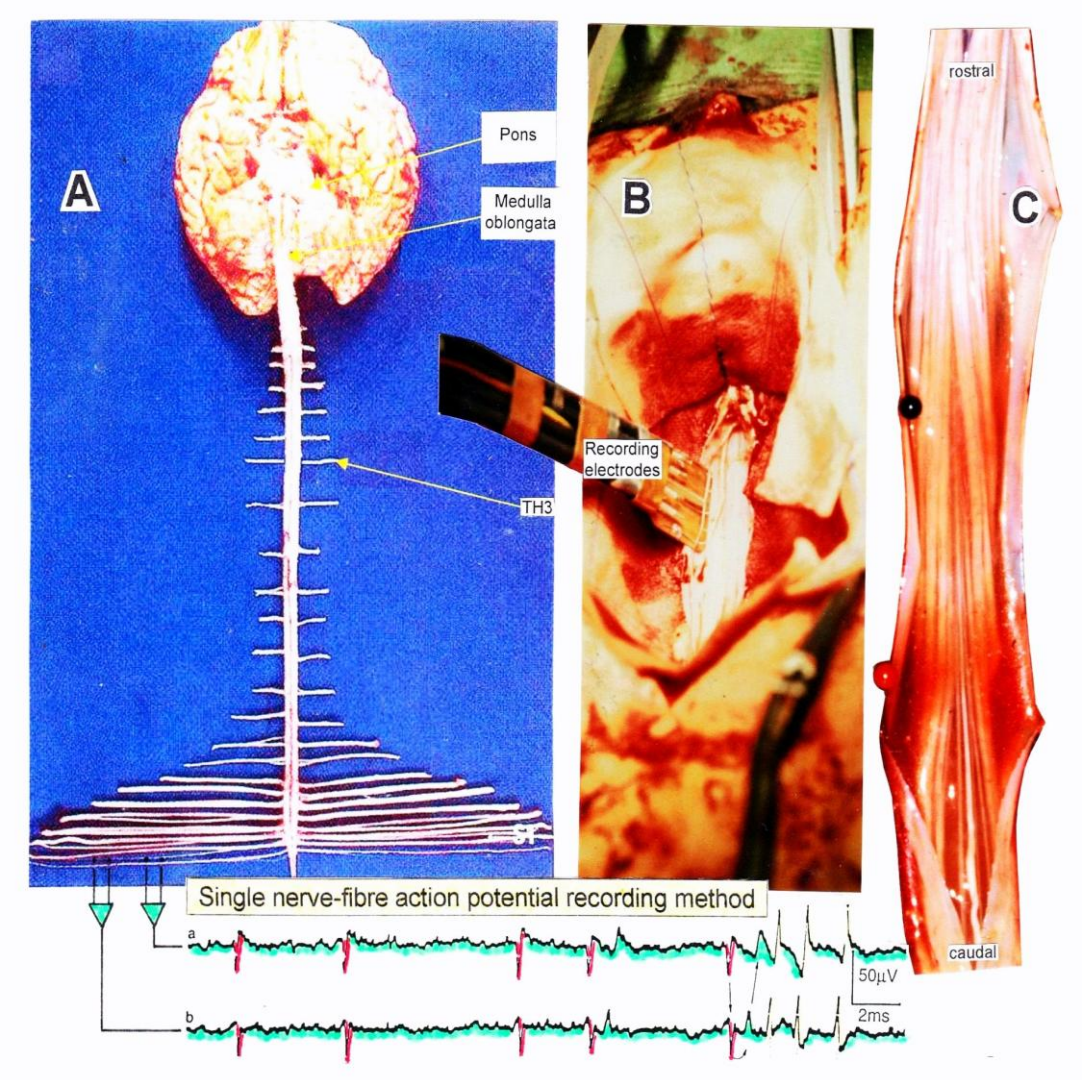


Fig. 4.11. Layout of the recording of single-nerve fiber action potentials to analyze the self-organization of neuronal networks of the human CNS under physiologic and pathophysiologic conditions. A, B, C. By recording with two pairs of platinum wire electrodes (B) from sacral nerve roots (cauda equina, C) containing between 200 and 500 myelinated nerve fibers, records were obtained in which single nerve-fiber action potentials (APs) were identified from motoneurons (main AP phase downwards) and afferents (main AP phase upwards). A. Human CNS with the schematic illustration of the recording layout and an original record of single nerve-fiber action potentials. Note the time calibration of 2ms. B. Intraoperative recording layout (when implanting a bladder stimulator) with two pairs of wire electrodes and one temperature sensor. A thin nerve root is positioned over the platinum wire electrodes. C. Dissection of the human cauda equina. At the caudal end, the filum terminalia and thin nerve roots can be seen. Dissections of the Author apart from the laminectomy in B

The most important finding with the single-nerve fiber action potential recording method was that nerve cells in the human CNS are organizing themselves through “Phase and Frequency coordination” [35, 36] (Figs. 4.16, 4.17). In nerve fibers, this phase and frequency coordination can easily be measured, because the three motoneuron types fire for high activation oscillatory [37] and offer in this way a structure to which the timed firing of neurons can be related to. Since the α_2-motoneuron oscillations are most stable, firing phases of neurons can be related best to the α_2-motoneuron firings.

Fig. 4.14 shows schematically the oscillatory firing patterns of the three kinds of motoneurons and the muscle fiber types they innervate.

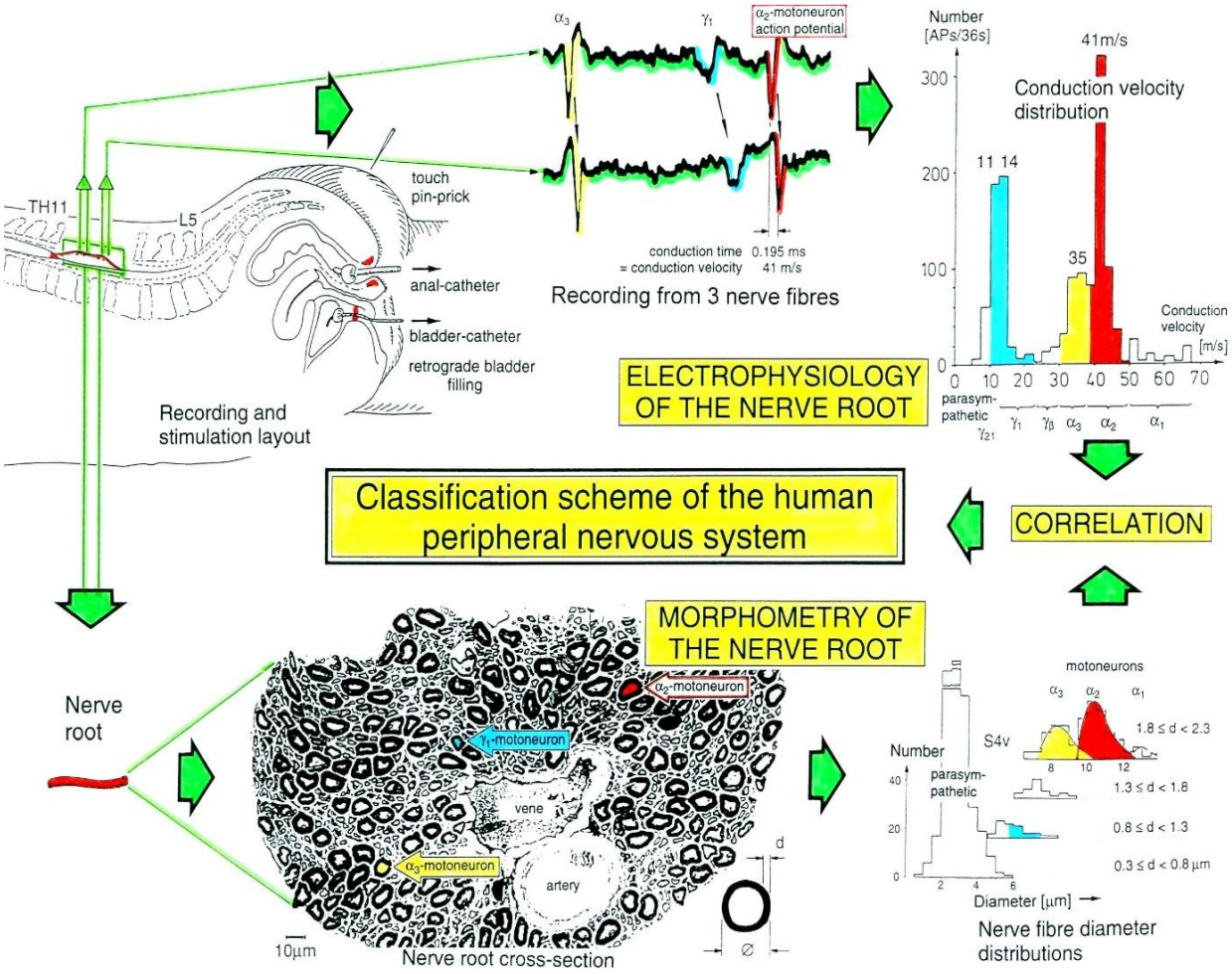


Fig. 4.12. Development of a classification scheme for human peripheral nerve fibers. Conduction velocities (V) and nerve fiber diameters (∅) of afferent (from receptors) and efferent (motor) nerve fiber groups in normal humans and in patients with a traumatic SCI for 0.5 to 6 years

By comparing CNS functioning in brain-dead humans (where the spinal cord is functioning rather physiologically) and patients with spinal cord injury, injury-induced changes of CNS functioning can be measured and partly repaired. Mainly the phase and frequency coordination of neuron firing becomes impaired following injury. This impaired coordination among neuron firings can efficiently be repaired through exercising on a special CDT device (Fig. 4.4).

The drawing back of the single-nerve fiber action potential recording method is that it is an invasive recording method. But with the surface electromyography (sEMG) [38] one can record non-invasively coordinated firing among motoneurons via their motor units if one records from suitable patients, like incomplete spinal cord injury patients, when a certain muscle is only innervated by a few motoneurons.

In Fig. 4.15, the recordings from motoneurons and motor units are compared. The firing patterns of α_1, α_2 and α_3-motoneurons can easily recorded with the single-nerve fiber action potential recording method but not with the sEMG (Fig. 4.15). From spinal cord injury patients, on the other hand, single-motor unit APs can be easily recorded from α_1 motor units but not from α_2 and α_3 motor units (Fig.

4.15), because their AP amplitude seems to be too small. Clinical sEMG recordings therefore show mainly the activity of α_1 motor units. The phase and frequency coordination among neuron firings can be measured in human with the single-nerve fiber action potential recording method (Fig. 4.16) and with surface EMG (Fig. 4.17).

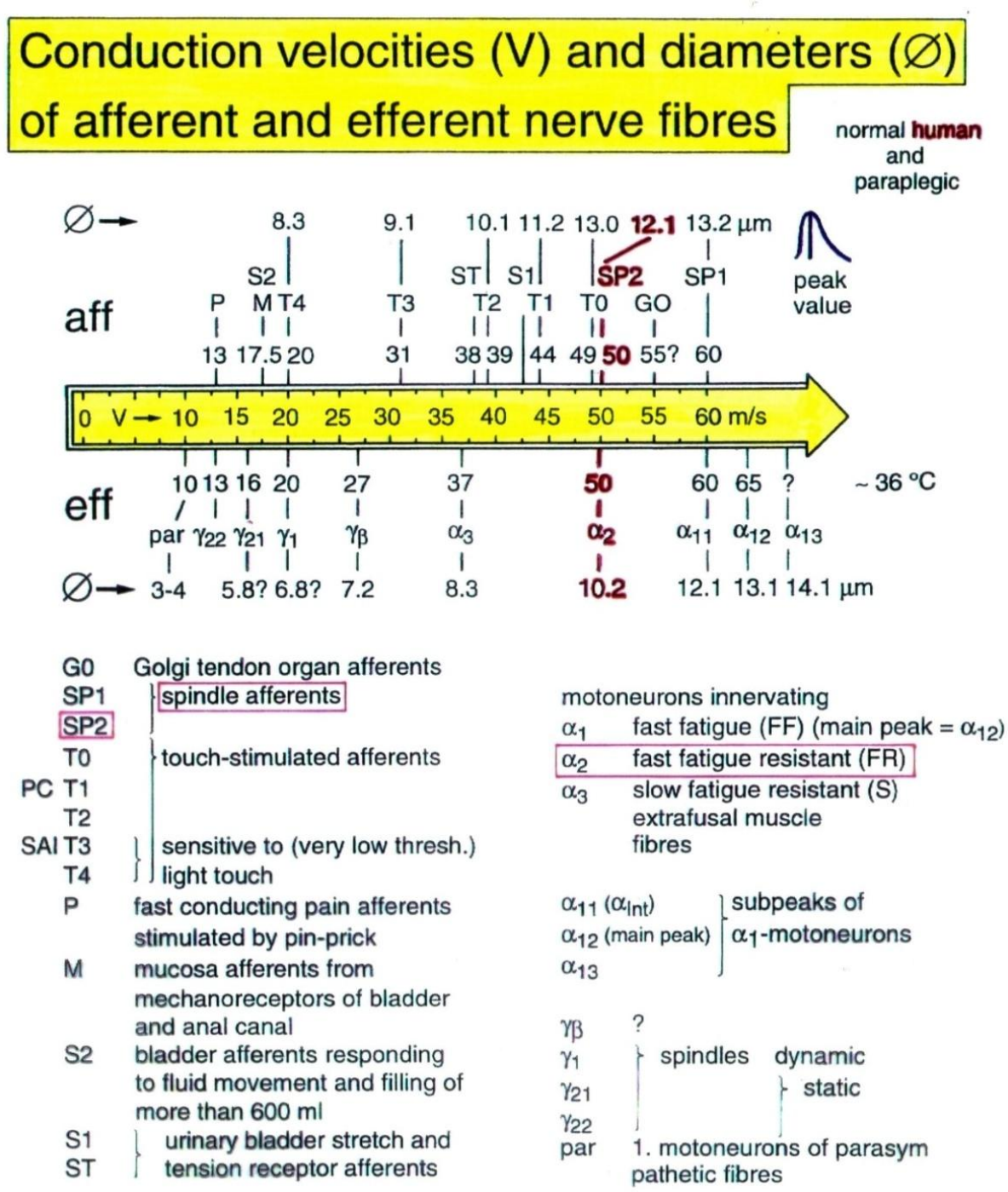


Fig. 4.13. Classification scheme for human peripheral nerve fibers. Conduction velocities (V) and nerve fiber diameters (∅) of afferent and efferent nerve fiber groups in normal humans and in patients with a traumatic spinal cord injury for 0.5 to 6 years. The splitting of the α_1-motoneurons into the 3 subgroups, α_{11}, α_{12}, α_{13}, has not yet been confirmed. This is the only existing classification scheme for human peripheral nerve fibers!

