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Reorganization of the Human CNS

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REORGANIZATION OF THE HUMAN CNS

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of the lesioned human brain and spinal cord.
Theoretical basis for modern neurorehabilitation (31 case reports)

CONTENTS

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REORGANIZATION OF THE HUMAN CNS

Neurophysiologic measurements on the coordination dynamics of the lesioned human brain and spinal cord.

Theoretical basis for modern neurorehabilitation (31 case reports)

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Abstract. The key strategies on which the discovery of the functional organization of the central nervous system (CNS) under physiologic and pathophysiologic conditions have been based included (1) our measurements of phase and frequency coordination between the firings of α- and γ-motoneurons and secondary muscle spindle afferents in the human spinal cord, (2) knowledge on CNS reorganization derived upon the improvement of the functions of the lesioned CNS in our patients in the short-term memory and the long-term memory (reorganization), and (3) the dynamic pattern approach for re-learning rhythmic coordinated behavior. The theory of self-organization and pattern formation in nonequilibrium systems is explicitly related to our measurements of the natural firing patterns of sets of identified single neurons in the human spinal premotor network and re-learned coordinated movements following spinal cord and brain lesions. Therapy induced cell proliferation and, maybe, neurogenesis seem to contribute to the host of structural changes during the process of re-learning of the lesioned CNS. So far, coordinated functions like movements could substantially be improved in every of the more than 100 patients with a CNS lesion by applying coordination dynamic therapy. As suggested by the data of our patients on re-learning, the human CNS seems to have a second integrative strategy for learning, re-learning, storing and recalling, which makes an essential contribution to the functional plasticity following a CNS lesion.

A method has been developed by us for the simultaneous recording with wire electrodes of extracellular action potentials from single human afferent and efferent nerve fibres of undamaged sacral nerve roots. A classification scheme of the nerve fibres in the human peripheral nervous system (PNS) could be set up in which the individual classes of nerve fibres are characterized by group conduction velocities and group nerve fibre diameters. Natural impulse patterns of several identified single afferent and efferent nerve fibres (motoneuron axons) were extracted from multi-unit impulse patterns, and human CNS functions could be analyzed under physiologic and pathophysiologic conditions. With our discovery of premotor spinal oscillators it became possible to judge upon CNS neuronal network organization based on the firing patterns of these spinal oscillators and their driving afferents. Since motoneurons fire occasionally for low activation and oscillatory for high activation, the coherent organization of subnetworks to generate macroscopic function is very complex and, for the time being,

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may be best described by the theory of coordination dynamics. Since oscillatory firing has also been observed by us in single motor unit firing patterns measured electromyographically, it seems possible to follow up therapeutic intervention in patients with spinal cord and brain lesions not only based on the activity levels and phases of motor programs during locomotion but also based on the physiologic and pathophysiologic firing patterns and recruitment of spinal oscillators. The improvement of the coordination dynamics of the CNS can be partly measured directly by rhythmicity upon the patient performing rhythmic movements coordinated up to milliseconds. Since rhythmic, dynamic, coordinated, stereotyped movements are mainly located in the spinal cord and only little supraspinal drive is necessary to initiate, maintain, and terminate them, rhythmic, dynamic, coordinated movements were used in therapy to enforce reorganization of the lesioned CNS by improving the self-organization and relative coordination of spinal oscillators (and their interactions with occasionally firing motoneurons) which became pathologic in their firing following CNS lesion. Paraparetic, tetraparetic spinal cord and brain-lesioned patients re-learned running and other movements by an oscillator formation and coordination dynamic therapy. Our development in neurorehabilitation is in accordance with those of theoretical and computational neurosciences which deal with the self-organization of neuronal networks. In particular, jumping on a springboard 'in-phase' and in 'anti-phase' to re-learn phase relations of oscillator coupling can be understood in the framework of the Haken-Kelso-Bunz coordination dynamic model. By introducing broken symmetry, intention, learning and spasticity in the landscape of the potential function of the integrated CNS activity, the change in self-organization becomes understandable. Movement patterns re-learned by oscillator formation and coordination dynamic therapy evolve from reorganization and regeneration of the lesioned CNS by cooperative and competitive interplay between intrinsic coordination dynamics, extrinsic therapy related inputs with physiologic re-afferent input, including intention, motivation, supervised learning, interpersonal coordination, and genetic constraints including neurogenesis.

The theory of reorganizing the lesioned human CNS, based on measurements in humans (brain-dead individuals (HT1-6) and patients with and without CNS lesion) of self-organization of the human spinal cord neuronal networks, is used to re-learn lost somatic, autonomic functions and higher mental functions in patients with CNS lesions, and will be shown to be in accordance with the data from animal research if comparable; some differences will be made clear. With the development of a special coordination dynamic therapy device to train simultaneously the coordinated movements of arms, hands and fingers, and legs, feet, and the trunk an essential further step has been done towards efficient reorganization of lesioned CNS.

With our tools and methods available to repair the lesioned CNS by reorganizing (re-learning), it became also possible to diagnose instability and deterioration of integrated functions of the CNS in patients with severe lesions or minor defficiencies in the organization of the CNS, such as scoliosis. The essential improvement of higher integrative functions in patients with severe brain lesions by coordination dynamic therapy opens up the possibility to improve higher mental functions in individuals with a severe CNS lesion or a physiologically functioning CNS.

Key-words: Human neurophysiology - Integrative CNS functions - Single nerve-fibre action potentials - Natural impulse patterns - Self-organization - Spinal oscillators - Phase and frequency coordination - Coordination dynamics - CNS lesion - Coordination dynamic therapy - Re-learning - Transfer of learning - Co-movements - Spasticity release - Neuro-rehabilitation - Rehabilitation

1. Introduction

The human CNS possesses billions of neurons each one of which having connections to an average of approximately 4000 other neurons. New concepts and tools are needed if the inherent complexity of the most complex system of all, the human CNS and its relation to behavior and thinking, is to be understood and repaired in the case of a lesion. Presently, there is a huge void between the knowledge what a single neuron does (which we know a lot of) and what many of them do when they cooperate. The understanding of the principles of organization among large numbers of neurons is of a paramount importance, as this organization lies at the root of the understanding of ourselves, of the world we live in, of how we touch, see, hear, plan, act and think and how we re-learn behavior and thinking in the case of a CNS lesion. Such fundamental behavioral functions depend on temporally coherent functional units distributed throughout different regions of the CNS, and standard methods have not the potential to elucidate them. For example, responses to sensory stimuli or activities in relation to motor acts are commonly averaged over successive trials in order to improve the signal-to-noise ratio. This averaging procedure destroys any temporal structure in the activation pattern that is not precisely locked to the stimulus or the motor response. Thus, temporal codes were either ignored or remained undiscovered with the commonly applied methods of single unit analysis [145]. In our human neurophysiologic studies [103-140,186-189,193] simultaneous natural firing patterns of several identified single afferent and efferent neurons were therefore recorded and analyzed, but not averaged. In this way we could discover the self-organization of premotor spinal oscillators (functional unit of a motoneuron and interneurons) and phase and frequency coordination between the firings of oscillatory and not oscillatory firing motoneurons and afferents.

By recording single nerve-fibre action potentials from nerve roots it is possible to analyze simultaneously afferent and efferent impulse patterns and investigate the coupling changes of self-organized premotor spinal oscillators to generate, under physiologic conditions and following a CNS lesion, rhythmic and non-rhythmic movements and autonomic functions like continence. These data partly enable the understanding of the integrated functions of the human spinal cord and supraspinal centres; moreover, they allow to substantially improve locomotor and other functions in patients with CNS lesions. With the improvement of the treatment applied within the first 7 hours following spinal cord lesion, including methylprednisolone [14] administration, more patients with spinal cord lesions are paretic and a reorganization of the integrative functions of the CNS is possible and needed. A first paradigm shift in the understanding of the functioning of the CNS concerning the self-organization of neuronal networks gives more reorganization possibilities by the so-called neuronal network plasticity. The second paradigm shift, namely that neurogenesis may be induced in the human adult spinal cord [186] and adult brain [31], opens further possibilities for repair, regeneration and reorganization of the CNS.

In the last 100 years, many authors have come to suggest that it is the rhythmic firing of human neuronal networks which is responsible for rhythmic movements (trembling, tremor) of the body (trunk) and legs, arms and fingers (for references, see [60,168]). Descartes tackled tremor as early as in 1649 [20]. The conclusions drawn by R. Jung from measurements on tremor and clonus in 1941 [60] were similar to the findings concerning the self-organization of premotor spinal oscillators in recent papers [118,120,127]. Only, R. Jung did not differentiate between different motoneuron types and analyzed tremor by only using mechanical and electromyographic recordings.

In 1939 and 1950 [52-54], E.v. Holst expressed his disagreement with the common regard of the CNS beeing only a reflex apparatus producing motor output. His ‘relative coordination’ of different rhythms [52] of the CNS in different species including man is very similar to recent findings of the relative coordination of human spinal oscillators [107,118,131]. It was the opinion of the Sherrington school that all reflexory, excitatory and inhibitory influences onto motor output are due to direct interactions at the motoneuron pool itself (reflex theory) [19]. The opinion of R. Jung was that the bottom-level coordination mechanism, at which all impulses run together, is the ‘Schaltzellenapparat’ (neuronal network apparatus) of the spinal cord [60].

Our current research on spinal oscillators and rhythm coupling supports the rhythm theory of R. Jung and E.v. Holst that assumes that the neuronal networks with their rhythmic properties driving the motoneurons are the bottom level basic mechanism for coordination, and essentially contribute to the coordination dynamics of arm and leg movements. At least to understand movements, the coordination dynamics of neuronal networks of the spinal cord must be understood and integrated in theories on human movements, since neuronal networks of the spinal cord show remarkable functions and plasticity, as has been shown by electromyography by the improvement of the motor program in patients with a complete rostral spinal cord lesion [177]. Brain-dead humans may be able to perform coordinated leg movements when kept at an intensive care unit for several weeks, anencephalic [91] and healthy newborn babies (Fig. 43) can step automatically, and spinal oscillators self-organize themselves and may fire rather coordinatedly in patients with a complete spinal cord lesion.

In the last 15 years the understanding of the functioning of the CNS has changed, moving away from the rigid reflex and neuronal response chain theories towards the concept of dynamic self-organization of neuronal networks [3,63], and this has direct implications for neurorehabilitation because of the increased network plasticity including large scale plasticity [143]. The regulation of neural stem cells and neurogenesis in the intact and damaged adult mammalian and human brain, and probably spinal cord, offers further possibilities with respect to the regeneration and reorganization of the injured human CNS [4,45,166,167].

This review is designed to build up a scientific basis to reorganize the lesioned human CNS by re-learning, so that motor, autonomic and higher mental functions of patients can be improved on the same basis. Since it seems impossible to review the functioning of the whole human CNS, the present review concentrates on oscillators and self-organization in neuronal networks. To get more hard data on the functioning of the human nervous system, new precise human neuroelectrophysiologic methods are needed, like single motor unit electromyography [97,147], the tungsten electrode method [59,67,158] and the single-nerve fibre action potential recording method [103-140].

The case reports are used here to document the theory, to derive human data from lesion studies and use them in theory and to explore possibilities in neurorehabilitation when extrapolating from theory to clinical settings (in similarity to pre-experiments in animal research), since full clinical studies for reorganizing the human CNS, requiring up to 5 years time and more are time, energy and money consuming. In the long term, the clinical trials have to be backed by full clinical studies. But in all patients who obtained coordination dynamic therapy from the author (G.S.) for at least 3 months, the functioning of the CNS could substantially be improved.

This review starts with the new development in human electrophysiology with which it is possible to analyze partly the organization of neuronal networks of the human CNS. As a first step, the firing of motoneurons in the occasional and oscillatory firing mode in relation to the skin and muscle spindle afferent activity is demonstrated; the recordings were obtained from brain-dead individuals (HTs). The partial loss of phase and frequency coordination following

CNS lesion was derived from recordings from paraplegics made during surgery for implantation of electrical bladder stimulators. Single motor unit firing was partly verified electromyographically from leg muscle recordings. The partial loss of phase and frequency coordination prompted the development of coordination dynamic therapy to restore the impaired coordination dynamics. The case reports show that the lesioned CNS can be repaired. With the knowledge derived from the case reports and other patients, the theory has been summarized and updated.

To improve motor, vegetative and higher mental functions in patients with CNS lesion, it is appropriate to observe neuronal network organization in the human lower sacral range, where motor and vegetative (volitional and automatic) functions are generated. Self-organized premotor spinal oscillators have been shown to have two driving phases per oscillation cycle [126] when primarily the somatic nervous system is activated (pin-pricking of sacral dermatoms to induce escape reaction), but the oscillators have three driving phases [126] when additionally the parasympathetic division is activated (stimulation of urinary bladder filling (vegetative) afferents by bladder catheter pulling). The complexity of neuronal network organization becomes obvious when in addition to somatic also vegetative functions are activated. It is further believed that the vegetative functions are the door to the higher mental functions.

A. Human neurophysiology: Self-organization of premotor neuronal networks in the spinal cord

2. Recording of single afferent and efferent action potentials from nerve roots

Our contribution to the understanding of human neurophysiology started from scratch; first, the basis of impulse pattern recognition, i.e. the identification and classification of peripheral nerve fibres had to be improved.

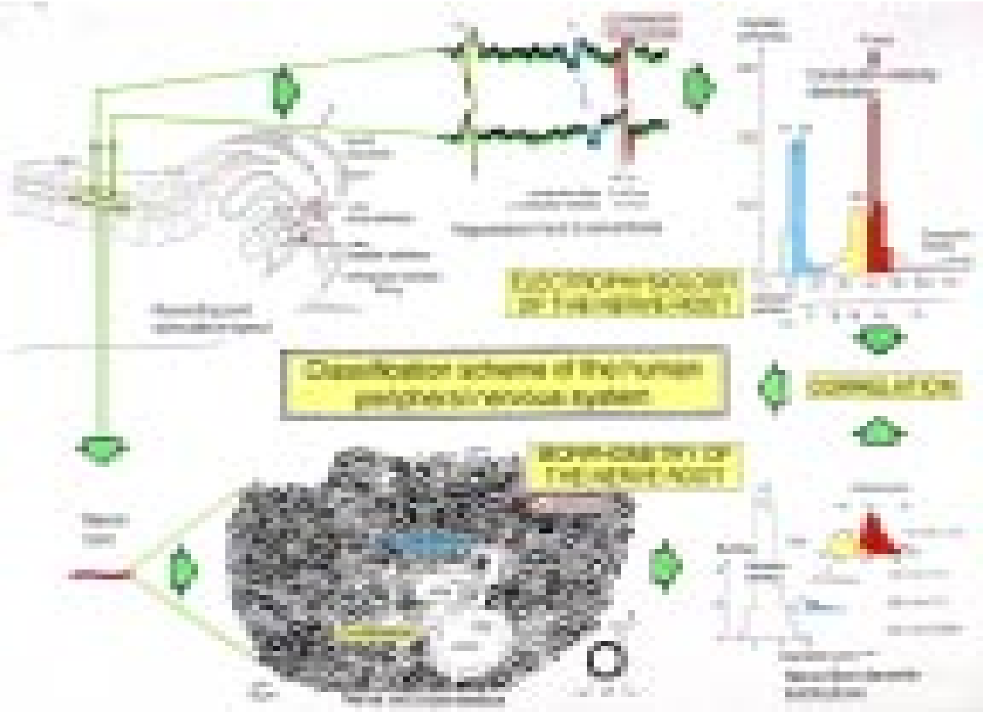

Figure 1
Schematic layout of the classification scheme of the human peripheral nervous system. By recording with two pairs of platinum wire electrodes from a nerve root containing approx. 500 myelinated nerve fibres, a record was obtained in which 3 action potentials (APs) from 3 motoneurons (main AP phase downwards) can be seen. By measuring the conduction times and with the known electrode pair distance (10 mm), conduction velocity distribution histogram was constructed in which the nerve fibre groups were characterized by ranges of conduction velocity values and peaks in asymmetrical distributions. After the recording, the root was removed, fixated, embedded and stained, cross-sections were prepared for light microscopy, and used to measure the mean diameter and the myelin sheath thickness (d). Distributions of nerve fibre diameters were constructed for four different ranges of myelin sheath thicknesses. 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 from the same root, a classification scheme was constructed of the human peripheral nervous system. Cross-section from an S4 ventral root of the brain-dead human HT1.

Because of the ascensus of the human spinal cord, thin long nerve roots exist in the lower sacral range through which mainly continence functions (urinary bladder and anal canal functions) are conducted, which are not covered by tail functions as in rat or cat [113,114]. Few nerve fibres of the lower sacral nerve roots supply lower leg muscles (M. flexor hallucis brevis, for example), so that also motor functions can be explored. Since nerve roots lack peri- and epineurium (Figs. 1,3), which shunt electrical activity, and lower dorsal and ventral sacral nerve roots contain afferent and efferent fibres [106,114], afferent and efferent single nerve-fibre action potentials (APs) can be recorded simultaneously with two pairs of wire electrodes from undamaged nerve roots or fascicles (for methods see [106,127]). Since conducted afferent and efferent APs arrive at the electrodes from opposite directions, for our wiring the main amplitude of extracellular afferent APs shows upwards and that of efferent APs downwards (Fig. 34). APs of afferent and efferent fibres can therefore safely be distinguished from each other [127].

3. Classification scheme of human peripheral nerve fibres

Conduction velocities of single nerve fibres were calculated from the conduction distance (electrode pair distance = 10 mm) and the conduction times (time difference of a certain AP between the traces from two pairs of wire electrodes). Velocity distributions of afferent and efferent fibres were constructed and distribution peaks were correlated to certain nerve fibre groups. From brain-dead humans and partly from patients during surgery, the nerve roots used

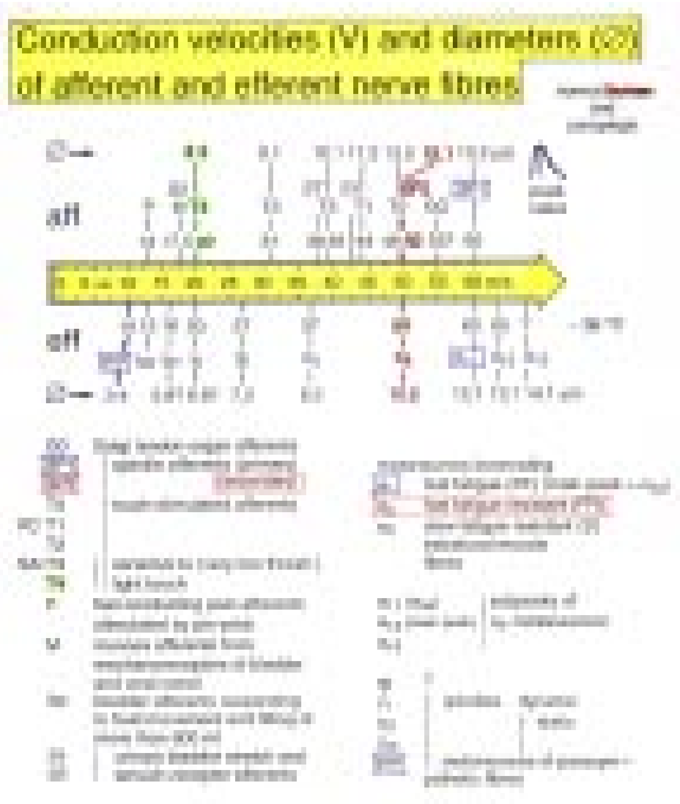

Figure 2
Conduction velocities (V) and nerve fibre diameters (∅) of afferent and efferent nerve fibre groups from normal humans and from patients with a traumatic spinal cord lesion suffered 0.5 to 6 years previously. The splitting of the α_1-motoneurons into the 3 subgroups, α_{11}, α_{12}, α_{13}, has not yet been confirmed.

