Neurotherapy

Definition: Medical discipline to improve the functioning of the human nervous system by learning, based on anatomy, human neurophysiology and medical research.

Repair of the human central nervous system

Key-words: Spinal cord injury, traumatic brain injury, stroke, cerebral palsy, cerebellar injury, Parkinson, aging, peripheral nerve injury – Neurorehabilitation, Schädel-Hirn-Trauma

1. A partial repair of the CNS is possible upon movement-based learning

The general belief is that a substantial repair of the injured, malformed or degenerating central nervous system (CNS) in humans is not possible. However, up-to-date medical (human) research shows that a partial repair of the injured nervous system is possible upon a special intensive movement-based learning therapy called **Coordination Dynamics Therapy (CDT)** (14). The extent of repair depends on the severance of the injury. The CNS of the patients learns to repair itself. CDT teaches the CNS how to repair itself by learning. All repair mechanisms are already in the nervous system, they just have to be activated by learning.

2. CDT can partially repair most CNS injuries, malformations and degenerations

CDT has been shown to be able to improve CNS functioning after stroke (1), traumatic brain injury (2,7), spinal cord injury (3,4,10,13), cerebral palsy (6), cerebellar injury (9), in Parkinson's disease (5) and after hypoxic brain injury (8). Speech had been induced and improved in a patient with severe cerebral palsy (14) and urinary bladder functions were repaired in patients with spinal cord injury (13,14).

3. CNS functioning can be measured non-invasively

When exercising on a special coordination dynamics therapy (CDT) and recording device (Figs.1,2C), coordinated arm, leg and trunk movements can be trained and CNS functioning measured non-invasively. Further, upon exercising with different combinations of arms and legs in forward and backward direction, right-left, rostral-caudal, and forward-backward symmetry impairments of CNS movement organization can be measured and repaired.

4. Movements, coordinated firing of nerve cells and neural network stability have to be trained for repair

With nervous system injury, movements and other patterns become impaired and the coordinated firing of nerve cells and neural network stability become impaired (12,14). To repair nervous system functioning, movements have to be re-learned, the coordinated firing of nerve cells has to be improved, the communication of neural sub-networks improved and the stability of physiologic patterns increased and those of pathologic patterns (spasticity) decreased. Movement-based learning can repair impaired CNS functioning, because this is the strategy which the CNS uses during development for correcting CNS development 'en route'. Trial and error eliminating processes are used to improve CNS self-organization (14). CDT uses these movements of the developing child for improving CNS functioning, namely creeping, crawling, up-righting, walking, running, jumping and training balance. Additionally, the coordinated firing of nerve cells is trained when exercising on the special CDT device (Fig.1), which works very exactly so that the CNS can re-learn the coordinated firing of nerve cells from the movement induced afferent input when the patient exercises on the device. Upon exercising, physiologic movement patterns improve and their stability increases and the stability of pathologic patterns decreases by learning transfer (12,14). Only those movements can be trained, which the patient is able to perform by himself or with support of therapists (Figs. 2,4,5,6).

Figure 1. Exercising on the special CDT device with crossed arms to train enhanced communication between the right and left cerebral hemispheres via the corpus callosum. One hand holds the leaver in suppination and the other hand in pronation for mechanical reasons.

5. Learning transfer from movements to improve autonomic and higher mental functions

A powerful tool to repair the injured CNS by movement-based learning is the learning transfer. By learning transfer (12,14) also those patterns can partly be repaired which cannot be trained as for example urinary bladder and higher mental functions. Upon movement-based learning (CDT) urinary bladder functions (13) and speech (14) could be repaired in patients with spinal cord injury and cerebral palsy. The scientific basis for learning transfer is given by the System Theory of Pattern Formation and Human Neurophysiology (12,14). Since sub-neural networks of the human CNS can generate different patterns and the CNS has to be seen as one network, one trained pattern will also influence the other not trained patterns to become more physiologic in functioning.

6. Different repair strategies in humans and animals: Learning for repairing the human CNS

Repair strategies of the nervous system in animals and humans are different. In animals, in which the neural networks are more hard-wired, the nerve fibre growing strategy is used. In humans, in whom the neural networks are more complex to generate also speech and reading, the movement-based learning strategy is used; learning is primarily used and not the enhancement of growing of nerve fibres. Animal research is therefore only of limited help for the repair of the human nervous system (14).

7. Limited neurogenesis in human from endogenous stem cells

Upon CDT a few new nerve cells (motoneurons) could be built from endogenous stem/progenitor cells in a patient with a cervical spinal cord injury to get some finger functions back (11). An exogenous stem cell therapy, however, is unlikely to be effective. The administered cells have to proliferate and have to be integrated into the injured adult neural networks. But this proliferation and integration does not seem to be possible, because physiological neural activity is required to stimulate the membranes of the administered stem/progenitor cells for proliferation and integration (Chapter VI of (14), 17). Further, the communication distance between nerve cells during development and repair seems to be in the range of 0.001mm, which is difficult to achieve during exogenous stem cell therapy (Chapter 1 of (14)).

8. Program for movement-based learning

To repair the severely injured human CNS by learning 20 to 30 hours training per week is needed for approximately 3 years. The patient has to train at his/her limits to induce all repair mechanisms including the building of new nerve cells. With intensive training new nerve cells and connections are built and the specific movements 'tell' the CNS where to locate the new cells and what connections have to be made. A therapist with an up-to-date education is needed to instruct the patients what movements are needed for repair and helps him to perform these movements. Therefore, even though a movement-based learning therapy seems to be simple, deep knowledge about human nervous system functioning under physiologic and pathologic conditions is needed to adapt the therapy optimally to the patient's CNS injury and its ongoing repair. The progress in CNS functioning has to be quantified clinically and measured objectively by a device.

9. Learning (treatment) strategies included in important training movements for repair

1. **Exercising on a special CDT device** (Figs.1,2C):

A. Training of phase and frequency coordination, which are impaired and are organizational principles of human CNS functioning.

B. Learning of pattern variability from the changing between pace and trot gait coordination of arm, leg, and trunk movements.

C. Training especially trunk stability from the performed rotational trunk movements, if the patient is exercising of the special CDT device in the lying position (Fig.21, right side, VideoKadri).

D. Upon exercising with the right hand at the left handle and with the left hand at the right handle (or vice versa) (Fig.1), the corpus callosum can substantially be activated and repaired, which is important in corpus callosum injury and aging.

2. **Walking and running** (Figs.2A;6G,H, VideoWalking):

A. Re-learning of an integrative innate automatism, which may get strong genetic support for repair.

B. The stepping automatism (= neonatal stepping movement (Fig.3)) is a movement element to be integrated (modified, refined and brought under volitional control) in the more integrative pattern walking.

C. Natural walking (or running) in the forward and backward directions, if necessary with support of therapists (Fig.2A), is the most specific human movement and must therefore be trained, because the CNS may use this movement also for other purposes.

D. Sky-walking (neuro-walking): Since in severe cervical spinal cord injury (injury level C5/C6) the physical load for therapists during supported treadmill walking is high and the weight support for the patient is large, sky-walking on an exactly functioning device helps to re-learn walking. Such a patient (tetra) with little trunk stability can re-learn the trot gait moving without weight-bearing support (Fig.4, VideoRuth).

E. Sky-walking enhances the stability of the trot gait pattern, which may have been weakened by the training of pattern variability and phase and frequency coordination upon exercising on the special CDT device (Fig.2C,D).

F. The support given by the therapist improves the movement performance and the movement induced afferent input and in turn the performed motor pattern.

Figure 2. Performed movements A,B,C,D

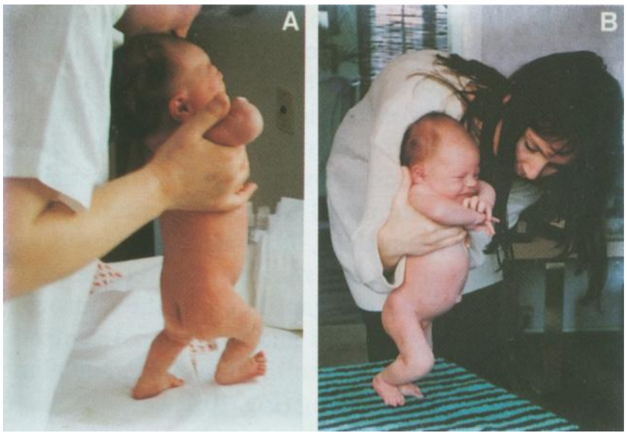

Figure 3. Automatic stepping in a newborn infant. A. A 5-day-old infant, Juliane, performing primary automatic stepping; slight backward posture. The heel of the right foot touched the ground first. B. Infant Juliane, 8-day-old, performing automatic stepping.

G. During fast running, if possible, the movement induced afferent input is higher per time and may be more physiologic, because the kinetics improves the performance. Because of the higher and more physiologic input, the pathologic CNS organisation (spasticity) may be reduced and the performance and learning improved. The higher physiologic afferent input improves the physiologic self-organization of the neural networks.

3. **Jumping or swinging on springboard** (Fig.2B):

A. Injured premotor spinal oscillators (14) (neural sub-networks of the CNS) are entrained upon the rhythmic, dynamic, stereotyped movements (partly imposed by the mechanical properties of the springboard or swinging device) to reduce their frequency range and to get a real 'Eigen frequency' again (Fig.2B).

B. Induction of learning transfer from arm, leg, trunk and pelvic floor movements to urine storing and continence functions of the urinary bladder (similar networks and receptors are activated) (12,13,14).

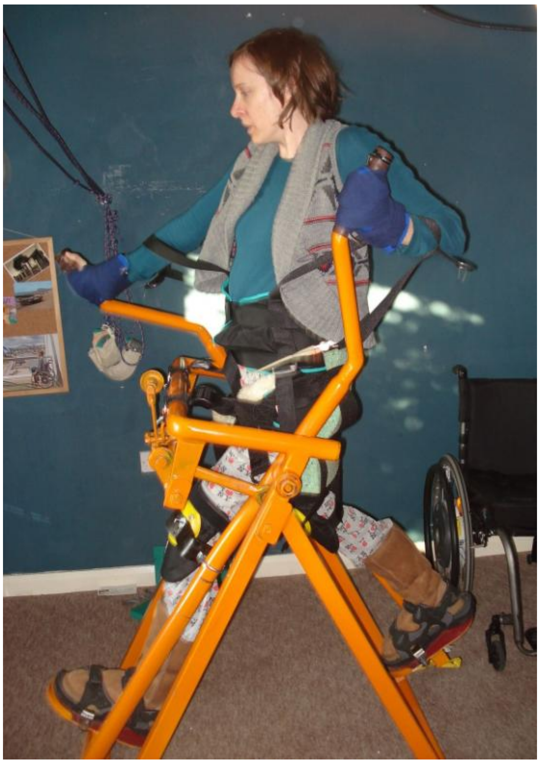

Figure 4. Patient with severe cervical spinal cord injury is exercising very coordinated trot gait movement without weight support on a sky-walker.

C. Swinging and jumping can also be performed in patients with severe SCI (C5/6) without weight-bearing support in the upright position (Fig.2B).

4. **Training of trunk stability**:

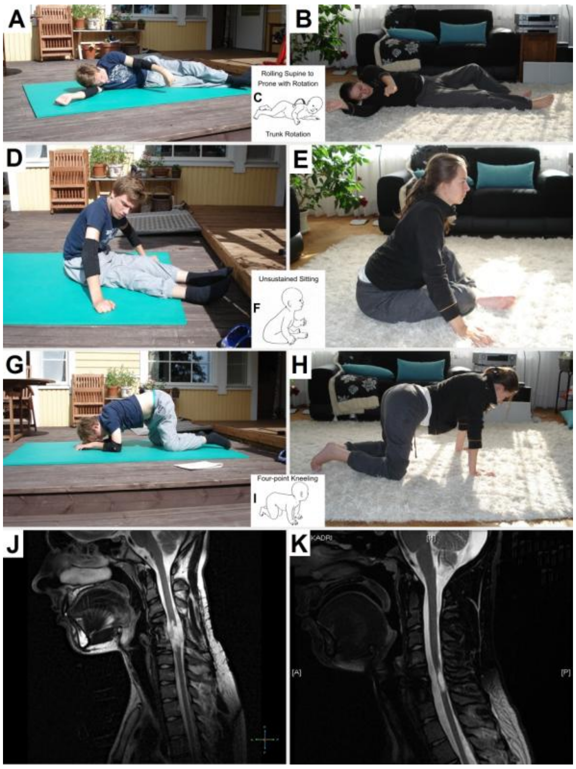

Figure 5. Comparison between development and the repair of an almost complete cervical spinal cord injury upon 0.5 years (A,C,G) (therapy started with 15.5 years) and 5 years of coordination dynamics therapy (B,E,H) (CDT started with 17 years). The MRI of the SCI of the patient of the left panel is shown in 'I' and those one of the right panel in 'K'. Trunk rotation (A,B,C), unsustained sitting (D,E,F), and four-point kneeling (G,H,I) is compared between 0.5 and 5years of CDT and with the positioning of an infant.

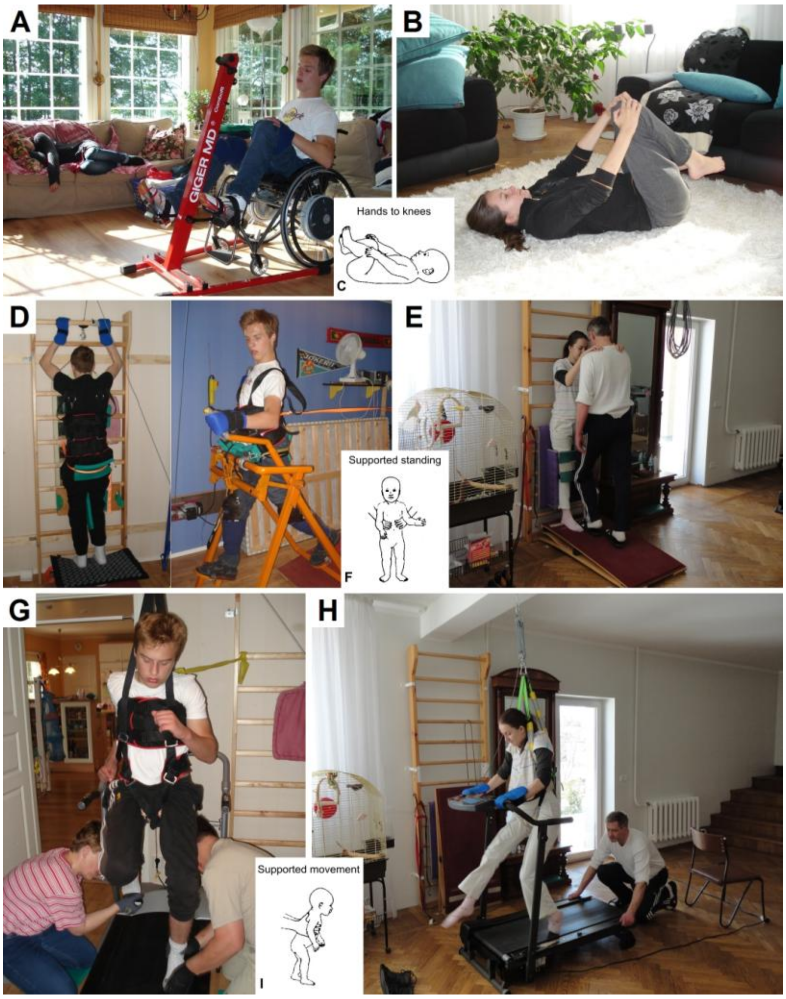

Figure 6. Comparison between the development of an infant and repair of a cervical spinal cord injury upon CDT. Left penal, positioning upon 0.5 years of therapy and right penal after 5 years of therapy. Same patients as in Figure 36. Reaching of hands to knees, supported standing, and supported walking are compared.