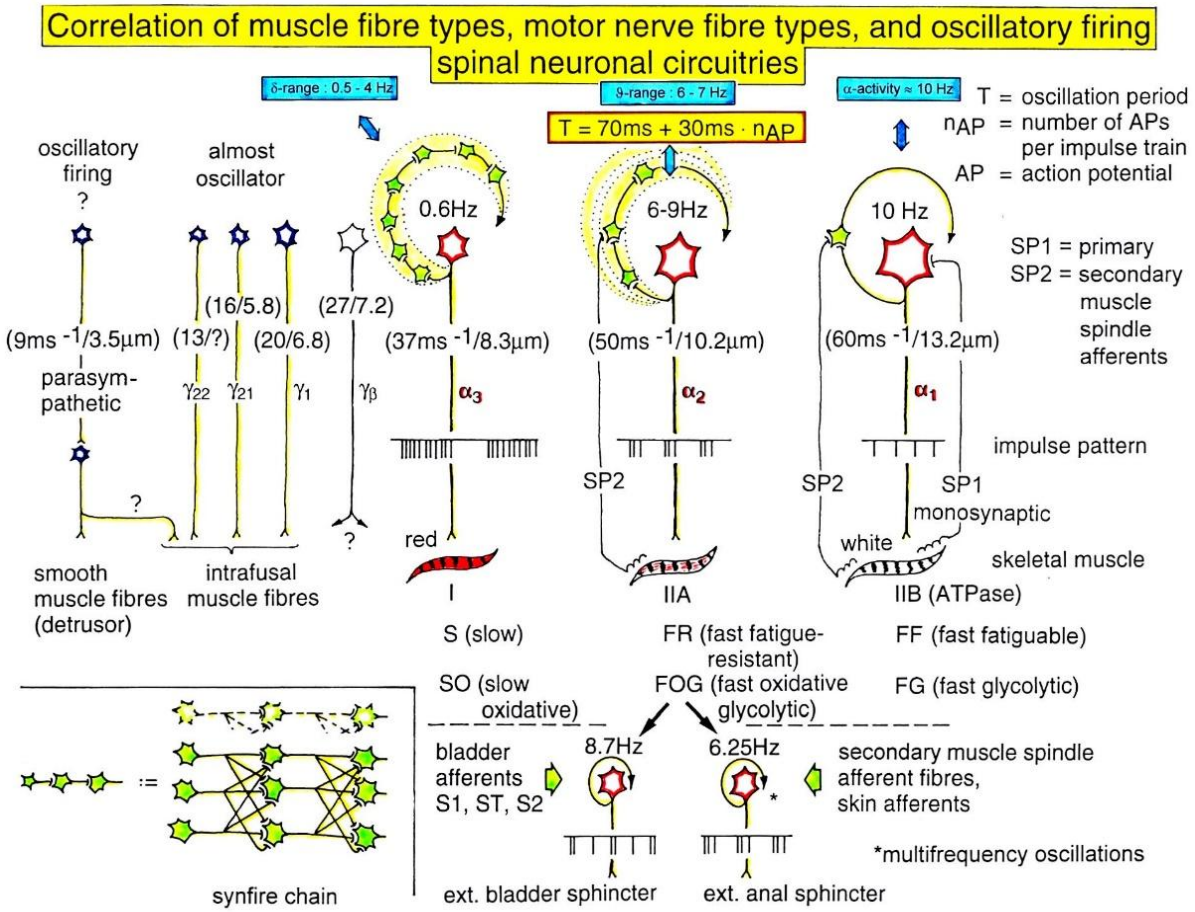


Fig. 4.14. Correlation of muscle fiber types, motor nerve fiber types, and oscillatory firing spinal neuronal networks (oscillators), based on histochemical, morphological and neurophysiological properties. This figure provides a simplified correlation between muscle fiber, motoneuron and sacral oscillator types. No additional subtypes have been included. The existence of α_1-motoneuron (FF) oscillators firing at 10 Hz has been predicted and they have been identified in paraplegics. α = motoneuron, γ_1, γ_2 = dynamic and static fusimotors, parasympathetic = parasympathetic preganglionic motoneuron. S1, ST, S2 = stretch, tension and flow receptor afferents

The neural networks of the human brain, including the cerebral cortex and the basal ganglia, organize themselves by phase and frequency coordination among neuron firings and neural subnetworks as for example the network oscillators of which the motoneuron is a part. This coordination is achieved by the organization tendencies of the network, the descending impulse patterns from the brain and the spatiotemporal afferent impulse patterns from the periphery.

If the premotor spinal oscillators would not coordinate their firing and synchronize their firing for longer periods of time, tremor would occur. Such pathologic synchronization can be observed in patients with Parkinson's disease [39, 40].

If the neural networks are damaged by trauma, degeneration or malformation, the coordination between neuron firings becomes impaired and has to be repaired by movement-based learning (CDT). Drugs and operations cannot repair neural network functioning.

The generation of motor patterns of α_1-motoneuron firings with increasing load and the phase and frequency coordination among single-motor unit firings can be recorded with sEMG (Fig. 4.17).

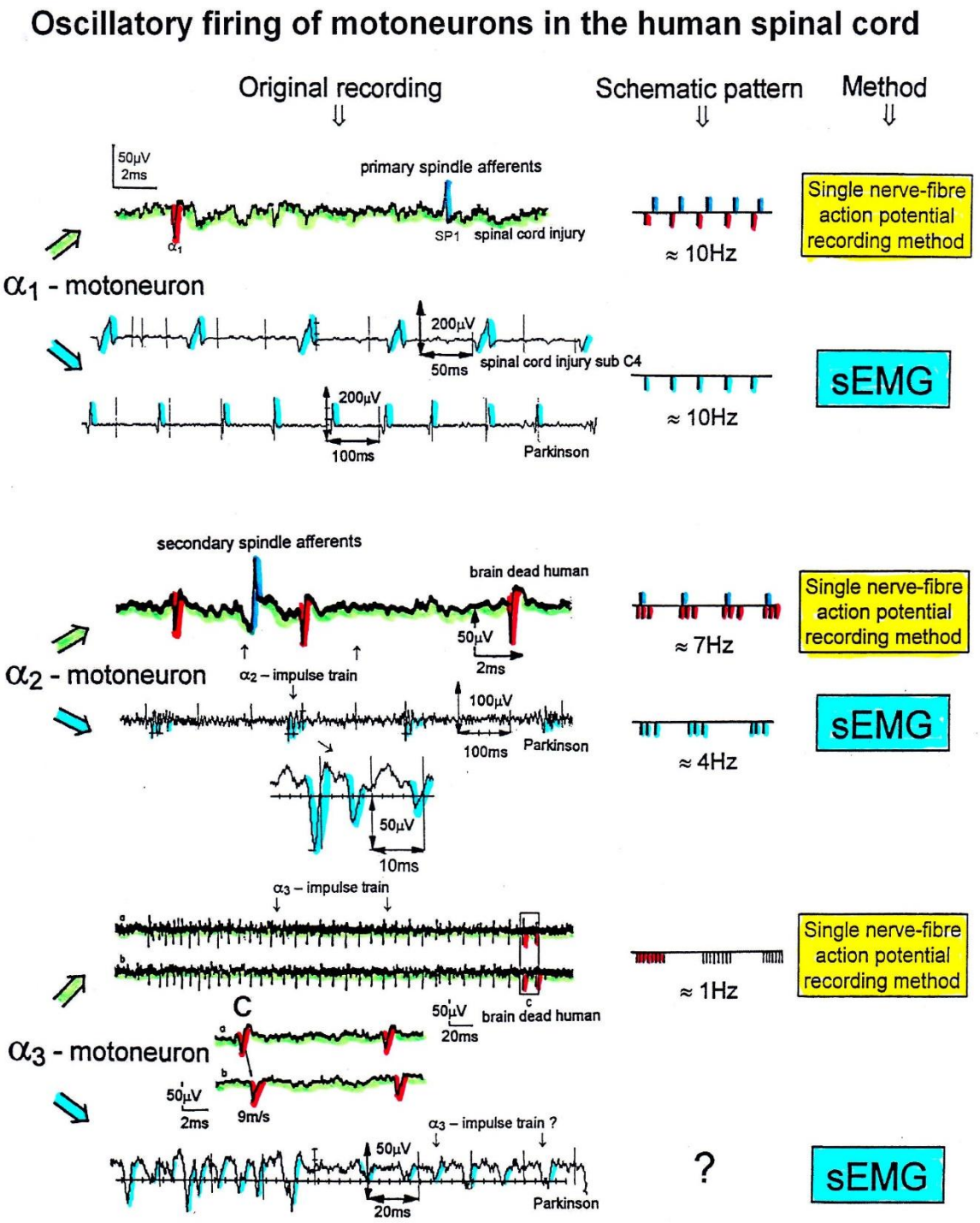


Fig. 4.15. Oscillatory firing patterns of α_1, α_2, and α_3-motoneurons recorded from motoneuron axons with the single-nerve fiber action potential recording method and by surface electromyography (sEMG) from FF, FR, and S-type motor units. The left panel shows original recordings, the middle panel the schematic patterns; the recording methods are indicated on the right side. The recordings were taken from patients with spinal cord injury and Parkinson's disease and from brain-dead humans

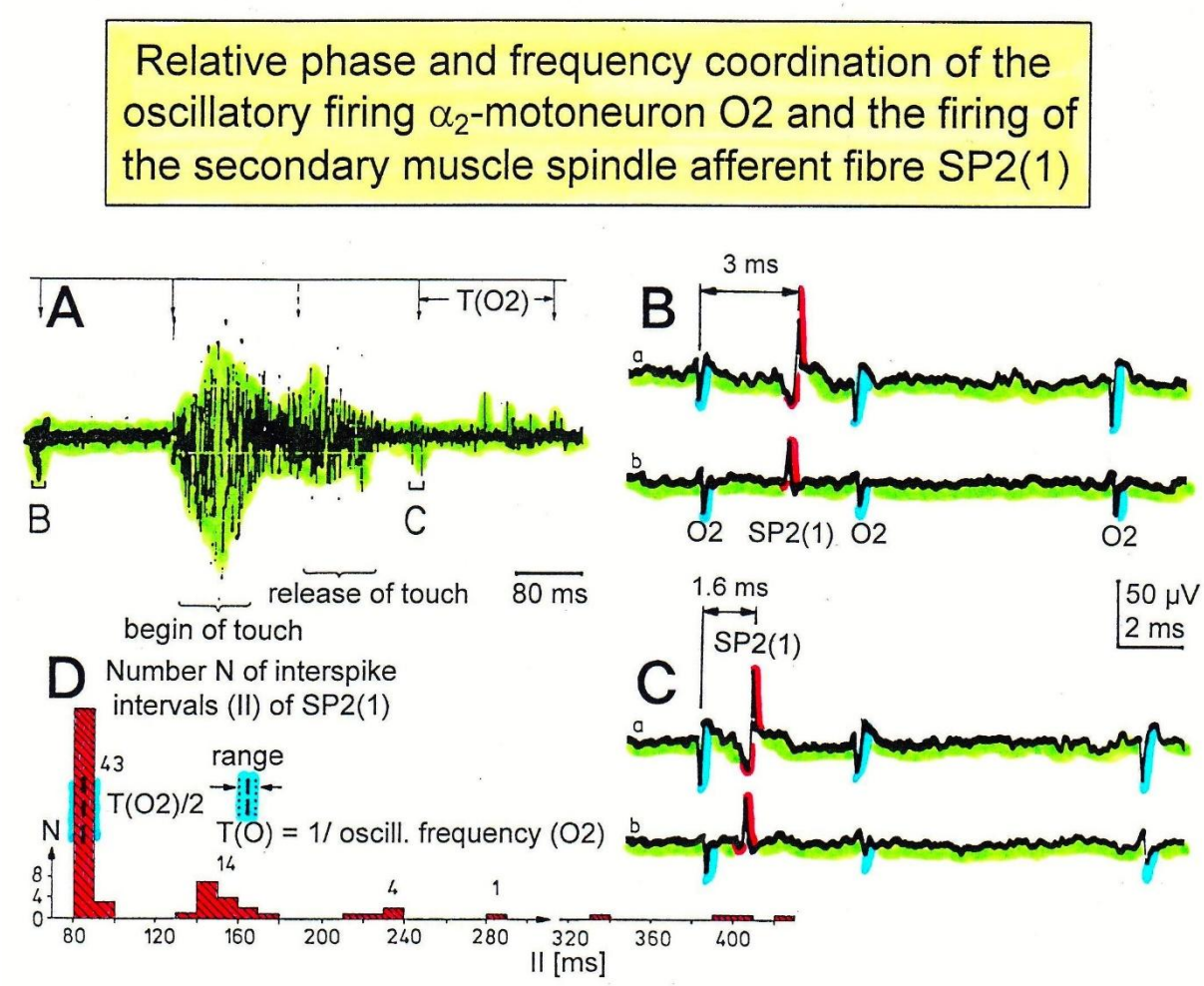


Fig. 4.16. Time relation between the occurrence of the action potentials (APs) of the oscillatory firing α_2-motoneuron O2 and the firing of the secondary muscle spindle afferent fiber SP2(1). Brain-dead human HT6. S4 dorsal root recording. A. Overall view of the used sweep piece; only trace "a" shown. Four oscillation cycle periods of the motoneuron O2 are indicated (T(O2)). The APs of the impulse trains can be recognized only partly, because of the slow time base and poor digitalization. One impulse train (dashed arrow) is lost in the touch stimulated activity, which consists of a touch (large overall activity) and a release part (lower overall amplitude). B, C. Sweep pieces from A, time stretched. In B, motoneuron impulse train APs are marked O2, spindle afferent APs are marked SP2(1). Note that the APs of the spindle afferent fiber are not time-locked to the first AP of the impulse train of the rhythmically firing motoneuron (relative phase coordination). D. Occurrence of interspike intervals of the secondary muscle spindle afferent fiber SP2(1). The numbers give the amount of IIs in each distribution peak. The oscillation period of motoneuron O2 (and the range of variation) and the half period are indicated by short dashed lines. Note that the IIs of fiber SP2(1) are very similar to the oscillation period (or the half of it) of α_2-motoneuron O_2 (relative frequency coordination)

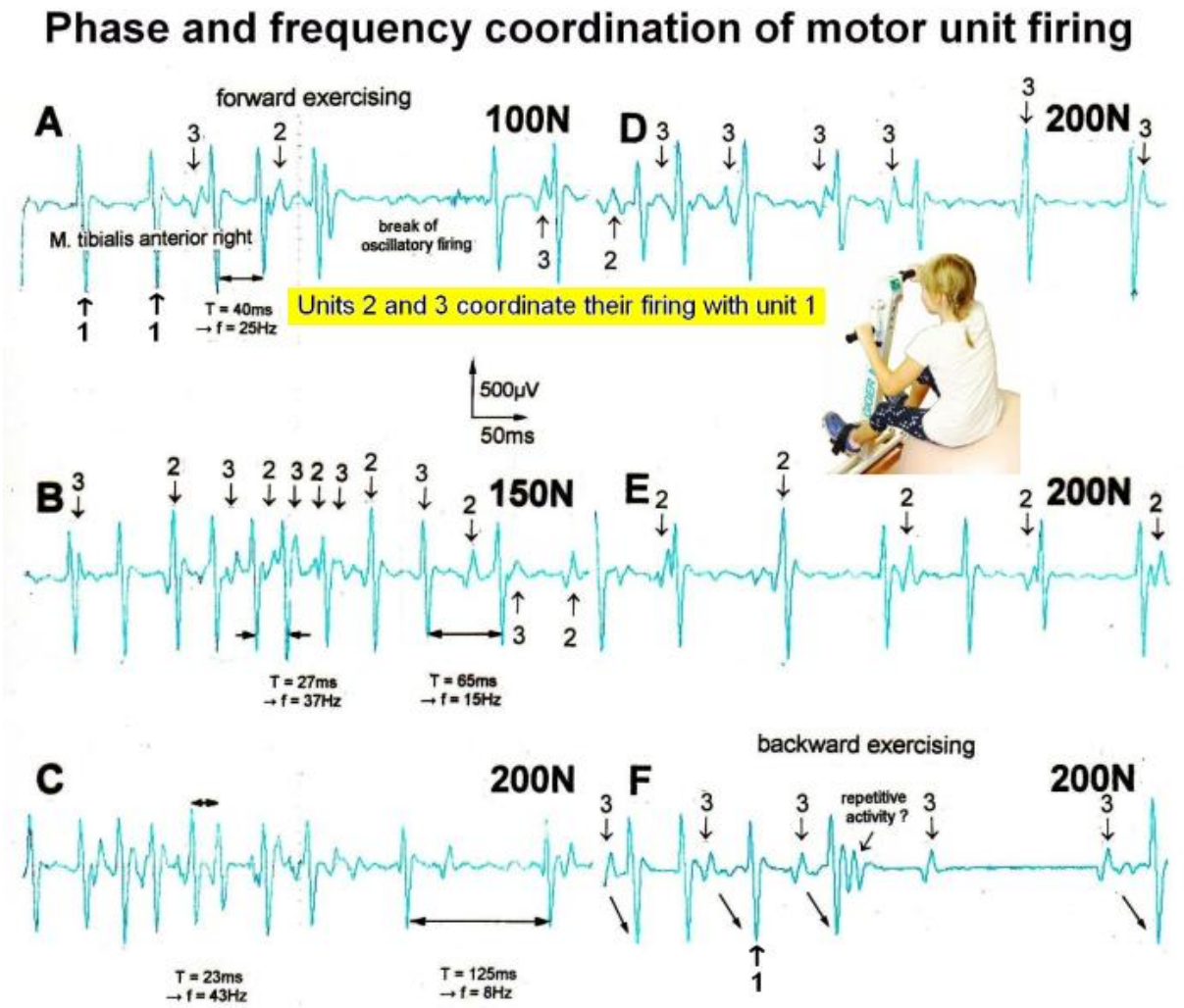


Fig. 4.17. Phase and frequency coordination between oscillatory firing of 3 motor units (FF-type, motor units '2' and '3' are partly marked) during the generation of a motor program when exercising on the special coordination dynamics therapy device at loads increasing from 100 to 200N. Oscillation periods (T) and oscillation frequencies (f [Hz]) of oscillatory firing motor unit 1 (largest motor unit) are partly indicated. In 'F', some coordination's between motor unit '3' and '1' are marked