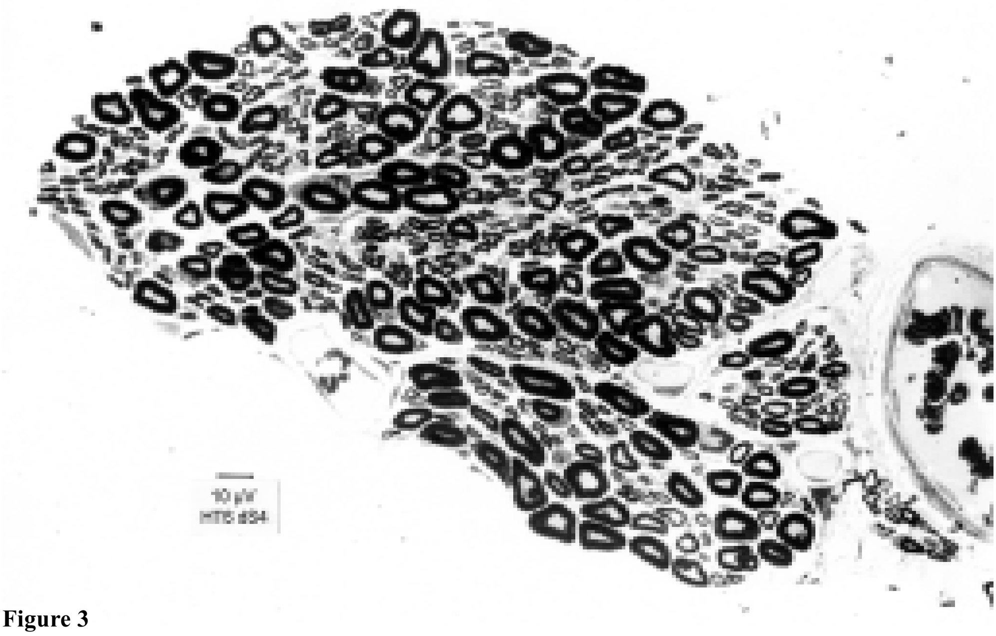

Figure 3
Cross-section from an S4 dorsal root of the brain-dead human HT6.

to record from could be removed, fixated, embedded and stained (Fig. 3). Mean nerve fibre diameters could be measured, and nerve fibre diameter distributions constructed (morphometry). Fibre diameter distribution peaks were identified to represent certain nerve fibre groups (Fig.1). To identify velocity peaks, different kinds of natural stimulation (touch, pin-prick, anal and bladder catheter pulling) were used (Figs. 17-20). In identifying nerve fibre diameter distribution peaks of nerve roots, a comparison of the root distributions with the distributions of known distant skin, muscle and autonomic nerves was useful. Such a comparison of root and distant nerve fibre diameter distributions is justified (different distances from the cell soma), because human nerve fibres taper only very little (approx. 0.3 % per 10 cm, unpublished measurement).

By correlating identified conduction velocity peaks with nerve fibre diameter peaks, a classification scheme for the human PNS was set up, in which individual groups of nerve fibres are characterized by group conduction velocities and group nerve fibre diameters [106,112,124,127] (Figs.1,2,5). The temperature dependence of conduction velocities was accounted for, by calibrating the velocity distributions of afferent and efferent fibres with the calibration relation, namely that secondary muscle spindle afferents conduct with the same velocity as α_2-motoneurons (FR) [127]. This classification scheme is still incomplete and only holds for nerve fibres thicker than approx. 3.5 µm (Fig. 2). The classification schemes developed by Grundfest, Erlanger and Gasser (A,B,C) and Lloyd and Hunt (I,II,III,IV) [46,57,58,77] do not apply to humans. E.g., conduction velocities in rats, cats and dogs (max ≈ 120 m/s) are much higher than those in man (max ≈ 70 m/s) (see below).

4. Single nerve fibre and compound nerve action potentials

By recording simultaneously single nerve fibre APs following no or natural stimulation and compound nerve action potentials elicited by electrostimulation of the nerve roots (Fig. 4), single nerve fibre conduction velocity spectra could be constructed and nerve fibre groups indentified (Fig. 5); moreover, compound AP sub-peaks could be measured and identified (Fig. 6) by comparing them to the single nerve fibre conduction velocity group values and to the available knowledge concerning electrical stimulation thresholds. Using additional literary data it was found that the primary spindle afferents likely have the lowest threshold upon electrical nerve root stimulation, followed by α_1-motoneurons (FF), secondary muscle spin-

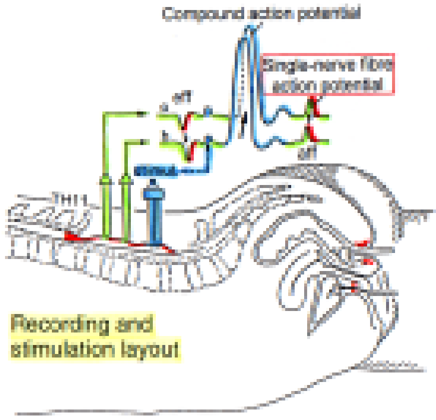

Figure 4
Layout for stimulation and recording of single fibre action potentials (APs) and compound action potentials (CAPs). Traces a and b are records taken from the two sites; downward arrow = efferent, upward arrow = afferent, the natural stimulation used were touch, pin-prick, and anal and bladder catheter pullings. Following electrical (artificial) stimulation with a ‘Brindley’ stimulator (stimul.), the compound action potential passes the 2 electrode pairs as a large afferent-like AP.

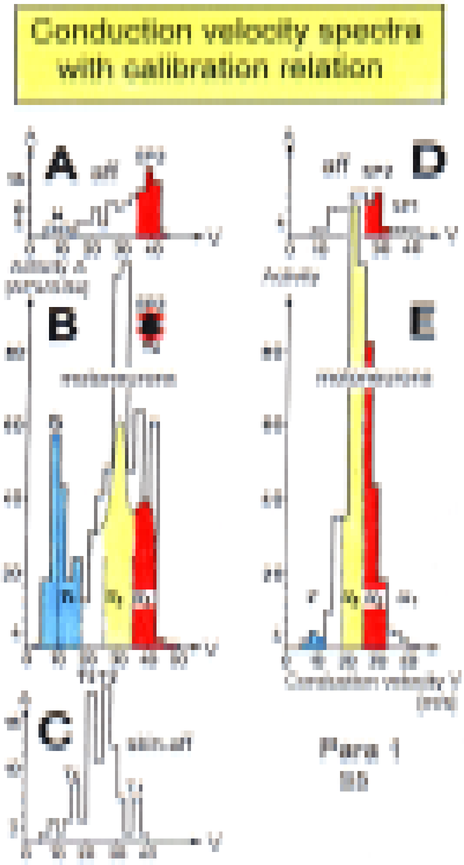

Figure 5
Distribution histograms of conduction velocities from recordings from the S5 root of paraplegic 1 at higher (A, B, C) and lower unknown root temperature (D, E). The calibration relation for the identification of distribution peaks, i.e. that the secondary spindle afferent fibres (SP2) and α_2-motoneurons conduct with the same velocity, is indicated by the thick arrow in B. The velocity ranges of the motoneurons are indicated in B and E by the vertical dotted lines. The oscillatory α_2 and α_3-motoneuron activities in B and E have not been excluded. The dotted curve in B indicates the approximate α-motoneuron distribution upon subtracting the oscillatory activity. Note that T1 skin afferents (probably innervating Pacinian corpuscles) conduct at slightly slowlier rates than do α_2-motoneurons, aff = aferent velocities; M = velocities from mucosal mechanoreceptor afferents.

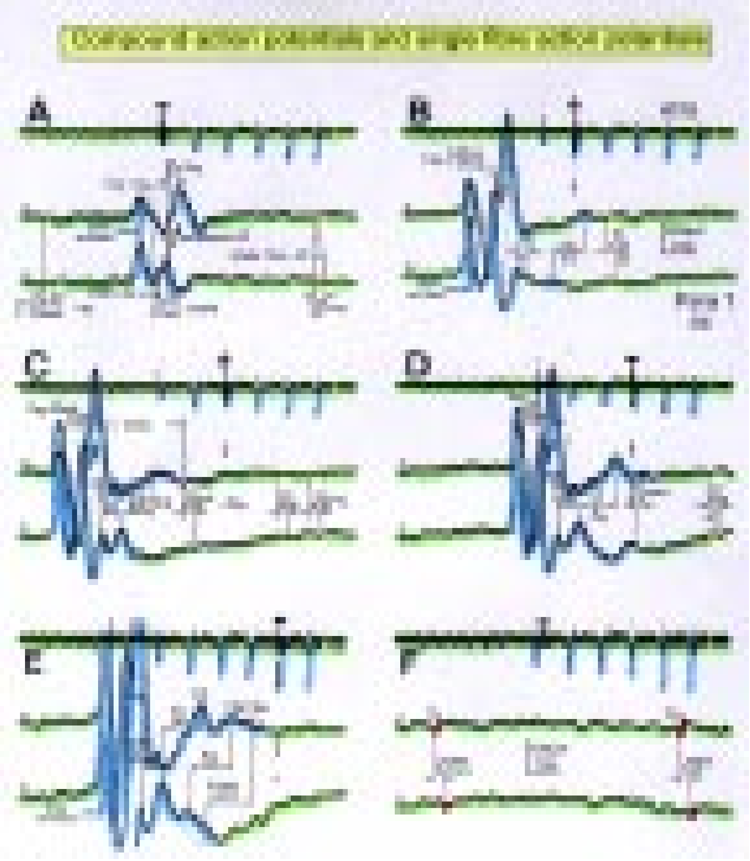

Figure 6
Size and form of the compound action potential (AP) in dependence on the strength of the stimulation and in relation to the single-fibre APs. Single-fibre APs are labelled according to the group they belong to (e.g., SP2, α_2); components of the compound AP are labelled according to the nerve fibre group they belong to, namely CSP2, Cα_3. Rα_3 designates possible reflected antidromically propagating α_3-motoneuron APs. Conduction time (ct) and conduction velocity (v) are indicated at single-fibre APs and peaks of compound APs. The large arrows in A, B, C, D indicate the main compound AP. Note that with increasing stimulation artifact (stim. artifact) from A to D also the slowlier conducting nerve fibre groups get excited. The small thick arrows on the summary trace (trace 'a'; time scale 40 ms) on top of A to F marks the first (A), second (B), third (C), fourth (D) and fifth (E) stimulation artifact. In E, the amplitudes are stretched (120 µV), to make compound AP components Cγ_{21} and Cγ_{22} visible. F shows single-fibre APs recorded between the first and the second stimulation. Para 1, S5 root, root temperature unknown.

dle afferents, α_2-motoneurons (FR), α_3-motoneurons (S), γ_β, γ_1 (dynamic), γ_{21} (static), γ_{22} (static), and parasympathetic motoneurons.

In first approximation, the AP duration increases in the same way as the AP amplitude decreases with the decreasing conduction velocity, and the area between the average single fibre AP curve and the baseline is the same for all single fibre APs with the same distance from the recording electrodes in the root cross-section. By comparing the mean area of a single AP with the areas of the peaks of the compound APs, 230 single fibre APs were found to contribute to the compound AP in the measured case (Fig. 6). In secondary spindle afferent fibres and α_2-motoneuron groups, 53 fibres were stimulated (23%). The α_3-motoneuron peak and the afferents in the same velocity range contained 101 fibres (44%), the γ_β peak contained 9 fibres (4%), the γ_1 32 (14%), the γ_{21} 23 (10%), and the γ_{22} contained 12 (5%) fibres. Additionally, two primary spindle afferents and two α_1-motoneurons most likely contributed to the compound AP. Since the large peaks in the compound APs did not change their area with the increasing stimulation, all muscle spindle afferents and α-motoneurons were most likely activated to contribute to the compound AP [122].

By comparing the different sub-compound APs comprised in a compound AP (CSP1, Cα_1, CSP2, Cα_2, Cα_3, Cγ_β, Cγ_1, Cγ_{21}, Cγ_{22}) (Fig.6) with the motoneuron group identification obtained from single nerve fibre conduction velocity distribution histograms (Fig. 5E), it can be seen that the compound AP with its peaks provides more conclusive information with respect to splitting. In unfavorable recording conditions (for example, low temperature) the compound AP can give additional information which can be used to identify nerve fibre groups [122].

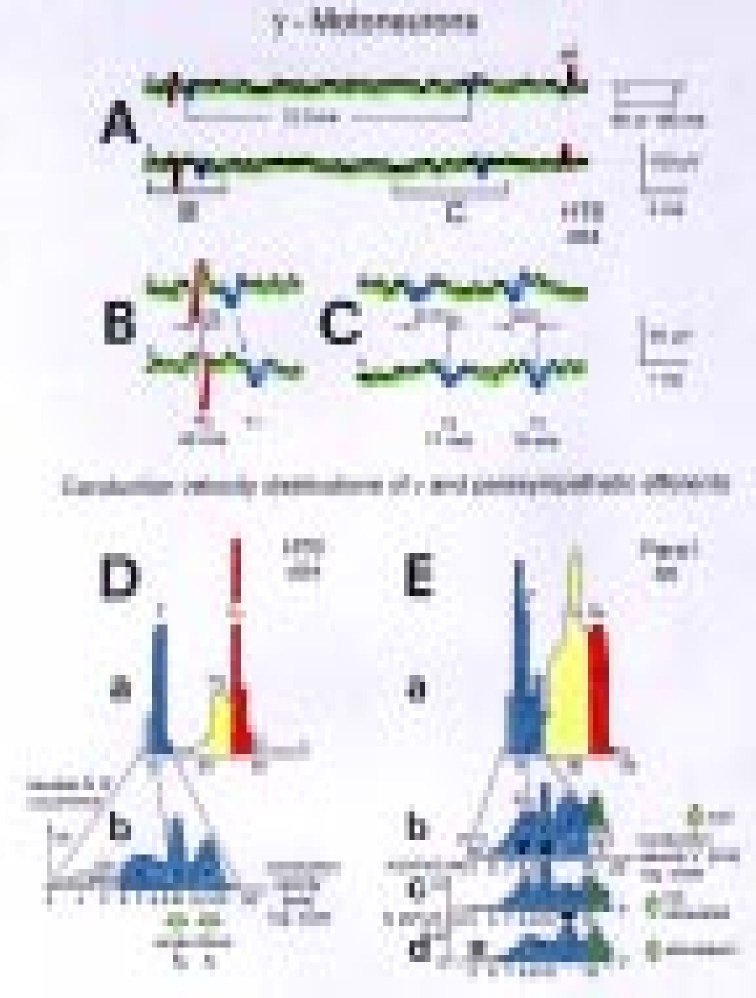

Figure 7
A. Activity from 2 γ-motoneurons and an α_2-motoneuron. The γ_1-motoneuron may have fired in the oscillatory mode for a few cycles with a period duration of 90 ms or 180 ms. Interspike intervals of the possible impulse train, consisting of 2 APs, are indicated (12.3 ms). The insert shows the possible oscillation cycle period. HT6; dS4. B,C. Time and amplitude expansions of A. Conduction velocities are indicated. Note that with the increasing conduction velocity, the AP amplitude increases and the duration decreases. D,E. Conduction velocity distributions of motoneurons for the brain-dead human HT6 (D) and paraplegic 1 (E). To make intrafusal motoneuron and parasympathetic peaks visible, the main γ-peak of Da and Ea was plotted on a log scale in Db and Eb. The distribution peaks are labelled with the groups, they most likely represent. In E, the distribution Eb is split into the distribution upon no additional stimulation (Ec) and upon additional stimulation (Ed). Note that in the non-stimulated distribution (Ec) the static γ-motoneuron peaks (γ_{22}, γ_{21}) are highest, whereas under stimulation (Ed) the parasympathetic (para) and the dynamic γ-motoneuron peaks (γ_1) are highest. When plotting the velocities in Db and Eb logarithmically, the conduction times were first grouped by a conduction time histogram and the column values were then used (conduction distance = 8 mm) to construct conduction velocity distribution curves.

5. Identification of γ and parasympathetic efferents in conduction velocity distributions on a logarithmic scale

To allow for a better identification of γ-motoneuron groups in conduction velocity distribution histograms, single-nerve fibre velocities were plotted on a log scale rather than linearly [121] (Fig.7). By comparing stimulated and non stimulated induced velocity distributions (Fig. 7E), peaks of static and dynamic γ-motoneurons and parasympathetic fibres could be identified.

By comparing Fig. 7 with Fig. 6, it can be seen that there is a similarity in the distributions of the motoneuron groups between the compound AP with its sub-compound APs and the nerve fibre groups in conduction velocity frequency distributions for single fibres.

6. Comparison of conduction velocity distributions of humans and animals

Fig. 8 shows conduction velocity distribution histograms of a human (B) and a dog (A) measured with the same method, the same equipment and at similar temperatures. It can be seen that the velocity distributions are very similar in their peaks, apart from the higher group velocity values. The dog α_2-motoneurons for example, conducted at 70 m/s whereas the human ones at 40 m/s at 34 °C.

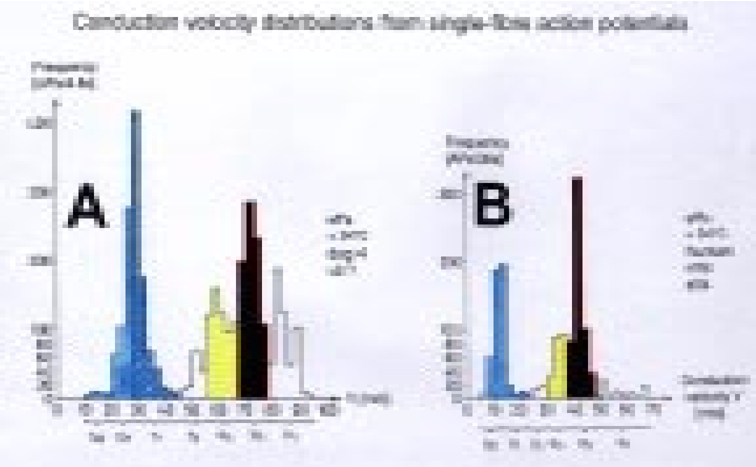

Figure 8 Distribution histograms of conduction velocities: efferent APs from dog (A) and human (HT6; dS4) (B) lower sacral nerve roots. The distribution peaks are labelled according to the respective groups they represent. Motoneuron velocity ranges are indicated. In A, 24 sweeps of 0.2s, and in B, 30 sweeps (stimulated and non-stimulated) of 1.2s duration were used.

The difference between the human and the animal peripheral nervous system may however not just be that human nerve fibres conduct proportionally slowlier. Transmission frequencies of secondary muscle spindle afferents in man were measured to be as high as 5000 Hz [125]. It may therefore be that other human neuron membrane parameters differ from those of animals. The lower conduction velocity values in man may be the price for a higher transmission frequency. A higher transmission frequency allows a higher pattern variability and more dynamic patterns.