A. Recapitulating development to repair trunk stability. Trunk stability can be trained by the change of the crawling posture, exercising on the special CDT device in the lying position, and by training patterns and reactions of infancy development (Figs.5,6).

5. **Endogenous stem cell therapy**:

A. Activating endogenous stem cells in or at blood vessels, especially when going to the physical limits will contribute to the adaptation and repair of the blood vessel system in general. The cardio-vascular performance will improve. When activating the neural networks, upon therapy, adjacent to the injury site (in SCI, Fig.7D), blood vessels are generated also specifically at the injury site. Multipotent stem cells, whatever way they migrate (or wherever they are generated) find the environment for integration. The naturally activated neural networks generate the electro-magnetic fields and guidance molecules for the integration of the different differentiated cells and for regenerating nerve fibres (see Chapters I and VI (14)). The more severe the injury is the less proper environment can be generated for structural and functional repair.

10. CNS functioning improvement in disabled and healthy humans

In principle, every nervous system can be improved in its functioning upon administering Coordination Dynamics Therapy (CDT). Exercising on the special CDT device will improve CNS functioning during development and will improve the performance in athletes, especially if the CNS of the athletes is not functioning optimally (Chapter II of (14)). But the importance of the improvement of CNS functioning lies in the repair of injuries, malformations and degenerations (Chapter II of (14)).

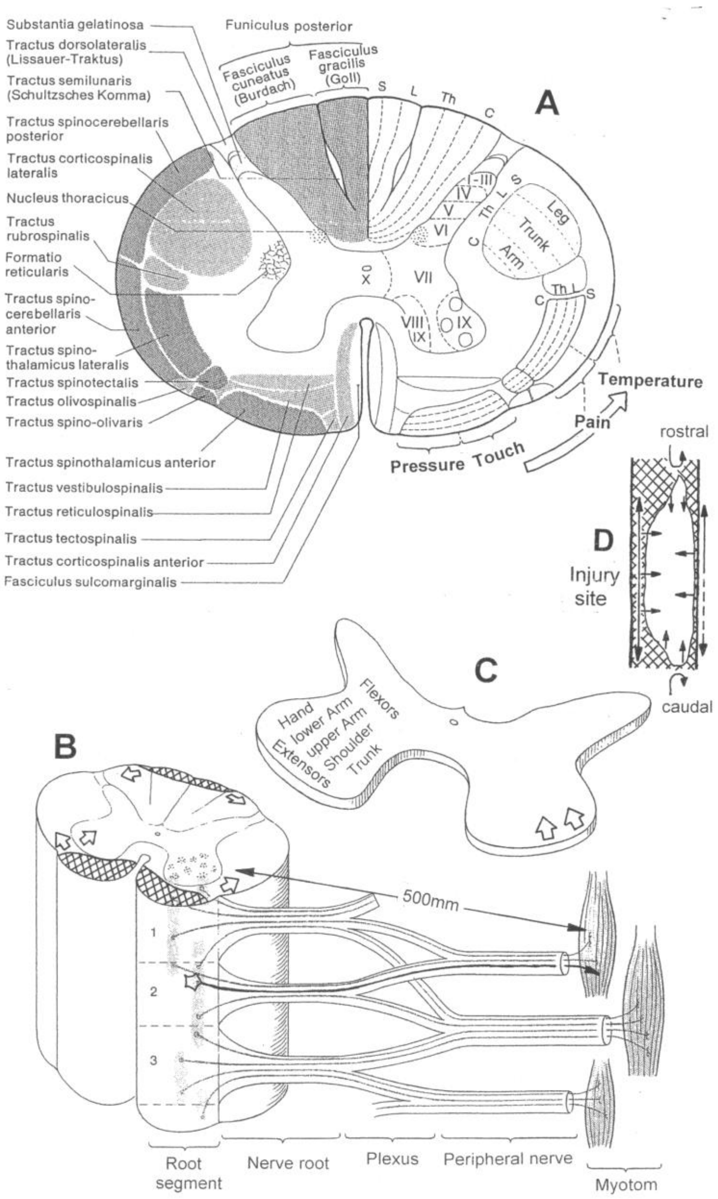

Figure 7. Schematic drawings of the human spinal cord with a cervical injury. A. Spinal cord cross-section with fibre tracts and grey matter. Note the regaining of sensitivity upon CDT from pressure to touch, pain, and temperature is indicated by an open arrow. B. Spinal cord section with suggested spared matter (cross-hatched). Open arrows indicate direction of structural repair. The axonal outgrow of a newly built motoneuron is indicated by a bended and long arrow. C. Motoneuron sites for serving different functions are indicated. Note that the extensor motoneuron cell bodies are sited more adjacent to the spared spinal cord matter than the flexors and should be generated first in this case, indicated by open arrows. D. Injury site of the patient. Small short arrows indicate the direction of structural activity-dependent repair. The structural repair starts from the activated spared matter into the cavity. The ascending and descending tract activity is indicated by long arrows, and the tract and network activity rostral and caudal to the injury site is indicated by bent arrows.

If a therapy method can partly repair the severely injured CNS, surely it can manage easily with the mild injuries. From the severe injuries we learn how the human CNS is functioning (Chapters III and V) and how to repair it (Chapter II) by comparing physiologic and patho-physiologic human CNS functioning. Because of limited neurogenesis (building of new nerve cells) in the human CNS, the largest contribution to the repair comes from the functional reorganization of the CNS. Probably the few newly built neurons will be generated at sites where they are needed most, as for example for learning and memory and creating important connections for the communication between neural sub-networks. An integrative healthy movement-based treatment as CDT is not only repairing the injury it is used for, but it improves also other functions of the human body. Here an example. A mother of a monastery suffered a spinal cord injury and trained only on the special CDT device. There was only some improvement with the spinal cord injury; but she cured her diabetes.

11. Repair in traumatic brain injury, cerebral palsy, stroke, Parkinson's disease and spinal cord injury

The largest repair can be achieved in babies and children because in addition to movement-based learning the development is influenced. The repair mechanisms of the development, namely the correction 'en route' upon trial and error eliminating processes, is used (Chapter II of (14)). Progress in stroke patients is good, but often they cannot train at physical limits because of other diseases. In degenerative diseases like the Parkinson's disease the problem is that more nerve cells are dying than new ones can be built upon CDT. But by functional reorganization the functioning of the degenerating CNS is optimized at any stage of degeneration. The quality of life is improved on the basis of the available neural network structure. In mild degenerative diseases the improvement of CNS functioning is higher.

12. Improvement of CNS functioning in aging

In aging the general health will improve upon CDT. The drawing back in elderly people, namely that not so many nerve cells can be built anew as in young ones, can partly be overcome. Upon exercising, nerve cells can be built anew and degenerative effects counteracted. The exercising on the special CDT device is more than just training some movements to stay fit. By exercising the complicated coordinations of arm and leg movements, complicated patterns can be reached (activated) and improved like autonomic (urinary bladder) and higher mental functions (intelligence, memory, speech, writing). It is not sufficient to generate new nerve cells but they have to be placed at or directed to sites where they are most urgent needed and this is partly possible by training complicated very coordinated movement patterns on the special device. With these special movements the therapy may offer better patterns for learning than the nature can offer with the natural movements. Nature also offers the possibility of training movements with complicated coordinations. When walking in the mountains, for example, and partly jumping from stone to stone, complicated movements are trained. However, not all elderly people are able to walk in the mountains. The advantage of the special CDT device is that a person can sit at home on a chair and train the complicated movement patterns on a device whenever he/she wants. Also with joint problems one can easily train on the special CDT device.

13. Different repair in peripheral nerve injury in human and rat

If peripheral nerves are injured (crashed or cut and sutured (fascicle to fascicle)), nerve fibres grow over the injury site along pathways (Bügners bands) to the target (muscle). Because of mismatch (taking the wrong path) they grow partly to wrong places. By movement-based learning, the mixed functions can be compensated for by a functional rewiring in the brain. Therefore, after peripheral nerve injury repair, movement-based learning is necessary to optimize functional recovery. Here an easy example for functional repair. If one transposes the nerves to extensor and flexor muscles, the human patient re-learns after a few trials to use the muscles in the right way again. A rat cannot relearn these nerve supply changes, because the CNS has not the necessary neural network complexity for re-learning. The higher regenerative capacity of nerve fibres is doesn't help the rat. Therefore, the rat's nervous system is different to that of humans and data from animals cannot easily be transposed from animals to humans.

14. Difficulty of functional repair after orthopaedic operations in cerebral palsy or brain injury

In cerebral palsy children, who can walk with a very poor performance, orthopaedic operations are performed to improve the positioning of legs and feet by changing, for example, the lengths of tendons. After the operation, the leg and feet are in a much better position, but the patient cannot walk any more, because the receptors from the legs are informing the CNS wrongly about the walking performance. A healthy human would quickly re-learn walking by movement-based learning. But the cerebral palsy or brain-injured child has big problems to re-learn the walking because the neural network complexity and pattern variability is too poor to relearn quickly.

15. Scientific basis for movement-based learning

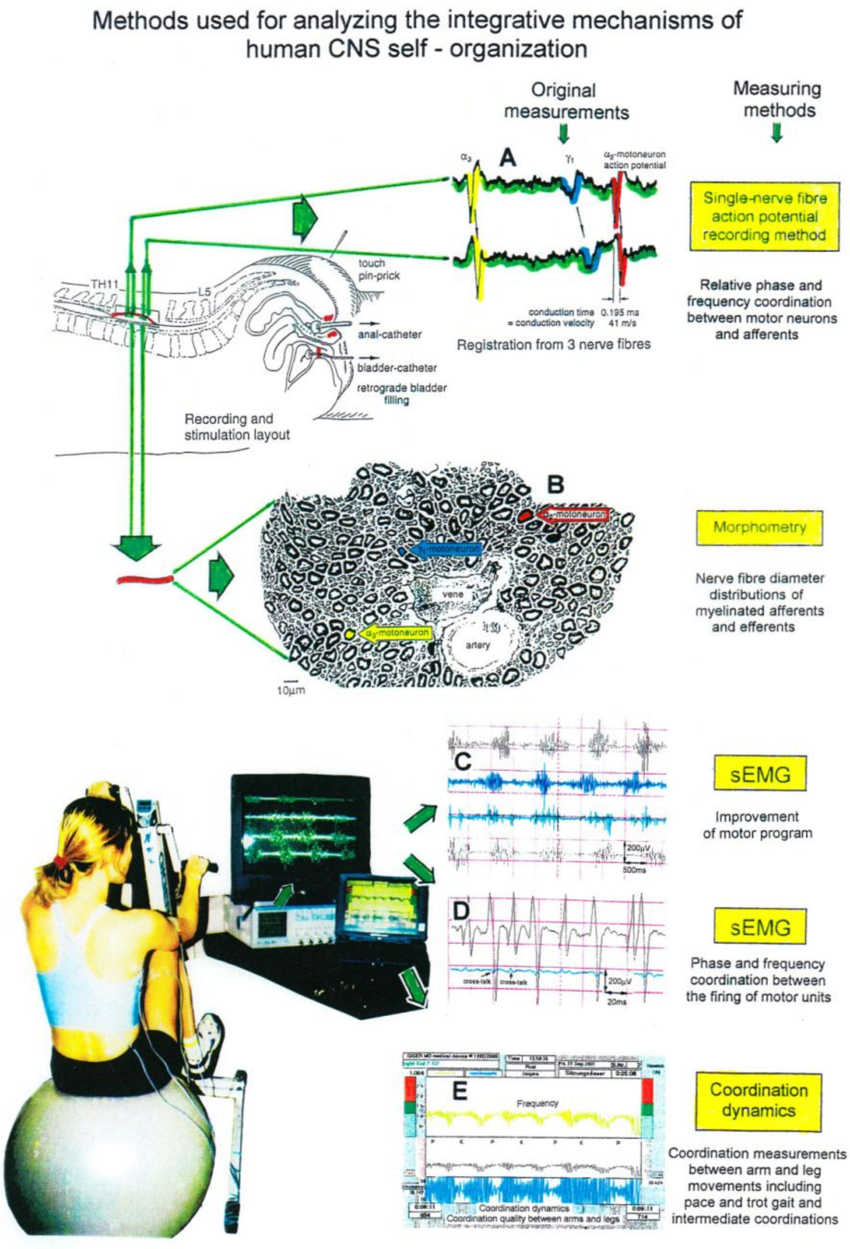

Figure 8. Schematic layout of the measuring methods used to study the self-organization of neuronal networks of the human CNS under physiologic and pathophysiologic conditions. A, B. By recording with two pairs of platinum wire electrodes from sacral nerve roots containing between 200 and 500 myelinated nerve fibres, records were obtained in which single-nerve fibre action potentials (APs) could be identified from motoneuron axons (main AP

phase downwards) and afferents (main AP phase upwards). By measuring the conduction times and with the known electrode pair distance (10 mm) conduction velocities could be calculated. Conduction velocity distribution histograms were constructed in which the myelinated nerve fibre groups larger than 4µm could be characterized by group conduction velocity values. Recording was followed by morphometry. Distributions of nerve fibre diameters were constructed and nerve fibre 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 of the human peripheral nervous system. It became thus possible to record natural impulse patterns simultaneously from identified single afferent and efferent nerve fibres and to analyse self-organizing mechanisms of the human CNS under physiologic and pathologic conditions.

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 legs 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.