4.2.7 Improvement of Stability and Exactness of Phase and Frequency Coordination to Allow Specific Patterns Formation and Learning Transfer (System Theory of Pattern Formation)

The importance of stable and exact phase and frequency coordination, to allow specific pattern formation and in consequence **learning transfer** [41] to other patterns, can be understood at the collective variable level (System Theory of Pattern formation [42-44]) and at the neuron level. The behavioural information F_{inf} of the coordination pattern dynamics, characterized by equations of motion of collective variables, $dX/dt = F_{intr}(X) + \sum c_{inf}F_{inf}(X,t)$, affect the whole coordination pattern dynamics, including stability, rather than only certain coordination patterns. If the behavioural information includes the exercising of extremely coordinated, integrative movements, like exercising on the special CDT device for turning, then the quality of CNS self-organization can be enhanced by improving the exactness of self-organization, namely the precision of phase and frequency coordination between neuron and neural assembly firings. By improving the precision of organization of the intrinsic dynamics $F_{intr}(X)$, that is, the specific variability of the injured networks, certain patterns

do then already reappear. In the 12-year-old patient Alen, the left hand became operational through 6 weeks of coordination dynamics therapy, first time in his life.

Neurons often serve more than one network pattern at the same time by time sharing of neuron firing and, in this way, give rise to learning transfer among the activated patterns. If subnetworks are improved in the organization of one pattern, the organization of the other pattern will also improve. Neurons involved in the organization of breathing and activating intercostal muscles, for example, are also involved in the organization of trunk stability. By reducing the spasticity of the trunk (in patients with Parkinson's disease), the breathing will also improve. Similarly, sphincteric motoneurons are involved in continence and pelvic floor weight bearing. If during pregnancy the pelvic floor is not trained, sometimes incontinence occurs. This stress incontinence after birth can be repaired by learning transfer from coordinated movements. By mainly exercising on the special CDT device and jumping on springboard, urinary bladder functions can be repaired by learning transfer in otherwise healthy women.

4.2.8 Measuring CNS Functioning by the Arrhythmicity of Exercising (Coordination Dynamics Value)

The impaired phase and frequency coordination at the single neuron level, the assembly level and the macroscopic level can be measured macroscopically when the patient is exercising on a special coordination dynamic therapy device (Fig. 4.28A) on which arms and legs turn with a slightly different frequency (transmission 19 (arms) : 18 (legs)). The phase coordination between arms and legs is imposed by the device. The loss of phase and frequency coordination between arm and leg movements becomes visible and measurable by the arrhythmicity of turning. During a turning cycle, the coordination between arms and legs changes between pace and trot gait and according to the difficulty of the coordination, the turning frequency increases and decreases. This frequency variation (df/dt; f = frequency) can be recorded, quantified and displayed on a computer screen (Fig. 4.51) and is called coordination dynamics value. CNS functioning is therefore measured though pattern change (continuous change from trot gait to pace gait and backwards) according to the System Theory of Pattern Formation.

During the functional reorganization of the injured CNS of patients, the relative phase and frequency coordination of neuron firing has to be trained as exactly as possible by the movement induced afferent impulse patterns from the receptors (learning through feedback information) to restore coordination in the range between 3 and 5 milliseconds (approximate lengths of postsynaptic potentials). The device has therefore to impose the exercising patient a coordination in the millisecond range for the different coordination's of arm and leg movements between pace gait and trot gait. The easy pace and trot gait coordination's, but not the difficult intermediate coordination's, can often be performed easily by the patient. Therefore, the continuous change from the easy to the difficult coordination's and backwards diagnoses the capability of the CNS to organize easy and difficult organizational states. If the movement states can be easily generated by the neuronal networks of the CNS, then the frequency variation of turning is small during the turning cycle, and if the movement state is difficult to be organized by the patient's CNS, then the frequency variation is large (the coordination dynamics value is large).

4.2.9 Unique Properties of Special CDT Devices

The special CDT device has three important properties. First, the patient performs coordinated arm, leg and trunk movements when exercising on it. The training of the integrative patterns take care of that the pathologic organization cannot escape from repair by shifting to another part of the CNS and the whole CNS, including the injured parts, is reorganized so that other CNS parts can take function over through plasticity. Second, the device is extremely exact, so that the endplate potentials in the neural networks (approximately 5ms long) overlap, to improve the efficiency of organization. In spinal cord injury, for example, the transmission over the injury site will increase. In basal ganglia and cortex repair, more action potentials will reach the motoneurons in the spinal cord for activating arm and leg muscle fibers. Third, the coordination between arm and leg movements changes from pace to trot

gait, imposed by the device. The intermediate coordination patterns between pace and trot gait are difficult to generate for the CNS neural networks. If the patients CNS learns to generate these intermediate patterns, imposed by the device, then the neural networks have learned to function better in the deep complexity of CNS organization. The patient's nervous system learns by turning from the device, to function more physiologically through improving especially the phase and frequency coordination among neuron firings. This phase and frequency coordination can be measured by the single-nerve fiber action potential recording method (Fig. 4.16) invasively and by single-motor unit surface electromyography non-invasively (Fig. 4.17).

4.2.10 Motor Learning and Problem-solving Therapy

Because of basal ganglia and cortex injury and atrophied pyramidal tract in the patient, there are retarded, accelerated or deviant development of motor and other functions. Some functions may not develop at all, while others show only a decrease in variability. Both impaired and healthy parts of the brain mature over time and thus lead to increased complexity, which has direct repercussions on the quality of the learning (trial-and-error-elimination [45]) processes. Processes that in themselves are normal cannot bring about good results because some areas of the brain which are also necessary for the accomplishment of the particular motor function are deficient.

The well-known symptoms and signs of cerebral palsy in the first year of life (poverty of movements, stereotypy of posture and motility, inability to "discover" new motor possibilities, neglect of one extremity, stereotyped extension of the legs during vertical suspension, head-lag during the traction test or during sitting) can all be traced back to a lack of trial-and-error-elimination processes (learning) as a consequence of deficient brain structure. In the case of an inability to "discover" new motor possibilities, there may be a disturbance in the chain of events because errors are not recognized (or not eliminated), with the result that the processes stop prematurely [46]. The learning therapy has therefore to be administered continuously over longer times to run through the whole chain of events. Further, learning 'tricks' have to be used to enhance the ability to discover new motor possibilities. In the case of Alen, know how has to be used so that he discovers movements of the left not functioning hand.

The System Theory of Pattern Formation of CNS development encompasses all areas of development and is derived from mathematics, physics, human neurophysiology, clinical research, and developmental psychology. The CNS is considered as one neuronal network. A new behavior is generated, which is dependent on the input of all subsystems. This behavior may have a characteristic that could not have been determined by evaluating the contributing behaviors individually [47].

The system repair approach is a "feed-forward system" that is self-correcting 'en route' rather than hardwired from the cerebral cortex. It also implies that all factors, subsystems, or structures contributing to the motor behavior (or patterns in general) are important and exert an influence on the outcome [47]. If cortex and basal ganglia are injured in an infant, then many patterns become abnormal or do not exist. The higher centers can no longer control movements or other patterns sufficiently. But through movement-based learning, a self-correction 'en route' may partly compensate for the missing contribution of a subsystem in the way that other subsystems take functions over and/or the cerebellum and pons are partly repaired.

The problem-solving learning tries to repair sub-networks that are necessary for functioning and learning. By inducing trial–and-error-elimination processes in subunits of the normal developing nervous system, an optimal development is achieved [45]. To teach the injured CNS to repair itself by trial–and-error-elimination processes, the CNS has to recognize upon CDT which sub-networks, regulation units or sub loops are not functioning properly (or are missing) and to repair them by error elimination, including the possibility that other brain parts partly take functions over, and sub-networks build anew to a limited extent.

4.2.11 Interpersonal Coordination and Co-movement

To induce learning of movements in the hemiparetic Alen, also interpersonal coordination and co-movement were used. When the therapist performs the movement simultaneously in interpersonal coordination (Fig. 4.23A), she can draw the patient into a better movement pattern.

When a hemiparetic patient performs with both arms, hands, fingers or legs the same movement, then the paretic side can learn from the good side the movement pattern. Such learning/pattern transfer can be very fast. In the patient Alen, the CNS learned the power (Figs. 4.29 and 4.30) and precision grip (Fig. 4.31) immediately, first time in life!

4.2.12 Repair Strategies at the Neuron Membrane and Genetic Levels

The building of functions/patterns in the 12-year-old Alen, first time in life, make it likely that excitation-neurogenesis coupling [48] contributed, stimulated through CDT.

1. Repair depends on learning and memory formation, mediated or supported by epigenetic mechanisms. Epigenetics is the interplay between genes and the environment resulting in phenotype and epigenetic landscape.

2. Epigenetic mechanisms, like DNA methylation, are probably sensors for movement-based learning and memory formation and fine modulators of neurogenesis though CDT (Fig. 4.18).

3. The epigenome consists of non-coding RNA and chromatin, a proteinaceous matrix surrounding DNA. The dynamic interactions of post-translationally modified chromatin proteins, covalently modified cytosines inside DNA and non-coding RNA define the complex pattern of gene expression beyond the four bases of DNA.

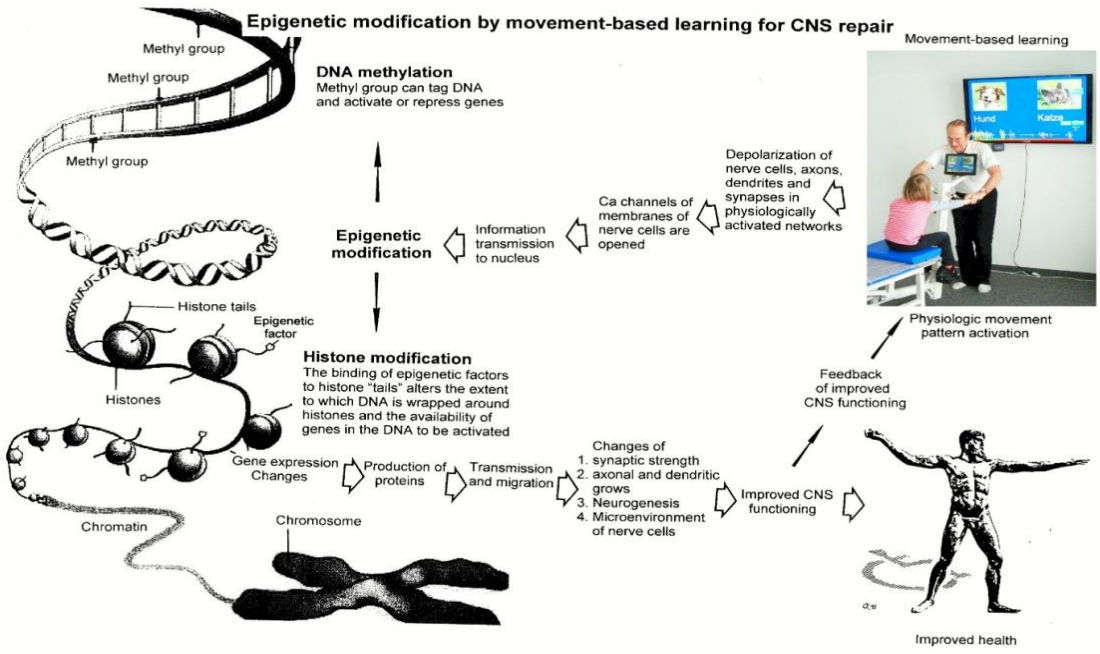


Fig. 4.18. Epigenetic regulation for repair by movement-based learning. CDT-induced stimulation of the pathways that regulate neural network repair is a proven therapeutic and preventive tool. Epigenetic mechanisms, stimulated by physiologic network activation, are likely key players within signaling networks, as DNA methylation, chromatin remodeling and small non-coding RNAs superfamilies' are required for the fine-tuning and coordination of gene expression during neural network repair by learning

4. The hippocampus plays an essential role in learning and memory. In the hippocampus there exists a specialized form of neural plasticity, which is, the generation of new functional neurons from stem cells occurring throughout life. Adult hippocampal neurogenesis contributes to learning and memory formation.

5. New neurons are important for learning and memory formation (besides functional reorganization), i.e., for increasing the rate of repair, for the following reasons:

a. The insertion of new neurons helps to store the memory of the same activity that led to the creation of the neuron.

b. Activity-dependent neurogenesis enhances the learning of new memories and degradation and clearance of previously stored unwanted memories like spasticity, because the synapses, dendrites and axons can be devoted more fully to the newer memories. The old neurons with large and complex axon and dendritic trees are difficult to change. They can only be changed with sustained effort.

c. New neurons seem to improve the accuracy of relearned patterns (from model study [48]). This means that new neurons help to improve phase and frequency coordination of neuron firing and pattern stability.

d. The advantage of new neurons seems to be dramatically greater in networks that had been more active and had been required to store more memories [48]. The advantage of neurogenesis for memory storage in heavily active networks is that it provides an increased rate of repair if movement-based learning is administered aggressively and if different movements are trained.

6. Specific natural network activity is required for multiple aspects of repair. Specific activity is essential for correct migration of interneurons and it also controls the development and repair of their axons and dendrites. During repair there is a specific requirement of network activity in shaping the cortical integration of specific neural subtypes. Newly build neurons are likely electrically active shortly after their birth and participate in the early network activity that contribute to circuit maturation during repair by CDT.

7. Specific activity is required for migration and maturation at several stages of repair. A break in CDT may invalidate the whole chain of repair events. Specific interneuron subtypes require activity for migration and morphological maturation at two distinct stages of development [35]. Newly built neurons may even require specific activity for migration and maturation at several distinct stages of repair. **During a break in CDT, the specific activity, required for neuron migration, maturation and network integration, may not be supplied at one of these stages so that the chain of repair events is severed, the whole repair chain has to be started anew.**

8. Drug application may undermine repair. Altering the level of neuronal excitability within genetically targeted neurons from drug application, for example antiepileptic drugs may have profound consequences on multiple aspects of the repair of select types of neurons within a population of neurons, as well as their associated gene expression. The pain-killer ‘Contergan’, taken during pregnancy, changed gene expression and the babies were born without arms.

9. Excitation-neurogenesis coupling [48]:

a. Excitation increases or decreases neuron production directly by excitation-neurogenesis coupling.

b. The excitation acts indirectly on the surrounding mature (hippocampal) cells through depolarization-induced release of growth factors.

c. Adult neurogenesis is enhanced by excitatory stimuli and involves Ca^{2+} channels and NMDA receptors.

d. The Ca^{2+} influx pathways are located on the proliferating stem/progenitor cells (NPCs), allowing them to directly sense and process excitatory stimuli. The Ca^{2+} signal in NPCs leads to rapid induction of a proneural gene expression pattern.