7. Recruitment of α and γ-motoneurons in rat, dog and man

Distribution changes of conduction velocities in each group of α_2, α_3 and γ-motoneurons were used for recruitment analysis. As will be shown below (Fig.14), the α-motoneurons will increase their firing rate upon the increase of their adequate afferent input from firing occasi-

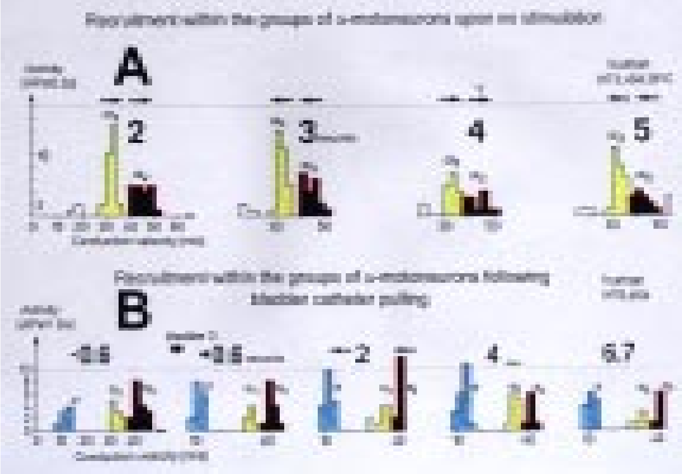

Figure 9
Frequency of the occurrence of changes of single-fibre conduction velocities (recruitment changes) within the groups of α- and γ-motoneurons in man upon no stimulation (no catheter positioned, A) and following strong bladder catheter pulling (B). The velocity ranges in B are taken from Fig.8. Time in seconds following start of measurement or stimulation is indicated (e.g. 2: 2.0 to 2.2s). The arrow directions on top of the histograms indicate stages, at which motoneurons in a certain group with low or high velocities are preferentially activated, as can be calculated from the histograms. Note in B the co-recruitment of γ_1 and α_2-motoneurons, and that α_2-motoneurons are recruited before α_3-motoneurons. HT3; vS4.

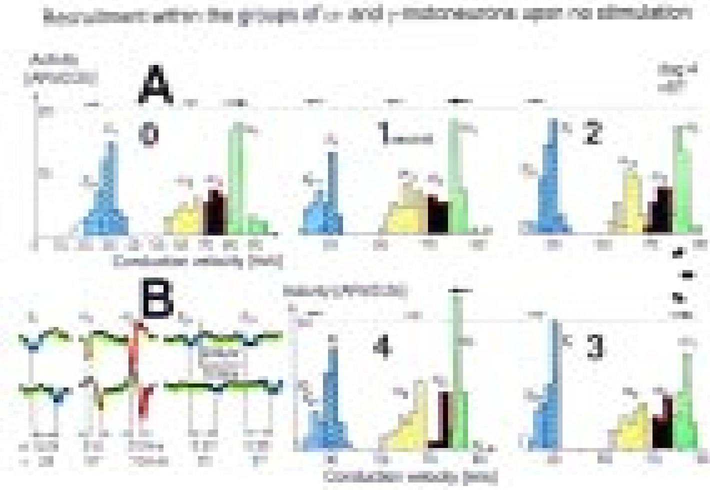

Figure 10
A. Frequency of occurrence changes of single-fibre conduction velocities within the groups of γ_1, α_3 and α_2-motoneurons (recruitment) in a dog sacral ventral root upon no stimulation. The group conduction velocity ranges are taken from Figure 8. Measurement times in seconds are indicated (e.g. 1 second: 1.0 to 1.2s). The arrow directions on top of the histograms indicate stages, at which motoneurons in a certain group with low or high velocities are preferentially activated, as can be calculated from the histograms. Columns for γ_1-motoneurons are cross-hatched, those for α_3 are dotted, and those for α_2 are filled. Dog 4, bladder catheter positioned. B. A sweep piece from a recording from dog 4. Conduction times (ct) and conduction velocities (v) and α and γ-motoneurons are indicated.

onally to firing oscillatory. It has been shown in humans for low activation that the α and γ-motoneurons are recruited with the increasing conduction velocity, i.e. according to the thickness of the axon, thus according to the motoneuron size. The slowlier conducting fibres are recruited before the faster conducting ones in each motoneuron group [113,9].

In man, with no additional stimulation, the slowly and fast conducting α_2 and α_3-motoneurons were recruited repeatedly every 2s (Fig. 9A). In the dog (for identification of nerve fibre

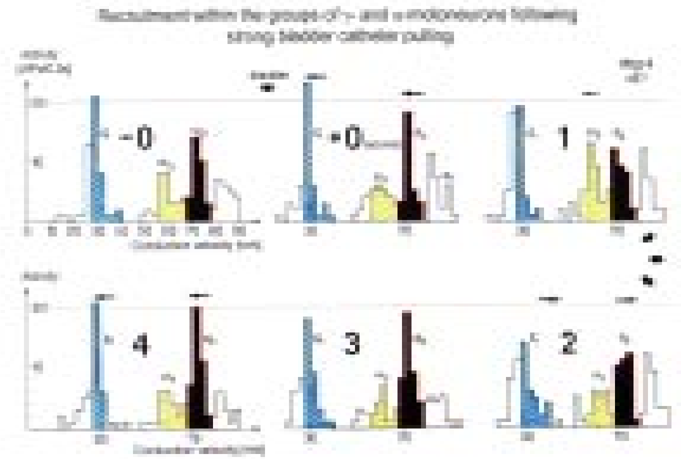

Figure 11
Recruitment of α and γ-motoneurons in a sacral ventral root of dog 4 following strong bladder catheter pulling. For further description, see legends to previous Figures. Note that α_2-motoneurons are recruited before α_3-motoneurons, and the co-recruitment of γ_1 and α_2-motoneurons.

groups, see Fig. 8A), with no additional stimulation, slowly (and fast) conducting γ_{21} and α_3-motoneurons showed repeated activation every 3 to 4s. A subgroup of α_1-motoneurons showed repeated recruitment every 2s (Fig. 10). In a slowlier conducting rat subgroup of α_1-motoneurons, without specific stimulation, the motoneurons were recruited according to the size principle every 2s. It seems therefore that in rat, dog and man with unspecific low level stimulation, α and γ-motoneurons are recruited repeatedly according to the size principle in each motoneuron group [113]. The period of repeated recruitment varied between 2 and 4s. The recruitment in the different groups may be synchronized or not.

Following bladder catheter pulling, the human slowly conducting γ_1 and α_2-motoneurons were recruited 2s after the pulling, the slowly conducting α_3-motoneurons 4s after the pulling (Fig. 9B). In the dog following bladder catheter pulling, the slowly conducting γ_1 and α_2-motoneurons were recruited directly following the pulling, and the slowly conducting α_3-motoneurons were recruited 1s later (Fig. 11). In the rat, the slowly conducting α_1-motoneurons were recruited directly following pin-pricking of the limb, the slowly conducting α_2-motoneurons 0.2s later, and the slowly conducting α_3-motoneurons 1s later. Therefore following specific additional stimulation, the more dynamic motoneurons (α_1, α_2, γ_1) are recruited according to the size principle before the more static motoneurons (α_3, γ_2), depending on the function stimulated. Often, there was co-recruitment of α and γ-motoneuron groups.

Hennemans's recruitment according to the size principle [9] can be understood as a special case of motoneuron recruitment (namely, recruitment among α_1-motoneurons only) of the above mentioned more general recruitment principle. Upon recording with EMG surface electrodes, e.g. from the musculus tibialis anterior of a healthy human individual, it can be seen that with low muscle activation, the single motor unit APs have a small amplitude, whereas with higher activation motor units with larger AP amplitudes are recruited. Since FF type motor units have much larger AP amplitudes than FR and S type motor units, one mainly recognizes the recruitment of FF type motor units.

The recruitment within the different α and γ-motoneuron groups for low level activation is important to understand muscle tone (apart from mechanical muscle properties); however, it is difficult to measure the recruitment because of low activity, which makes the sampling intervals large to get enough events.

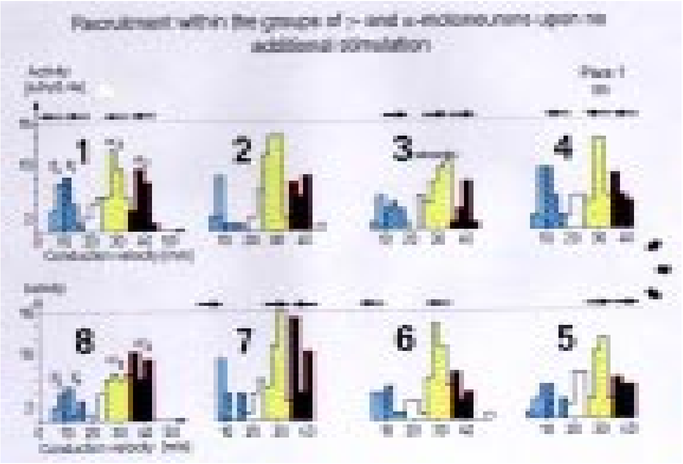

Figure 12
Frequency of the occurrence of changes of single-fibre conduction velocities in paraplegic 1 upon no stimulation, with the anal and bladder catheters positioned. The arrows on top of the histograms indicate stages at which α and γ-motoneurons in a certain group are preferentially activated with low or high conduction velocities. Note that there is mainly co-recruitment of γ_1, α_3 and α_2-motoneurons with rhythmicity.

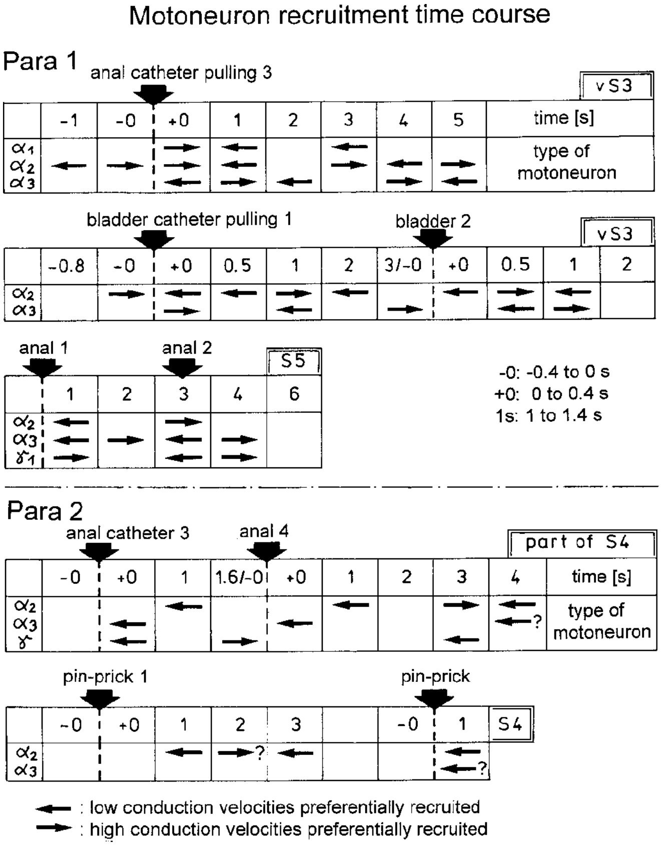

Figure 13
Summed recruitment changes in the occasional firing mode with ongoing time as measured in two paraplegics (1 and 2). The arrows direction indicates whether preferentially motoneurons with low or high axon conduction velocities are recruited (within the time interval of 0.4s) after a certain time. Para 1; Para 2.

8. Recruitment of motoneurons in the occasional firing mode following spinal cord lesion - pathologic recruitment

Upon no additional stimulation in a paraplegic patient, slowly and fast conducting motoneurons were recruited repeatedly within the groups of α_2 and α_3-motoneurons every 2.5s in similarity to the rather physiologic case (HT3, Fig. 9). But the level of activation of the α and γ-motoneurons was higher in the paraplegic patient (Fig. 12) than in the brain-dead human (Fig. 9), even though the vS4 roots (Fig. 9) are expected to contain more fibres than an S5 root (Fig. 12). The higher activation of the neuronal networks of the spinal cord below the lesion is in accordance with the pathologic overactivation of muscles (spasticity) in para- and tetraplegia.

Following anal catheter pulling, the slowly conducting α_3-motoneurons (S) were recruited directly following the stimulation, whereas the faster conducting α_2-motoneurons (FR) were recruited approx. 1s later (Fig. 13). The faster recruitment of α_3-motoneurons (more static) in comparison to the α_2-motoneurons (more dynamic) differed from the recruitment observed during measurements in brain-dead humans and in rats and dogs, and was discussed with respect to the loss of interneurons in the spinal cord, and is in accordance with the pathologic activation of muscles in paraplegia. Bladder catheter pulling does not activate so many α_3-motoneurons (the external urethral sphincter mainly contains α_2-motoneurons), and is therefore not suitable for comparing the recruitment speed between α_2 and α_3-motoneurons.

9. Self-organization of a premotor spinal oscillator

The self-organization of a premotor spinal α_2-oscillator innervating the external striated urinary bladder sphincter is shown in Fig.14D. Because the motoneuron axon of O1 had a recurrent fibre (A) at the recording site, each single AP of this motoneuron could be identified safely by the AP of the recurrent fibre. The function of the motoneuron was to secure bladder continence. The activity from urinary bladder receptors, i.e. the activity of bladder stretch (S1), tension (ST) and flow receptor afferents (S2) (Fig. 14E), was an adequate afferent input to the motoneuron. For retrograde bladder filling up to 550 ml, motoneuron O1 only fired occasionally (D,F). This was the storage phase of the bladder, during which the intravesical bladder pressure increased only little. For higher bladder filling volumes, the motoneuron switched via the transient oscillatory firing mode to the continuous oscillatory firing mode (D) to generate a higher activity (F) for a stronger drive of the urethral sphincter to more strongly secure continence when the storage phase was nearly passed and the bladder pressure increased more strongly. For bladder filling volumes higher than 800 ml, the activity of the spinal oscillator decreased again; probably, the oscillator became inhibited (D). Pain fibres (not shown in Fig. 14G) may have inhibited the oscillatory firing to protect the bladder from mechanical damage. The overflow mechanism was started. Probably, fluid entered the trigonum vesicae to activate flow receptors, so that the flow receptor activity (S2) increased strongly (E). The premotor spinal oscillator O1, of which motoneuron O1 is probably a part [118], was organized by the adequate afferent input (S1, ST, S2, ...) induced by bladder filling. The oscillator to be formed in the premotor neuronal network in the spinal cord, consisting of a motoneuron and interneurons, needs a certain preformation of the networks (connectivity, synapse efficacies, membrane properties of neurites, ...) and adequate afferent input patterns. In modeling such networks, the organization of the premotor spinal oscillators in the spinal cord neuronal networks cannot be separated from its space-time distributed adequate afferent input patterns, giving rise to self-organization. From Fig. 14B it can be seen that the stretch receptor afferent APs (S1(1)) show a relative phase correlation to the impulse trains of the oscilla-

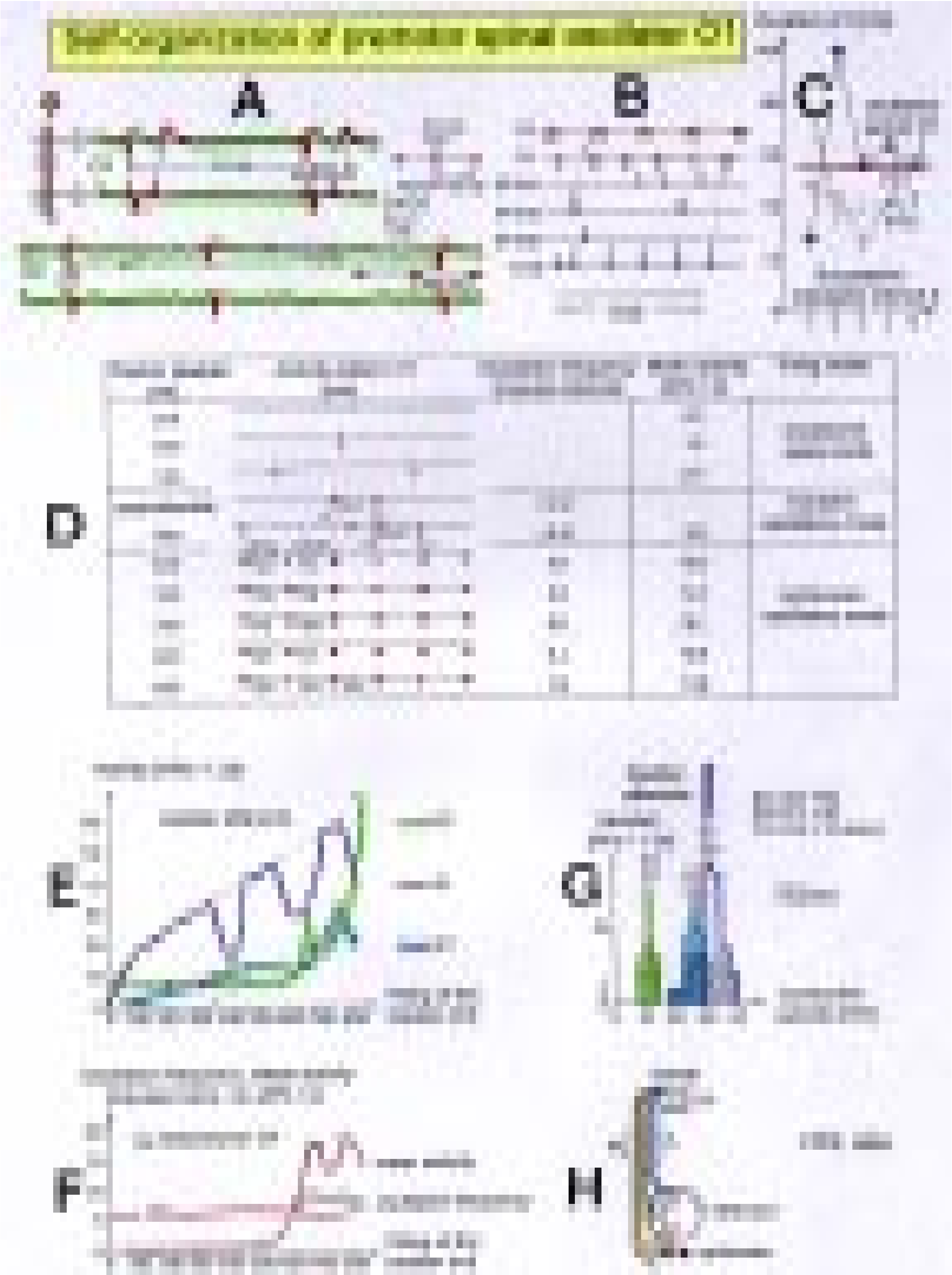

Figure 14
Self-organization of premotor spinal α_2-oscillator O1, which innervates the external urinary bladder sphincter (skeletal muscle). Brain-dead human HT6; recording from a dorsal S4 nerve root. A. Recordings from α_2-motoneurons O1 and O2, firing in the oscillatory mode with impulse trains of 2 (uppper recording) and 3 (lower recording) action potentials (APs). The durations of the oscillation periods were 110 (O1) and 164 ms (O2). The interspike intervals of the impulse trains were 5.9 ms (O1) and 4.6 and 7.4 ms (O2). Motoneuron O1 conducted at 36 m/s; its recurrent fibre conducted at 21 m/s. The measurment layout is shown schematically. The inserts show the oscillatory firing modes; they have not been drawn to

tory firing motoneuron O1. The successive interspike intervals (IIs) of the S1(1) afferents have, on the average, a value similar to that of the oscillation period of oscillator O1 (Fig. 14C).