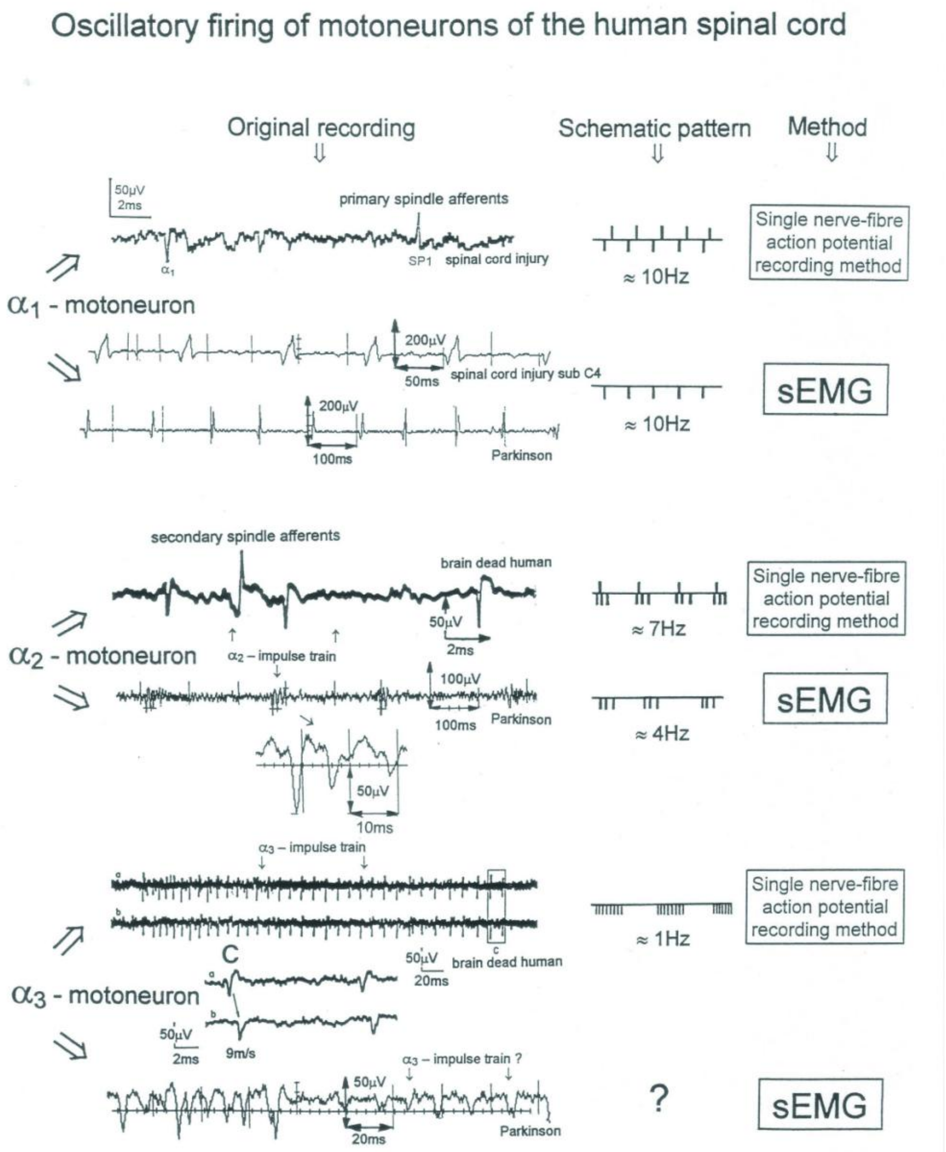

Figure 9. Oscillatory firing patterns of α_1, α_2, and α_3-motoneurons recorded from motoneuron axons with the single-nerve fibre action potential recording method and by surface electromyography (sEMG) from FF, FR, and S-type motor units. The left panel shows original recordings, the middle panel the 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 movement-based learning therapy, called Coordination (Pattern) Dynamics Therapy (CDT), is based on measurements at the neural level (single-nerve fibre action potential recording method, single motor unit surface EMG), the neural sub-network level and the pattern level (surface EMG (electromyography) of motor patterns and coordination pattern dynamics measurements with the special CDT device) (Fig.8). The oscillatory firing of premotor spinal oscillators, generated by neural sub-networks could be measured with the single-nerve fibre action potential recording method and surface EMG (Fig.9). The whole theory and praxis of CDT (with case reports of treatment up to 11 years) is presented in the book “Human Neurophysiology: Development and Repair of the Human Central Nervous System” (14). Besides some anatomy, detailed functioning of human skin, urinary bladder and muscle spindle receptors are included in this book of human neurophysiology. The book extracts the knowledge from approximately 100 scientific publications of theory and praxis (www.cdt.host.sk; publication list) and goes beyond that knowledge level. Some measurements and aspects of human neurophysiology will be given here to better understand the different trained movement patterns and to realise that CDT has really a scientific basis which is supported by measurements in the human nervous system.

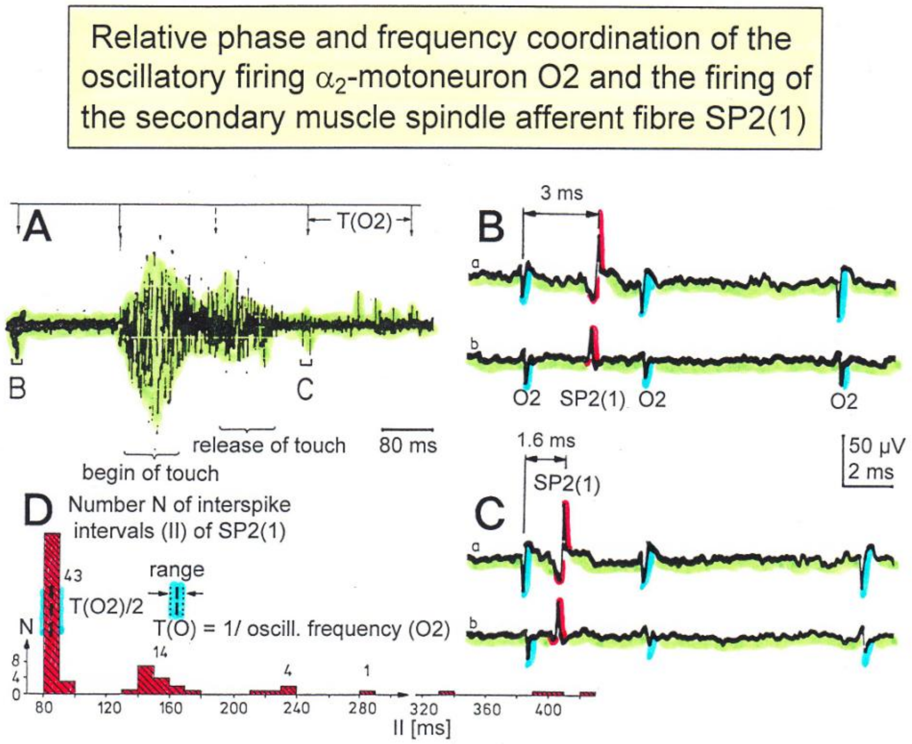

Figure 10. Time relation between the occurrence of the action potentials (APs) of oscillatory firing α_2-motoneuron O2 and the firing of the secondary muscle spindle afferent fibre SP2(1). HT6. S4 dorsal root recording.

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 is marked O2, spindle afferent APs are marked SP2(1). Note that the APs of the spindle afferent fibre are not time-locked to the first AP of the impulse train of the rhythmically firing motoneuron (relative phase coordination). Digitalization 4 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 fibre 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 fibre SP2(1) are very similar to the oscillation period (or the half of it) of α_2-motoneuron O2 (relative frequency coordination).

<u>16. Coordinated firing of neurons, their impairment and repair by learning</u>

In every CNS injury, degeneration or malformation the phase and frequency coordination of neuron firing becomes impaired and has to be repaired by learning. Figure 10 shows the coordinated firing between a secondary muscle spindle afferent fibre and an oscillatory firing α_2-motoneuron. The coordination is approximately 3 to 5 ms exact. The coordinated firing of motor units in the same muscle or in different muscles can be recorded by surface EMG (Figs.11,12). The impaired coordination between nerve cells and arm and leg movements following injury (14) can be improved especially upon exercising on the special CDT device, which is working mechanically very exact. The exactness of the device guaranties that the coordinated arm and leg movement induced afferent input can teach the neurons of the CNS to improve their coordinated firing up to a few milliseconds. Since the neurons are coincidence, or even better, coordination detectors (Fig.13), this improved coordinated firing improves for example the communication among nerve cells and neural sub-networks (especially between networks across an injury site as for example in spinal cord injury) because the threshold of neuron excitation is reached earlier. However, the training of phase and frequency coordination via coordinated arm, leg and trunk movements improves the self-organisation of the corresponding sub-networks and the functioning of the CNS neural networks also in general. Some motor and other patterns re-appear upon this improved coordination at the neural and movement level. A cerebral palsy child became able to speak upon exercising on the special device (14).

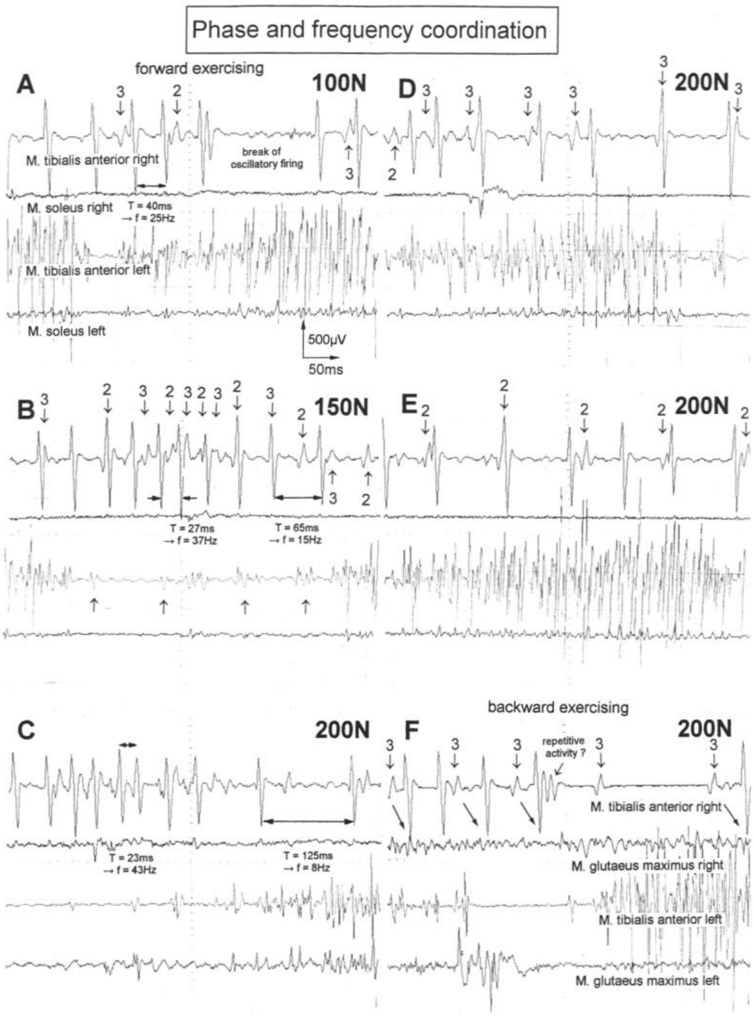

Figure 11. Phase and frequency coordination between motor unit firing (in the same muscle) during the generation of a motor program during exercise on the special coordination dynamics therapy device at loads increasing from 20N to 200N. The wave forms of 3 identified motor unit potentials of FF-type ‘1’, ‘2’, and ‘3’

are inserted in ‘A,C’ and some of them are marked in ‘A,B,C’. Note in ‘A’ that motor unit ‘1’, firing at approx. 9Hz, coordinates its firing with motor unit ‘2’, firing at approx. 4.2Hz, by firing twice as often. In ‘B’ both motor units fire non-synchronously at around 10Hz with relative phase and frequency coordination. A, B. No motor program can be seen in the right tibialis anterior muscle as in the biceps brachii and quadriceps femoris muscles during exercising at 20N and 50N. C. The oscillatory firing of motor unit 1 and 2 (and 3) was transiently interrupted (inhibited) upon exercising at 100N, thus showing the beginning of a motor program. In the motor program burst, the frequencies of the motor units are increasing and decreasing. D. Upon exercising at 200N, the motor program became more pronounced. Probably two more high-threshold motor units contributed to the motor program burst in addition to the 3 motor units identified in ‘A-C’. E, F. Improvement of the motor program from ‘E’ to ‘F’ in the right tibialis anterior muscle of the same patient on another day. But due to a flu the motor program of the right tibialis anterior muscle was in ‘F’ not as good as in ‘D’. The activity in the left gastrocnemius muscle consists partly of cross-talk. Recording from a patient with a complete spinal cord injury sub L3 after trauma.

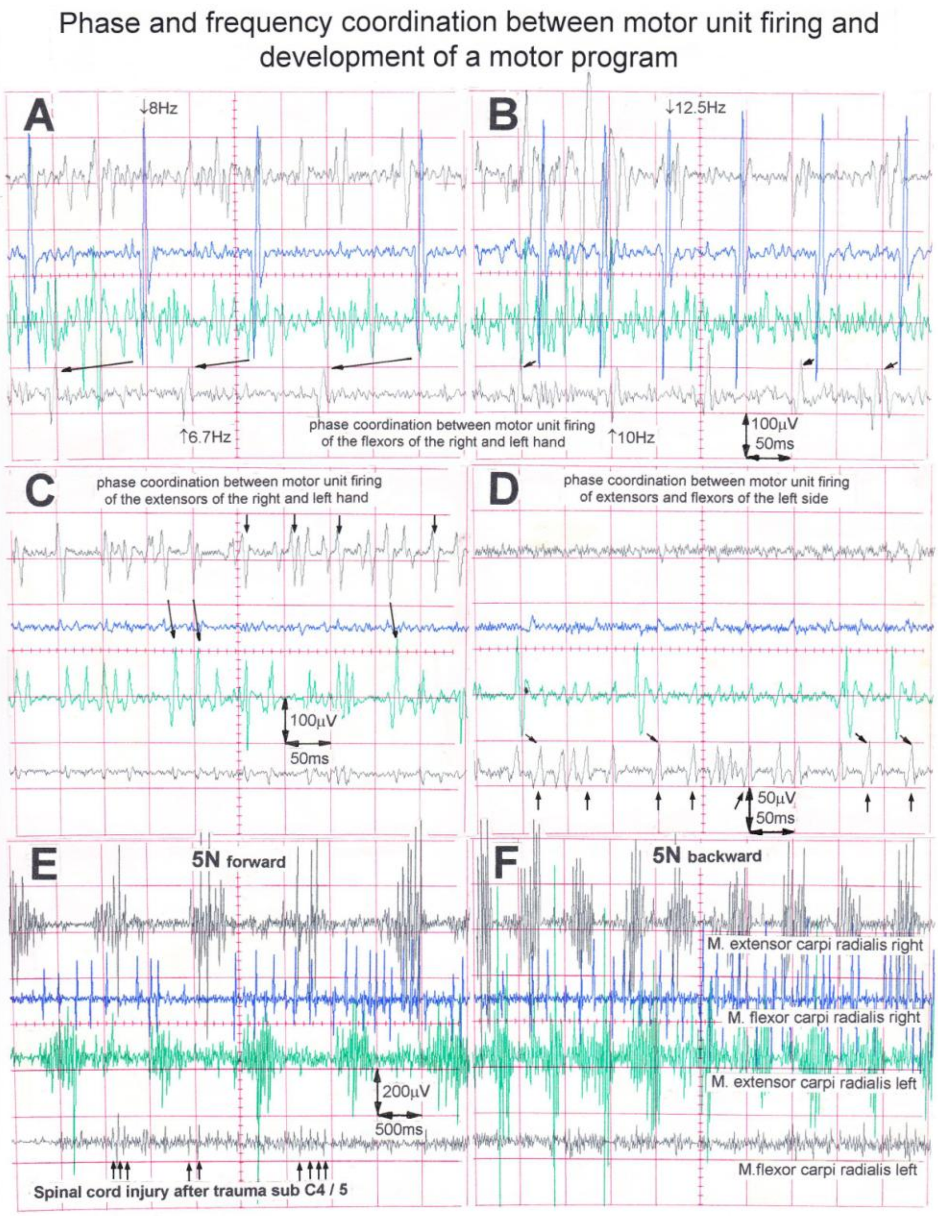

Figure 12. Phase and frequency coordination of single-motor unit firing between different muscles and between different arms. Phase coordinations are indicated by arrows between unit potentials. A-D. The patient with a spinal cord injury was in position at the special coordination dynamics therapy device but activated muscles on volition upon looking onto the oscilloscope screen. E,F. Patient is exercising on the special device. Note the beginning of generating a motor program in the right flexor carpi radialis muscle for 5N forward turning (similar to Fig.4E, right tibialis anterior sweep). Recordings from a patient with a complete spinal cord injury sub C4/5.