10. Integrative coordinated movements have to be trained to allow functional reorganization and new nerve cell integration across very large distances. CDT has to activate injured and uninjured networks to enhance physiologic CNS functioning and learning transfer.

11. Conclusion for optimal therapy according to the present stage of knowledge. If there is similarity between development and repair, animal (mice) data also hold in humans and the principles of neurogenesis of the hippocampus also hold in other parts of the brain, albeit to a much lesser extent, then the patient has to be trained at his limits (1) to induce substantial building of new nerve cells [49]. The treatment has to be continuously administered (2) to support all stages of repair at the progenitor level as migration, maturation and integration. The networks, requiring repair, have to be activated specifically (3) to generate repair-friendly, micro-environmental properties in the networks. No drugs should be administered that change neuron excitability (4). The exercises have to include coordinated arm, leg and trunk movements (if possible) to improve the impaired phase and frequency coordination for CNS self-organization (5). The performed movements have to be as integrative as possible to reconnect distant brain parts and to induce learning transfer.

This short introduction to the theory of coordination dynamics therapy may help to understand the substantial progress achieved in the patient Alen.

4.3 RESULTS

4.3.1 CNS Functioning at the Beginning of Coordination Dynamics Therapy

4.3.1.1 Location of the injury

The patient Alen suffered a perinatal insult with asphyxia. He sustained a cerebral hemiplegia on the left side, a parenchyma defect of the basal ganglia and a degeneration of the pyramidal tract. Fig. 4.19A, B shows the MRI of the 9-year-old Alen. The insult with asphyxia changed the brain. Rather normal ventricles are shown in Fig. 4.19C-E for comparison. Since there is no MRI available from after birth, it is not clear how much a subependymal germinal matrix bleeding is involved in the changes.

Alen was born through a cesarian. He could not breathe. When the fluid, mixed with blood, was removed from the lung, he started to breathe. The time period of apnea is unknown. At an age of 9 years, a parenchyma loss of the basal ganglia was diagnosed and a Wallerian degeneration of the pyramidal tract at the site of the pons found, indicating a degeneration of the lateral corticospinal tract and the anterior corticospinal tract (Fig. 4.20A). The loss of the parenchyma of the right basal ganglia was probably caused by post-ischemia and/or post-hemorrhage following a subependymal germinal matrix bleeding with pressure onto the close pyramidal tract. Brain injuries could therefore be caused at different sites of the brain (Fig. 4.20).

An injury involving the cerebral cortex, causes weakness of part of the body of the opposite side. Hemiparesis is seen in the face (not in Alen) and hand more frequently than elsewhere, because these parts of the body have a large cortical representation (Fig. 4.4 and 4.20B). The typical finding is a predominantly distal paresis of the arm, most serious functional consequence of which is an impairment of fine motor control of hand and finger. The weakness is incomplete (paresis rather than plegia), and is flaccid, rather than spastic, because the accessory (nonpyramidal) motor pathways are largely spared.

If with hemorrhage or ischemia the internal capsule is involved (Fig. 4.20), there will be a contralateral spastic hemiplegia. In the patient Alen, no real spastic could be found so far. He could not use the left hand and had to manage everyday life with one hand. School medicine did not try to repair or did not succeed to repair the left-hand functions during his life.

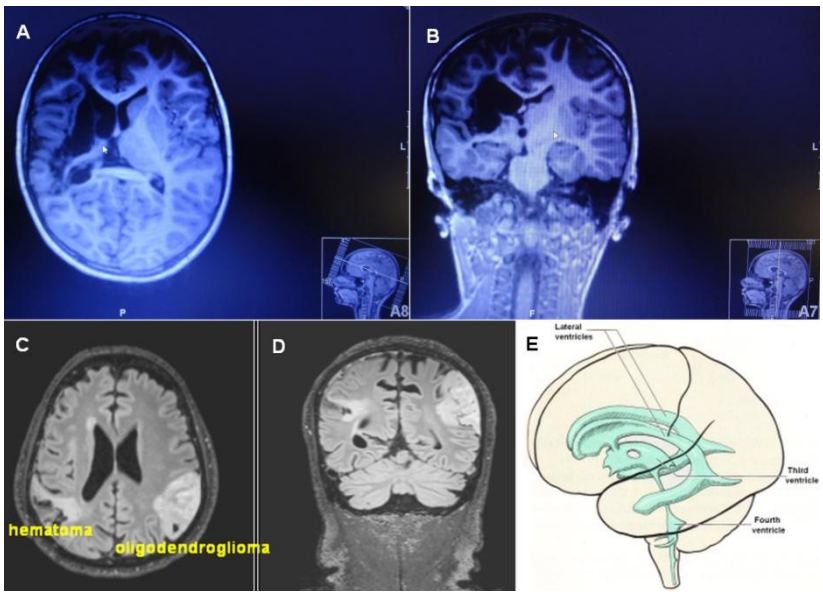


Fig. 4.19. A, B. MRI (with movement artifacts) of the 9-year-old Alen: Strongly changed brain and ventricles, parenchyma loss of the basal ganglia and a Wallerian degeneration of the pyramidal tract and the anterior corticospinal tract. C, D. For comparison, MRI of a cancer patient, ventricles are somehow normal [23]. E. Picture of the ventricles (taken from [26])

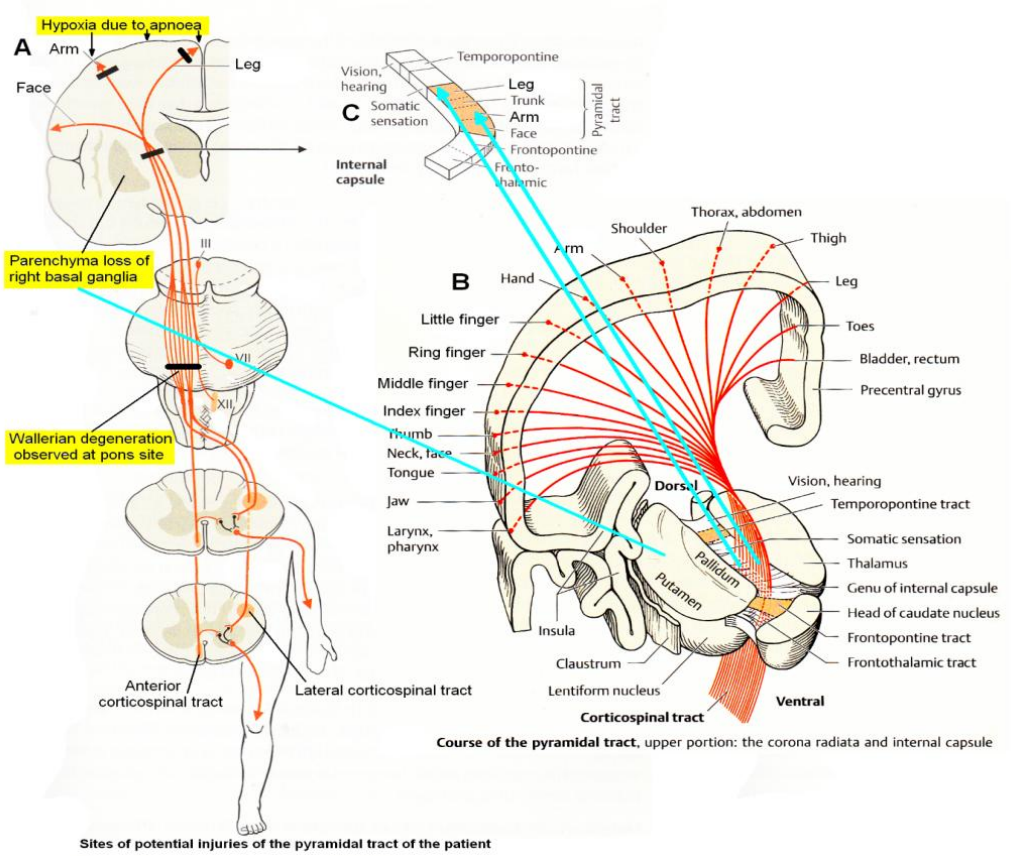


Fig. 4.20. Sites of injuries of the CNS of the patient Alen. The Wallerian degeneration of the right pyramidal tract has consequences also on the 'good' right side through the anterior corticospinal tract. Figures partly taken from [26]

4.3.1.2 Sensitivity in the left hand

By examination touch and pain, it was found that there was full sensitivity in the left hand and fingers. He could distinguish between warm and cold. Therefore, the thalamus was not or only little damaged through the hypoxia, because the thalamus 'tells' you that you have a feeling. In comparison to the blood supply of the basal ganglia, the thalamus may obtain more oxygen with the blood than the basal ganglia because of the artery communicans posterior (Fig. 4.2). But when exercising strongly, Alen showed cold sweating in the left hand, indicating also an impairment of the vegetative nervous system.

The next question was, whether the sensory cortical fields were damaged? Since with closed eyes, Alen could clearly say where he was touched and he had the same feeling than on the right hand, the sensory cortical fields (Fig. 4.4) were not or only little injured. Since, apart from the pyramidal system, the spinal cord was not injured, the intrinsic apparatus of the spinal cord was probably functioning and could be used for repair of the left-hand functions.

4.3.1.3 Deficits of the motor functions

When starting CDT, the 12-year-old Alen could not **creep** in a physiologic pattern (Fig. 4.21c). Rather physiologic trot gait creeping patterns are shown in Fig. 4.10ab. The patient Nefeli with a spinal cord injury (SCI) and the patient Sophie with an atrophy of the cerebellum and pons are creeping in interpersonal coordination. Apart from the spasticity of the pelvis (lifted pelvis), Nefeli creeps physiologically. Sophie creeps with deficits. During moving she overstretches (Fig. 4.21a) and overswings the legs (Fig. 4.21b). The creeping of Alen is worse than that of Sophie. His legs are swinging about and the pelvis is not moving on the ground (Fig. 4.21c). This very poor creeping performance may indicate an injury preferentially of the paleostriatum (globus pallidus), because over the course of phylogeny, phylogenetically old species (Tiktaalik 375 million years ago, phylogeny between fish and Ichthyostega) (Fig. 4.6) may also moved in a creeping way or performed salamander crawling (Fig. 4.10).

Fig. 4.21. a, b. The patients Nefeli (SCI) and Sophie (atrophy of cerebellum and pons) during creeping in interpersonal coordination in antiphase. Sophie is overstretching (a) and overswinging the legs (b) in comparison to Nefeli. She had not fully learned so far to control the inertia and centrifugal forces of leg movement. She cannot stop leg movement in time. The spinocerebellum (vermis) had not been repaired sufficiently so far. c. The boy Alen with injured basal ganglia, caused by hypoxia, during trying to creep. The performance of the pattern is very pathologic in comparison to that of Nefeli. Strong overshoot (dysmetria) of the left leg can be seen (marked). The left marked hand is also activated pathologically due to the atrophy of the pyramidal tract

At the beginning of therapy, Alen was able to **crawl in pace gait coordination** (one body side against the other) in quite a good coordination (Fig. 4.22). But he could not crawl continuously. The maintenance of the pace gait crawling performance was inexistent. This means, the automatic control of the pace gait crawling was impaired.

Fig. 4.22. The patient Alen during in-phase crawling. At the start of pace gait crawling, the left hand is positioned rather physiologically (A). Then he loses the hand pattern. Only one finger is activated (B). And then the left hand is not included in the crawling pattern anymore (C). But he has no spasticity in the hand, like in stroke. He only cannot hold the starting pattern and the hand and the fingers are not activated.

The **trot gait crawling** was continuously in Alen. Only there was no coordination between arm and leg movements and the left hand was not activated (Fig. 4.23B). For comparison, Fig. 4.23A shows a rather coordinated trot gait crawling of a cerebral palsy girl in interpersonal coordination with a physiotherapist.

Fig. 4.23. A. Trot gate crawling of a cerebral palsy girl in interpersonal coordination with the therapist. The crawling performance of the therapist is not optimal. The right arm is leading with respect to the left knee. The crawling performance of the girl is also not optimal; the knees are too much apart. B. The trot gait crawling of the patient Alen is continuously, but the coordination between arms and legs is between the pace and trot gait pattern (pathologic)

Alen could **walk** speedily (Fig. 4.24). The stride length was quite large and the positioning of the hands were not normal. Especially the posture of the left hand was pathologic, due to the atrophy of the right pyramidal tract. At the beginning of walking (Fig. 4.24A), the performance was best. But after 3 to 5 steps the performance got worse (Fig. 4.24B, C). The maintenance of the starting pattern was not possible. This means, the automatic control of the walking was impaired, due to the injury of the basal ganglia and the left hand was not activated properly because of the atrophy of the pyramidal tract.

The patient could also **run** speedily (Fig. 4.25). As for walking, the running stride length was quite large (Fig. 4.25A) and the positioning of the hands pathologic. Again, at the beginning of running, the pattern was best (Fig. 4.25B) and deteriorate with ongoing running steps (Fig. 4.25C,D,A). Therefore, also during running, one could see that the automatic control of locomotion was impaired due to the injury of the basal ganglia.

Fig. 4.24. The patient Alen during walking. The performance is suboptimal

Fig. 4.25. The patient Alen during running. At the beginning the running performance is quite good (B), but he could not maintain the good performance (A)

Also, during **jumping in anti-phase** at a fixed place, he started with a quite good performance, apart from the hand positioning (Fig. 4.26). But then he lost the jumping pattern after 3 to 5 jumping steps. The pattern stability was low during jumping. Further, Alen had also some problems to initiate (to start) the jumping pattern. After approximately three weeks of CDT, he had no problems any more with the initiation of the jumping pattern.

Fig. 4.26. Jumping in antiphase of Alen. He was able to jump 3 to 5 steps

The **speech** of Alen was quite good. He spoke German, Serbian and English. The Author could communicate with him in German or English. He was attending a special language school for pupils with impaired speech. Accidently a good school choice because the other healthy pupils accepted him fully since they also had a problem (the speech).

Alen could **write** with the right hand (Fig. 4.27). Probably he was right-handed. In the 5th class, he had not learned so far, the continuous writing.

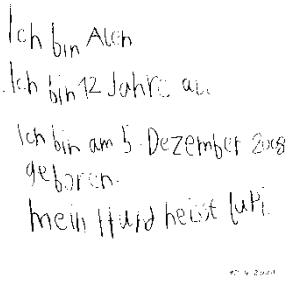
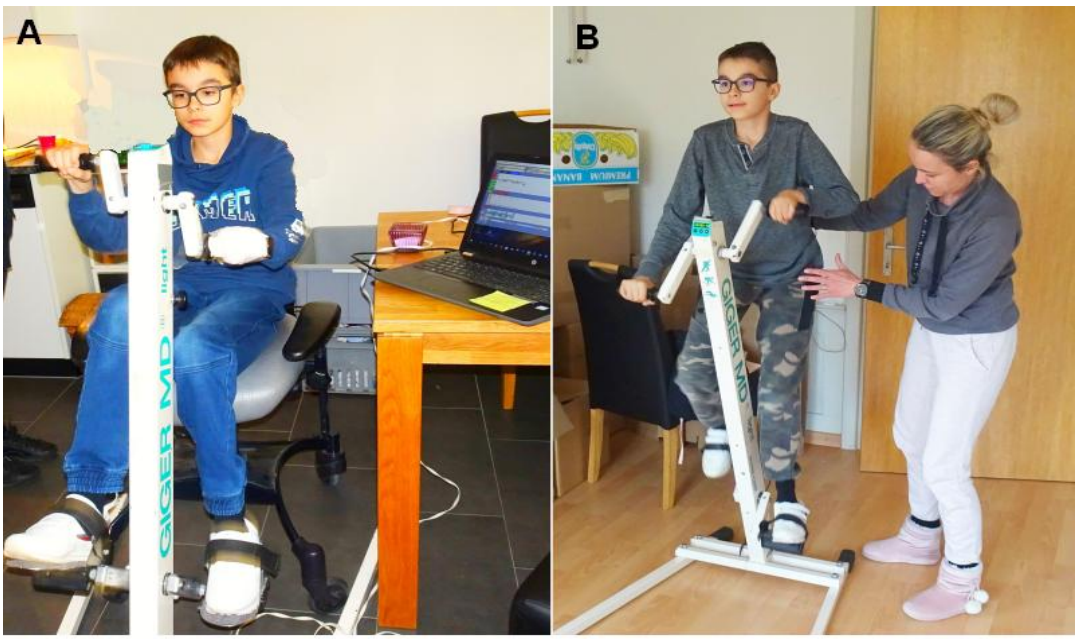


Fig. 4.27. Writing of the patient Alen, attending the 5th class

The patient Alen was able to exercise on a **special CDT** device in the sitting and standing position (Fig. 4.28). For turning in the sitting position (A), for measuring the coordination dynamics values, the left hand had to be fixed, because it would slip from the handle after 10 to 20 turns. Astonishing is that he could **exercise in the standing position** quite well (A), in spite of the deficits of the left arm and hand. He could only put little weight on the left hand and arm, because of the atrophied pyramidal tract due to the injury of the right cerebrum. Probably the not crossing extrapyramidal tract of the left side contributed to the performance of the left arm and hand, even though the basal ganglia were also injured. The hand grip power of the left hand was nearly zero, therefore the mother supported him.