Other premotor spinal oscillators, activating the external striated bladder sphincter not shown here, will also have self-organized themselves by the same or similar afferent input. However, these oscillators subserving the same function will be correlated in their firing in the way that they do not fire in synchrony but distributed in their phases with respect to one another (probably by relative inhibition with respect to each other) to secure that the sphincter muscle does not show rhythmic movements (tremor). Such non-synchrony correlated oscillatory firing of several oscillators has in a small time window been measured [118] (Fig. 39).

In the case of a non-lesioned CNS, this premotor spinal oscillator O1 could also be activated volitionally from supraspinal centres. It would be very interesting to see how the afferent input patterns from supraspinal centres to the spinal premotor network would look like.

By recording from the dorsal S4 root of the brain-dead human HT6, impulse trains from another oscillatory firing motoneuron and its driving afferents were measured, which served quite a different function (Fig. 14F). The α_2-oscillator O2 (Fig. 14A,B) innervating the striated external anal sphincter was activated by secondary muscle spindle afferent activity, induced by the anal catheter-stretched muscle spindles, probably located in the anal sphincter or functionally associated pelvic floor muscles. Also, mucosal and skin receptors within the anal reflex area will induce self-organization of premotor oscillators activating the external anal sphincter to secure anal continence. The self-organization and drive of this spinal oscillator upon adequate afferent input from muscle spindles and skin receptors will be tackled below. It is evident from the impulse patterns shown schematically in Fig. 14B that the impulse trains of this oscillator O2 show a phase relation and an interspike interval relation to its driving spindle afferent APs.

The self-organization of the spinal oscillators in the premotor neuronal network cannot be separated from its adequate forming and driving afferent impulse patterns. It is not clear whether

scale. B. Impulse patterns of oscillatory firing α_2-motoneuron O2 innervating the external anal sphincter, in relation to the muscle spindle afferent activity SP2(1 to 3), activated by the stretch of the anal sphincter by the anal catheter, and impulse patterns of oscillatory firing α_2-motoneuron O1 innervating the external urethral sphincter, in relation to the stretch receptor afferent activity (S1(1)) of the urinary bladder, activated by 750 ml bladder filling. Phase relations between APs of SP2(2) and O2 and between APs of S1(1) and O1 are indicated by the small arrows. C. Three series of successive interspike intervals of the 2 stretch receptor afferent fibres S1(1) and S1(2) activated by retrograde bladder filling. The oscillation period of oscillatory firing motoneuron O1, activated only by bladder filling is shown. D. The firing in the occasional spike mode, the transient and the constant oscillatory firing mode of α_2-motoneuron O1 in response to filling of the bladder. In the 'activity pattern' column changing durations of oscillation periods are given. The oscillation frequencies in the brackets give the frequencies at the moment of oscillation for the transient oscillatory mode. Downward deflections are schematized APs. Interspike intervals of the close APs ~ 6.0 ms (A). E. Activity levels of stretch (S1) and tension (ST) and flow receptor afferents (S2) (E) and of sphincteric α_2-motoneuron O1 (F) in response to retrograde filling of the bladder. The activity values of the S1, ST and S2 afferents are taken from histograms like the one in G. Filling of the bladder was stopped once between 600 and 650 ml. F. The small dotted lines represent mean activity (APs/s) and oscillation frequency (impulse trains/s) of α_2-motoneuron O1 if bladder filling were not stopped in between. Note that the mean activity increases continuously with the filling of the bladder from 550 to 650 ml, even though motoneuron O1 started to fire in the oscillatory mode from 620 ml on (D). Note further that the oscillatory firing motoneuron O2 (frequency of firing with impulse trains is shown) is nearly not affected by the filling of the bladder and by the start of the oscillatory firing of motoneuron O1. G. Conduction velocity frequency distribution histogram of stretch, tension and flow receptor afferent activity at 750 ml. The activities of afferents S1, ST and S2 are quantified by counting the afferent conduction velocities under the peaks (open plus hatched part), with the conduction velocity limits given in the insert. The counts (27, 33, 59) are given below the peak labelled S1, ST and S2 and plotted into E for the afferent activity at 750 ml. H. Schematic drawing of the anatomical arrangement of the afferents and the motoneuron O1.

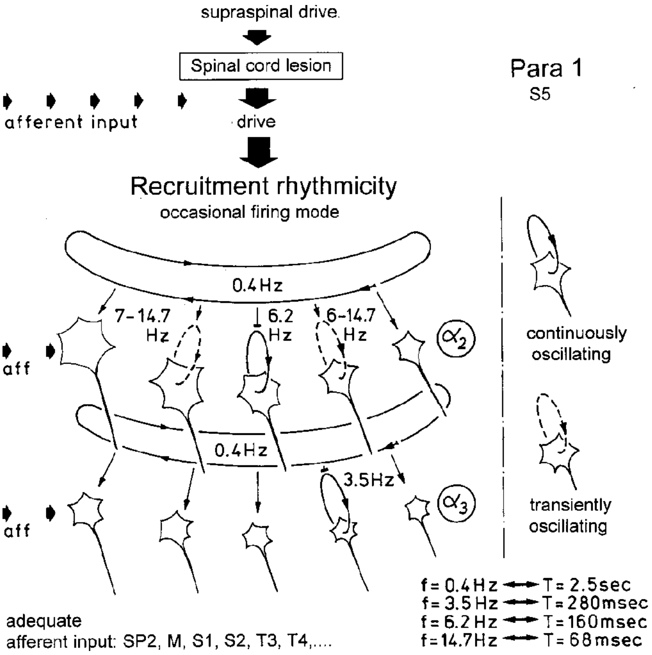

Figure 15
Recruitment rhythmicity of firing, drawn for α_2 and α_3-motoneuron axons, in an S5 nerve root in paraplegic 1. The changes in γ-motoneuron recruitment are not shown; neither the co-recruitment of γ_1 and α_2-motoneurons is indicated. The arrows pointing towards the motoneuron somas indicate recruitment; no arrow = no recruitment. SP2 = secondary muscle spindle afferents (affs), M = mucosal affs, P = pain affs, S1 = bladder stretch receptor affs, S2 = flow receptor affs, T3 = low threshold skin affs.

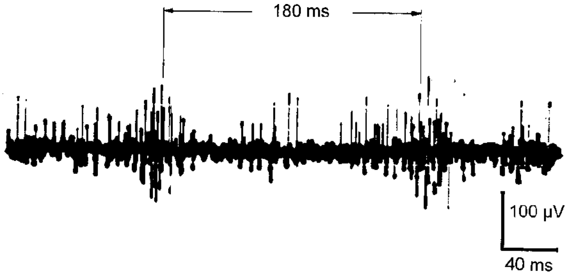

Figure 16
Overall efferent activity recorded from an S5 dorsal root 20 s after pulling the bladder and anal catheters. The rhythmic activity interval is marked by a 180 ms distance. Brain-dead HT4.

during phylogenesis and ontogenesis the CNS neuronal networks adapted to the impulse patterns of the receptors or whether the receptors adapted their firing to the network organization or both. But it would be far from reality to model self-organization of the human spinal cord (and more generally the CNS) neuronal networks without taking into account the space-time distributed adequate afferent impulse patterns from the periphery and the supraspinal centres, giving rise to self-organization.

Before going into further details of the self-organization of premotor spinal oscillators, some data will be presented on the simultaneous firing of motoneurons in the occasional and oscillatory firing mode.

10. Simultaneous firing in the occasionally and oscillatory firing mode

If motoneurons fire occasionally, transiently oscillatory or continuously oscillatory in dependence on their activation (Fig. 14), then in a population of motoneurons one should observe all the three firing modes.

Fig. 15 (and Figs. 17-19) schematically shows how all the three firing modes of the motoneurons interact with each other. The data were obtained from a recording from a paraplegic patient. The α_2 and α_3-motoneurons were recruited repeatedly every ~ 0.4 Hz according to the size principle in each motoneuron group. One α_3-motoneuron and one α_2-motoneuron were firing continuously oscillatory. Two further α_2-motoneurons fired transiently oscillatory. It is unclear how the firing of the motoneurons in the occasional and oscillatory firing mode were correlated. By splitting the summed impulse traffic (Fig. 16) it was found that very approx. 50% of the motoneurons in the occasional firing mode fired in relative coordination with the oscillatory firing motoneurons (they fired in relative coordination with the spinal oscillators), and the remaining 50% of motoneurons seemed to fire with no correlation to the spinal oscillators. This can be understood in the way that the motoneurons and the interneurons contributing to a network organization to generate a certain function fire relatively coordinatedly, and that the neurons not firing in relative coordination with the spinal oscillators are not or only little contributing to the organization of that particular function. The self-organization of a certain function in the neuronal networks therefore occurs through the neurons in the subnetwork to generate this function becoming more activated and correlated with each other in response to the adequate afferent input. The motoneurons most strongly contributing to a certain function (contraction of the external anal or bladder sphincters to secure continence) fire oscillatory, motoneurons contributing less strongly to the generation of this function fire occasionally but correlated to the oscillators, and the motoneurons firing occasionally with seemingly no phase correlation to the firing of the oscillators contribute little if at all to that function. If the recruitment according to the size principle is given by the different thresholds of the motoneurons (the smaller motoneurons have a lower threshold), then the drive potential to activate the motoneurons in the occasional firing mode is changing periodically (in this case at 0.4 Hz). It is interesting to know how this rythmicity is correlated to the rhythms of the self-organized premotor spinal oscillators.

Figures 17 through 19 show some data on the simultaneous firing of motoneurons in the occasional and oscillatory firing mode [105].

Figure 17
Activity of occasionally active α_2, α_3 and γ-motoneurons (A) and simultaneously measured mean activity and oscillation frequency of α_2-motoneuron O2 (B) in response to touching the lower sacral dermatomes (outside the anal reflex area) with a ball or pricking them with a pin (pain). The activity values have been obtained from conduction velocity distribution histograms. HT6; dS4.

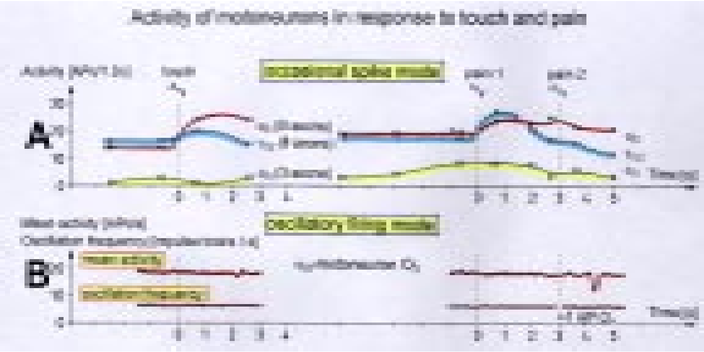

Fig. 17A shows the response of occasionally firing α and γ-motoneurons to touch and pain applied to sacral dermatomes outside the anal reflex area (see Fig. 37). While the α_2-motoneurons and γ-motoneurons showed a transient activity increase for about 2 seconds, the α_3-motoneurons with their polymodal afferent drive did not respond specifically. Also, oscillatory firing α_3-motoneurons (Fig. 24) showed little dynamic response. The one or two α_1-motoneurons which may be running through the dorsal S4 root were not activated. Mostly α_1-

motoneurons do not contribute to continence function. The very constantly oscillatory firing α_2-motoneuron O2 (Fig. 17B), innervating the external anal sphincter and activated by the constant drive of muscle spindle afferents and anal mucosa afferents induced by the positioned anal catheter, showed nearly no response to the touch. Upon pin-pricking, the α_2-motoneuron O2 fired further continuously oscillatory, but switched once from firing with 3 AP impulse trains to two AP firing and backwards. The α_2-motoneuron O1, activated later on to fire oscillatory upon urinary bladder filling (Fig.14), was not firing because of no bladder filling. Upon the pain application, motoneuron O1 fired once with 1AP (Fig. 17B).

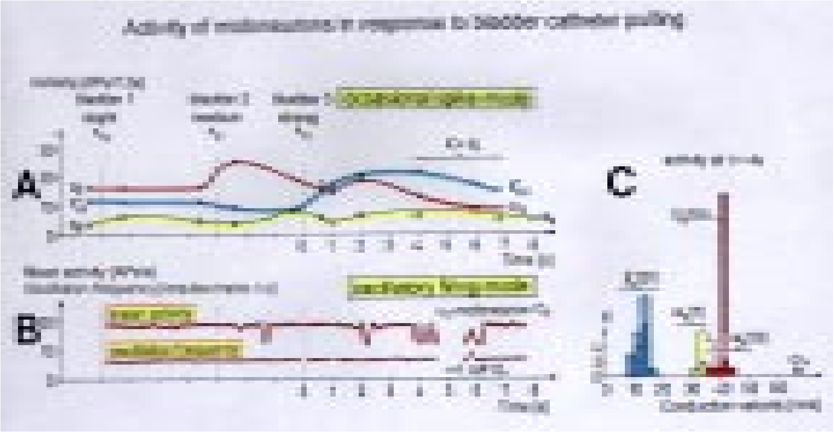

Figure 18
A,B. Activity of occasionally firing α_2, α_3, γ_1 and γ_2-motoneurons (A) and mean activity and oscillation frequency of oscillatory firing α_2-motoneuron O2 (B) in response to pulling the bladder catheter slightly, moderately and strongly. Note that in the case of a strong bladder catheter pulling the increased γ-activity lasted longer than the α_2-motoneuron activity, and this prolonged activity increase came from the γ_2-motoneurons (the higher activity of γ_2-motoneurons in comparison to the activity of γ_1 is indicated as $\gamma_2 > \gamma_1$). '1 AP O1' in B marks the appearance of 1 AP of sphincteric motoneuron O1. The α_2-motoneuron O2 stopped transiently firing oscillatory 5 s after strong bladder catheter pulling (B).
C. Conduction velocity distribution histogram of motoneuron activities at t = 4 s. Distribution peaks and ranges of single motoneuron types are indicated. The figures in the round brackets give the activities counted from open plus cross-hatched histogram parts (all conduction velocity values are used). The horizontally hatched part of the α_2-motoneuron peak indicates the activity from oscillatory firing α_2-motoneuron O2. The approximate number of activated motoneurons ($\alpha_2 = 8$, $\alpha_3 = 3$, $\gamma_{1,2} = 8$) was calculated from means of the cross-hatched parts of the histograms (each conduction velocity value only taken once). HT6; dS4.

Upon pulling the bladder catheter moderately or strongly (Fig. 18A,B), the occasionally firing α_2-motoneurons increased their activity transiently (for approx. 3 s) (A). The α_3-motoneurons may have shown a bit of a transient activity increase. The response of the γ-motoneurons seemed to be a mixture of excitation and inhibition. Following strong bladder catheter pulling (bladder 3), the prolonged response was due to the activation of also static γ-motoneurons ($\gamma_1 < \gamma_2$). The continuously oscillatory firing α_2-motoneuron O2, innervating the anal sphincter, responded more strongly to bladder catheter pulling (Fig. 18B) than to touch and pin-prick (Fig. 17). Because in most (but not all) people the urinary bladder function and the anal canal function inhibit each other, the strong bladder catheter pulling probably induced inhibition of the oscillatory firing α_2-motoneuron O2, so that the motoneuron reduced its activity by firing alternatingly with 2 APs and 3 APs and then even stopped oscillatory firing for one second. The α_2-motoneuron O1 fired once with 1 AP when the motoneuron O2 stopped firing (reciprocal response).

Fig. 18C illustrates an efferent conduction velocity distribution histogram based on the above measurements. For a comparable low activity, it is important to distinguish between the activity of occasionally firing motoneurons and that of oscillatory firing motoneurons (hatched horizontally, Fig. 18C).

Best would be to count the conduction velocity of each motoneuron in the summed impulse traffic of a nerve root only once (cross-hatched in C) which is somethimes roughly possible. For a high activation of nerve fibres, the separation of the oscillatory activity is not so important since the time interval within which the velocities are collected is short. Anyhow, for a detailed analysis of the afferent and efferent impulse traffic in a nerve root, including the identification of the nerve fibres also from conduction velocity distributions, one has to be careful when counting APs of the individual nerve fibres. Namely, if a fibre has a higher activity than another one, and its APs are therefore counted several times, the velocity distribution histogram (used to identify the fibre types) can be strongly biassed. A comparison with the components of compound APs may help (see Fig. 6) to identify group conduction velocities in critical cases, because with electrical stimulation each fibre will be excited only once (apart from rebound APs).

Upon anal catheter pulling (Fig. 19), the occasionally firing α_2-motoneurons increased transiently their firing, the γ-motoneurons decreased their firing, and the α_3-motoneurons showed no specific response. The oscillatory firing α_2-motoneuron O2 was strongly affected, it changed the impulse train length, the oscillation period and stopped oscillating several times. Obviously, the α_2-motoneuron O2 was adequately activated, and it may have been overactivated (inhibited) by its adequate afferent input from anal canal receptors. The α_2-motoneuron O1 fired once transiently oscillatory.

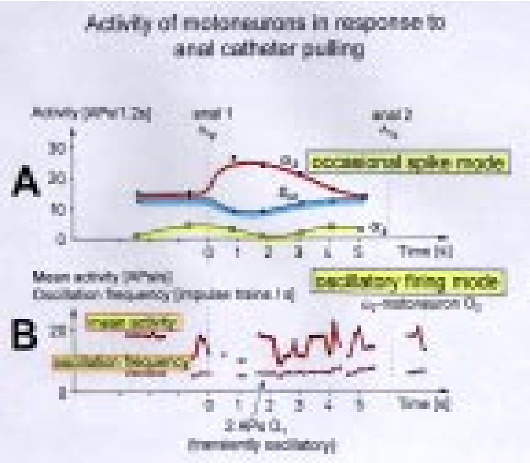

Figure 19
Activity of occasionally firing α_2, α_3 and γ-motoneurons (A) and mean activity and oscillation frequency of α_2-motoneuron O2 (B) in response to pulling the anal catheter, marked ‘anal 1’. ‘2 APs O1’ mark transient oscillatory firing of α_2-motoneuron O1, innervating the external bladder sphincter. The α_2-motoneuron O2 stopped firing oscillatory several times (B). HT6; dS4.

It is unclear, whether all motoneurons can fire oscillatory. In records from ventral sacral roots often many motoneuron axons fired oscillatory. Then, the problem arose that it was difficult to extract the firing patterns of single fibres because the template recognition was not safe and the summed rhythmic activity became too complicated for a separation on the basis of rhythmic firing patterns of single motor axons.

11. Mixed functions in dog sacral nerve roots

It has been shown that the conduction velocity distribution histogram for dog efferents is very similar to those of humans apart from the higher velocity values (Fig. 8). It should therefore also be possible to set up a precise classification scheme for the dog peripheral nervous system in analogy to the one in man. As has further been shown (Figs. 10,11), also the recruitment according to the size principle in each motoneuron group can nicely be measured.