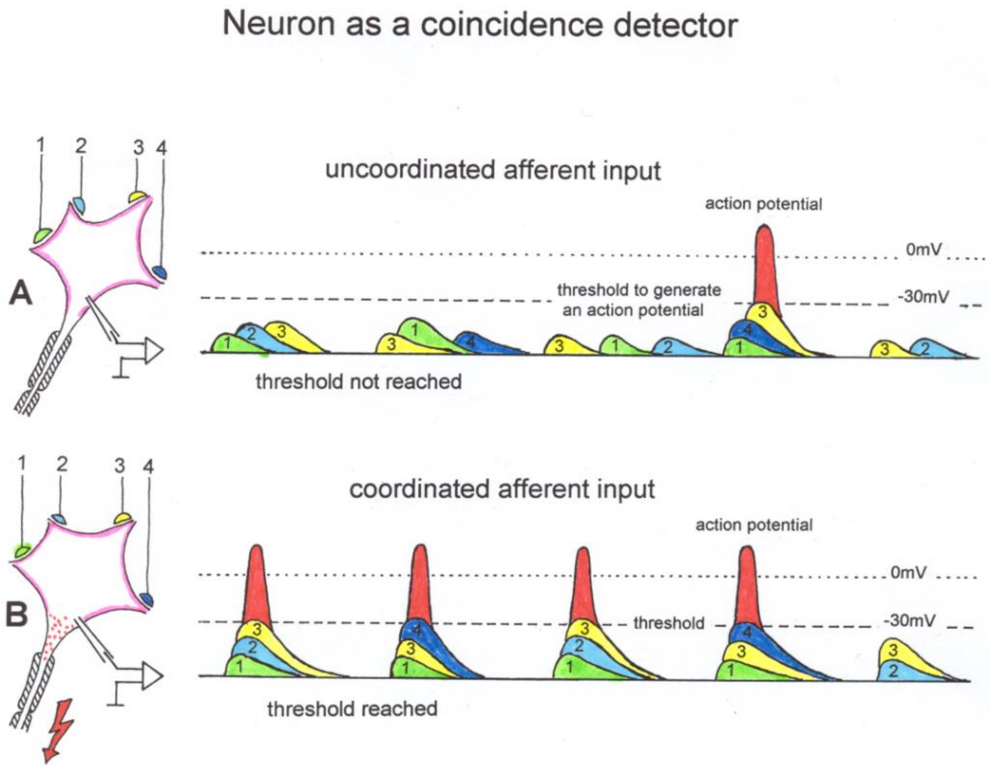

Figure 13. Neuron operating as a coincidence detector. A. Afferent input is reaching rather uncoordinated the cell soma. Only sometimes an action potential is generated, because the threshold of action potential generation is mostly not achieved. B. The action potentials in fibres 1 through 4 are reaching 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.

17. CNS repair by functional reorganisation upon exercising different automatisms

The repair of phase and frequency coordination of neuron firing, however, is not sufficient repair in severe injuries. Functions of destroyed brain parts have to be taken over by other parts or the CNS in general. For this functional CNS repair, different movements have to be trained. Important are the movement automatisms which the CNS is using during development for a correction 'en route', namely creeping, crawling, fast walking, running, jumping and training balance. The movements should be integrative, so that the pathologic neural network organisation cannot escape to other network parts. The network as a whole has to be repaired. Finger functions can nicely be trained when exercising simultaneously arms and legs on the special CDT device (Fig.2D). Nearly all movements improve CNS functioning. But since the repair of complex neural networks is slow, those movements have to be administered primarily to the patient who has the highest rate of repair.

18. The System Theory of Pattern Formation for understanding Neurotherapy

To understand the ongoing changes of movement performance in the patient, the System Theory of Pattern Formation is used. In a complex system like the human CNS, patterns are generated by the system seeking 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, its arms and legs are strongly attracted to the pace and trot gait patterns. The attraction is that strong so that intermediate crawling patterns do not seemingly exist, as if the patterns were 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 (because of the injury) and has to relearn the pace and trot gait coordinations for CNS repair and shifts in this way the attractors for crawling to the pace and trot gait coordinations. Attractive states and attractors of CNS organisation are pictured as a ball in a potential well or more generally in an attractor layout (Fig.14). Changes in CNS functioning are characterized as continuous stabilization and destabilization, over time, of preferred attractor states.

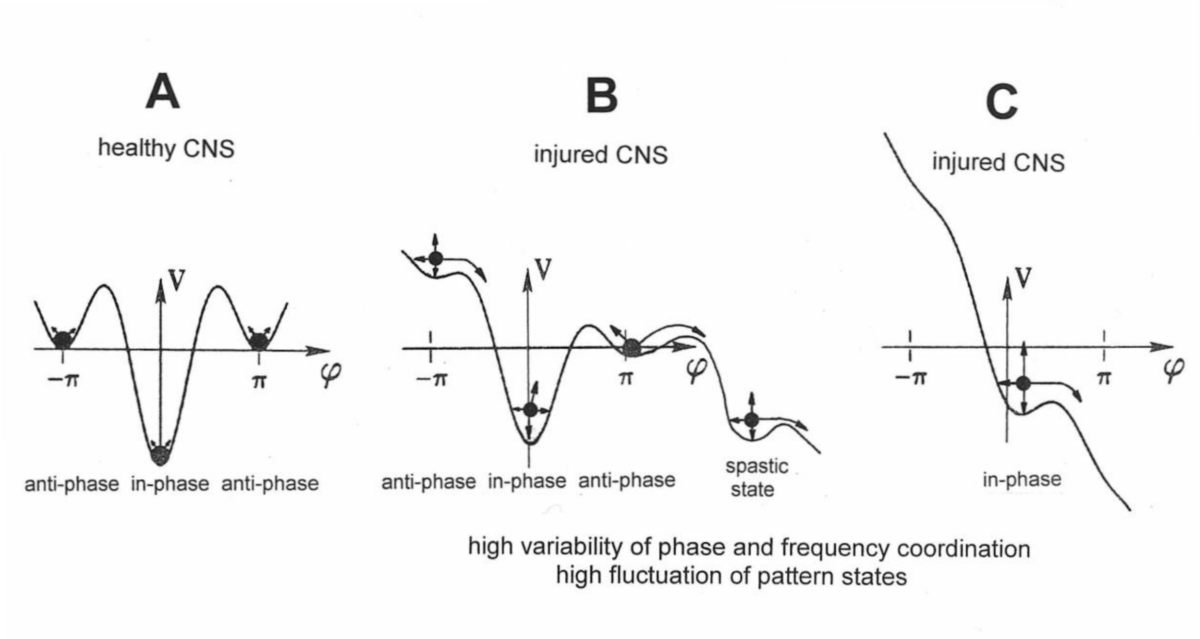

Figure 14. The potential, V(φ), of the coordination dynamics for jumping on springboard of a healthy (A) and injured CNS (B,C). The region around each local minimum acts like a well that weakly traps the system into a coordinated state. Behavioural changes are represented by the over-damped movement 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 the healthy case). 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 that high that there is high probability that the system is kicked out of the basin of attraction. The patient cannot jump any more anti-phase and has problems to jump in-phase. The stability of jumping depends on the motor program (the deepness of the 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.

To reduce for understanding the complexity of human neural networks of the many billions of neurons, order parameters or collective variables are introduced for 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, memory, intention, and support given by a therapist. The specific requirements are captured by the concept of behavioural 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, takes the general following form (15):

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

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 behavioural information $\mathbf{F}_{inf}(\mathbf{X},t)$ includes cognitive states, emotional states, intentions, motivations, instructions, inter-personal coordination, movement support etc. While applying therapy to the 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 behavioural information, the intrinsic dynamics of the neuronal networks can be influenced further, if CDT is no longer efficient any more in repairing the injured CNS (updating of the therapy).

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, that is, the specific variability of the injured networks, certain patterns do already re-appear.

19. Clinical implications for treatment derived from the equations of motion of the collective variables (formula 2)

1. Behavioural 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 behavioural information **is one scientific basis for learning transfer** between different patterns and stability changes of patterns (as for example the reduction of spasticity). The other scientific basis for learning transfer was followed from human neurophysiology, namely that nerve cells or neural sub-networks are involved in different neural network organisations.

2. Intrinsic coordination tendencies captured by the intrinsic dynamics influence the performed pattern systematically because the degree to which intrinsic tendencies conflict or agree with the required patterns determines the variability of the performed coordination pattern.

3. Reduction in stability (of movement and other patterns) when intrinsic and informational requirements conflict, may lead to loss of stability and abrupt change as behavioural information changes smoothly.

4. 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 instructions ($\mathbf{F}_{inf}$), urinary bladder function, intelligence and speech may partly be repaired following CNS injury or malformation.

5. When in an injured CNS with a certain set of behavioural information ($\sum c_{inf}\mathbf{F}_{inf}$) the intrinsic coordination dynamics ($\mathbf{F}_{intr}$) cannot be changed any more during coordination dynamics therapy, then this set of behavioural information has to be changed (using different $\mathbf{F}_{inf}$) or balanced differently (using different $\mathbf{c}_{inf}$) to further improve CNS organization dynamics.

6. However, the equations of motion of the coordination pattern dynamics (formula 2) provide no information about the specific behavioural information (F_{inf}) and training intensity ($\mathbf{c}_{inf}$) with the use of which the CNS can be efficiently repaired in the given patient. We need to have detailed knowledge of the human CNS on the single neuron and neural assembly level (14), besides the knowledge at the integrative level, to find the specific behavioural information for the repair of the human CNS.

A novel step in coordination dynamics therapy is the inference derived from the formula 2 of the equation of motion. It suggests that the movement training not only improves the performance of that particular movement, but also improves the other non-trainable functions by transfer of learning. These functions include vegetative functions like bladder control, speech, and higher mental functions. Furthermore, we have an applicable tool at hand with which the stability of physiological network states can be increased (e.g. movements, continence, continuous concentration to 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 thus offers us an important theoretical basis and a practical tool to diagnose, quantify and repair the malfunctioning human nervous system at the macroscopic level.

20. 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.14) we get a theoretical basis to understand and measure the 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.

21. CNS repair upon stability changes of physiologic and patho-physiologic patterns: improvement of the geographical landscape of attractors

When jumping on springboard (Figs.2B,21) the pattern changes can be represented by the over damped movement of a rolling ball in the potential landscape for the physiologic (Fig.14A, little fluctuation of phase and frequency coordination) and the pathologic case (Fig.14B,C, large = large variability).

In the healthy CNS, the phase and frequency variability is small (short arrows of the moving ball) and the jumping in in-phase and in anti-phase is stable (Fig.14A). Following injury, the potential landscape is deformed and the fluctuation of the network states, generating jumping, is high (Fig.14B). The in-phase jumping is still stable in spite of the increased fluctuation (larger fluctuation arrows), because the basin of attraction is deep. The jumping in anti-phase becomes 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.14C). The attractor layout is asymmetrical and deformed. Support is needed for anti-phase jumping. The jumping in in-phase is still possible but unstable.

Upon performing very exact coordinated movements, imposed by devices (as for example shown in Fig.1), 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.14A. The progress in treatment (learning) is that the in-phase jumping in Fig.14C and the anti-phase jumping in Fig.14B become stable (Fig.14A) again. 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 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). But exercising only on the special device is not sufficient for improving the attractor layout sufficiently. There is no miracle device. Many different movements have to be trained to repair the CNS.

22. Reduction of spasticity

When performing movements like walking, running, crawling, or exercising on a device which imposes highly coordinated movements on the patient, the coordination dynamics can be changed in the way that the stability of spastic states decreases and the stability of the movement states increases. Such changes of coordination dynamics are pictured commonly by means of an attractor layout. An attractor is pictured as a potential well (attractor valley) into which a rolling ball is attracted. The position of the ball represents the momentary state of the system. Figure 15 shows schematically such an attractor layout with the two attractors *spasticity* and *coordinated movement*. At the beginning of the exercising (A), the spastic state is very stable (the attractor valley is deep) and the state of the system is attracted towards the attractor state *spasticity*. With exercising, the attractor layout is changing in the short-term memory in the way that the attractor *spasticity* is getting shallower (less deep) and the attractor *physiologic movement* is getting deeper (B). Because of fluctuation due to variability of phase and frequency coordination, the position of the ball, which represents the momentary state of the system, switches between the attractor states *spasticity* and *movement*. Spasticity and movements are present simultaneously in the patient. With further exercising the attractor *movement* becomes deeper (more stable) than the attractor *spasticity*. The patient can now perform the movements with little or no spasticity. The transient reduction of spasticity in the short-term memory, achieved by many hundred of coordinated movements lasts minutes till several hours; it is indicated in Fig.15 by the two long arrows. The shorter backward arrow (from right to left) indicates that spasticity has slightly reduced in the long-term memory. The coordination dynamics have changed. Repeated exercising will further reduce the stability of *spasticity* and increase the stability of the coordinated *movement* and will further change intrinsic coordination tendencies in the long-term memory.