A possible motor program for exercising in the sitting or standing position would probably be like the one of a Parkinson's disease patient (Fig. 4.28C), because Parkinson's disease patients have also impairment of basal ganglia regulatory circuits (Fig. 4.5B), because of the degeneration of a nigrostriatal projection.



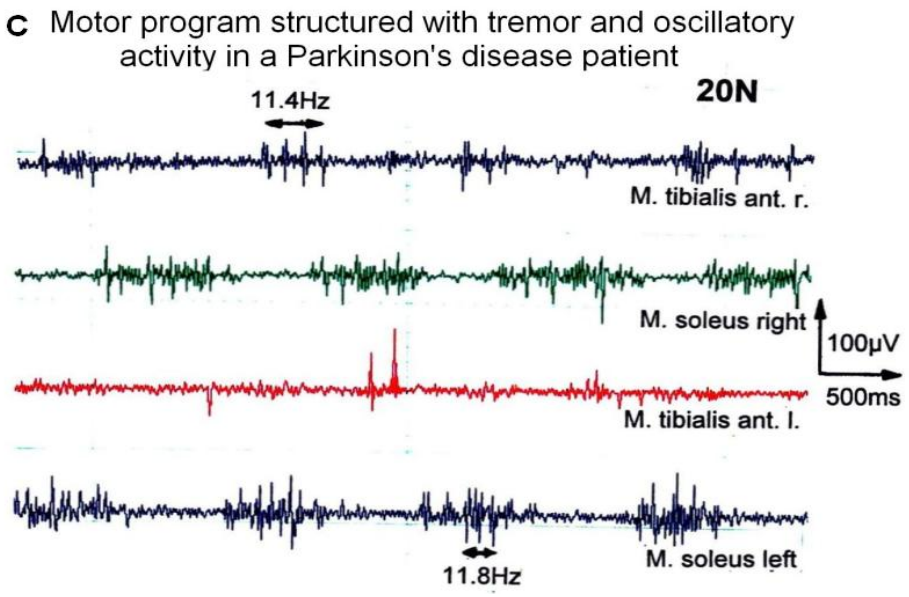


Fig. 4.28. A,B. The patient during exercising on the special CDT device in the sitting (A) and standing position (B). In the sitting position, his CNS was measured to obtain the coordination dynamics value. The left hand had to be fixed, otherwise it would slip from the handle. C. sEMG motor programs of a patient with Parkinson's disease during the exercise on the special coordination dynamics therapy device at a low load of 20N. The motor program muscle bursts are more or less structured by rhythmicity (no rhythmic structure occurs in normal motor bursts). Rhythmic activity at a frequency of 11.4 and 11.8Hz is indicated

Impaired coordination among motor and other neurons, leading to oscillatory firing (Fig. 4.14), synchronized oscillatory firing of FR and FF-type motor units, tremor and other dysfunctions, will have consequences for the general organization of CNS neural networks and can be repaired [50,51]. In the motor program bursts, shown in Fig. 4.28C, rhythmic activity can be identified, which cannot be seen in the rather physiologic motor pattern. The highlighted rhythmic firing at 11.4 and 11.8Hz may indicate oscillatory firing of FF-type motor units innervated by α_1-motoneurons.

The main disability of Alen was, that he could not move on volition the left hand and fingers because of the cortex damage and the atrophy of the pyramidal tract. Losing one hand function is a disability of 50% (in Switzerland).

4.3.1.4 Strategy for the brain repair

Because the brain-injured patient Alen had big problems to perform creeping and crawling, but could perform the upright movements walking, running, jumping and exercising on the special CDT device in the standing position quite well, the brain injury was located more in the phylogenetically old structures like the paleostriatum (globus pallidus) and the neostriatum (caudate nucleus and putamen), apart from the injury of the right cerebrum.

To repair/re-organize the cerebrum, walking, running, jumping and exercising on the special CDT device in the standing position have to be trained with the inclusion of the left arm and hand as much as possible. The repair of the finger functions will be most difficult, because the neural networks activating them are very complex which means very difficult to repair. For the repair of the basal ganglia, creeping and crawling have to be trained in a continuous way with good coordination performance between arms and legs. Further, movements have to be trained, which phylogenetically older species may have used for locomotion (Method).

He can crawl in pace gait and in trot gait, but with poor coordination. He has especially big problems with the left hand, but the hand is not spastic. He can walk and jump in antiphase with poor

performance. When jumping in anti-phase, he can hold the pattern for approximately 3 jumps. Then he is losing the pattern (very poor pattern stability).

The 12-year-old Alen has a good prognosis to catch up with normal pupils, if coordination dynamics therapy is administered to him at his limits for more than a year. The most important repair steps are to improve the cognitive functions through learning transfer from movements and to get the left hand and finger functions working.

4.3.2 Brain repair through 6 weeks of Coordination Dynamics Therapy

Through 6 weeks of CDT, Alen's motor functions improved and he could hold longer times the left hand on the leaver when exercising on the special CDT device. But he was still not using the left hand in every-day life. Therefore, the Author started to work with know-how on the left hand to get it functioning.

4.3.2.1 Power grip

To induce the power grip pattern, the Author used the co-movement strategy. Alen was asked to take with the right good hand the glass with no water in and should simulate the water drinking. Of course, there was no problem. Then he was asked, to hold strongly with the right one glass and take with the left had the second glass (Fig. 4.29A) and bring it to the mouth for drinking (Fig. 4.29B,C) and put it back then to the table (Fig. 4.29D). Unbelievable, he could manage through strong concentration. And then he was asked, by the mother, to perform the drinking performance with the left bad hand without holding with the right good hand the glass (Fig. 4.29E-H). Unbelievable, he could manage. The power grip worked a bit.

Fig. 4.29. A-D. The patient Alen learned the power grip. A-D. Through co-movement from the right good hand to the left bad hand, he could initiate the power grip in the left bad hand. E-H. After realizing that the left hand can do the drinking performance, he became able to use only the left bad hand for the drinking pattern

The next step is the reality test. Is Alen able to perform the drinking in reality? Mother Alen and the Author were going to the kitchen to see whether Alen could drink by himself with both hands. Alen opened the tap with the right good hand (of course no problem), took the glass with the bad left hand, filled the glass with water (Fig. 4.30A), did drink water in the normal way (Fig. 4.30B), and pore the rest of water to the basin (Fig. 4.30C). After finishing the drinking, he was crying for joy, because first

time in life, he managed to drink water in the normal way (Fig. 4.30D). Before he had to open the tap with the right hand, take a glass with the right hand, get water into the glass, drink, put the glass back with the right hand and close the tap with the right hand.

Fig. 4.30. After 6 weeks of CDT, the patient Alen with a Cortex and a basal ganglia injury learned at an age of 12 to drink with both hands (A-C), first time in life. Ale is crying for joy because he succeeded (D)

4.3.2.2 Precision grip

After being very successful with the learning of the power grip, the question arose, is Alen able to generate the precision grip, first time in life. Again, the co-movement strategy was used. First, he took a glass ball with the right good hand, which was of course working. Then, when holding one glass ball with the right good hand, he became able to take a second glass ball with the bad left hand (Fig. 4.31A), bumping both balls together (Fig. 4.31B) and put them back to the table. Then he was asked by the mother, to take a glass ball with the left hand only and he succeeded (Fig.4.31C,D). Even though, the right good hand was not in the precision grip pattern, still the fingers are a bit in that position (Fig. 4.31C,D).

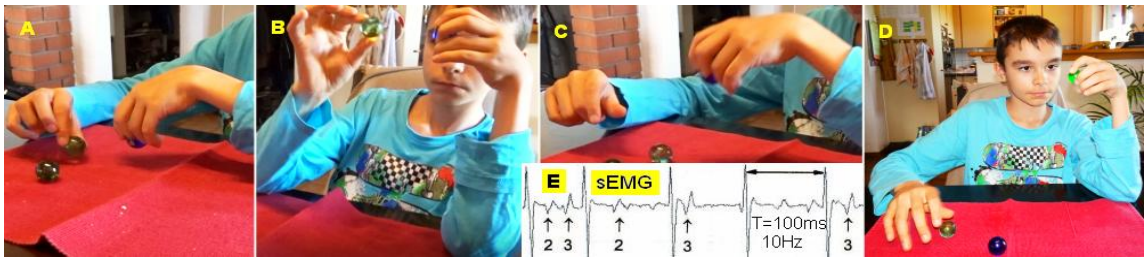


Fig. 4.31. Through co-movement, the patient Alen became able to generate the precision grip pattern. Note, the positioning of the left wrist joint is plantar flexed (A-C). In D the wrist joint is in a quite well position. Note further, with the right good hand, he took the ball with two fingers (A,) and with the bad left hand he used 3 fingers for the precision grip. Motor units could be activated coordinately in finger muscles (E)

That Alen learned the power grip and precision grip patterns through 6 weeks of CDT is a dimensional step forward (reduction of disability by approximately 30%). Still much more has to be learned by him through repair. As can be seen from Fig. 4.30C,D and Fig. 4.31, the fingers and the wrist of the left hand are often not activated in right way. Also the power was missing. Anyway, some motor units were activated in the fingers in a very important physiologic pattern (Fig. 4.31E). Alen became able to eat a bit with both hands, but the pattern of the left hand was pathologic.

4.3.2.3 Training of other arm, leg and trunk movements to improve symmetrical grows of the body

Alen could exercise on the special CDT device, but only having the hands in the prone position and not in supination, because he could not rotate arm and hand. Other brain-injured patients also have

that problem. But when exercising on the special CDT device, he slowly learned to shift the hand positioning from pronation to supination.

To train the left hand and to play at the same time, Alen was allowed to play sometimes with a video game, where he had to use the left hand and fingers. He had to hold the handle and use the thumb (Fig. 4.32). For efficient repair, the exercising on the special device is much more efficient.

Fig. 4.32. The patient Alen during playing a video game in which he has to use the left arm and hand

To improve the functioning of the left side and to induce as much growing of the left body side in comparison to the right side, Alen had also to train the jumping on one leg (Fig. 4.33). He easily managed to jump on the good right leg (A), but he succeeded with the left bad leg only one jump so far (B). It can be seen from Fig. 4.33 that he could easily jump with the right leg, that means, no special concentration was needed. But when jumping with the left leg, he had to concentrate very much. He looked down to realize visually the task (jumping) to be managed. The visual feedback is very efficient to train and learn a task. It was reported that a visualization of a task is very important for relearning movements [55]. For movement control Alen also used a mirror. To force himself to jump with the left leg, Alen clenched the right hand to a fist, to get more power to the left leg (B). The left hand could probably not contribute in that way.

Fig. 4.33. The patient could easily jump continuously with the right leg (A), bad managed with the left bad leg only one jump (B). Note the clenched fist of the right hand in B. When trying to jump with the poor left leg, he looked down for realizing and controlling the jumping (visual feedback)

Because Alen could not crawl properly and was not able to use the left hand properly (Figs. 4.22,4.23), the crawling position was trained with the left hand in the physiologic position (Fig. 4.34A-E). To get an absolute simultaneous afferent input to both hands for co-activation, sometimes the hands were put on top of each other (Fig. 4.34F, G). In Fig. 4.34H, the first step to a push up movement pattern is trained.

Fig. 4.34. The mother during training with Alen the crawling position: Backward moving (A), forward (B), up (C), down (D), up without hand support (E), shift to the right side (F), shift to the left (G). In H, the first step to the push up movement is trained

Coincidence detector and improving regulation circuits of basal ganglia and optimizing functions in the pyramidal tracts and enhance co-movement concentration

4.3.2.4 Neuron as a coincidence detector with respect to coordinated afferent input

How is it possible that Alen learned the precisian grip within 6 weeks, what he did not learn in the 12 years of his life? A regeneration of neurons in the pyramidal tract is unlikely, because with a regeneration growing speed of approximately 1mm/day [7] and a growing distance of 200 to 300mm, more than 200 days would be needed already for the growing of axons from the cortex to reach the cervical motoneurons for hand functions. Further time would be needed for the reorganization of the cortex and the synapse formation at the motoneurons. Therefore, the repair of hand function was coming from a functional reorganization and not from a structural repair so far.

Through exercising on a special CDT device, the coordinated firing of neurons is improved in the whole CNS, and especially in Alen in the cortico-striato-pallido-thalamo-cortical regulatory circuits (Fig. 4.5B) and also among the damaged or atrophied pyramidal tract neurons. Existing connections were reorganized in the way to make them functional for power and precision grip and other functions. When offering the thalamus of both brain sides simultaneous coordinated afferent input in the range of a few milliseconds from the left hand and right hand (Fig. 4.34F, G) (co-movement), then the neurons get even more activated for repair because neurons are coincidence detectors and excitation threshold are reached earlier (Fig. 4.35). They become now able to activate pyramidal tract neurons and in turn the motoneurons to activate motor units in hand muscles, including those for the precision grip (Fig. 4.31E).

Alen's teacher at school reported, that Alen could through the treatment concentrate longer times during the lessons. This means, the whole brain optimized its functioning including those of the cognitive functions.