The drawback with respect to rat, cat and dog recordings from nerve roots is that the anatomy of the spinal canal of those animals is different from that of man. Because of the ascensus of the human spinal cord and as man has no tail, the continence functions are mainly represented in the lower sacral nerve roots only, and they are not mixed with tail functions.

In the dog (and other animals), functions are mixed in the sacral nerve roots. Even though recruitment can nicely be measured in the dog, functions could not be identified so far in the measurements performed in the same way as in man (Fig. 2 of ref. [113]). Animal research certainly allows the use of additional invasive methods to split the functions conducted in the roots.

12. Need for improved classification schemes of the peripheral nervous system of animals

An improved classification and identification of peripheral nerve fibres in the rat, cat, dog, pig and monkey would be of great value, so as to enable a direct comparison of the human data with those of animals, to make use of the animal data in human research, and thus make patients also benefit from animal research. The classification schemes of Grundfest, Erlanger and Gasser, and Lloyd and Hunt [46,57,58,77], and the measurements of Boyd and Davey [13] on peripheral nerve fibres were brilliant for their times, but are insufficient for the present needs of measuring natural impulse patterns to get information concerning the self-organization of neuronal networks. In physics and mathematics, the basis for the resolution of new problems keeps improving. Often, the coordinate system is adjusted to the specific problem to be solved.

It is important to have a precise classification of peripheral nerve fibres by group conduction velocities, group nerve fibre diameters and impulse patterns as it would enable extraction of natural impulse patterns of several identified afferent and efferent fibres from the summed impulse traffic in nerve roots or nerves [110], so that the self-organization of CNS neuronal networks (at least in the spinal cord) can be analyzed under physiologic and pathophysiologic conditions.

13. Correlation between the activity of γ-motoneurons and secondary muscle spindle afferents

So far, the oscillatory firing of γ-motoneurons has not been observed under physiologic conditions. Following spinal cord lesion, the firing of the γ-motoneurons can become rhythmic (Fig. 37). Since α and γ-motoneurons are partly co-recruited in the occasional firing mode, it could be that the firing of some γ-motoneurons becomes more rhythmic if the α-motoneurons fire oscillatory and the α and γ-motoneurons are co-recruited for a certain function.

The γ-motoneurons drive muscle spindle afferents via the muscle spindles and a time lag of 400 ms has been measured upon natural stimulation (Fig. 20) [105], in accordance with the γ-loop scheme.

It will be shown below by the impulse patterns of single fibres (Fig. 32) and cross-correlations (Fig. 37,38) that α and γ-motoneurons and secondary muscle spindle afferents can have similar interspike intervals and similar phases in their firing (if harmonics are included), so that premotor spinal oscillators can build up an external oscillator loop (via the γ-loop) to the periphery. But we have to remember that the muscle spindles are included in a network of γ-motoneurons and spindle afferent connections: one γ-fibre may innervate several muscle spin-

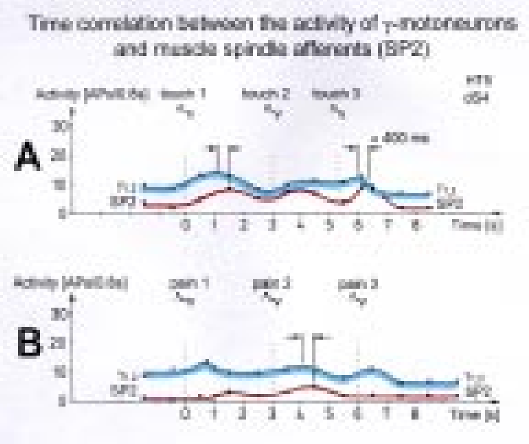

Figure 20
Time correlation between the activity of γ-motoneurons and secondary muscle spindle afferents in response to touch (A), marked 'touch 1, 2, 3', and pricking with a pin (B), marked 'pain 1, 2, 3', lower sacral dermatomes. The delay of the spindle afferent activity is indicated as 400 ms. HT6; dS4.

dles and one spindle afferent fibre will project onto many α-motoneurons. A single muscle spindle afferent fibre may even have several encoding sites [115]. It is therefore likely that the firing of many α and γ-motoneurons and spindle afferent fibres is relatively coordinated, as can nicely be seen when α-motoneurons fire oscillatory (Figs. 31-38).

14. Premotor spinal oscillators

So far, the firing of motoneurons in the occasional firing mode was mainly considered. The demonstration that neurons of the CNS (here motoneurons) can fire oscillatory and non-oscillatory (occasionally) (Fig. 14) is very important for the understanding of the functioning of the human CNS. To describe the functioning of the CNS merely by reflex pathways and loops or coupling of rigid oscillators (of cellular or network origin) is in contradiction to hard human data, namely that premotor spinal oscillators self-organize as was concluded from measurements of simultaneous natural impulse patterns of afferent and efferent fibres. In what follows, we shall concentrate on the oscillatory firing of motoneurons, which takes place for high activation.

For high and rather constant afferent input it was found that α-motoneurons fire repeatedly with impulse trains according to their type (Fig. 21). The α_1-motoneurons (FF) fire rhythmically at around 10 Hz (range 8 to 12) with an impulse train consisting of 1 AP; α_2-motoneurons (FR) fire at approx. 6 to 9 Hz with 2 to 5 APs per impulse train, and α_3-motoneurons (S) fire with a frequency in the range of 1 Hz and with long impulse trains consisting of up to 40 APs (and more) (Fig. 22) [107,118]. The rhythmic firing patterns of α-motoneurons are generated by probably local neuronal networks of the spinal cord since oscillatory firing can be recorded from motoneurons of the disconnected spinal cord. There is indication that the motoneuron is a part of the spinal oscillator [118]. The oscillation period (T) is roughly related to the number of action potentials (APs) per impulse train (nAP), and this can be expressed by the formula: T = 70ms + 30ms • nAP. A typical premotor α_2-oscillator fires with 3 APs every 160 ms (T = 70 ms + 30 ms • 3 = 160 ms), and can change its firing pattern to 2 APs every 130 ms for less activation or to 4 APs every 190 ms for higher activation.

It is assumed as a simplified working hypothesis that these spinal oscillators are organized by excitatory reverberatory loops of interconnected interneurons in the form of synfire chains [118,161] to which inhibitory interneurons essentially contribute because their inhibition time, 30 ms (rat) and 150 ms (cat) (page 103 of [162], [88]), falls within the range of the 30 ms building time block of the oscillation period and the oscillation period itself (160 ms) (see

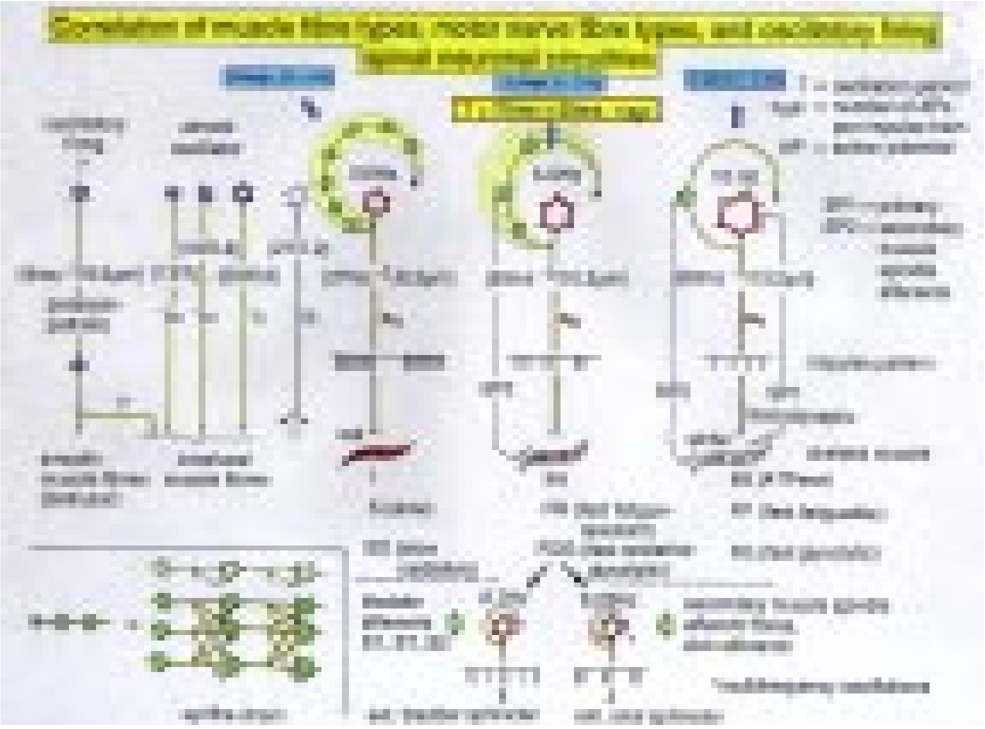

Figure 21
Correlation of muscle fibre types, motor nerve fibre types, and oscillatory firing spinal neuronal networks, based on histochemical, morphological and physiological characterization. This Figure shows a simplified correlation between muscle fibre, motoneuron and sacral premotor oscillator neuronal network types. The neuron chain loops of α_2 and α_3-oscillators have to be replaced by a neuronal network of recurrent excitation and inhibition of which the synfire chain is a simple example. No additional subtypes of motoneurons have been included. α = motoneuron; γ_1; γ_2 = dynamic and static fusimotors; parasympathetic = parasympathetic preganglionic motoneuron; S1, ST, S2 = stretch, tension and flow receptor afferents. α_2-Oscillators innervating the striated ext. anal sphincter show multifrequency oscillations (e.g., f = 5.25, 6.25, 7.7 Hz), as predicted mathematically. The dashed line neurons in the synfire chain, in the left lower part indicate the functional fringe of subthreshold excitation of the synfire chain. Frequency ranges of field potential oscillations from EEG (delta, theta, alpha) are indicated.

above). Premotor α_1-oscillators show little rhythmicity generated by small networks, whereas α_3-oscillators show much rhythmicity generated by a larger local subnetwork [118]. The oscillator loops consisting of chains of neurons (Fig. 21) are therefore only schematized network loops. This network loop seems to be rather continuous for α_3-oscillators, whereas the α_2-oscillator loop may show rather discrete subloops accounting for the firing with different impulse trains length (Fig. 21) and therefore different loop periods according to T = 70ms + 30ms • nAP. The network loop of an α_1-oscillator is more in the direction of a single neuron chain loop. The measurements give no direct information about the number of neurons contributing substantially to the self-organization of the spinal oscillators. But since α_2-motoneurons show multifrequency oscillation and α_3-motoneurons show a rather continuous change of the frequency (indicating rather complex local neuronal networks), one can speculate that the number of neurons contributing substantially to the oscillation may vary between a few (α_1-oscillators) and a few hundred (α_3-oscillators). The characteristic of α_2-oscillators to be

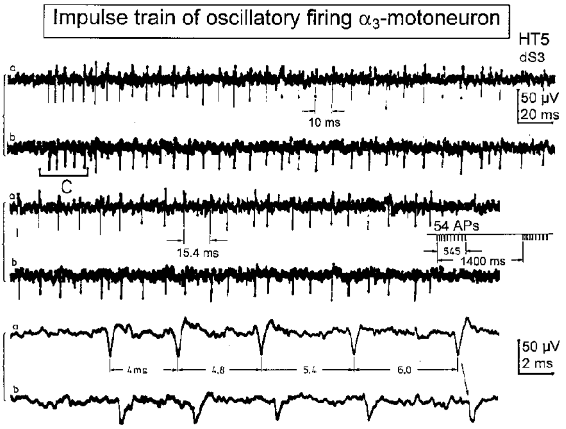

Figure 22
An impulse train (54 APs) of oscillatory firing α_3-motoneuron O3 of brain-dead HT5. ‘B’ is the continuation of ‘A’. The duration of the oscillation period was approximately 1400 ms (insert ‘B’). The start of the impulse train is shown time-expanded in C.

able to change their organization when activated also by the parasympathetic nervous system division (the number of driving phases changes from 2 to 3) [126] points also towards complex local oscillators, consisting of many neurons. The rhythmically firing of the local subneuronal networks (oscillators) is mainly coordinated, similarly as the whole neuronal network of the CNS, by the organization tedencies of the network, the descending impulse patterns and the spatiotemporal afferent impulse patterns (see below). The differences between the 3 premotor oscillator types will be considered now in more detail.

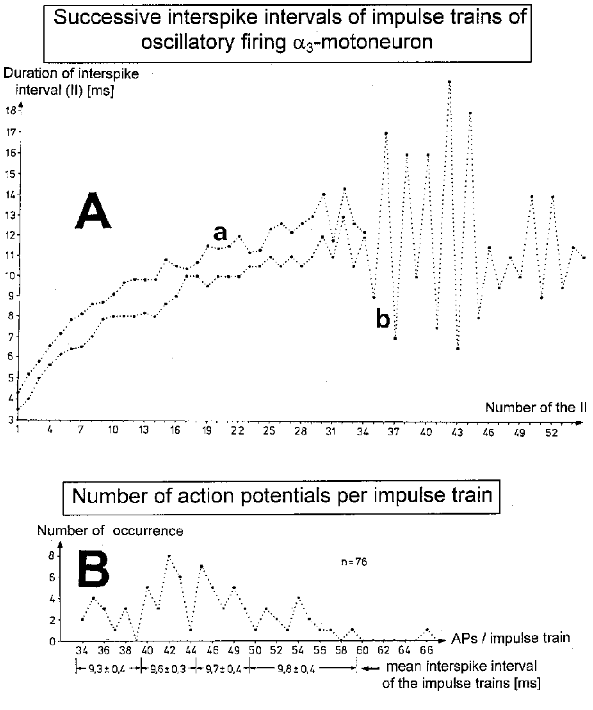

Figure 23
A. Interspike intervals (IIs) of successive APs of a short (a) and a long impulse train (b) of α_3-motoneuron O3. The large dots give the values of the IIs, and the dotted lines connect successive IIs. Note that the IIs from impulse train ‘b’ are very unequal from II 34 on. HT5; dS3 root.
B. Occurrence of APs per impulse train. The large dots give the numbers of how often an impulse train of a certain number of APs occurred; the dotted lines connect the values. Note that the AP numbers per impulse train do not follow a Gaussian distribution. The lower part of the Figure gives mean IIs for ranges of impulse train lengths.

α_3-oscillators

In Fig. 22, an original recording from an α_3-oscillator is shown. The insert in 'B' shows a schematic layout of the firing. The duration of the interspike intervals of the impulse train increases regularly at the beginning of the impulse train and does alternate between long and short values at the end of the impulse train. The firing with alternating long and short interspike intervals from the 30th AP on can be better seen in Fig. 23A. This long-short alternation of interspike intervals may be due to a coupling phenomenon between oscillators. The alternation becomes only visible at the end of the impulse train close to the threshold of excitability of the motoneuron. Alternating firing with short and long oscillation periods has been observed for α_2-oscillators (Fig. 14 of Ref. [127]), and may be connected with the existence of antagonistic inhibition of network structures similar to half-centre oscillators (see below, Fig. 41). If one measures the mean interspike interval of different parts of an α_3-impulse train (Fig. 23B), then the feature of alternating interspike intervals is lost.

The static behavior of α_3-motoneurons can also be seen when they fire oscillatory (and not only when they fire occasionally (Figs. 17-19)). In Fig. 24, the oscillatory firing α_3-motoneu-

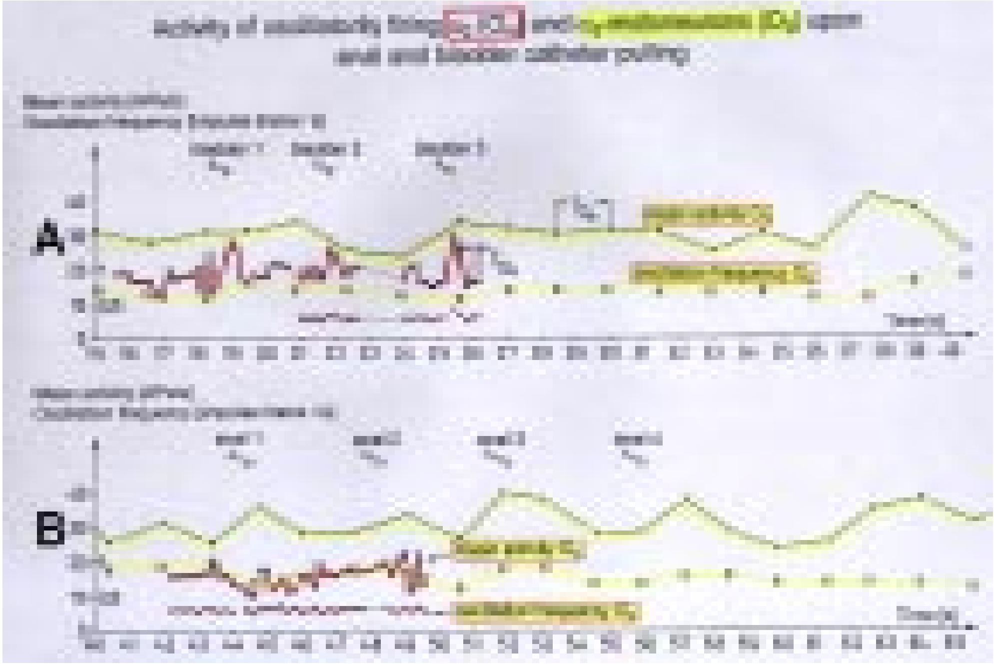

Figure 24

Mean activity (APs/s) and oscillation frequency (impulse trains/s) in response to urinary bladder (A) and anal catheter pulling (B) from oscillatory firing α_2-motoneuron O4 and α_3-motoneuron O3, recorded simultaneously. Dots = mean activity, crosses = oscillation frequency, large dots and crosses refer to α_3-motoneuron O3, the small ones to α_2-motoneuron O4. Values from α_2-motoneuron O4 only calculated for certain periods; the dashed lines indicate that the oscillation was not interrupted. The scale 0 to 1 relates to the oscillation frequency of α_3-motoneuron O3; scale 0 to 40 relates to the mean activity of α_3-motoneuron O3 and the mean activity and oscillation frequency of α_2-motoneuron O4. T(O3) and T(O4) mark oscillation periods. Dots and crosses mark the mean activity and oscillation frequency at the end of the oscillation cycle period. Lines connect discrete values of mean activity to make trends more obvious. The time and duration of the pulling of bladder and anal catheters are marked; repeated stimulation is marked with numbers. Time, in seconds, continuous. HT5, dS3 root.

ron shows only little or no specific reponse to natural stimulation like bladder or anal catheter pulling. The dynamics of the response is weaker in comparison to that of the oscillatory firing α_2-motoneuron. In Fig. 4 of Ref. [128], it has been shown that an α_2-oscillator responded still less dynamically than an α_1-oscillator. The dynamics therefore increases from α_3 to α_2 to α_1-oscillator, in accordance with the dynamics of responses of the α-motoneuron firing in the occasional firing mode and in accordance with the muscle fibre types the 3 types of α-motoneurons innervate. The slow (S), medium fast (FR) (fast fatigue-resistant) and fast contracting muscle fibres (FF) (fast fatiguable) have their own corresponding premotor networks in the spinal cord, namely the α_1, α_2 and α_3-networks (Fig. 21).