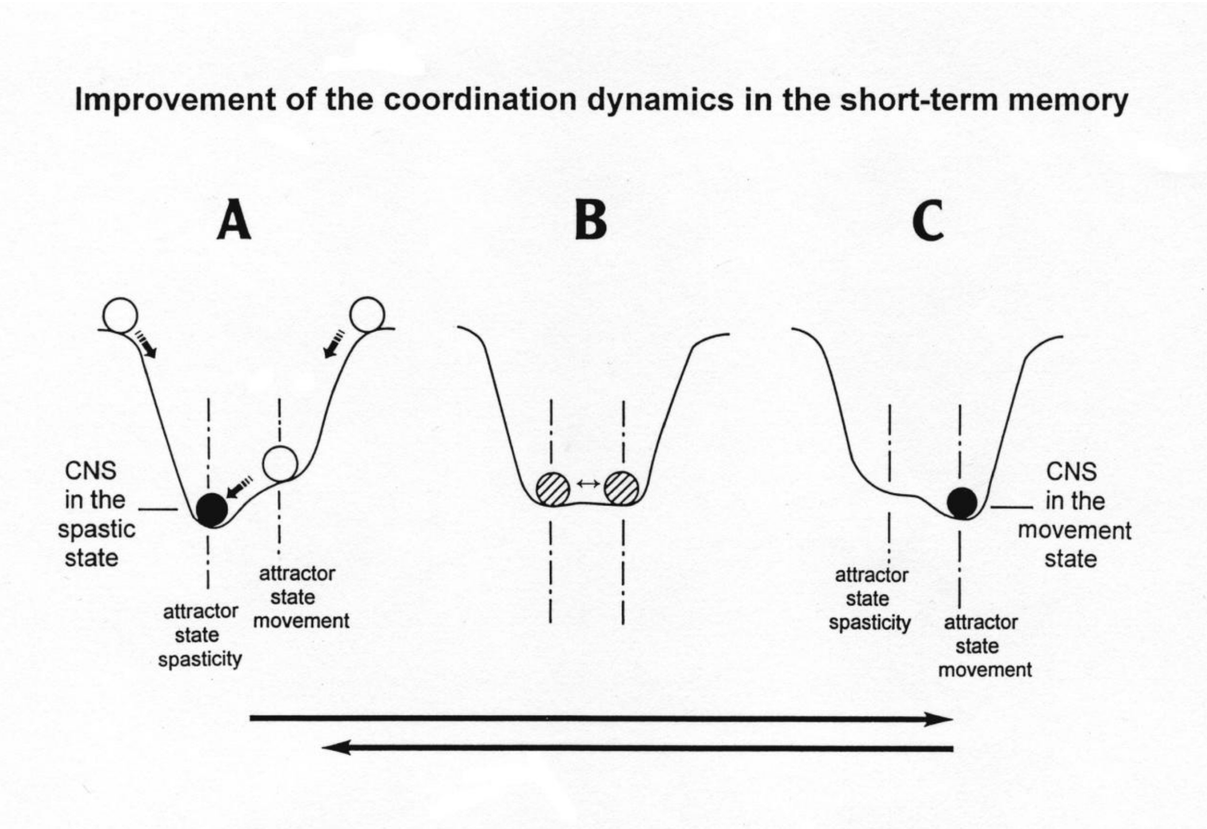

Figure 15. Therapy-induced spasticity reduction in the short-term memory. The position of the ball represents the state of the system and the potential well the attractor. The ball is attracted to the stable position in the deepness of the hole, called attractor state. The attractor layout, consisting 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.

<u>23. Quantifying CNS functioning by measuring pattern stability upon pattern change when exercising on the special CDT device</u>

Experimentally, the underlying dynamics of coordinated movements can be found in the temporal stability of coordination patterns and can be assessed through patterns change. A change of the coordinated movement patterns is generated, when a subject is exercising on the special CDT and recording device, where the coordination between arms and legs, imposed by the device, changes continuously between pace and trot gait and backwards. The stability of the intrinsic coordination tendencies is measured by the deviations and differential stability during the performance of these rhythmic movements. The plotting of the differential stability over time of the frequency of exercising generates an attractor layout for this special movement (Fig.16) and the mean stability per one minute can be measured by the arrhythmicity of exercising (df/dt, f = frequency). Such value, the so-called coordination dynamics value, quantifies CNS functioning objectively, integratively, and non-invasively. The assessment of quality of CNS organization by pattern change is a novel step in CDT.

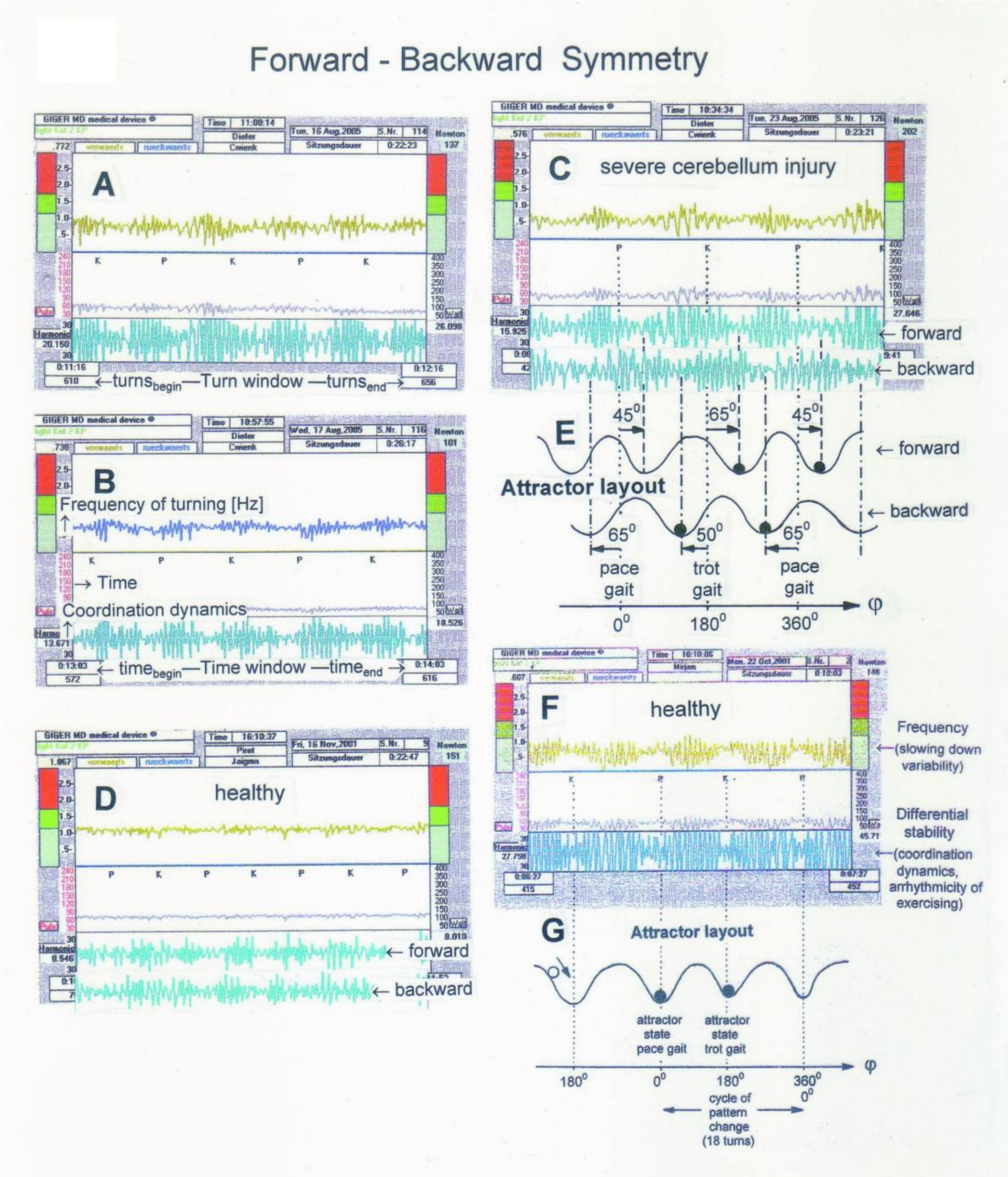

Figure 16. Forward-backward movement symmetry impairment in a patient with severe cerebellum injury for exercising on the special coordination dynamics therapy device (A-C). Coordination dynamics figures of a healthy person are shown for comparison (D).

24. Forward-backward symmetry impairment

As the coordination dynamics traces in Fig.16 show, the lack of symmetry between forward and backward exercising can be made visible and quantified in a patient with cerebellum and cerebrum injuries by measuring the coordination dynamics (temporal stability) through pattern change. When exercising at a load of between 100N and 200N, the values for the exercising frequency and the coordination dynamics increased and decreased rhythmically both for forward (Fig.16A) and backward turning (Fig.16B). But when exercising forwardly, the arrhythmicity was small to the right side of the pace (P) and trot gait (K) coordinations (Fig.16A) and when exercising backwardly (Fig.16B), the arrhythmicity was small to the left side of the pace (P) and trot gait (K) coordinations. Therefore there seems to be a mirror picture shift of the arrhythmicity between exercising forwardly and backwardly with respect to the pace and trot gait coordinations.

In a healthy case, the lowest arrhythmicity of exercising (the highest pattern stability) was positioned at the pace and trot gait coordinations (Fig.16F). To make this seemingly mirror picture change with respect to forward and backward exercising better visible in the patient, the coordination dynamics traces for forward and backward exercising are arranged together in Fig.16C (lower part). The recordings were taken from one week later to show that patterns of highest stability were at the same place with respect to the pace and trot gait coordinations to show that there was no phase drifting. It can clearly be seen Fig.16C that the periods of lowest arrhythmicity shifted rather symmetrically away from the pace (P) and trot gait (K) coordination positions with respect to forward and backward exercising. When picturing this rather opposite symmetric shift of the arrhythmicity of exercising in an attractor layout of pattern formation in the framework of the system theory of pattern formation, the attractor states (patterns with highest stability) shifted away from the pace and trot gait coordination patterns (Fig.16E). In the attractor layout of a healthy sporty girl (Fig.16G), drawn from the coordination dynamics recording of Fig.16F, the stable movement patterns (when exercising on the special device) are lying at the pace and trot gait coordinations. For the patient with a brain injury, the stable movement patterns (small arrhythmicity of exercising) shifted with respect to the cycle of pattern change (lower part of Fig.16G) between $\varphi = 45°$ and $65°$ forwardly for forward exercising, and between $\varphi = 50°$ and $65°$ backwardly for backward exercising (Fig.16E). This rather opposite shift of the attractor states shows similarity to the rather mirror picture change of the antagonicity impairment of the antagonistic muscle activation of the tibialis anterior and gastrocnemius muscles, measured by surface EMG in this patient (see below). We can therefore measure symmetry impairment of CNS organization with respect to forward and backward exercising with the special CDT device. Symmetry diagnostic with the special CDT device can also be performed with respect to right and left and rostral and caudal.

25. **Motor pattern diagnostic by surface electromyography (sEMG) for updating CDT**

In Figures 8, 9, 11 and 12 sEMG demonstrated coordinated firing of single motor units. But sEMG can also be used to improve or update CDT. Above in the coordination pattern dynamics, characterized by equations of motion of collective variables, it was emphasized that the intrinsic dynamics $\mathbf{F}_{intr}(\mathbf{X})$ (CNS functioning) can be modulated by the treatment (behavioural information $\sum c_{inf}\mathbf{F}_{inf}(\mathbf{X},t)$) upon changing the equation of motion, if CDT is no longer efficient any more in repairing the injured CNS (updating of the therapy). The system theory of pattern formation, however, gives no information on how to change the therapy for further improvement of CNS organization. But such information can come from human neurophysiology. It will be demonstrated now how motor patterns, recorded with sEMG, from different movements can show us what movements have the best motor patterns and should be trained most because of the highest rate of learning. It will be started with recorded motor patterns when the patient with the brain injury is exercising forwardly and backwardly on the special CDT device. The coordination pattern dynamics give us information about CNS functioning in general. But sEMG motor patterns shows what is wrong in the different motor patterns and gives hints on what to change in the administered therapy.

26. Symmetry improvement of motor programs of antagonistic muscles by increasing the integrativity of the movement

In a patient with cerebrum and cerebellum injury, surface electrodes were placed on the right and left tibialis anterior and the right and left lateral gastrocnemius muscles. When the patient only exercised with the legs (like on a fitness bicycle), the left gastrocnemius muscle became activated too late with respect to the left tibialis anterior muscle (Fig.17A, at $\varphi = 200^0$ instead of 180^0 (antagonistic muscles)) for exercising in the forward direction, and it became activated to early for exercising in the backward direction (Fig.17B, at 150^0 instead of 180^0). The antagonicity of the motor programs thus showed pathologic symmetry between exercising in the forward and backward directions, namely $\Delta\varphi_{forward} = 20^0$ against $\Delta\varphi_{backward} = -30^0$. When exercising with arms and legs (Fig.17C,D) this asymmetric coordination did not change in the (better) left leg.

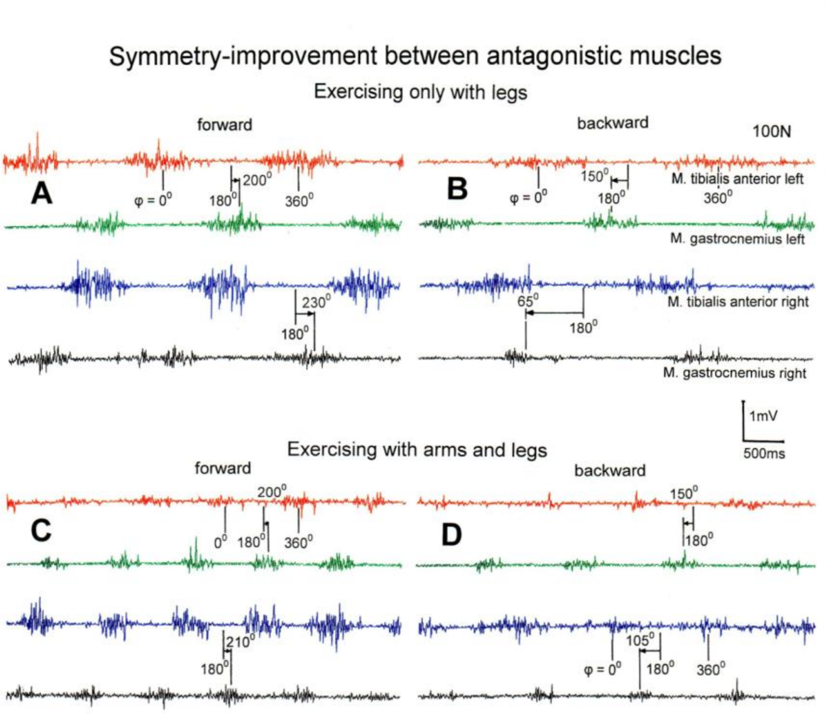

Figure 17. Motor programs of right and left tibialis anterior and gastrocnemius muscles recorded by sEMG for the patient with a severe cerebellar injury upon exercising on the special coordination dynamics therapy device in the forward (A,C) and backward direction (B,D) only using legs (A,B) and with arms and legs (C,D). Note that the gastrocnemius muscle is not activated properly antagonisticly with respect to the tibialis anterior (at 180 degree): it gets activated ealier or later, depending on whether movements are performed in the forward or backward direction and upon whether only legs or arms and legs are used.