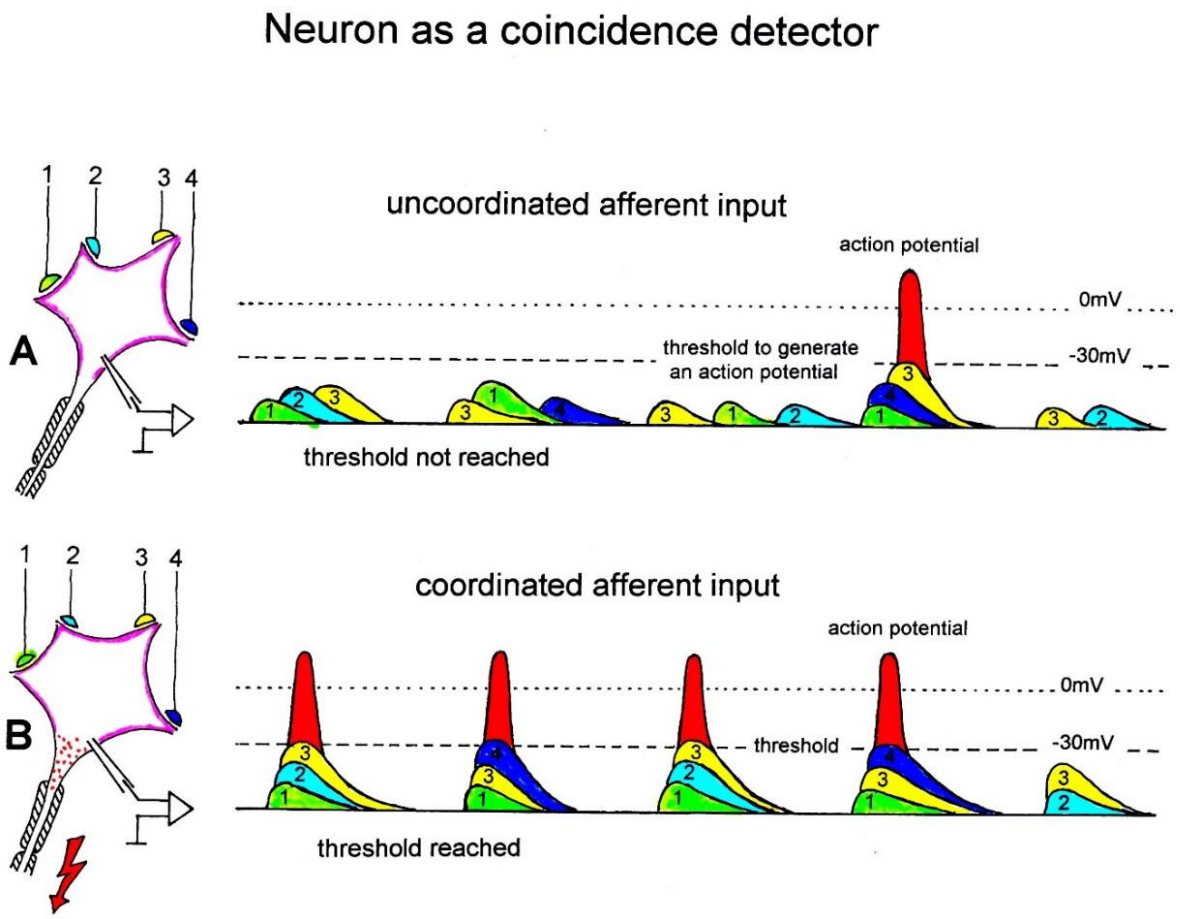


Fig. 4.35. Neuron operating as a coincidence or coordination detector. A. Afferent input is reaching rather uncoordinated the cell soma. Only sometimes an action potential is generated, because the threshold of action potential generation is mostly not achieved. B. The action potentials in fibers 1 through 4 are reaching time-coordinated the dendrites or the cell soma. The postsynaptic potentials add up and the threshold is achieved at approximately –30mV, and action potentials are generated time-coordinated at the axon hillock. In the real CNS mostly, many more smaller postsynaptic potentials will contribute to the generation of an action potential and passive conduction from the dendrites to the cell soma has to be taken into account. Coordinated afferent input may thus induce or enhance (coordinated) communication between neuronal network parts following CNS injury

4.3.3 CNS repair through 3 months of CDT

4.3.3.1 Improvement of hand and finger functions on the paretic (left) side

Within 6 weeks of CDT Alen learned to use the left hand for the power grip (Fig. 4.29), the precision grip (Fig. 4.31) and to use the learned functions for drinking water with both hands (Fig. 4.30). But his nervous system could not generate other left-hand functions. Especially he was not able to rotate the left hand.

The rotational movements of the left (bad) hand were trained now on the special CDT device by changing from the prone to the supination pattern. The left hand was fixed to the leaver. Such rotational hand movement pattern training is more efficient than just trying to rotate the hand, because such movement training is more integrative. After 10 weeks of CDT, he learned a bit to rotate the left hand. He became able to turn a bit in the supination pattern on the special CDT device without fixing the hand (Fig. 4.36). The consequence of this new movement was that he could exercise better on

the special CDT device in the standing position in the way that he could hold stronger the left leaver and the left wrist positioning was more physiologic, as can be seen when comparing the wrist positioning of Fig. 4.37 with Fig. 4.28B.

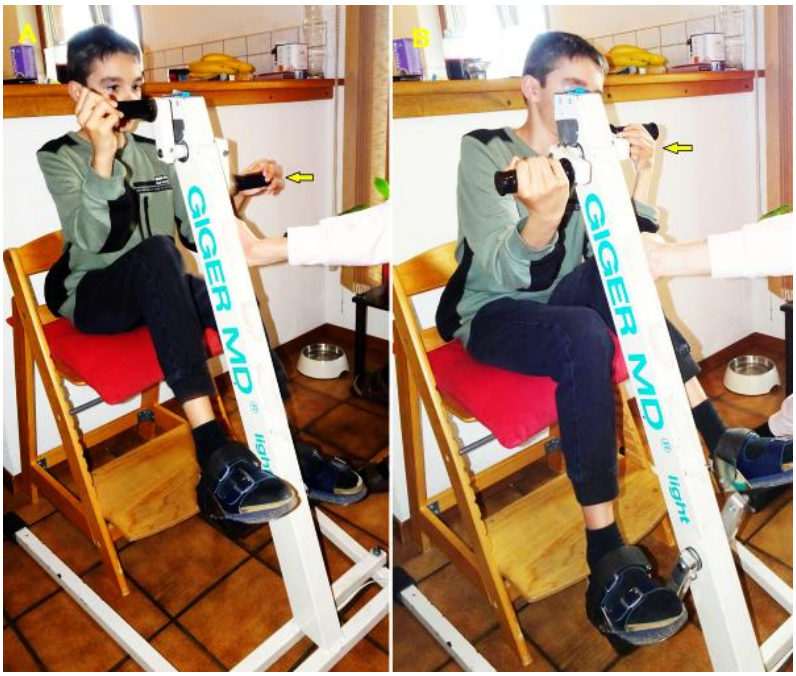


Fig. 4.36. Patient Alen during the training rotational wrist and arm movements on the special CDT device, when the left (bad) hand was not fixed (arrows). The right good hand had no problems to turn in the supination position (B)

Fig. 4.37. Patient Alen during exercising in the standing position. Note the more physiologic left wrist positioning in comparison to that in Fig. 4.28B (marked with an arrow)

When exercising on the special CDT device, the holding of the leavers was similar to the power grip pattern. But more functions of hand and fingers were needed for everyday life. The next step of hand repair was to get more finger functions.

Alen was not able so far to force the left fingers apart. With the right hand he could. To make the patients CNS to learn this finger movement, again specific knowhow was used. The mother was holding both hands of Alen together (Fig. 4.38A) and he tried then to put the fingers apart of both hands (Fig. 4.38B). Unbelievable, it worked continuously. Alen was now able to open and close the fingers, apart from the thumb. The absolute simultaneous afferent input from both hands induced the pattern in the left (bad) hand. Therefore, the co-movement between the right and left hand, the simultaneous afferent input, the strong concentration and the visualization of the task started/organized the pattern in the left hand.

When the mother did not push the two hands together, Alen could not activate/generate the pattern in the left hand (Fig. 4.38C, D). Therefore, so far, after 10 weeks of CDT, the co-movement and the concentration alone were an insufficient stimulus to activate these left finger functions; the simultaneous afferent input of the touch from both hands was needed additionally.

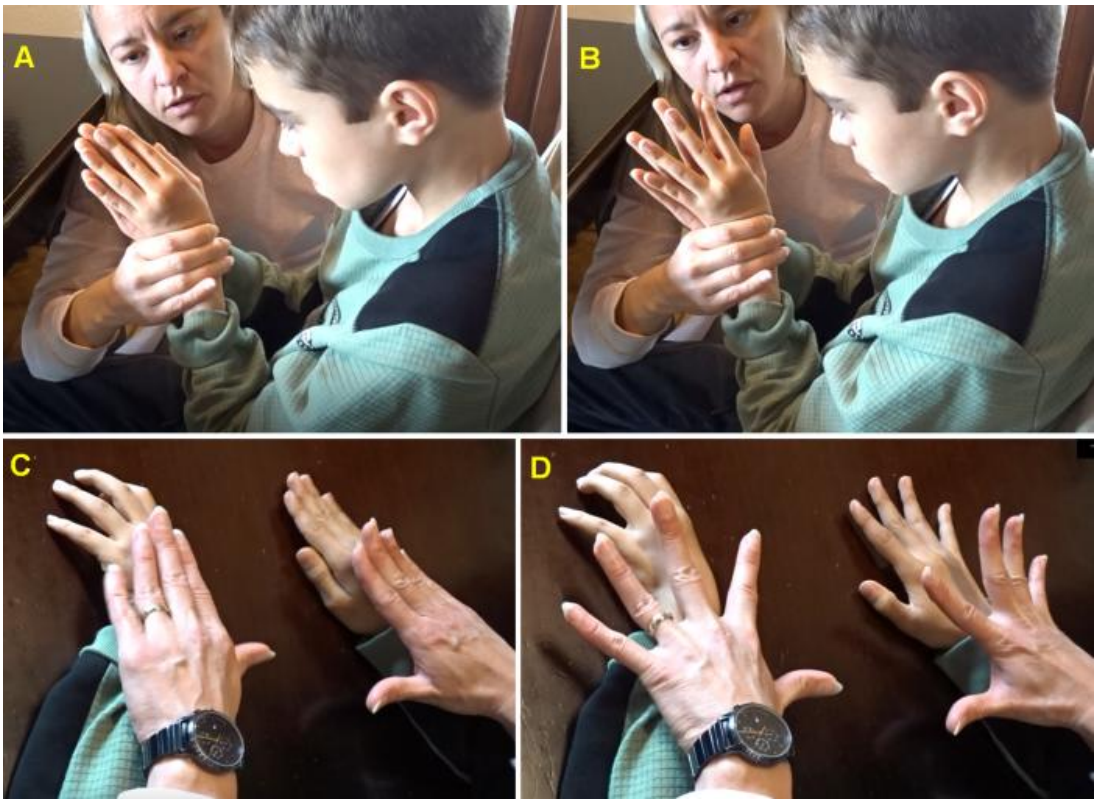


Fig. 4.38. When the mother holed both hands together, Alen was able to force the fingers apart and together (A, B). When having the hands apart for opening and closing the fingers (C, D), co-movement, concentration and visualization of the task were insufficient to activate the pattern in the left hand.

The consequences of the improvement of the left hand and left finger functions was that the patient Alen became able to eat pasta with both hands in a rather physiologic way (Fig. 4.39).

4.3.3.2 Plasticity

Approximately 75 years ago, Sperry transposed the nerve supply of flexor and extensor muscles in the rat [52] and in the monkey [53]: the monkey relearned the task, the rat did not. In Sperry's

experiment on monkeys, their learning to flex or extend the elbow in one situation did not necessarily become generalized to other performances. This indicates that the neural readjustment was not localized solely in the spinal centers, but involved reorganization at the supraspinal levels, including the red nucleus [54]. Surprisingly few trials were required for poliomyelitis patients to use transposed tendons successfully. The visualization of the task seemed to be the prime aid to the patients [55].

Fig. 4.39. Patient Alen during mixing the pasta (A) and turning the pasta in the spoon (B)

As shown here, repair through plasticity can be enhanced even more strongly, when using in addition to the visualization of the task, concentration, co-movement and simultaneous afferent input from the fingers in this case. May be other nuclei than the red nucleus, including the repair of the basal ganglia, contributed to the tremendous speed of hand repair.

4.3.3.3 Training of left leg functions

To visualize the hemiparesis of the patient with respect to the leg, Alen was exercising without trousers and shirt (Fig. 4.40). When standing, one could see that the proximal leg muscles were little or not atrophied, but the lower leg muscles were (Fig. 4.40A). The circumference around the calves, when sitting, were 21.5cm on the left and 28.3cm on the right side. But when jumping with the mother in anti-phase (Fig. 4.40C-D), the gastrocnemius muscle was activated (Fig. 4.40B, arrow) in the phase when jumping upwards. Because of the atrophy of the lower leg muscles, the muscular strength was reduced. It was hard work for him to jump with the mother and he complained to be exhausted.

This jumping in antiphase is a very good movement pattern for training especially leg muscles, to stimulate the growing of the left leg (which was 4cm shorter), to train the coordination between arms and legs and to train the left-hand function of Alen.

Fig. 4.40. A. It can be seen that the left calf muscles were strongly atrophied. B-C. During jumping in anti-phase with the mother, the gastrocnemius muscle was activated in the lift-off phase (B, arrow) and not so much in other jumping phases (C, D)

Orthopedics intended to stop the growing of the right good leg by putting transiently plates into the knee, so that the lengths of the legs would not differ so much in the future anymore (see below). The strategy of CDT is different. The growth of the left bad leg has to be stimulated. The Author believes in CDT because it is natural and not only the legs are growing when getting older.

A one year and 10 months old patient with spina bifida and brain injury learned within 2 years of CDT to creep, crawl, stand and walk a few steps. With the therapy also hip joints were build [19].

4.3.3.4 Further improvement of hand functions

Within 8 weeks of CDT, Alen learned further hand functions. When fixing the two thumbs together, he was able to move the fingers of both hands apart (Fig. 4.41A, B). A tiny bit he became able to wash his hands with soap (Fig. 4.41C).

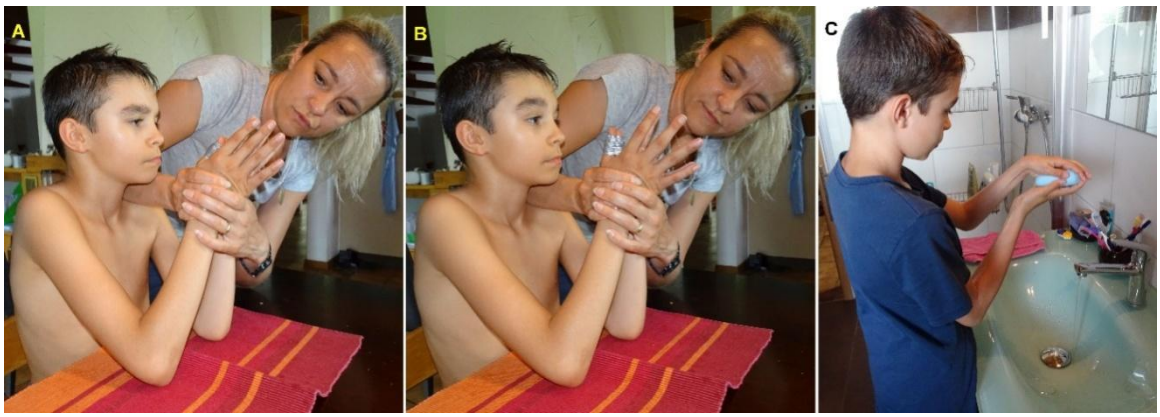


Fig. 4.41. A, B. Opening and closing of the fingers, including the thumb. C. First try in life to wash the hand with both hands and soap

It is not sufficient that hands and fingers can perform certain movement patterns, also power is needed. On the special CDT device, Alen trained also to generate power, when training at higher loads (Newton). So far, he succeeded to train up to 50N. A healthy pupil could approximately exercise against 100N. To see the increase of power with respect to CNS repair, the grip force was measured (Fig. 4.42A). Within 8 weeks the grip force of the left bad hand increased from around zero to 2.5kp and of the good right hand from 10 to 11kp (Fig. 4.43). The power improvement in the left (bad) arm as can be seen from the size of the biceps muscle (Fig. 4.42B). Alen was proud of the increase of the

biceps because even a girl at school noticed it. With therapy continuation, the hand grip force further increased (Fig. 4.43).