α_1-oscillators

With respect to dynamics, α_1-oscillators are the opposite of α_3-oscillators. The α_1-oscillators respond very dynamically, but have only little oscillator network properties. In Fig. 25 it can be seen that the firing of the α_1-motoneuron is absolutely correlated (Fig. 25C) to the firing of the primary spindle afferent fibre SP1. Each AP of the SP1-fibre is correlated to an

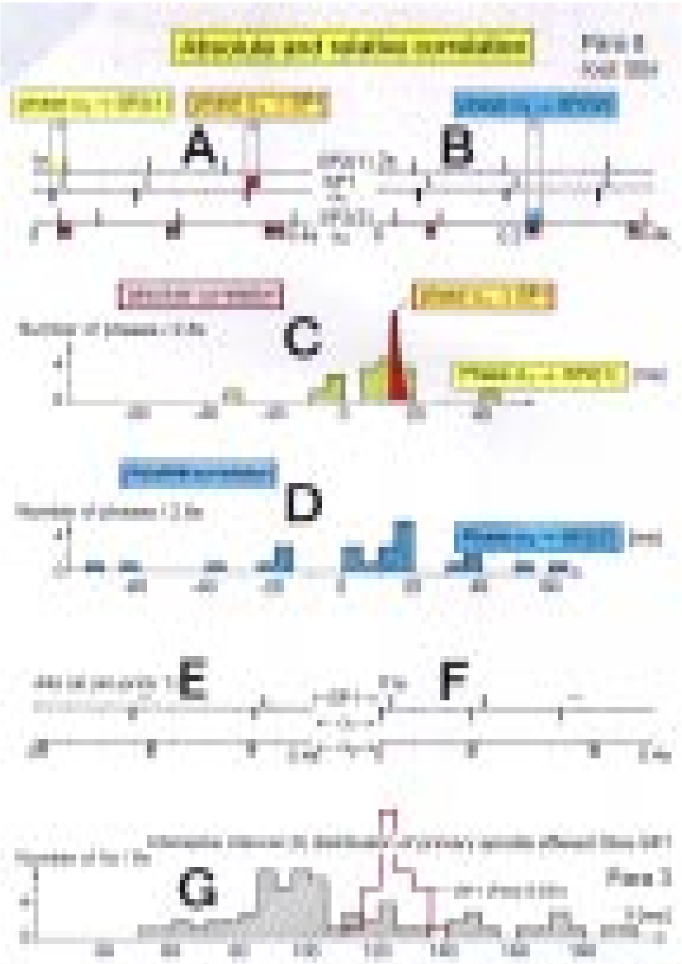

Figure 25
Absolute and relative correlation quantified by phase relations between the α_1 (FF) and α_2-motoneurons (FR) and their driving primary (SP1) and secondary (SP2) muscle spindle afferent fibres. A, B. Definition of the different phases. C. Distribution of the phases between α_1-motoneuron and the secondary muscle spindle afferent fibre SP2(1). Note that the phase distribution $\alpha_1 \rightarrow$ SP2(1) is approx. 40 times wider than that of the $\alpha_1 \rightarrow$ SP1 distribution (phase $\alpha_1 \rightarrow$ SP1 taken from [128]). D. Distribution of the phases between α_2-motoneuron and the secondary muscle spindle afferent fibre SP2(2). Note that the phase distribution $\alpha_2 \rightarrow$ SP2(2) is similar to that of $\alpha_1 \rightarrow$ SP2(1) (approx. 4 times wider). E, F. Note that every α_1-AP of the oscillatory firing α_1-motoneuron is accompanied by a time-locked SP1-AP. ‘A’-’F’ = para 8. G. Interspike interval (II) distribution for a primary spindle afferent fibre of paraplegic 3. Note that the distribution peak is at approx. 95 ms; probably, this fibre was driving an α_1-motoneuron with an average oscillation period of 95 ms. The SP1 fibre distribution for paraplegic 8 is included for comparison. Para 8; Para 3.

AP of the α_1-motoneuron. The SP1-fibre and the α_1-motoneuron fire rhythmically in absolute correlation (Fig. 25E,F), but the firing of α_1-motoneurons has also some correlation to secondary muscle spindle afferent activity: When the SP1-fibre stopped firing, the oscillatory firing α_1-motoneuron continued firing for one more oscillation period; in other words, it fired 1 further AP (Fig. 25F). The α_1-motoneuron could also start to fire before the SP1-fibre (Fig.

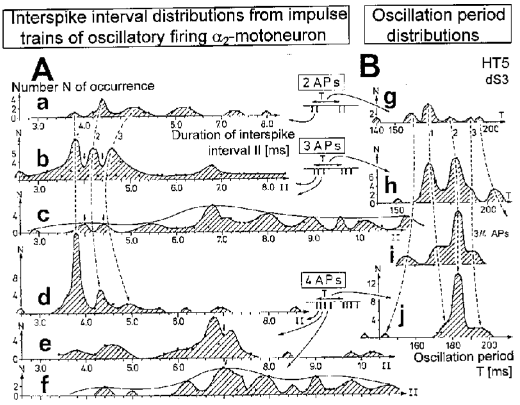

Figure 26
Interspike interval frequency distribution (A) and the corresponding oscillation period frequency distribution (B) for different lengths of impulse trains. The corresponding distribution peaks of the first interspike intervals and the oscillation period are connected by the dashed lines. The corresponding interspike interval peaks and oscillation period peaks are labelled in the same manner (1, 2 and 3) (b and g). Distributions of the second (c, e) and third interspike intervals (f) are also shown. The small arrows indicate opposite trends of occurrence between the first (b) and the second (c), and between the second (e) and the third (f) interspike intervals. HT5; dS3.

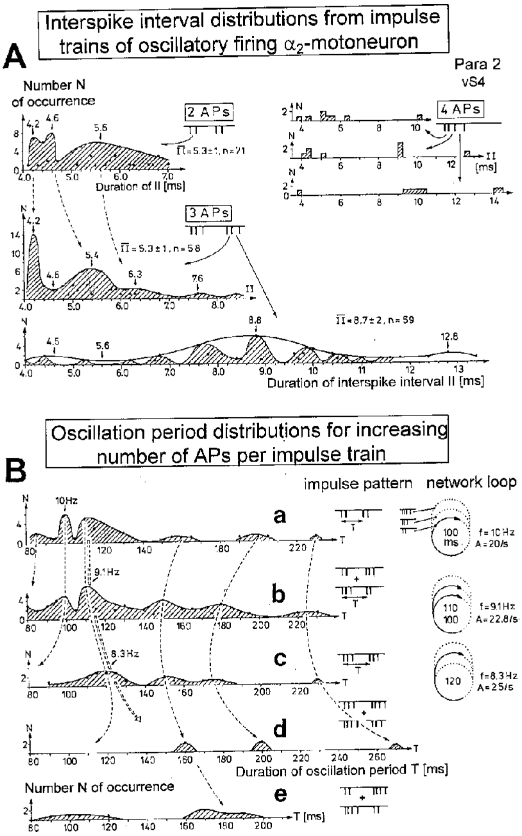

Figure 27
A. Interspike interval frequency distributions from impulse trains of oscillatory firing α_2-motoneuron O4. Owing to systematic errors, e.g. between even and odd values, enveloping curves were drawn. For impulse trains of 4 APs only histograms were plotted because of rare occurrence. The dotted lines mark the corresponding peaks in the occurrence patterns of the first interspike interval (II). Note that mean interspike intervals (II) provide only little information about the distribution of IIs. Two enveloping curves are drawn for the distribution of the second II.
B. Distributions of oscillation period frequencies: impulse train lengths of 2 APs (a), 2/3 APs (b), 3 APs (c), 3/4 APs (d) and 2/4 APs (e). The corresponding peaks are connected by the dashed lines. The double dashed line indicates mean shift of the distribution. A very simple loop interpretation is given for the increasing oscillation period at the right side of the Figure. Para 2; vS4.

25E), which means that the α_1-motoneuron was getting also drive from other afferents, probably secondary muscle spindle afferents as the α_1-motoneuron fired also in relative correlation with a secondary spindle afferent fibre (Fig. 25C, phase distribution $\alpha_1 \rightarrow$ SP2(1)). A simultaneously recorded oscillatory firing α_2-motoneuron fired oscillatory in relative coordination with a secondary muscle spindle afferent fibre (SP2) (Fig. 25D).

The weak oscillatory characteristic of the α_1-motoneuron (Fig. 25) can also be judged upon from its sharp (absolute) firing correlation with the SP1-fibre (~ 5ms) (Fig. 25C) in comparison to the wide range of oscillation periods of α_1-oscillators (~ 120 ms, very similar to Fig. 25G).

α_2-oscillators

The characteristics of α_2-oscillators are in between those of the α_1 and the α_3-oscillators. They are self-organized by the adequate afferent input patterns from several kinds of receptors. The α_2-oscillator O1 (Fig. 14) was e.g. organized from receptors sensing bladder filling and emptying (stretch (S1), tension (ST) and mucosal (S2) afferents). The α_2-oscillator O2 (Fig. 14) was organized at least by the activity from secondary muscle spindle afferents (SP2) and skin and mucosal afferents from the anal reflex area. The α_2-oscillators may have several rather discrete network loops (Figs. 21,28) and oscillation frequencies, and they do respond less dynamically than α_1-oscillators (Fig. 4, page 64 of [128]) and more dynamically than α_3-oscillators (Fig. 24).

The distributions of the occurrence of interspike intervals within the impulse trains (Figs. 26A, 27A) and of oscillation periods (Figs. 26B, 27B) provide information concerning the

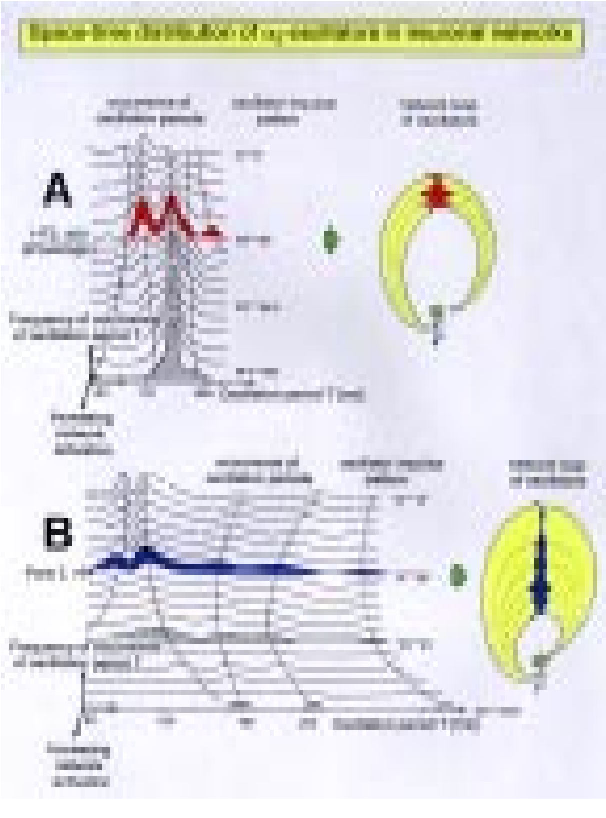

Figure 28
Space-time distribution of activated neuronal networks of α_2-oscillators from a brain-dead human (HT5; dS3) (A) and following spinal cord lesion (Para 2; vS4) (B). The oscillation period distributions for different impulse lengths were taken from Figures 26 and 27 and interpolated so that the frequency of occurrence of the oscillation period be obtained in dependence on increasing network activation (the activity of an oscillator increases with the increasing impulse train length, as can easily be calculated). The frequency of the occurrence for a medium impulse train length was used to draw schematically the network loops of an oscillators in brain-death and in paraplegia (right side of the Figure). The network loops give the impression of probabability distributions of excitation in neuronal networks. Note that in paraplegia, the activated network loop is much more space-time distributed, as if lateral field inhibition were missing.

organization of the neuronal networks of the medulla. The shape of the distributions of the interspike intervals shows similarities to coupling properties of mechanical oscillators (coupled pendulums). Also, similar subpeaks in oscillation period distributions of different motoneurons indicate rhythm coupling between oscillators (compare Fig. 12C of [127] (α_2-oscillator) with Fig. 1C,G of [128] (α_1-oscillator)). The shift of the corresponding distribution peaks in oscillation period distributions with the increasing oscillator network activation (increasing impulse train length) suggests the existence of several rather discrete network loops of α_2-oscillators (Figs. 26B, 27B). Such oscillator loop distributions are pictured on the right side of Fig. 28. Interpolation of the oscillation period distributions of Figs. 26,27 shows how the excited network loops shift with increasing excitation (Fig. 28).

The network loop of the α_2-oscillator of the neuronal network caudal to a spinal cord lesion is more distributed than that of a brain-dead human, indicating a widening of the network loops (further spread of the excitation), and is in connection with the loss of phase and frequency coordination (see below), an indication for the loss of specificity of oscillator properties due to the loss of supraspinal control including descending inhibition.

14 A. Similar frequencies of premotor spinal oscillators and field potential oscillations in the cortex

The frequencies of field potential oscillations in electroencephalography (EEG) [145] are very similar to those of the premotor spinal oscillators. The frequencies within the delta range (0.4 to 4 Hz) are similar to those of α_3-oscillators (0.4 to 4 Hz), those within the theta range (6 to 7 Hz) are similar to those of α_2-oscillators (6 to 9 Hz), and the α-activity (8 to 12 Hz) is similar to the frequency of premotor spinal α_1-oscillators (8 to 12 Hz).

The high frequency oscillations in the EEG recordings in the β (15 to 30 Hz) and γ range (30 to 60 Hz) have so far no counterpart in the premotor neuronal network of the spinal cord. But the oscillations measured in EEG recordings are changes in field potentials, whereas the measured oscillations of the premotor spinal oscillators are rhythmic activity of individual nerve cells (motoneurons) of the CNS. Moreover, the natural impulse patterns of single neurons provide more information on the functioning of the human CNS than do frequency ranges in a Fourier spectrum. A typical α_2-premotor spinal oscillator fires every 160 ms (= oscillation period T) with an impulse train of 3 APs. The oscillation period of 160 ms is most likely generated by the local neuronal network (the loop (as one possibility) time is 160 ms) whereas the 3 AP impulse train with interspike interval durations of 4.6 and 7.4 ms is most likely generated in the motoneuron itself (a longer depolarizing pulse excites the motoneuron to fire repetitively (with an impulse train) [107]). Therefore, the directly measured natural impulse pattern provides structural information; the interspike intervals of the impulse train of 4.6 and 7.4 ms duration provide primarily information concerning the membrane properties of the activated motoneuron, and the oscillation period of 160 ms provides primarily information concerning the network properties of the oscillatory firing cell assembly. And of course, the natural impulse patterns of motoneurons can be compared with the natural impulse patterns of afferents, and the changing phase relations between motoneurons and afferents can be analyzed to provide clues for an analysis of integrative CNS functions. Fourier analysis provides mixed information concerning rhythmicity of network properties and membrane properties of neurons. When analyzed using Fourier analysis, the membrane properties of the motoneuron, giving rise to the interspike intervals of 4.6 and 7.4 ms of the impulse train, suggest rhythmic network or single neuron firing in the range of 22 and 14 Hz, even though these frequencies do probably reflect the rhythmicity of repeated firing of the depolarized motoneuron membrane. Therefore, direct analysis of natural impulse patterns provides more information concerning the structure of the neuronal network of the human CNS than does Fourier analysis.

Spontaneously occurring field potentials appear to follow the rule that the amplitude of the fluctuations decreases with the increasing frequency of oscillations. This suggests that rapidly oscillating cell assemblies comprise fewer neurons than slowly oscillating assemblies [145]. The same conclusion was arrived at with the formula for the oscillation period of premotor spinal oscillators $T = 70\text{ ms} + 30\text{ ms} \bullet n_{AP}$ (n_{AP} = number of APs per impulse train), namely that the premotor spinal α_1-oscillator (10 Hz) comprises fewer building blocks of T, and therefore interneurons [107] than α_2 (6-9 Hz) and α_3-oscillators (0.4-4 Hz) if one assumes that the oscillation period in the local neuronal network is generated by a series of neurons connected to a reverberatory loop (Fig. 41A), of which the motoneuron is a part (Fig. 21).

Since there is similarity in the frequencies of oscillatory firing cell assemblies of the most caudal CNS (premotor spinal oscillators of the conus medullaris) and the rostral CNS (cortex), and the oscillatory firing cell assemblies are most likely quite different (there are no motoneurons in the cortex), the similarity of the frequencies of the spinal cord and the cortex may indicate rhythm coupling as a coupling or activation mechanism of the spinal cord by the cortex. Relative coordination, with synchronization as the simplest type of coordination, may be used throughout the CNS for self-organization. It should be simultaneously recorded from the cortex (EEG) and from muscles (EMG) during coordinated movements, to see whether there are phase relations (relative coordination) between the firings of single motor units and the changes of the field potential.

15. Natural afferent impulse patterns from the skin

The neuronal networks of the spinal cord do self-organize by the natural impulse patterns from the receptors in the periphery (in spinal cord lesion) and from supraspinal centres (physiologically both contributions). It is difficult to say whether the networks adapted their self-organization to the impulse patterns of the receptors of the periphery or whether, during phylogenesis or ontogenesis, the receptors adapted their firing to the needs of the neuronal network. Nevertheless, it is obvious that the natural firing patterns of the afferents and their space-time distributions give rise to the self-organization of the neuronal networks, and are therefore of utmost importance for the understanding of the functioning of the CNS. Such parameters are difficult to measure.

To make a conclusion on the organization and reorganization of neuronal networks from the wiring of the neurons (see in [3]) is risky, because one would need to know, for example, the efficacies of the excitatory and inhibitory synapses (LTP, LTD), the membrane properties of local critical areas of neurites, and how membrane properties change with learning and reorganization following CNS lesion.

Two original recordings of simultaneous skin afferent patterns of 14 and 22 receptors are shown in Fig. 29. The summed natural firing patterns upon touch (Fig. 29Ea) are split and are schematically drawn in Fig. 29Eb, and those upon pin-prick (Fig. 29A-D) can be seen in Fig. 29F [106,111]. Below we shall discuss the fact that the spatio-temporal touch afferent patterns give rise to a self-organized network state subserving anal continence, whereas additional activated pain afferents stimulate a network state inducing an escape and protection response.

Electrostimulation of nerves in patients cannot mimic such spatio-temporal impulse codes elicited by natural stimulation, and will give rise to non-natural neuronal network organization of the CNS. When performing electrostimulation in patients, it should be therefore clear what network states are about to be activated in the CNS and how the artificial patterns differ from the natural impulse patterns.