However, an improvement of the symmetry of antagonistic coordination between the gastrocnemius and the tibialis anterior muscles could be observed in the right leg when exercising in the forward or backward direction using arms and legs as compared to only using the legs. Upon exercising in the forward direction only using legs, the right gastrocnemius muscle became activated too late with respect to the right tibialis anterior muscle (Fig.17A, at 230^0 instead of 180^0; $\Delta\varphi_{forward} = 50^0$), and too early for exercising in the backward direction (Fig.17B, at 65^0 instead of 180^0; $\Delta\varphi_{backward} = -115^0$). When exercising in the forward direction with arms and legs, the right gastrocnemius muscle was not activated that late (Fig.17C, only at 210^0 instead of 180^0; $\Delta\varphi_{forward} = 30^0$). When exercising in the backward direction, the right gastocnemius muscle did not get activated as early with respect to the right tibialis anterior muscle (only at 105^0 instead of 180^0; $\Delta\varphi_{backward} = -75^0$). Thus, it may be stated that the antagonistic coordination between the right tibialis anterior and the right gastrocnemius muscles improved for exercising in the forward and backward directions by 20^0 and 40^0 respectively upon exercising with arms and legs, as compared to using only the legs (like on a fitness bicycle). More generally speaking, this antagonistic symmetry between the tibialis anterior and the right gastrocnemius muscles improved by 60^0 for exercising in the forward and backward directions upon exercising with both arms and legs. During this more integrative exercising on the special CDT device using both arms and legs, the antagonistic activation of the tibialis anterior and the gastrocnemius muscles improved in the short-term memory. Therefore in this patient the antagonicity impairment could be treated by exercising very coordinated movements with arms and legs on the special device. Probably other very coordinated four-limb movements could also improve the antagonicity of muscle activation. But a fitness bicycle would not improve the antagonicity of muscle activation.

<u>27. Learning in the short-term memory from the better opposite side</u>

The better (with respect to antagonistic activation) left side did not improve in this patient, whereas the poor right side did improve by 36% ($\Delta\varphi_{forward}$ - $\Delta\varphi_{backward}$ reduced from 165^0 to 105^0). With the integrativity increasing from coordinated leg movements to coordinated arm and leg movements, the better left side remained unchanged, whereas the poor right side improved by 36%. This one-sided symmetry improvement can be interpreted in the way that the poor right side learned in the short-term memory from the good left side. This learning effect may be sited in the spinocerebellum and/or in the spinal cord (co-movement).

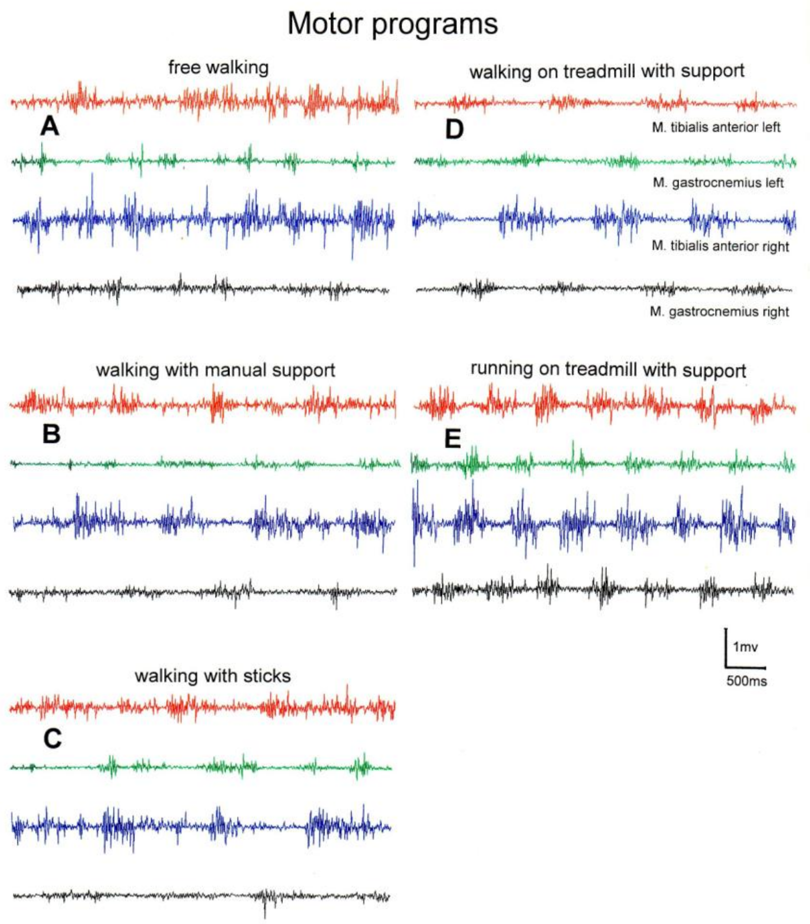

Figure 18. Surface EMG motor program of the right and left tibialis anterior and gastrocnemius muscles for free walking (A), walking with manual support (B), walking with sticks (C), walking (D) and running (E) on the treadmill with support. Note that the motor programs for walking with strong support (D,E) are much better than those for walking with little or no support (A,B,C).

28. Judgement of motor walking programs in a patient with balance problems

In the patient with cerebellum and cerebrum injury, changes in the walking program will be analysed when the patient had to keep balance by himself. Since the vestibulocerebellum was also heavily damaged, increasing motor program deficits for increasing balance needs can be expected. Figure 18 shows sEMG motor programs for free walking (Fig.18A) and for supported walking (manual support) (Fig.18B), walking with sticks (Fig.18C), walking on treadmill (Fig.18E), and running on treadmill (Fig.18E). The motor programs for free walking (A) were worse than those for the different kinds of supported walking (B-E). With the increasing support (from B,C to D,E) the motor programs improved. Obviously, the patient had balance problems: upon spending efforts to keep more balance by himself, his motor programs became worse. The interpretation of this worsening of the motor programs with the increasing balance needs is that upon free walking, the damaged vestibulocerebellum could not sufficiently coordinate balance any more with walking. The motor program for supported walking or running (B-E) were best for running (E), which indicates that the higher speed improves the performance and the learning as long as the patient can manage the speed.

29. Comparison between motor programs when swinging and jumping on springboard

To find out what motor programs are best upon performing rhythmic, dynamic, stereotyped movements (functional repair at the neural ensemble level) on springboard, sEMG was recorded for the different kinds of springboard movements.

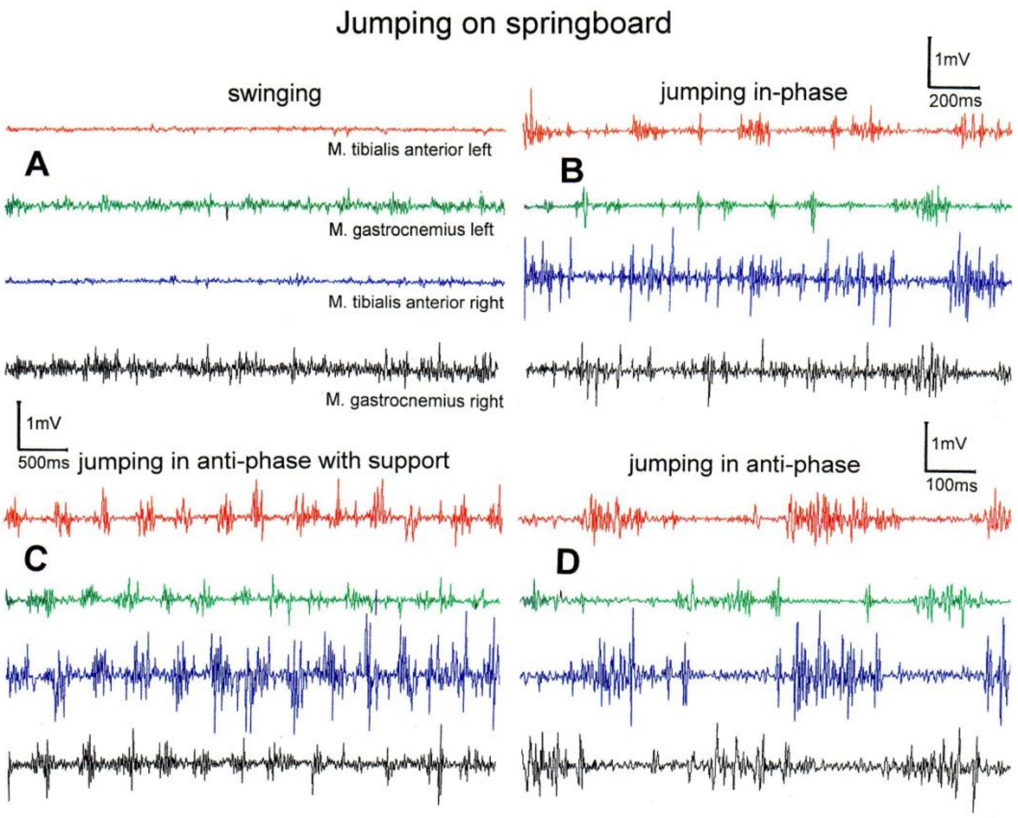

Figure 19. Surface EMG motor program of the right and left tibialis anterior and gastrocnemius muscles for swinging (A) and jumping on springboard in-phase (B), in anti-phase with support (C), and in anti-phase without support (D). Note that the motor programs are better for jumping in anti-phase (C,D) than for jumping in in-phase and swinging. Note further that continuous synchronous oscillatory firing of motor units can be seen on the trace taken from the right tibialis muscle for jumping in in-phase (B).

Motor programs upon swinging and jumping on springboard are shown in Figure 19. For swinging (Fig.19A) the tibialis anterior and gastrocnemius muscles were only little activated rhythmically, i.e. no real motor program could be seen. When jumping in in-phase, the leg muscles were more activated and motor programs could partly be identified (Fig.19B). In the right tibialis anterior muscle there can be seen synchronized oscillatory firing of motor units (pathologic). For jumping in anti-phase with (Fig.19C) and without support by a therapist (Fig.19D) the motor programs were quite good, even though rhythmic firing of motor units can also clearly be identified during the motor bursts (right gastrocnemius muscle in Fig.19D).
The conclusion for the treatment with respect to exercising on springboard is that jumping will entrain the neuronal networks of the patient better than swinging, since real motor programs could only be identified for jumping. The general conclusion for treatment is that **sEMG can help to improve the rate and understanding of repair.**

30. Symmetry learning to enhance the efficiency of CNS repair

Learning transfer from one hand movement to the symmetric one has been reported to occur (15), which means that the symmetry counterpart improves without being trained itself. It has been shown herein (see above) that the antagonicity between the tibialis anterior and gastrocnemius muscles in the poor right leg improved in the short-term memory by 36% when increasing the integrativity of exercising by changing from only leg movements to coordinated arm and leg movements. Assuming that repeated improvements in CNS functioning in the short-term memory will repeatedly slowly also become reflected in the long-term memory would mean that there is learning transfer with respect to the improvement of antagonicity from the left leg to the right leg.
Improvements of symmetries of movements are used in CDT. A certain movement can be also improved by training the symmetry counterpart. If for example, the walking pattern on the right side has been impaired in a stroke patient for a few years, this pathologic walking pattern has become an old-learned movement and is difficult to improve. The symmetry counterpart, namely backward walking, has however not become an old-learned movement after injury. Additional training of backward walking will therefore more efficiently improve forward walking by learning transfer.
In conclusion, movements and especially automatisms have to be trained with their symmetry counterparts to enhance the efficiency of CNS repair.

31. Symmetry improvement of CNS functioning during development in comparison with those after CNS injury

Coordination dynamics between arm and leg movements in the forward and backward direction has been shown to substantially improve during CNS development by exercising on the special coordination dynamics therapy device (16). Also, the symmetry between exercising in the forward and backward directions improved (16). Besides coordination dynamics improvement also symmetry improvements may thus be of importance to improve CNS functioning in the injured as well as normally functioning CNS. It seems worthwhile to further study improvement in CNS organization with respect to coordination and symmetries during individual development to see what can be learned from the improvements of CNS organization during individual development for CNS repair.

32. Giving emphasis upon training movements for which the motor programs are best

The motor programs of the tibialis anterior and gastrocnemius muscles were shown to be better for jumping than for swinging on springboard (Fig.19). Since the motor programs were still better for jumping in anti-phase than for jumping in in-phase (Fig.19), jumping in anti-phase will be more beneficial for improving neuronal network organization than jumping in in-phase and should be trained more often. Also the pathologic synchronized oscillatory firing of motor units (see below) seamed to be reduced in the anti-phase jumping mode. Jumping in anti-phase may activate more inhibition. Consequently, jumping in anti-phase should be predominantly trained in this patient at that repair stage.

33. Improvement of higher mental functions, speech, and writing in elderly people

The coordination dynamics therapy the patient with cerebrum and cerebellum injury (see sEMG recordings (Figs.17-19)) was receiving was far from being optimal. As a consequence, improvement in coordination dynamics and movements were limited. It is nevertheless sure that the therapy was worthwhile since considerable improvements could be achieved in higher mental functions and speech. At the beginning the patient showed scanning speech and it was difficult to listen to him over longer periods of time. Over the years, a normal discussion became possible. The patient also received speech therapy, mostly during the exercising on the special CDT device. Hyper-salivation subsided already after 6 months of therapy.

Figure 20. Therapy-related improvement of the impression of the face of the patient who suffered severe cerebellar injury: before the accident (a), after the accident (1995) till 2006 (b-i).

Improvements of higher mental functions became partly reflected in the improved impression of the patient’s face (Fig.20). Before the accident (a), the face shows mental strength. Four months after the accident (b), the face seems to be that of another person: as if everything was lost. Seven (c) and 10 months after the accident (d), the impression of the face partly recovered, but there is a strong over-emphasizing of the feelings reflected in the face. Nineteen (e) and 20 months after the accident (f), a further recovery in the impression is distinguishable. Still, a slight over-emphasizing of the feelings can be seen. Forty months after the accident (g), some of the old impressions of the face is back. Forty-four months after the accident, the face became really similar to that seen before the accident; the face still misses mental strength. Ten years after the accident (i), also some of the mental strength re-appeared in the face.

In reality and as suggested by his appearance, the patient is still not the old one. His mental strength has not been fully repaired. He himself says that before the injury he could do two things at the same time: “Listening to somebody and developing at the same time a strategy against the opponent person. This is not possible any more”. In practical life he has still problems. His injury included a frontal lobe injury.

After the accident that caused the severe cerebral and cerebellar injury, the patient’s wife was advised to place the patient in a place, where human bodies are kept until they die. Instead of following the advice, the wife was fighting for her husband’s future; having learned about CDT, she organized to start it approximately 2 years after the accident.

Dr. Cwienk’s (the patient) intellect recovered that much that the Author sometimes asks him for advice, since the patient has much more expertise than the Author in certain fields. This is actually a bit of a dream of a research worker who tries to repair the human CNS. One gets a patient after CNS injury, who has been given up by the school medicine, and after treatment the patient’s intellect partly exceeds that of the research worker himself. It was this Dr. Dieter Cwienk (Austria) who asked in the past why we don’t let patients who suffer severe brain injury die if we don’t give them the proper available treatment. To leave the patient to vegetate until the remaining functions of his body die is undignified for the humans.