Fig. 4.42. A. Measuring of hand grip force. B. The increase of size of the biceps muscle in Alen can clearly be seen. Even at school it was noticed

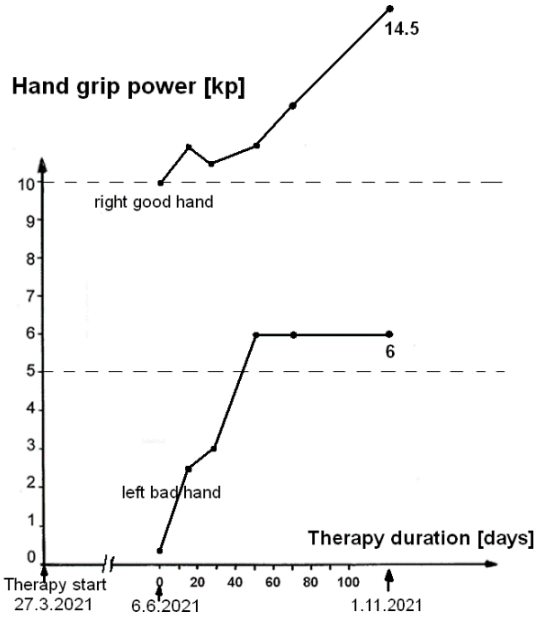


Fig. 4.43. Development of hand grip power of the 12-year-old patient Alen. Note the strong improvement of the left and right hand

4.3.3.5 Pattern variability and forefoot training by running backwards

Because of basal ganglia and cortex injury and atrophied pyramidal tract in Alen, there were retarded, accelerated or deviant development of motor and other functions.

Characteristic for normal development is variability in motor performance [45]. But the impaired nervous system is not able to attain such variability in motor performance because the structure of the CNS is deficient in enabling the infant to use various modes of operation for single performance. When there is serious damage to the CNS, it is even possible that the usual modes cannot be developed at all; the brain has to resort to unusual modes. Distorted motor patterns arise, which fall

outside the range of the normal variability and which are stereotyped, due to the deficiency of the "hardware."

At the beginning of therapy, Alen was only able to run and walk with a large stride length (Fig. 4.25), possibly because of a mild cerebellum injury due to hypoxia. Rather quickly he learned to reduce the stride length. The question was now, how much did the nervous system of Alen could improve his CNS functioning with respect to the pattern variability of running. As can be seen from Fig. 4.44, Alen learned to run backwards with large and small steps. This means, the pattern variability of the neural networks for running improved strongly. His CNS functioning improved strongly.

Fig. 4.44. The patient Alen during running backwards with small (A) and large steps (B). Mother and father are motivating him. During this backward running, he is running on the forefoot and training in this way the forefoot muscles and the neural networks activating them

The importance of backward walking and running is that the patient trains forefoot muscles and the neural networks activating them. With the forefoot walking and running, the foot arch can be built on the long-term, which is often impaired in children with CNS injury.

In Alen the left leg was 4cm shorter than the right one. Therefore, he was wearing in Fig. 4.44 still orthoses, to adapt partly the difference in leg length to run properly and "discover" more quickly the new motor possibility running backwards. Generally, it was fascinating how quickly Alen in general "discovered" with professional help new motor possibilities of arms and legs.

4.3.4 CNS repair through 4 months of CDT

With 4 months of therapy, the 12-year-old Alen, with diagnosed persistent hemiparesis on the left side, learned to brush the teeth with the left hand (Fig. 4.45).

Fig. 4.45. Alen during brushing the teeth with the left hand

Importantly, Alen became able to move a bit the bad left foot from right to left (Fig. 4.46).

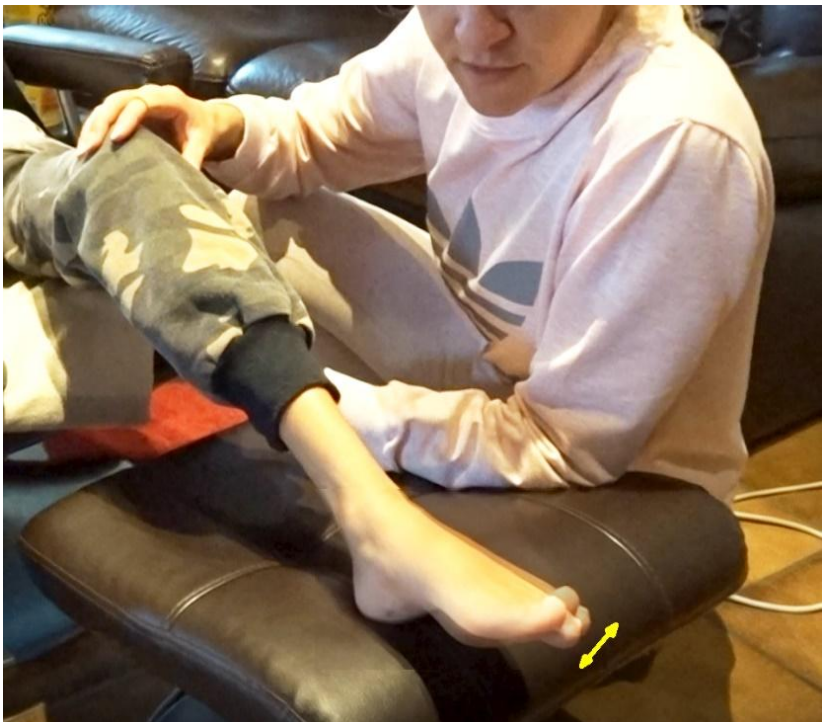


Fig. 4.46. Right-left movement of the left bad leg. The arrow indicates the movement direction

This became possible, because Alen trained for one month walking (Fig. 4.47), running (Fig. 4.48) and jumping without orthosis (Fig. 4.49). The orthosis hindered the CNS to learn more left foot movements. When walking and running in the forward and backward direction on the forefoot without orthosis, the CNS of Alen had the chance to learn more foot movements. The jumping in anti-phase will have contributed to the foot learning process.

Fig. 4.47. Walking on forefoot in the forward (A) and backward direction (B) without orthosis

Fig. 4.48. Patient Alen running on forefoot in interpersonal coordination with the mother. Note the atrophied left triceps

Fig. 4.49. Jumping of the patient in anti-phase with the father without orthosis

4.3.4.1 Correction of leg length discrepancy

Because of the hemiplegia from birth, the left bad leg of the 12-year-old Alen was with 88.5cm 4cm shorter than the right good leg (92.5cm). Orthopedic surgery suggested a hemiepiphysiodesis of the good right leg to stop its grows and correct the leg length discrepancy.

Epiphysiodesis is a pediatric orthopedic surgery that aims at or stopping the bone growth naturally occurring through the grows plate also known as the physeal plate. Temporary hemiepiphysiodesis works through arresting or inhibiting the physeal growth at one hemi-side of the growth plate. In consequence the other hemi-side is allowed to grow normally and unhindered.

The strategy of CDT was, to stimulate the grows of the too short left leg to catch-up with the length of the right leg. To stimulate the growth of the too short left leg, Alen trained especially the turning on the special CDT device (Fig. 4.28), jumped in antiphase (Fig. 4.49) and tried to jump with the left leg only, which was not possible so far, because of too little muscle power.

4.3.5 CNS repair through 6 months of CDT

The diminished muscular strength and impaired fine motor control on the left paretic side and the other (rather healthy) side further improved. The hand grip force of the left hand did not increase further over 6kp. The right-hand grip power increased up to 14.5kp (Fig. 4.43). The strong increase of also the right-hand grip power can be understood, because also the right side was impaired by the

Wallerian degeneration at the pons side via the not crossing anterior corticospinal tract (Fig. 4.20A). Even though the power grip force of the left hand did not increase further so far, the precision grip improved. Alen became able to throw a small ball downwards and catch it again with the left hand when coming up (Fig. 4.50B). He learned a bit to coordinate the precision grip with arm movement, which is an important functional improvement. The power and the coordination of the muscles of the left leg improved in the way that Alen became able to jump a few times with the left leg (Fig. 4.50A). This jumping with only the left leg may help that the left leg grows faster than the right leg to reduce the 4cm length difference between the legs. The mother refused a hemiepiphysiodesis for her son.

That the left-hand playing with the ball (Fig. 4.50B) became possible was found by Alen himself. To "discover" new motor possibilities of the left and right side increased. Often Alen was angry that he had to train so much. But when he learned a new pattern, then he was using it in different motor patterns.

Fig. 4.50 A. Alen during jumping a few times with the left leg only. B. The patient during throwing the blue ball down and catching it again. The small ball is marked with a double arrow. As can be seen, Alen is too much standing on the right leg. More training on specially the left side/leg (A) is necessary

The low-load coordination dynamics (CD) values (Fig. 4.51) did only improve (decrease) by 10%, probably because of the large neural network reorganization changes taking place.

Normally, when exercising on the special CDT device, the CD values get better. But on the other hand, with every bit of reorganization, the CD values get worse because of neural network changes. So far, the increase and decrease of the CD values canceled mainly each other out. When the main reorganizations for repair will have been done, then the CD values will improve (decrease) more.

Therefore, probably the main brain repair so far came from large reorganizations of the neural networks.

Fig. 4.51 shows the CD values for low load (A, B) and higher load (C, D). It can be seen that for higher load the CD values get worse (higher). In comparison to the CD values of the Author, the patients' values are much worse (higher) for low and for high load. A lot of further therapy is needed to

improve the functioning of the patients' CNS. The dreaming goal is that Alen can attend a normal school.

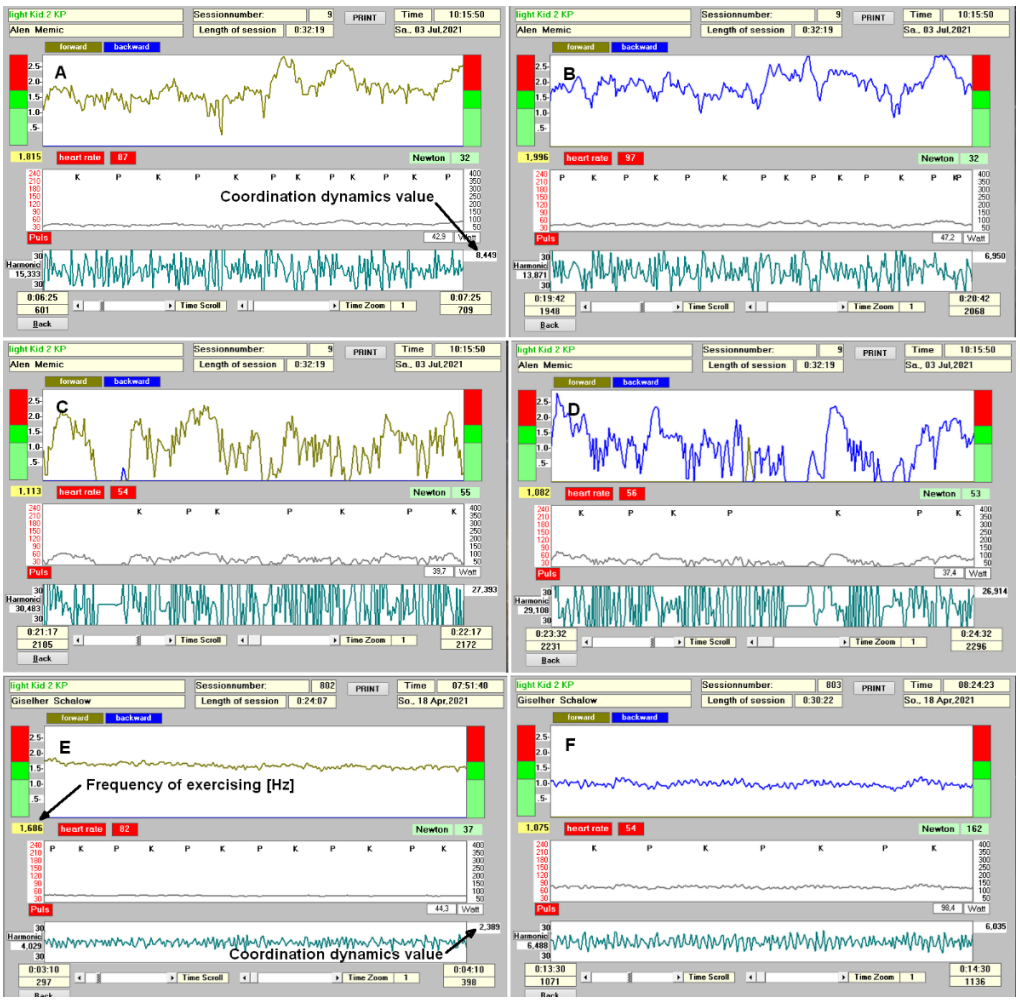


Fig. 4.51. Low-load (32N) coordination dynamics in the forward (A) and backward (B) direction of the patient Alen. For higher loads (55N) (C, D) the coordination dynamics values are much worse (increase from 8.4 to 27.3 and from 6.9 to 26.9). E, F. Nearly ideal values from the Author for comparison (CDvalue37N = 2.4 and 162N = 6.0)

4.4 DISCUSSION

4.4.1 General State of the Treatment and the Educational Systems

It is shown that the patient Alen with a so-called persistent hemiplegia for 12 years could learn functions on the paretic side. Most importantly he learned to a certain extent to use the left plegic hand in everyday life through suboptimal coordination dynamics therapy (CDT) for 6 months. His motor and cognitive functions could substantially further be improved with an optimal CDT for a few years.

A drawing back in therapy was that the educational and therapy systems were out-of-date and members of these systems were not interested to update their knowledge. If the patient Alen could leave out school for one year for an optimal CDT, his cognitive functions would improve and he could learn afterwards much better and could attend a normal school. So far, he attended a school for disabled. In Switzerland disabled children get support, but the parents cannot choose the best therapy for their child. They are forced to use the out-of-date therapy system. Since the repair progress is not coming from the offered treatment (neurology, rehabilitation, physiotherapy), the parents are not using

the offered treatments and, in this way, it is cheaper for the system on the short-term, but not on the long term and anyway it is not ethical.

4.4.2 Basal Ganglia Repair

The improvement of creeping, walking, running and hand functions indicate repairs of the basal ganglia through functional reorganization, because the basal ganglia play an important role in **initiation, maintenance** and **modulation** of these movement patterns. Alen learned to initiate the power and precision grip and learned to initiate finger functions. He learned to maintain these patterns better and longer and learned to variate the stride length of walking and running. The regulation circuits were therefore partly repaired through reorganization of their neural networks, especially the cortico-striato-pallido-thalamo-cortical regulatory circuit.

4.4.3 Comparison of Basal Ganglia Repair with Cerebellum Repair

Cerebellar injuries manifest themselves with disturbances of movement and balance. Dysmetria, the inability to stop a directed movement on time, typical for cerebro-cerebellum injury (Fig.4.21A, B; Sophie) was at the beginning of CDT also observed in Alen (Fig. 4.21C and 25A). But quickly Alen could repair his dysmetria, whereas Sophie with the cerebellum atrophy had not completely solved the dysmetria over 6 years of CDT. Possibly Alen had with the hypoxia only a mild injury of the cerebellum.

Apart from the hemiparesis, Alen with the basal ganglia injury had no problems with the protection automatisms when falling during walking or running. Sophie with the cerebellum atrophy learned through CDT the protection automatisms in 1 year [15] and the patient Dr. Cwienk, who lost 80% of the cerebellum in a traumatic injury [14], after 20 years of CDT. Sophie learned to keep balance, but Dr. Cwienk could not overcome the balance problem in 20 years. Sophie and Dr. Cwienk had no trunk stability problems, because they could exercise on the special CDT device in the standing position (Fig. 4.52) like Alen (Fig. 4.28B). Alen had no principal problems with balance, protection automatisms and trunk stability.

But the severance of a hypoxic injury depends strongly on the duration of the hypoxia. A 25-year-old woman suffered a severe hypoxic brain injury in an accident and had big problems with standing, walking and balance and could not improve them substantially within 6 months of CDT.

Fig. 4.52. Exercising on the special CDT device in the standing position of the 7-year-old Sophie with cerebellum and pons atrophy and the 60-year-old patient Dr. Cwienk with traumatic cerebellum, pons and cerebrum injury. Note that when no balance is needed, both can perform this coordinated arm and leg movement, but the girl with more elegance

4.4.4 Basal Ganglia and Cerebellum Repair with Respect to the Ontogenetic Landscape for Locomotion

A physiologic landscape for locomotion [56] is shown in Fig. 4.53. Because of basal ganglia and cerebrum injury and the degeneration of the pyramidal tract, Alen's landscape for locomotion would be completely different and cannot be analyzed because of missing data.