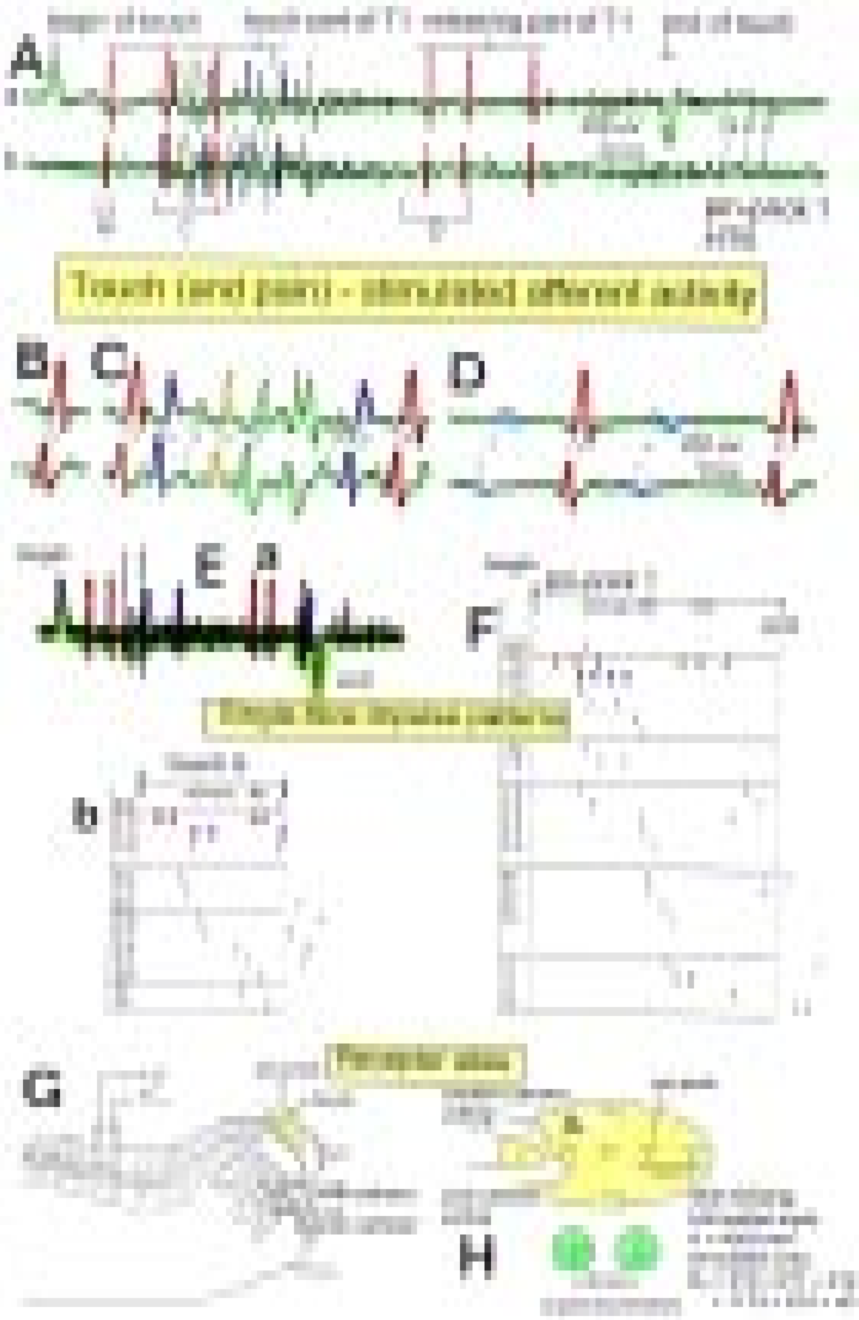

Figure 29 Touch (and pain)-stimulated afferent activity. Touch and pain activity stimulated by pin-pricking (A) and touching (Ea) at S5 or Co dermatomes and recorded extracellularly from a dorsal coccygeal root (brain-dead human HT6). T1, T2, T3, T4, P = mark action potentials (APs) from single touch and pain fibres. Subscripts 1, 2, 3 mark single fibres. A. Whole sweep following pin-prick 1 shown at a slow time base. The large upward artifact on trace 'a' marks electronically the beginning of the pin-prick. The large downward artifact on trace 'a' marks the end of the pin-prick. Note that 2 intervals of high activity of large APs occur, one after the beginning of the pin-prick with 1 AP in front, and a second before the end of the pin-prick; potentials with small amplitude follow potentials of large amplitude. Time intervals B, C and D are shown in a time-expanded form in B, C and D. B, C, D. Time expanded sweep pieces of A. Identified APs are indicated. Note that the APs from the $T1_1$ touch unit can be safely identified by the waveforms in B, C, D. Eb, F. AP occurrence patterns of single touch and pain fibres following short touch 6 and pin-prick 1. No pain afferents are stimulated upon touch 6. Upon pin-prick 1, the single-fibre AP activity of the different touch and pain groups is identified by the AP waveforms

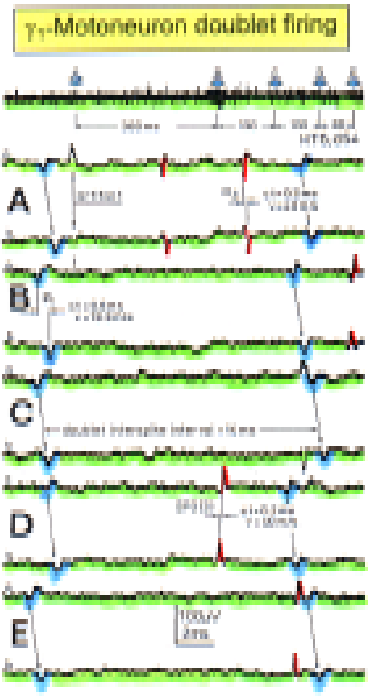

Figure 30

Doublet firing from a single γ_1-motoneuron (intrafusal, dynamic). From the sweep on the top of the Figure, successive AP doublets are shown on an expanded time scale in A to E. Conduction times (ct), conduction velocities (V), a doublet interspike interval and interspike intervals from doublet to doublet are indicated. An artifact (A) can clearly be distinguished from real action potentials by the mirror picture potentials and the missing of the conduction time. HT6, dS4.

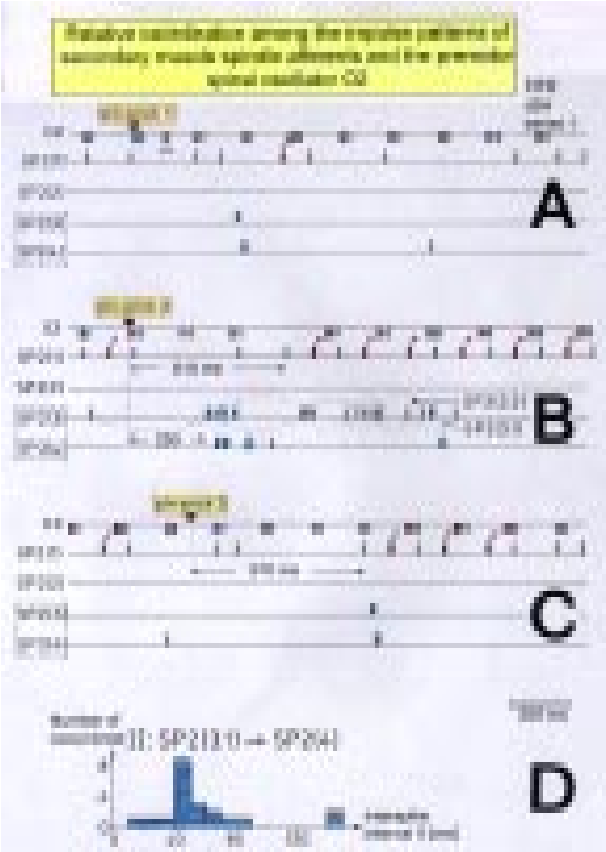

Figure 31

Impulse patterns of simultaneously recorded secondary muscle spindle afferent fibres (A, B, C) following pin-prick. Each bar represents an AP; upward = afferent, downward = efferent. In B, the activity from 2 single endings (SP2(3.1) and SP2(3.2)) is marked by dotted lines. The small arrows indicate similar time intervals between muscle spindle afferent APs and motoneuron O2 APs. D. Interspike interval distribution between SP2(3.1) and SP2(4)-fibres (cross-correlation). Since there is relative phase coordination between fibres SP2(3.1) and SP2(4) fibres, the spindle afferents may belong to the same spindle (indicated in A,B,C by the dashed box), or fibre SP2(4) belongs to a spindle which is in tandem with the spindle of fibre SP2(3) or the spindles of the two fibres are innervated partly by the same γ-motoneurons. HT6; dS4.

on traces ‘a’ and ‘b’, and by the conduction times. The single touch afferents of the T1 group are marked with subscripts. One active secondary muscle spindle afferent fibre (SP2) could always be identified in F. Note that for pin-prick 1, touch and pain afferents are stimulated whereas for touch 6 only touch afferents. G. Recording and stimulation arrangement for simultaneous recording of several single touch and pain units. A = area stimulated by skin folding, drawn in H in more detail. $T1_1$, $T1_6$ = suggested touch points of the $T1_1$ and $T1_6$-units. H. Drawing of the very approximate skin area stimulated by skin folding. $T1_{1\text{-}6}$ = suggested focal T1 touch points. Two-point discrimination indicated for the sake of comparison. N_A = number of stimulated units in the dorsal coccygeal root. Skin tractions evoked by anal and bladder-catheter pulling are indicated by the large open arrows.

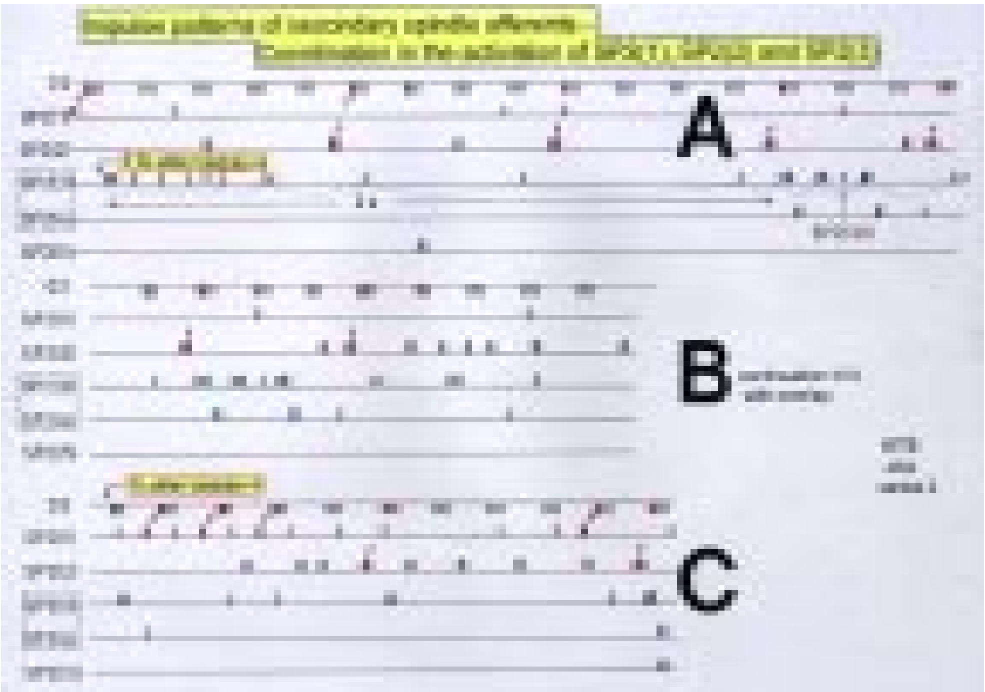

Figure 32
Impulse patterns of the 5 secondary muscle spindle afferent fibres SP2(1) through SP2(5) in relation to the impulse pattern of oscillatory firing α_2-motoneuron O2 following bladder catheter pulling. Bars represent APs. Very short IIs (as in doublets) are not drawn to scale; only the first APs are in their exact position. The dashed rectangle around SP2(3) and SP2(4) indicates that both afferents probably innervate the same spindle. The dotted curves, connecting certain APs of the SP2(3) activity, most likely represent the activity from single endings. Note that doublet firing occurs in spindle afferents SP2(2), SP2(3) and SP2(5); the doublet firing builds up in fibre SP2(3) from A (no doublet firing) to C (rather doublet firing). Note further the more static behavior of fibre SP2(4) in comparison to fibre SP2(3)(delayed response, lower activity changes); fibre SP2(4) may be a tertiary spindle afferent fibre. The small arrows indicate similar time intervals from the afferent APs to the motoneuron APs (phase coordination). HT6; dS4.

In basic research, it also should be borne in mind that artificial electrostimulation patterns give rise to artificial neuronal network organization of the CNS. Electrostimulation is therefore not very suitable to analyze natural integrative functions of the CNS.

16. Natural firing patterns of proprioceptive afferents and α and γ-motoneurons measured simultaneously, and the phase relations between them

Original recordings of the oscillatory firing of α-motoneurons are shown in Figs. 34,35. An original recording of the natural firing patterns of α γ-motoneuron is shown in Fig. 30 [121]. The γ-motoneuron in Fig. 30 was firing with doublets, which makes it possible to safely identify the single fibre APs. The doublet-firing of secondary muscle spindle afferents, and probably γ-motoneurons is correlated with the activation of the parasympathetic division [125]. The significance for the network organization is not known.

Schematic natural impulse patterns of secondary muscle spindles afferents are shown in Fig. 31 together with those of the oscillatory firing of the α_2-motoneuron O2. For original recordings of secondary muscle spindle afferent activity, see Figs. 34-36 [115,121]. The secondary muscle spindle afferent fibre SP2(1) (Fig. 31A,B,C) fires in relative phase coordination with the impulse trains of motoneuron O2, and contributes therefore to the self-organization and drive of the α_2-oscillator O2. The spindle afferents SP2(2) through SP2(4) do not, or only little contribute to the drive of the oscillator. It can be seen in Fig. 31A,C that the secondary spindle afferent fibres SP2(3) and SP2(4) fired in relative phase correlation. The cross-correlation diagram (Fig. 31D) shows that there is a relative phase coordination of ~ 42 ms between the firings of the two spindle afferents. The dotted lines in Fig. 31B indicate the firing patterns from single encoding sites of the secondary spindle afferent fibre SP2(3) (SP2(3.1); SP2(3.2)). It is obvious that there is a lot of relative phase coordinations between the firings of the secondary spindle afferents (including their single encoding sites), α-motoneurons and γ-motoneurons (see below; Figs. 33,38B).

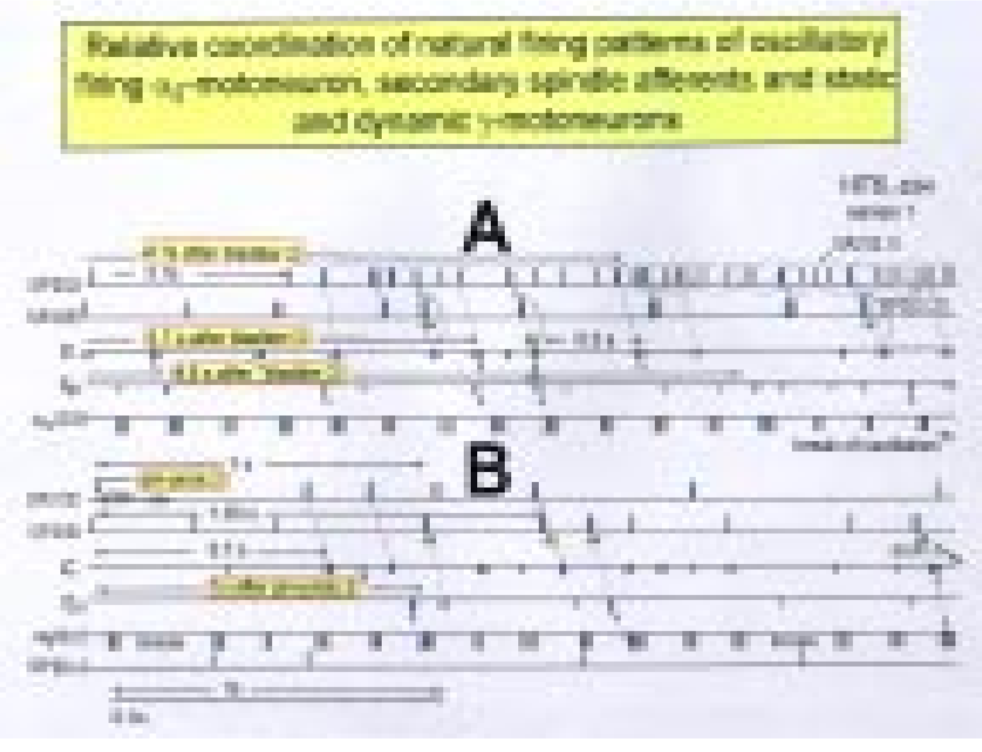

Figure 33
Impulse patterns of simultaneously recorded γ-motoneurons (γ_1 and γ_{21}), secondary spindle afferent fibres (SP2(2), SP2(4), SP2(5)) and oscillatory firing α_2-motoneuron O2 following bladder catheter pulling (bladder 3) (A) and pin-prick 2 (B). B was recorded before A. In A the impulse patterns of the 2 encoding sites SP2(2.1) and SP2(2.2) of the single parent fibre SP2(2) are indicated by the dotted curves. Times to the activity increases of γ-motoneurons and secondary spindle afferents following stimulation are indicated. Similar time intervals of the occurrence of γ-motoneuron APs and SP2(5) fibre APs (phase coordination) are indicated by the open arrows, and the similar time intervals of γ-motoneuron APs and α-motoneuron APs are indicated by small arrows. Similar time intervals of the APs of fibres SP2(2) and SP2(5) are indicated by the double dotted lines, those of γ_1-APs and the SP2(2) fibre APs by a dotted line, and those of γ_1-APs and the SP2(2)-SP2(5) correlation by a curved dashed line. HT6; dS4.

Following stimulation of the parasympathetic division by pulling the urinary bladder catheter, the secondary spindle afferents SP2(2), SP2(3) and SP2(5) switched partly into the doublet firing mode (Fig. 32). The interspike interval distribution of the SP2 afferent doublets overlaps within 9 to 14 ms with those of γ-doublets (Fig. 5 of [125]).

During the recording time of the impulse patterns shown in Fig. 31 only the SP2(1)-fibre contributed substantially to the drive of the spinal oscillator O2 (apart from non measured activity of afferents running through other roots). At a later point during the recording, shown in Fig. 32, there also was a contribution from SP2(2)-fibre. The activity and the regularity of the oscillatory firing of motoneuron O2 increased with the additional drive from SP2(2)-fibre as can be seen from a comparison of the impulse patterns of Fig. 31 and Fig. 32.

Fig. 33 shows schematic natural simultaneous impulse patterns of a static and a dynamic γ-motoneuron, two secondary muscle spindle afferents and the oscillatory firing α_2-motoneuron O2. The small arrows and the dotted lines indicate relative phase coordinations between the static and the dynamic γ-motoneurons and motoneuron O2, and between γ-motoneurons and secondary muscle spindle afferents. The dashed-circle line indicates a phase relation between the APs of the dynamic γ-motoneuron (γ_1) and the cross-correlation between SP2(2)-fibre (single ending 1 of the mother fibre) and SP2(5)-muscle spindle afferent fibre. Including the phase relations between the firings of secondary muscle spindle afferents and the oscillatory firing motoneuron O2 we obtain interlaced loops of coordinations between the firings of γ-motoneurons and secondary muscle spindle afferents, and between secondary spindle afferents and α-motoneurons and between α-motoneurons and γ-motoneurons (co-activity of α and γ-motoneurons). It becomes obvious from the correlations between the natural impulse patterns (including those of single encoding sites of spindle afferents) that the γ-loop is not a single loop, but a network of loops, because of the divergent projections of γ-motoneurons onto muscle spindles and the probably divergent and convergent projections of secondary muscle spindle afferents into the neuronal network of the spinal cord, consisting of α and γ-motoneurons and interneurons.