Figure 21. Some coordinated movements used at the therapy place. Three patients can be seen who had suffered spinal cord injuries and one patient who had suffered a severe brain injury (on the treadmill). The exercising is assisted by two physiotherapists. The patient on the left (incomplete cervical spinal cord injury) is jumping on

the springboard to entrain neuronal networks on the assembly level by performing rhythmic, dynamic, stereotyped movements. The patient on the treadmill is exercising the automatism walking. Support is provided by the therapist to arm movements to bring them in coordination with leg movements. The patient in the front (formally complete spinal cord injury Th5/6) is exercising the automatism crawling. Support is provided by a therapist to leg movements. The patient on the right (formally complete spinal cord injury sub Th10/12) is exercising highly coordinated arm and leg movements on the special coordination dynamics therapy device in the lying position; the coordination between arm and leg movements is imposed by the device.

34. Neurotherapy: Human Neurophysiology and its application to human patients (unit of theory and praxis)

Figure 21 shows a small efficient Neurotherapy place. Patients are seen who exercise on the special CDT device in the lying position (KadriVideo), walk on treadmill (VideoWalking), jump on springboard (VideoKadriJumping), and crawl. Sky-walking (Fig.4)(VideoRuth) cannot be seen. Two master degree physiotherapists give support to patients. To be able to administer Neurotherapy to patients with nervous system injuries they took at least 5 courses in Coordination Dynamics Therapy (CDT), including surface electromyography (sEMG). Figure 22 shows the performance of sEMG on a healthy child and in Figure 2C sEMG is performed to a patient with severe cervical spinal cord injury (Fig.5K). This patient in Figure 2 was arguing why she should go to a Neurologist? He tells me what is wrong with my nervous system, but he doesn't tell me how to repair it. When performing sEMG on suitable patients (spinal cord injury patients) the organisation of motor programs (Fig.11) and the coordination among motor units (Figs.11,12) can be studied. When recording motor programs from patients performing different movements (Figs.17,18,19), those movements can be identified which are most suitable for training. The non-invasive sEMG can therefore help the therapist to improve and update the therapy administered to the patient. Further, being familiar with human Neurophysiology, the therapist really understands what she/he is doing and needs not to speculate.

Figure 22. Supported walking of an 8-month-old healthy boy.

35. **Repair of premotor neural networks by exercising rhythmic, dynamic, stereotyped movements**

It is now tried to make understandable how the neural networks are repaired upon rhythmic, dynamic, stereotyped movements.

35.1 Building up of external loops to the periphery by premotor spinal oscillators

It will be shown now that with the building up of simultaneous phase relations between α, γ and secondary muscle spindle afferent fibres (SP2) (Fig.23) and the assimilation of interspike interval (II) distributions (coordination's of rhythms), an external loop of premotor spinal oscillators is built up to the periphery, which makes it possible to directly influence the firing of spinal oscillators by a rhythm training. The somatic and parasympathetic pattern organizations in the sacral micturition centre can simultaneously be entrained by jumping on springboard (Fig.24g) (including the stimulation of movement (Fig.24f) and bladder receptors (Fig.24h)) to allow movement-based learning in the continence and movement patterns and to induce learning transfer from movements to urinary bladder functions. A repair of neuronal network patterns of the functionally disconnected sacral micturition centre in spinal cord injury is possible (12,13).

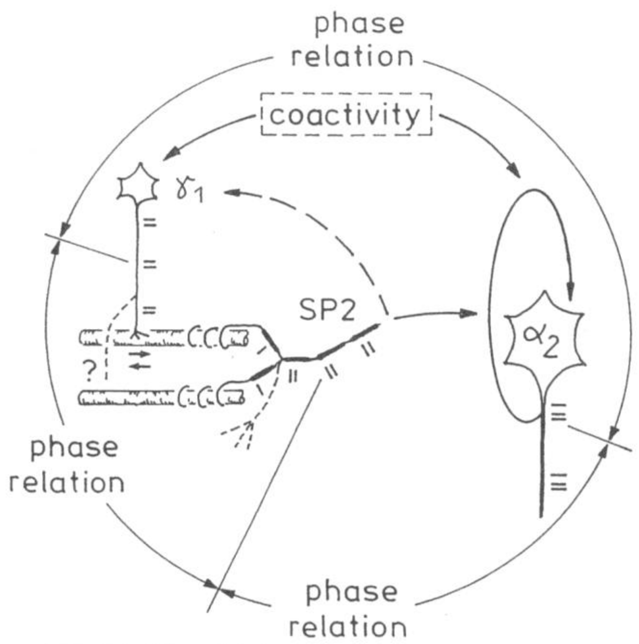

Figure 23. Schematized existing phase relation between α_2 and γ_1-motoneurons and a secondary muscle spindle afferent fibre (SP2). Parallel existing phase relations between other parent afferents and the α_2-motoneuron and between parent secondary spindle afferents are not shown. Phase relation means, the increased occurrence of phases in ms in a certain phase range between the action potentials (APs) of the two compared nerve fibres. The complex afferent and efferent muscle spindle innervation was not tried to show. Small arrows at intrafusal muscle fibre indicate local contraction, which is in nuclear chain fibres readily transmitted to the place of afferent innervation. A possible reason of the doublet firing of the SP2 fibre is pictured to occur from single APs (schematized by bars) of two myelinated endings, not necessarily from pacemaker switching. More endings of the parent SP2 fibre and γ_1-motoneurons are indicated by dashed line branches. "Coactivity" indicates a correlation between γ and α-motoneuron spinal cord circuitries for higher activations.

At the beginning of stimulation there existed two phase relations between the firings of the α_3, γ_1 and SP2(1) fibres (Fig.23), which means that the γ-loop, including the γ_1 and SP2(1) fibres, contributed to the drive of the α_3-oscillator. However, since the II distributions were different, the γ-loop was not a part of this spinal oscillator; it was only contributing to the drive of it, as pictured in Fig.24a. Since the II distribution of the fusimotor γ_1 was often rather broad, its driving network was not or only almost oscillatory firing (dashed line loop in Fig.24a).

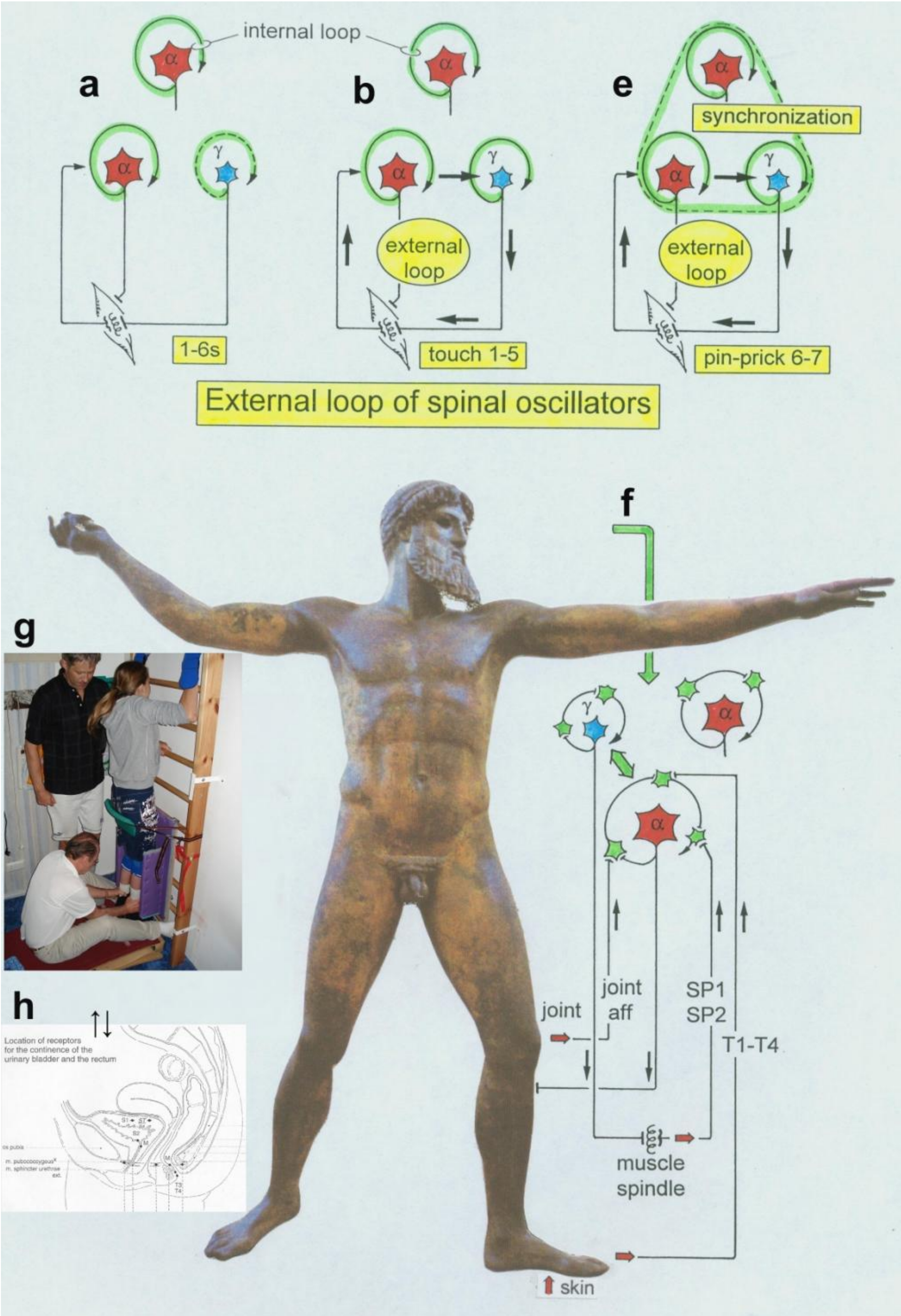

Figure 24. Spreading of oscillatory firing from α-motoneuron neuronal network to include muscle spindles (periphery) and synchronization of different α and γ-motoneuron neuronal networks caused by touch and pin-prick stimulation.

(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; taken from Fig. 3Aa,Ba of (8).

(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, taken from Fig. 1Ab, Bb (8).

(e) Oscillatory firing α (internal circuitry loop) and γ-motoneuron neuronal networks (external loop) synchronized (broad peak phase relation) upon pin-pricks 6-7, taken from Fig. 1Ae,Be of (8). 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-preformate the neuronal circuitry by synapse remodelling to fire

more physiologically oscillatory to reduce spasticity and improve locomotion. Extensive pathologic movement like tremor may entrain neuronal circuitry to increase tremor movement. The Greek good is a bronze statue of Zeus found close to the cape of Artemision 460 BC.
(g) Supported jumping on the springboard in anti-phase. The patient with the severe cervical spinal cord injury is supported by the Author.
(h) Location of receptors for the continence of urinary bladder and rectum stimulated upon jumping on springboard. For further details, see Fig.10 of Ref.42.

Upon touching sacral dermatomes repeatedly approximately every second, phase relations occurred between the α_3, γ_1 and SP2(1) fibres (not shown), even though reaching a different value and the II distributions of the α_3 and γ fibres and the SP2(1) fibre became assimilated. The γ-loop became directly connected to the oscillatory firing network: the premotor spinal oscillator built up an external loop to the periphery (Fig.24b).
Upon pin-pricking sacral dermatomes repeatedly, one phase relation occurred between the firings of the α_3, γ_1 and SP2(1) fibres and also the II distributions assimilated. The spinal α_3-oscillator had built up a full external loop to include the γ-loop in its oscillatory firing (Fig.24e). Since there was transient synchronous firing with another α_2 motoneuron, probably also that α_2-oscillator built up an external loop to the periphery.

35.2 Extension of the external loop generation of spinal oscillators to non-continence muscles

If one extends the integration of the γ-loop in the oscillatory firing of spinal oscillators innervating striated continence muscles to muscles activated for locomotion (Fig.24f), then for example during jumping, running or other coordinated, rhythmic, dynamic, stereotyped movements, at least oscillatory firing α_2 or α_3-oscillators build up external loops to the periphery. It is partly possible during jumping on springboard to synchronize spinal oscillators with the jumping rhythm, mainly given by the properties (Eigenfrequency) of the springboard. Especially the α_3-motoneuron networks can be entrained efficiently by jumping on springboard, since the 'Eigenfrequency' of the springboard and that of the α_3-oscillator network are both in the range of 1Hz. The extension of premotor network organizations serving bladder functions to premotor network organizations serving movement functions is justified, since rhythmic firing of single FF and FR-type motor units, which are innervated by α_1 and α_2-motoneurons, has been recorded by surface electromyography (sEMG) during rhythmic, coordinated movements (Eigenfrequency around 1 Hz) in patients with spinal cord injury (Fig.9). Upon exercising on the special CDT device, single FF-type motor units in arm and leg muscles coordinated their rhythmic firing with respect to phase and frequency (Figs. 11,12).

35.3 External loop of premotor spinal oscillators for entrainment and rhythmic, dynamic stimulation of motor and bladder functions

Upon jumping on springboard (Fig.24g) and other rhythmic movements like running premotor spinal oscillators organize themselves to fire transiently oscillatory according to the motor pattern and build up an external loop to the periphery (Fig.24). If the frequency of the rhythmic movement has an integer relationship to the 'Eigenfrequencies of the premotor networks and more rostral networks, these premotor networks get entrained for more specific self-organization. When jumping on springboard (Fig.24g) not only the motor networks get activated; also the external sphincteric motoneurons, innervating the external bladder and anal sphincter, as a part of the pelvic floor, get rhythmically activated to counteract the rhythmic weight changes of the intestine. Further, the rhythmic, dynamic, stereotyped up and down movements do stimulate stretch, tension, flow, and mechanical receptors of the bladder (detrusor and proximal urethra) (Fig.24h). Since the neurons involved in the generation of movement and continence (and micturition) patterns (especially if the neurons serve both functions at the same time) are synchronously, rhythmically activated, the pathologic bladder patterns get entrained from the rather physiologic jumping movement, in some similarity to co-movement. The synchronized activation of the somatic and parasympathetic networks allow efficient learning transfer, since the neurons work as coincidence or more general as coordination detectors (Fig.13). If there is fluid in the bladder and material in the bowel and rectum, the continence stimulus is stronger. Also walking and running will stimulate and change the intrinsic dynamics of the micturition and defecation centres, but not as strong as the jumping on springboard. The walking and running on a treadmill of patients with SCI is performed under weight support, whereas during jumping on springboard no weight support is given and needed (Fig.24g). The sympathetic nervous system division, probably innervating the internal urinary bladder sphincter (smooth muscle), will also be activated synchronously. Since the frequency of jumping is with around 1 Hz similar to the 'Eigenfrequency' of the α_3-motoneuron oscillators, these oscillator networks should be entrained most efficiently.

35.4 Entrainment of premotor spinal oscillator networks by rhythmic movement-induced afferent input and inputs from supraspinal centres

If one approximates for high activation spinal neural networks into premotor spinal oscillators (driving the motoneuron) and propriospinal oscillators (generating by coupling with one another movement patterns) then premotor spinal oscillators can be handled in a first approximation as single linear oscillators. The premotor spinal oscillators and the spinal pattern generating networks are self-organized and driven by afferent and supraspinal inputs. When training rhythmic, dynamic, stereotyped movements, the premotor spinal oscillators approximated as linear oscillators are driven by movement-induced afferent input from the periphery (mainly the legs), the surrounding pattern generating networks and possibly supraspinal inputs. These spinal oscillators and most likely their neuronal networks can be entrained at least by use of the external loop for a better self-organization. But the functional repair becomes only physiologic if volitional control (by ascending and descending tracts) is intertwined and activated.