CDT partly recapitulates the development. But the learning process is hampered by the deficiency of the basal ganglia, cerebrum injury and pyramidal tract, on which the learning process also depends.

To teach the injured CNS to repair itself by trial-and-error elimination processes, the CNS has, in similarity to the development, to recognize through CDT which subnetworks, regulation units, subloops or tracts are not functioning properly (or are missing) and to repair them by error elimination, including the possibility that other brain parts take functions partly over and subnetworks and tract fibers built anew to a limited extent.

In cerebellum injury the ontogenetic landscape would also different from the normal one. At the beginning of CDT, at an age of 5.5 years, Sophie could only crawl in antiphase to cover distances at home by herself, whereas healthy children at that age can creep, crawl, upright, walk, run and jump. Because of missing dynamic balance, she relearned the jumping on springboard late and the running very late. The functioning of the cerebellum and pons was pathologic and too slow to be able to generate in time the patterns jumping and running, according to the ontogenetic landscape. When she eventually learned the running, her dynamic balance had improved strongly.

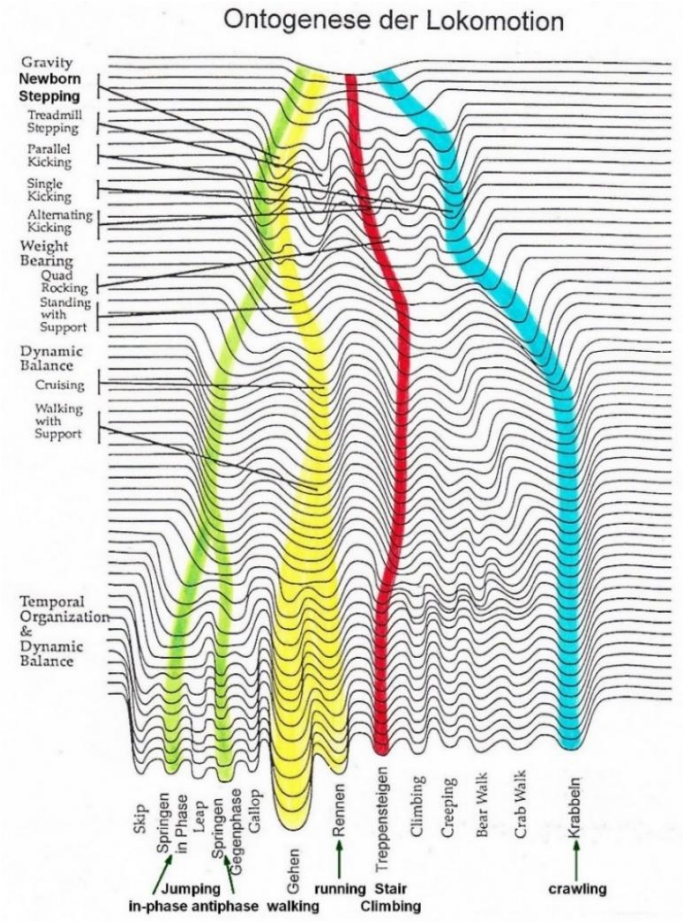


Fig. 4.53. Ontogenetic landscape for locomotion. The evolution of the attractor layout (System Theory of Pattern Formation) for different movements. Permission of Esther Thelen (†) [56]

REFERENCES

1. Schalow G (2013) Human Neurophysiology: Development and Repair of the Human Central Nervous System. Nova Science Publishers, Inc, Hauppauge NY, USA, 734 pp.
2. Schalow G (2015) Repair of the Human Brain and Spinal Cord. Nova Science Publishers, Inc, Hauppauge NY, USA, 525 pp.
3. Schalow G (2015) Neural network learning in human. Nova Science Publishers, Inc, Hauppauge NY, USA, 324 pp.
4. Schalow G (2002) Stroke recovery induced by coordination dynamic therapy and quantified by the coordination dynamic recording method. Electromyogr. Clin. Neurophysiol. 42: 85-104.
5. Schalow G (2002) Improvement after traumatic brain injury achieved by coordination dynamic therapy. Electromyogr. Clin. Neurophysiol. 42: 195-203.
6. Schalow G and Jaigma P (2006): Improvement in severe traumatic brain injury induced by coordination dynamics therapy in comparison to physiologic CNS development. Electromyogr. Clin. Neurophysiol. 46: 195-209.
7. Schalow G (2019) Regeneration of the human spinal cord via coordination dynamics therapy. Peertechz Publications, 97 pp. eBook.
8. Schalow G (2009) Partial cure achieved in a patient with near-complete cervical spinal cord injury (95% injury) after 3 years of coordination dynamics therapy. Electromyogr. Clin. Neurophysiol. 49: 199-221.
9. Schalow G (2002) Recovery from spinal cord injury achieved by 3 months of coordination dynamic therapy. Electromyogr. Clin. Neurophysiol. 42: 367-376.
10. Schalow G (2003) Partial cure of spinal cord injury achieved by 6 to 13 months of coordination dynamic therapy. Electromyogr. Clin. Neurophysiol. 43: 281-292.
11. Schalow G, Jaigma P and Belle VK (2009) Near-total functional recovery achieved in partial spinal cord injury (50% injury) after 3 years of coordination dynamics therapy. Electromyogr. Clin. Neurophysiol. 49: 67-91.
12. Schalow G (2010) Cure of urinary bladder functions in severe (95%) motoric complete cervical spinal cord injury in human. Electromyogr. Clin. Neurophysiol. 50: 155-179.
13. Schalow G (2021) CNS Repair in a Girl with a Spinal Cord Injury. Adv. Pub. Health Com. Trop. Med. 121: 201-226.
14. Schalow G (2006) Cerebellar injury improvement achieved by coordination dynamics therapy. Electromyogr. Clin. Neurophysiol. 46: 433-439.
15. Schalow G (2021) Cure-like brain-repair in a girl with atrophied cerebellum and pons through Coordination Dynamics Therapy. Adv Pub Health Com Trop Med 123: 1-47.
16. Schalow G, Jaigma P (2005) Cerebral palsy improvement achieved by coordination dynamics therapy. Electromyogr. Clin. Neurophysiol. 45: 433-445.
17. Schalow G (2006) Hypoxic brain injury improvement induced by coordination dynamics therapy in comparison to CNS development. Electromyogr. Clin. Neurophysiol. 46: 171-183.
18. Schalow G, Pääsuke M, Ereline J and Gapeyeva H (2004) Improvement in Parkinson's disease patients achieved by coordination dynamics therapy. Electromyogr. Clin. Neurophysiol. 44: 67-73.
19. Schalow G and Nyffeler T (2001) Koordinationsdynamik-Therapie: Myelomeningozele (Spina bifida). Physiotherapie.
20. Schalow G and Nyffeler T (2000) Koordinatiosdynamik-Therapie: Skoliose. Physiotherapy.
21. Schalow G (2019) Permanent coma patient re-learned to speak via Coordination Dynamics Therapy. Arch. Clin. Med. Case Rep. 3(2): 33-50.
22. Schalow G (2017) Breast cancer growth inhibition via Coordination Dynamics Therapy. In: "Horizons in Cancer Research. Volume 68". Editor: Hiroto S. Watanabe. Nova Science Publishers, Inc, Hauppauge NY, USA, pp. 125-151.
23. Schalow G (2020) Anaplastic oligodendroglioma WHO III brain cancer-patient recovered following operation, radiation and chemotherapy through Coordination Dynamics Therapy, which is also a Covid-19 treatment without ventilator. Int. J. Med. Clin. Imaging 5(2): 165-210.
24. Christensen JF, Jones LW, Andersen JL, Daugaard G, Rorth M and Hojman P (2014) Muscle dysfunction in cancer patients. Ann. Oncol. 25: 947-958.

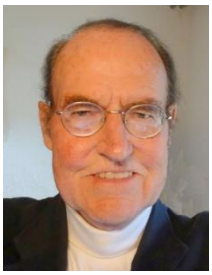
25. Schalow G (2020) To live longer with a better quality of life through coordination dynamics therapy especially in patients with severe brain injury and brain-cancer. Int. J. Med. Clin. Imaging 5(2): 118-155.
26. Baehr M and Frotscher M (2005) Duus‘ Topical Diagnosis in Neurology. Thieme Verlag, Stuttgart. (a very good book for medical neuroscience since it correlates structure and function in human nervous system injuries; only human neurophysiology is missing).
27. Kahle W (1984) Nervensystem und Sinnesorgane. Thieme Verlag, Stuttgart.
28. Schmidt RF und Thews G (1976) Physiologie des Menschen. Springer-Verlag, Berlin.
29. Daeschler, E.B., Shubin, N.H. and Jenkins, F.A. (2006). A Devonian tetrapod-like fish and the evolution of the tetrapod body plan. Nature 440 (7085), 757-763.
30. Shubin, Neil (2008). Your inner fish: A journey into the 3.5-billion-year history of the human body. University of Chicago Press, New York.
31. Shubin, N.H., Daeschler E.B. and Jenkins, F.H. (2014). Pelvic girdle and fin of Tiktaalik roseae. Proceedings of the National Academy of Sciences 111, 893-899.
32. Schalow G and Lang G (1987) Recording of Single Unit Potentials in Human Spinal Nerve Roots: a New Diagnostic Tool. Acta Neurochir. 86: 25-29.
33. Schalow G (2009) The classification and identification of human somatic and parasympathetic nerve fibres including urinary bladder afferents is preserved following spinal cord injury. Electromyogr. Clin. Neurophysiol. 49: 263-286.
34. Schalow G (2020) Classification and Identification of Human Peripheral Nerve Fibers by Conduction Velocity, Nerve Fiber Diameter and Natural Firing Patterns with Consequences for CNS Repair and Covid-19 Infection Treatment. Int. J. Med. Clin. Imaging 5(3): 231-314.
35. Schalow G (2005) Phase and frequency coordination between neuron firing as an integrative mechanism of human CNS self-organization. Electromyogr. Clin. Neurophysiol., 45: 369-383.
36. Schalow G (2021) Phase and frequency coordination improvement among neuron firing for improved CNS self-organization and neural repair in Parkinson and spinal cord injury. Int J Med Clin Imaging 6(1): 350-425.
37. Schalow G (1993) Spinal oscillators in man under normal and pathologic conditions. Electromyogr. Clin. Neurophysiol. 33: 409-426.
38. Schalow G (2006) Surface EMG- and coordination dynamics measurements-assisted cerebellar diagnosis in a patient with cerebellar injury. Electromyogr. Clin. Neurophysiol. 46: 371-384.
39. Schalow G (2005) Tremor in Parkinson’s disease patients can be induced by uncontrolled activation and uninhibited synchronization of α_2-motoneuron firing to which α_1-motoneuron firing synchronizes. Electromyogr. Clin. Neurophysiol. 45: 393-406.
40. Schalow G (2021) Phase and frequency coordination improvement among neuron firing for improved CNS self-organization and neural repair in Parkinson and spinal cord injury. Int J Med Clin Imaging 6(1): 350-425.
41. Schalow G (2010) Scientific basis for learning transfer from movements to urinary bladder functions for bladder repair in patients with spinal cord injury. Electromyogr. Clin. Neurophysiol. 50: 339-395.
42. Kelso JAS (1995) Dynamic Patterns. The Self-Organization of Brain and Behavior. MIT Press, Cambridge.
43. Schöner G, Zanone PG and Kelso JAS (1992) Learning as change of coordination dynamics: Theory and experiment. Journal of Motor Behavior 24: 29-48.
44. Zanone PG and Kelso JAS (1992) Evolution of behavioral attractors with learning: Nonequilibrium phase transition. Journal of Experimental Psychology: Human perception and Performance, 18 (2): 403-421.
45. Popper KR (1972). Objective knowledge: An evolutionary approach. London: O.U.P.
46. Touwen B (1987) Variability and stereotypy in normal and deviant development. In: Care of handicapped child. Apley, J. (Ed.). Clinics in Developmental Medicine No. 67. Philadelphia, pp. 99-110.
47. Thelen E (1987) The role of motor development in developmental psychology: a view of the past and an agenda for the future. In: Eisenberg, N. (ed.): Contemporary Topics in Developmental Psychology. New York, Wiley, pp 3-33.
48. Deisseroth K, Singla S, Toda H et al (2004) Excitation-neurogenesis coupling in adult neural stem/progenitor cells. Neuron 42: 535-552.

49. Schalow G (2009) Building of New Motoneurons in the Human Spinal Cord upon Coordination Dynamics Therapy to Improve Finger Functions in Motoric Complete Cervical Spinal Cord Injury. In: Berkovsky, T.C. (Ed.), Handbook of Spinal Cord Injuries, Chapter 4. pp. 231-264, Nova Science Publishers.
50. Schalow, G. Tremor in Parkinson's disease patients can be induced by uncontrolled activation and uninhibited synchronization of α_2-motoneuron firing to which α_1-motoneuron firing synchronizes. Electromyogr. Clin. Neurophysiol., 45: 393-406, 2005.
51. Schalow, G., Pääsuke, M., Jaigma, P. Integrative re-organization mechanism for reducing tremor in Parkinson's disease patients. Electromyogr. Clin. Neurophysiol., 45: 407-415, 2005.
52. Sperry RW (1945) The problem of central nervous reorganization after nerve regeneration and muscle transposition. *Quart. Rev. Biol.,* 20, 311-369.
53. Sperry RW (1947) Effect of crossing nerves to antagonistic limb muscles in the monkey. *Arch. Neurol. Psychiat.* Chicago, 58, 452-473.
54. Tsukahara, N. (1978). Synaptic plasticity in the red nucleus. In: Cotman, C.W. (ed.), Neuronal plasticity. Raven Press, New York, pp. 113-130.
55. Weiss P and Brown PF (1941) Electromyographic study on recoordination of leg movements in poliomyolitis patients with transposed tendons. Proceedings of the Society for Exper. Biology and Medicine, 48, 384-387.
56. Thelen E and Smith LB (1994) A dynamic approach to the development of cognition and action. MIT Press, Cambridge.
57. Schalow G (2021) Euthanasia in organ donation can be avoided through Coordination dynamics therapy. Adv Pub Health, Com Trop Med: APCTM-132. Volume 3: 1-34.

COMPETING INTERESTS

Author has declared that no competing interests exist.

Biography of author



Dr. Giselher Schalow
NGOMR: Non-Government-Organized-Medical-Research, Switzerland.

Born in Berlin. Son of the artist painter Edmund Schalow. Degree in Electronics at Engineering School Gauss (Dipl.Ing.), PhD in Theoretical Physics at Free University of Berlin, Germany and Promotion in Physics (Dr.rer.nat). Scientific assistant at Hahn-Meitner-Institute for Nuclear Physics and Research assistant at Institute of Biophysics, University College London with R. Miledi and Sir B. Katz. Study of Medicine (MD) and Promotion in Medicine (Dr.med.) at University of the Saarland, Germany. Research assistant at Turku University, Finland (Anatomy for Nerve Anastomosis in Spinal Cord Injury), Research assistant at Greifswald-University at Departments of Neurosurgery and Pathology (Measurements on Brain-Dead Humans (HTs)) and Habilitation in Medicine (Dr.med.habil.). Leading doctor for clinical research at Swiss Paraplegic Center Nottwil, Switzerland (Improvement of motor and urinary bladder functions in patients with Spinal Cord Injury). Guest Professor for Human Neurophysiology, Kinesiology and Physiotherapy at University of Tartu, Estonia, Institute of Exercise Biology and Physiotherapy. He is now a Researcher in Human Repair-Neurophysiology (Non-Government organized Medical Research).

London Tarakeswar

Registered offices
India: Guest House Road, Street no - 1/6, Hooghly, West Bengal, PIN-712410, India, Corp. Firm Registration Number: L77527, Tel: +91 7439016438 | +91 9748770553, Email: director@bookpi.org, (Headquarters)
UK: 27 Old Gloucester Street London WC1N 3AX, UK
Fax: +44 20-3031-1429 Email: director@bookpi.org, (Branch office)