35.5 Entrainment of loop network circuits for repair

If one assumes that loop circuits do not only exist between the premotor spinal oscillators and the periphery, but are a general structure in the CNS, then **motor learning involves the formation of** loop circuits (or better **loop network circuits**) **between the cortex and the periphery involving the sensory cortex and the thalamus**.

35.6 Harmonic, subharmonic and superharmonic entrainment

When a linear oscillatory system is driven by an external periodic input, its response contains both frequency components. However, if the external frequency is close to the Eigenfrequency of the oscillator itself, then it is possible to have a response at the external frequency only. This phenomenon is known as entrainment or synchronization. It is of paramount importance with respect to biological oscillators because it allows them to 'latch on' to the environment. Thus a rhythm with a free-running period of 24.7 hours may be synchronized to 24 hours when exposed to the natural sequence of day and night.
The entrainment of an oscillator with one degree of freedom can be described by the equation:

$$d^2x/dt^2 + f(x, dx/dt) + \omega_0 x = E \cos\omega_1 t$$

(x = variable, t = time, f = nonlinear term, $\omega_0 = 2\pi f_0$ = frequency of the oscillator, ω_1 = entrainment frequency, E = amplitude)

Upon jumping on springboard, the entrainment frequency ω_1 (the jumping frequency) is with 0.9 to 1Hz close to the Eigenfrequency of the premotor spinal α_3-oscillators (Eigenfrequency $\approx$ 1Hz, innervating S-type muscle fibres (red)). The α_3-oscillators and the networks they are integrated in are entrained directly. For the entrainment of the α_2-oscillators (Eigenfrequency $\approx$ 6Hz, innervating FR-type muscle fibres) and α_1-oscillators (Eigenfrequency $\approx$ 10-30Hz,

innervating FF-type muscle fibres (white)) subharmonic and superharmonic entrainment has to be considered.
When a nonlinear oscillatory system is driven by an external periodic input z_k, the entrainment can be harmonic (z_k itself has the oscillation period T of the oscillator; case of the α_3-oscillators), subharmonic (z_k has a period which is an integer multiple of T, mT; case of the α_2 and α_1-oscillators) or superharmonic (z_k has a period which is an integer fraction of T, T/m). With the increasing order of subharmonic entrainment, the entrainment strength reduces for the same coupling strength or entrainment amplitude E. For the α_2 and α_1-oscillators the entrainment is subharmonic and the entrainment strength therefore reduced. In α_2-oscillators, two entrainment phases per oscillation period were mostly observed, which correspond to 'in-phase' and 'anti-phase' coordination of arms and legs, which enhances entrainment. Also, the change of the number of phase relations between the neural assemblies in the sacral micturition centre may indicate changing entrainment or coupling communication between the somatic and parasympathetic nervous system divisions.
However, oscillator models are still far away from human network properties. The jumping on springboard is very rhythmic and stereotyped (frequency of jumping ≈1Hz). But firstly, the movement-induced afferent input enters the network at different levels (premotor neuronal network, propriospinal oscillatory network, brainstem network and higher centres); secondly oscillators can get drive from different sources; and thirdly often the rhythmic input patterns consist of impulse trains with increasing interspike intervals and with delays between the responses from different receptors and receptor types.
Even though the used oscillator model is far away from human self-organization network forms, their results are still very useful for the interpretation, under certain conditions, of measured data and to understand better the jumping on springboard training (as a part of the CDT) which contributes substantially to the cure of urinary bladder functions.
That the human CNS can be repaired by rhythmic, dynamic, stereotyped movements, including learning transfer, cannot fully be understood from this section. A step deeper into human neurophysiology is needed with definitions of phases and interspike intervals (II) (12,14) and documentation of further measurements. But the **measurements of phases and II's really do show that loops are built up from the premotor spinal oscillators (networks) to the periphery** (Fig.24) by phase and frequency coordination and that premotor networks are getting entrained. A functional repair of human neural networks is possible by formation and entrainment of complex network loops and their changes according to the pattern organisation of the networks. All details of theory, praxis and human neurophysiology are given in the book on **Human Neurophysiology: Development and Repair of the Human Central Nervous System** (14).

<u>35.7 Relative frequency coordination</u>

For the building up of an external loop to the periphery to entrain premotor oscillators (networks), phase and frequency coordination of α and γ-motoneurons and muscle spindle afferents is needed. Figure 10 showed an original recording of the phase and frequency firing coordination between a secondary muscle spindle afferent action potential and the impulse trains of an oscillatory firing α_2-motoneuron. In Figure 25, considerations concerning the relative frequency coordination are extended to the activity of further afferent fibres and γ-motoneurons. Figure 25G shows sweep pieces of the original recordings; Figures A through F show the interspike interval distributions of spindle afferents and γ-motoneurons. It can be seen from the overlapping of the oscillator frequency distribution ranges (and the half of it), and from the interspike interval distributions of the afferents that, from the viewpoint of frequency coordination, fibre SP2(1) contributed strongly to the drive of oscillator O2, whereas there was a weaker contribution from other afferents (less overlapping between the distributions of the afferents and the range of the basic frequency or the first harmonic of the oscillator). Also, γ-motoneurons showed only little frequency correlation at that time period.

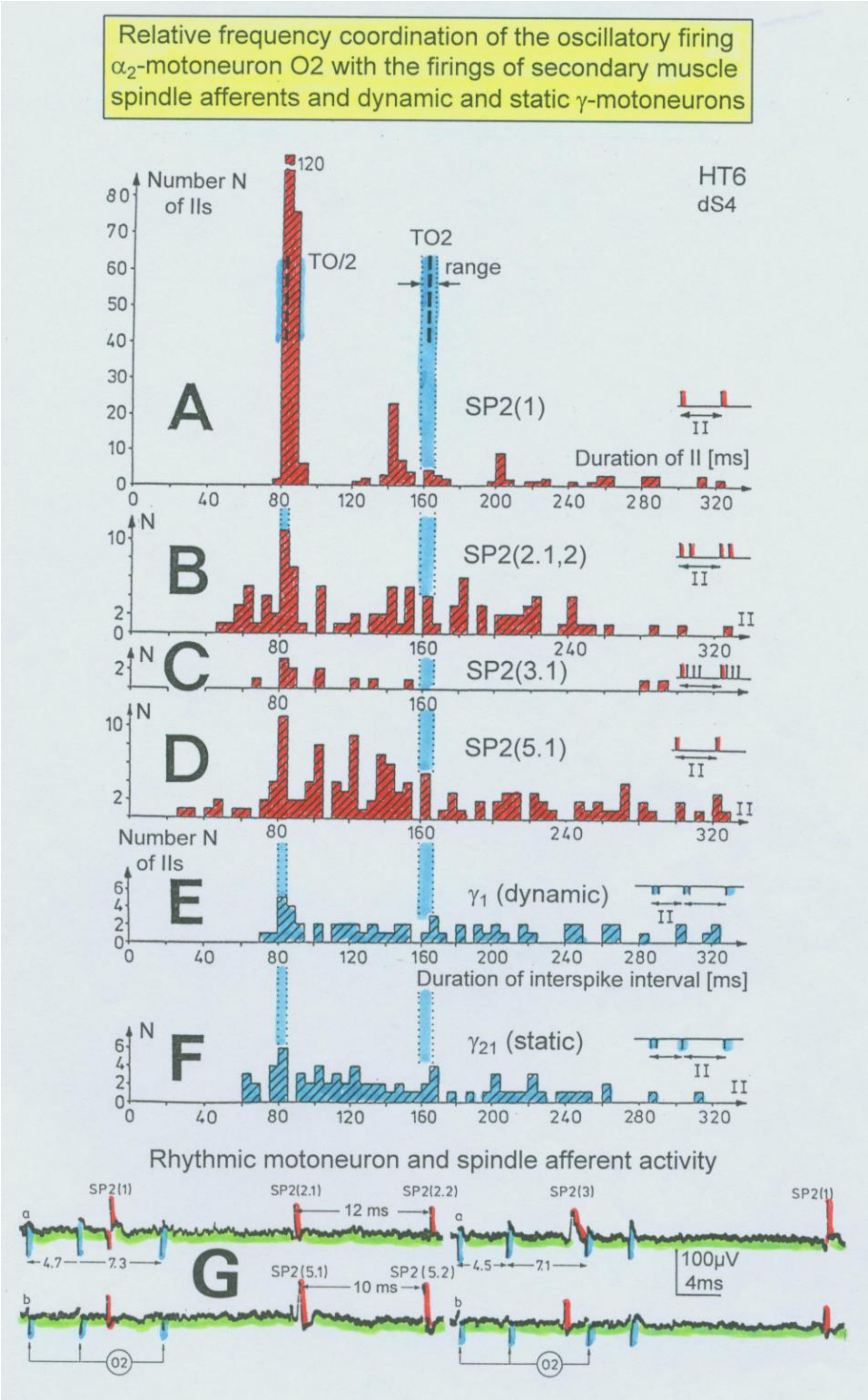

Figure 25. Interspike interval distributions of single endings of four secondary muscle spindle afferents (SP2) and two γ-motoneurons, recorded simultaneously. In A, the oscillation period TO2 (impulse train length = 3 APs) with its range of simultaneously recorded oscillatory firing α_2-motoneuron O2 (see G) is drawn for comparison; also, the halves of the oscillation period TO2/2 are indicated. Note that the interspike interval distributions of spindle afferents and γ-motoneurons have the shortest interspike interval, nearly identical to the half of the oscillation period (relative frequency coordination). The schematic impulse pattern in A to F shows the procedure for measuring the interspike intervals. Original records of the firing patterns of α_2-motoneuron O2 and the secondary muscle spindle afferents SP2(1), SP2(2), SP2(3) and SP2(5) are shown in G. Brain-dead human HT6, dS4 root.

As indicated by measurements, the coupling and the relative coordination during the self-organization of the neuronal networks of the human CNS are of an enormous complexity; this self-organization is induced by sets of mutual impulse patterns from stimulated receptors which are ordered, in time and space, so as to reflect, in the spinal cord and higher centres, the interplay of the body with the external world.

36. World-wide out-of-date teaching and treatment system to repair human nervous system injury or malfunctioning

Genetics, Epigenetics, Molecular and Cell Biology are important disciplines. But they cannot substitute for human Neurophysiology and medical research. If one wants to repair the human nervous system, one has to know how it functions under physiologic and patho-physiologic conditions. The medical faculties of universities are world-wide 20 years out-of-time, since they have not yet realised that human neurophysiology is needed and exists and has to be read for medical students to give them the knowledge to treat human patients. For example detailed knowledge of the human muscle spindle is needed with its different fusimotor, sympathetic and parasympathetic efferent innervation to understand the learning transfer from motor to vegetative and higher mental functions (12,14). Further, it is difficult to see, how one can perform movement sciences without sufficient knowledge of premotor spinal oscillators and human muscle spindles and their network of communication. Already John C. Eccles argued 25 years ago: “From mere behavioural descriptions we shall never come to understand how the brain is effective in the learning of motor skills”. The situation of physiotherapy schools or colleges is even worse. They are more than 20 years out-of-date. Names are upgraded, but the taught knowledge seems to decrease. Students do not learn sEMG (Figs.8,9,11,12) and do not learn about different treatments and their efficiencies. They do not learn the repair methods which they do need for treating human patients. An indicator that medical knowledge to treat nervous system injuries is decreasing is that the only international EMG journal “Electromyography and Clinical Neurophysiology” was closed down at the end of 2010 after 50 years of publishing.

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Chapter I: Competitive interaction between two kinds of motoneurons for the innervations of two types of muscle fibres during development and repair in frog, discussed with respect to **axon guidance** and endogenous stem cell supported structural repair by motor learning in human cervical spinal cord injury.

Chapter II: Development and repair of the human CNS.

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4. Repair in cerebral palsy
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6. Repair of traumatic brain injury in 3 children upon an 11-year-therapy: An outcome comparison between conventional neuro-rehabilitation, treatment by the mother, and Coordination Dynamics Therapy (CDT)
7. Cerebellum repair achieved by 10-year-CDT
8. Surface EMG- and coordination dynamics (CD) measurements-assisted cerebellar diagnosis and improvement in a patient with cerebellar injury
9. Health care in Aging
10. Improvement of movement performance in sportspeople, musicians, and other healthy adults
11. Different membrane properties in animal and human with possible consequence for intelligence
12. Pathologic pattern stimulation upon electro stimulation – physiologic pattern stimulation from natural afferent impulse patterns from the skin
13. Improvement after CNS injury in comparison with physiologic development with respect to urinary bladder functioning

Chapter III: Neurophysiology and pathophysiology of the neural networks of the human caudal spinal cord and their communication with skin, urinary bladder and muscle spindle receptor afferents – a scientific basis for the repair of the human central nervous system.

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4.2 Functional morphometry
5.1 Tapering of nerve fibres
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5.4. Correlation between electrophysiology and morphometry

5.5 Nerve compound action potentials analysed with the simultaneously measured single-nerve fibre action potentials

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9. Natural firing patterns of the different α and γ-motoneurons and muscle spindle afferents upon natural stimulations

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10. Premotor spinal α_1, α_2 and α_3-oscillators - Oscillatory firing of single human sphincteric α_2 and α_3-motoneurons for the continence of urinary bladder and rectum

11. Impaired organisation of Human spinal oscillator following injury

12. Impulse patterns of single encoding sites of human secondary muscle spindle afferents

13. Phase correlated adequate afferent action potentials as a drive of human spinal oscillators

14. Natural action potential patterns of intrafusal γ and parasympathetic motoneurons, secondary muscle spindle afferents and an oscillatory firing α_2-motoneuron, and the phase relations among them in humans

Chapter IV: Translational medicine. (Single-nerve fibre action potential recording method and morphometry is used as human research)

1. Rat model to study neural network organization
2. Rat model to study regeneration
3. Frog model for teaching and research: the power of electrophysiology

Chapter V: From the measured impaired phase and frequency coordination in and between the somatic and parasympathetic nervous system divisions in severe cervical spinal cord injury to the repair of the urinary bladder upon 3 years of movement-based learning.

1. The classification and identification of human somatic and parasympathetic nerve fibres including urinary bladder afferents and efferents is preserved following spinal cord injury.
2. Coordination impairment between the somatic and parasympathetic nervous system divisions in the human sacral micturition centre following spinal cord injury.
3. Phase relation changes between the firings of α and γ-motoneurons and muscle spindle afferents in the sacral micturition centre during continence functions in brain-dead human and patients with spinal cord injury.
4. Scientific basis for learning transfer from movements to urinary bladder functions for bladder repair in human patients with CNS injury.
5. Cure of urinary bladder functions in severe (95%) motoric complete cervical spinal cord injury in human.

Chapter VI: Movement-based learning in human for CNS repair compared with hippocampus learning in animals quantified at the cellular, molecular and epigenetic levels.

Supplement: The adventure of performing medical (human) research.

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