Two phase relations have been observed to occur mostly between the APs of the secondary muscle spindle afferents and the oscillatory firing motoneuron per one oscillation period (Fig. 5 (p.103) of [130], Fig. 38Ba). The two phase relations per oscillation period are in accordance with the ‘in phase’ and ‘antiphase’ movement in coordination dynamics of fingers, arms and legs (see below).

17. Phase and frequency coordination between oscillatory firing α_2-motoneurons and their adequate afferent drive

The relative phase and frequency coordination between the APs of the oscillatory firing α_2-motoneuron O2 and the secondary muscle spindle afferent fibre SP2(1) has partly been shown in Figs. 31 through 33, and can directly be seen in the original recordings in Fig. 34. The firing of the oscillator and the sweep pieces which are shown time-expanded are indicated at the summary trace. Fig. 34B,C shows the AP-impulse train of oscillator O2 in connection with one of its driving spindle afferent AP. Because of the duration of the phase relation of around zero milliseconds between the firing of the driving SP2(1)-fibre and the impulse train of the oscillatory firing motoneuron O2, the SP2(1)-fibre AP (every second AP) appeared at a similar time as the impulse train. Because the AP of the spindle afferent fibre had a characteristic waveform, it was easy to extract its impulse pattern from the summed impulse traffic of this S4 dorsal root. During touch-induced skin afferent activity (Fig. 34A), the activities of the motoneuron and the spindle afferent fibre were covered by the skin afferent activity. After the cessation of the skin afferent activity the afferent and efferent APs were found again at their expected time positions of the regular firings. The phase coordination between the firings of the oscillatory firing motoneuron O2 and the secondary muscle spindle afferent fibre SP2(1) at the time when records B,C were taken, was 1.6 ms (3 ms - 1.4 ms, Fig. 34B,C). In Fig. 34D, the relative frequency coordination between the firings of the SP2(1)-fibre and the impulse train of the oscillator is indicated. For the time period evaluated, the correlation between the firing of the motoneuron and the spindle afferent fibre was in the range of between 3 and 5 ms (Fig. 34D). The fact that neurons fire in a relatively coordinated way of up to a few milliseconds will be used (see below) to reorganize the lesioned CNS by re-learning phase and frequency coordination between neuron firings when exercising movements coordinated with an exactness of up to a few milliseconds, using a special coordination dynamic therapy device, i.e. by instrumented supervised phase and frequency re-learning (Figs. 50; 68G, H; 80D; 82B, C; 89B, D; 92C, D; 109; 111; 113; 117).

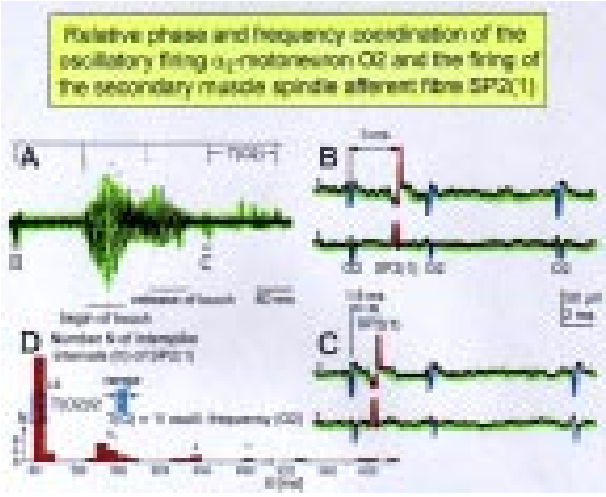

Figure 34
Time relation between the occurrence of the action potentials (APs) of oscillatory firing α_2-motoneuron O2 and the firing of the secondary muscle spindle afferent fibre SP2(1). HT6, S4 dorsal root recording.
A. Overall view of the used sweep piece; only trace ‘a’ shown. Four oscillation cycle 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 digitization. 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). Digitization 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).

In Fig. 35, considerations concerning the relative frequency coordination are extended to the activity of further afferent fibres and γ-motoneurons of the same root. Fig. 35G shows sweep pieces of the original recordings; 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

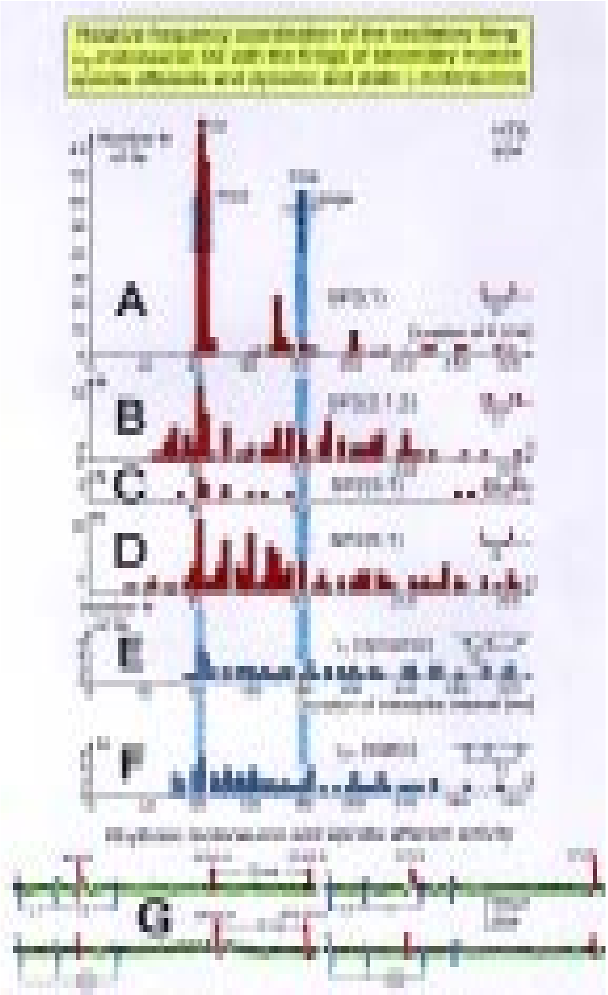

Figure 35
Interspike interval distributions of single endings of four secondary muscle spindle afferents (SP2) and two γ-motoneurons, recorded simultaneously. In A, the oscillation period TO2 (impulse train length = 3 APs) with its range of simultaneously recorded oscillatory firing α_2-motoneuron O2 (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 shortest interspike interval, nearly identical with 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.

frequency or the first harmonic of the oscillator). Also, γ-motoneurons showed only little frequency correlation at that time period.

Fig. 36 shows the interspike interval distributions of more afferents (including the afferents for bladder filling) of another root, together with the oscillation period range (and the half of it) of a second α_2-oscillator (O1). By comparing the oscillation periods and their ranges (their halves) with the interspike interval distributions of the afferents, it can be suggested which afferents made a (frequency coordination) contribution to the drive of what oscillator at that time interval. For example, the S1(1) urinary bladder afferent fibre activity contributed to the drive of oscillator O1 (activating the external bladder sphincter) because its interspike interval distribution overlaps with the range of the oscillation periods of O1. But the S1(1) distribution does not overlap with the range of the oscillation periods of oscillator O2, or with their halves or quarters. The S1(1) afferent fibre will therefore not have made a substantial contribution to the drive of oscillator O2. On the other hand, the secondary muscle spindle afferent fibre SP2(12) activated oscillator O2 innervating the external anal sphincter, since its interspike interval distribution overlaps with the range of O2 oscillation periods. But the secon-

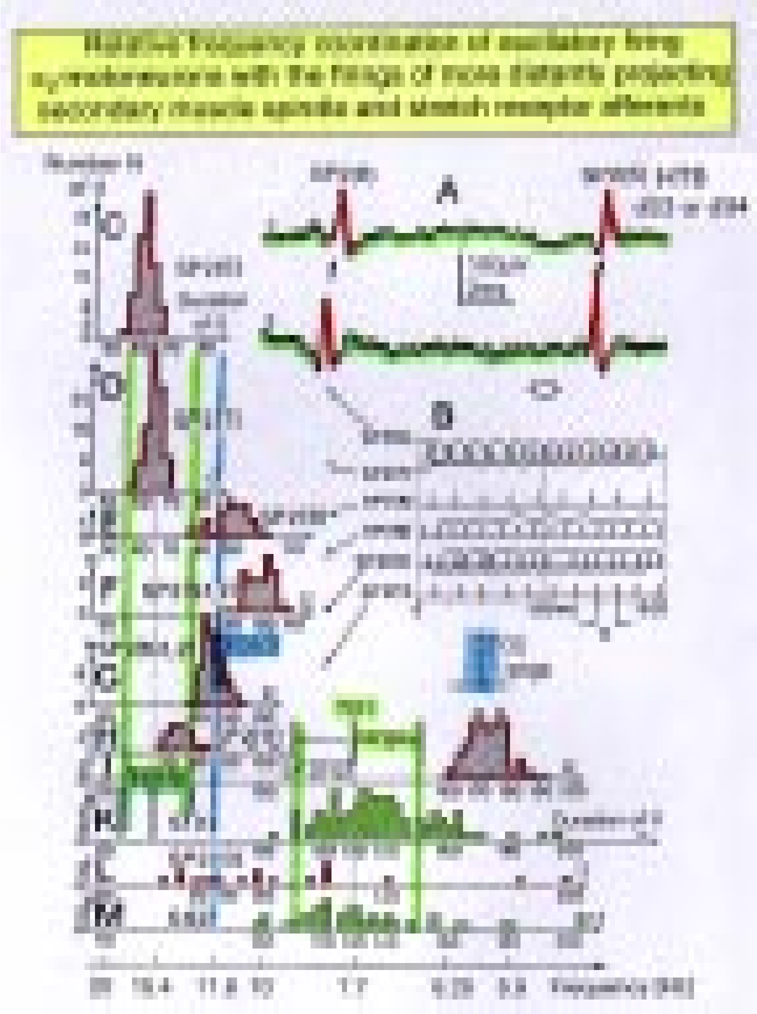

Figure 36
Measurements from brain-dead human HT6 from different spinal cord segments after retrograde bladder filling (700 to 800 ml), with the exception of ‘I’, which was obtained before filling. A. Sweep trace of a recording from a dorsal S3 or S2 root filament. It can be seen that the secondary muscle spindle afferent SP2(6) AP can be distinguished by the wave-form on the two traces from the secondary spindle afferent fibre SP2(8) AP (different amplitude of the three phases of the triphasic APs). B. Simultaneously recorded impulse patterns of the six parent secondary spindle afferents SP2(6) through SP2(11) obtained from dS3 or dS2 root recordings. The impulse patterns of SP2(6) and SP2(7) fibres are not separated to show the similarity of the patterns. The impulse patterns of the parent spindle afferents SP2(9) and SP2(10) are split into patterns of the single endings (single ending activity partly connected by circle lines) with the assumption that single endings of parent secondary muscle spindle afferents should have interspike intervals of duration longer than 50 ms. C to H. Interspike interval distributions of six simultaneously recorded single secondary spindle afferent endings. F, G. Interspike interval distributions of parent fibres, which are the sums of the distributions from the two activated endings. I. Interspike interval distributions of a secondary spindle afferent fibre (SP2(12)) of a coccygeal root. K, L, M. Interspike interval distributions of single-fibre afferent activity from a lower sacral dorsal root. In 4L, most likely the activity from a secondary spindle afferent fibre is shown. In K and M most likely the interspike intervals from afferents (S1(1) and S1(2)), innervating stretch receptors of the urinary bladder wall, are shown. In G, H and K, the durations of the oscillation periods (mean and range) of the oscillatory firing α_2-motoneurons are indicated by thick dashed and dotted lines; the motoneurons innervate the external anal sphincter (TO2) and the external bladder sphincter (TO1). The sites of innervation of the oscillatory firing motoneurons are identified (and distinguished from each other) by anal reflex stimulation, bladder filling and catheter pullings. Note that the TO1 and TO2 ranges and their halves overlap with the interspike interval distributions of the secondary spindle and stretch receptor afferents (relative frequency coordination).

dary muscle spindle afferent fibre SP2(12) did not activate oscillator O1, as its interspike interval distribution does not overlap with its oscillation period range or the half of it (Fig. 36).

By comparing interspike interval distributions of afferent fibres with oscillation period distributions it can be estimated what afferents made a (frequency coordination) contribution to the drive of the spinal oscillators. These considerations need no knowledge of the connectivity of the neuronal networks.

In the frequency coordination between the firings of afferents and oscillators and among oscillators, entrainment or coordination may occur sub- or superharmonically. The energy transfer, and therefore the coupling strength will be smaller if the APs coincide in their firing less often. As indicated by our measurements, the coupling and the relative coordination during the self-organization of the neuronal networks of the human spinal cord 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.

18. Relative phase and frequency coordination of α and γ-motoneurons, and the 'Magnet-Effect'

When two oscillatory firing local subnetworks with slightly different freqencies reduce their frequency difference in the way that one rhythm accelerates and the other one decelerates to achieve a favoured integer relationship between the period durations, it is called relative coordination according to E. v. Holst. Such 'Magnet-Effect' has been observed by R. Jung [60] with different tremor frequencies, and will be shown here for the rhythmic firing of motoneurons, measured with the single-fibre action potential recording method.

In Fig. 37B, the synchronization of the firing patterns of two α-motoneurons and one γ-motoneuron and two secondary muscle spindle afferents is shown (dotted rectangles) following pin-pricking (pp 6) inside the anal reflex area (dotted line area). The durations of the oscillation periods of the two α-motoneurons differ from each other by the integer number 3 (~ 100 ms and ~ 300 ms) (Fig. 38A). Following pin-prick 1-5 (20-24s), the frequency distributions of the α_3 and γ_1-motoneuron moved towards each other (Fig. 38A). With pin-prick 6 and 7, synchronization of the three motoneurons was achieved. With a set of relative phase relations (Fig. 38B) a phase and frequency coordination was achieved, which can directly be seen in Fig. 37B. Synchronization of the rhythmically firing subnetworks was achieved by the skin afferent input upon pin-pricking skin sites 1,2 and 6,7 (Fig. 37B) inside the anal reflex area. Pin-pricking sites 3 through 5 and 8 through 10 (outside or at the fringe of the anal reflex area) was less effective for the transient synchronization of the oscillators. Touching the anal reflex area resulted only in a weaker 'Magnet-Effect' of the rhythms with a partial synchronization (Fig. 38A, touch 1-5 and 6-10).

The relative phase and frequency coordination in the spinal cord of the paraplegic patient illustrated in Figures 37,38 was not as exact as in the brain-dead individual (Fig. 30-36). This is because the relative phase and frequency coordination of neuron firing in the CNS is partly lost following CNS lesion whereas the functioning of the spinal cord of the brain-dead individual is believed to be rather physiologic.

19. Change of neuronal network states takes time

With a catheter positioned in the anal canal, the motoneurons innervating the external striated anal sphincter fired oscillatory to activate the sphincter to secure continence. By dimpling or touching the perianal skin, the oscillators transiently reduced their oscillation period

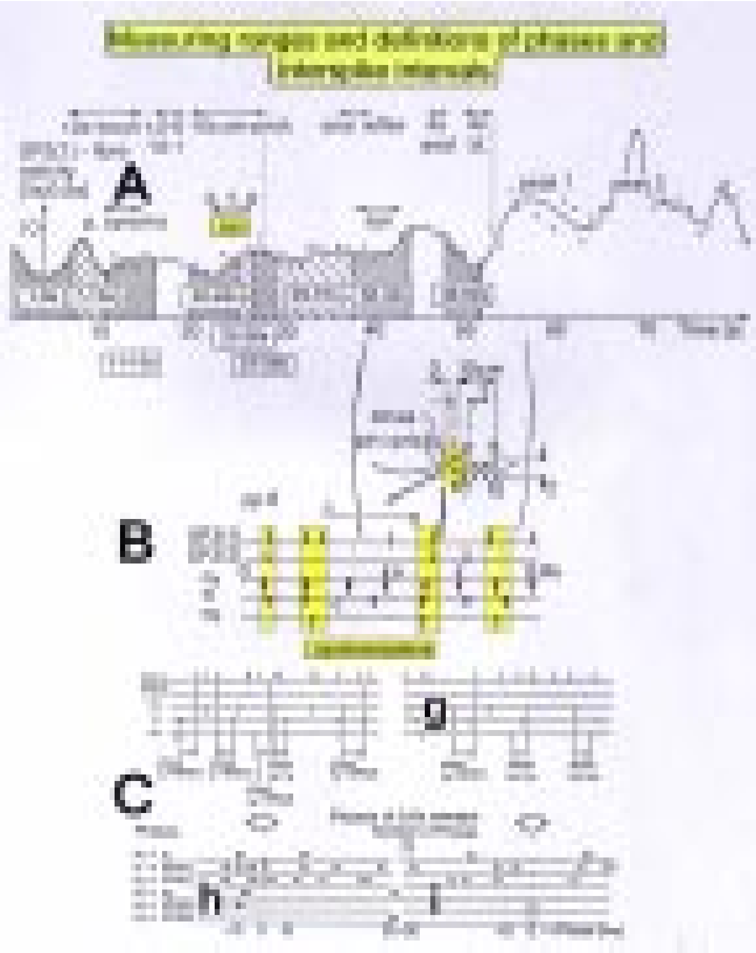

Figure 37 Measurement ranges and definitions of phases for the analysis of phase and frequency coordinations between motoneurons and spindle afferents. Coordination (synchronization) between firing patterns can directly be seen in B. A. Activity level of secondary muscle spindle afferent fibre SP2(1) in dependence on time. 10x touch = touching sites 1 to 10 shown in B; t. 5-6 = touching alongside the skin from site 5 to site 6; 10x pin-prick = pin-pricking sites 1 to 10; anal reflex = anal reflex stimulation; 4x anal = fourfold anal catheter pulling; 4x bladder = fourfold bladder catheter pulling; peak 1- peak 2 - 3 = first, second and third peak of spindle afferent activity due to parasympathetic activation; p. synchro = partial synchronization; syn = synchronization of α and γ-motoneurons and secondary muscle spindle afferents. Note the synchronization of the firing patterns following pin-prick 6 inside the anal reflex area. B. A set of single impulse patterns of secondary muscle spindle afferents (SP2(1,2)) and α and γ (intrafusal)-motoneurons and sites of stimulation. The small arrows in the impulse pattern of α_3-motoneuron (S) point to a shortening of the oscillation period following pin-prick 6 (pp6). The triangles indicate the beginning and the end of pin-pricking. Cg, h, i. Definitions of the phases between the different motoneurons and spindle afferents in 2 sets of impulse patterns (g), and the corresponding sets of phase relation distributions (h,i). Para 9; vS4.

(increased frequency) to enhance the continence function. Pin-pricking the perianal skin also shortened transiently the oscillation period of the oscillatory firing sphincteric motoneurons. The latency to the reduction of the oscillation periods was 10 ms (and longer) for touching the skin and 110 ms (and longer) for pin-pricking (Figs. 2, 3, 4 of Ref. [129]). This difference can be interpreted as follows. The touching of the perianal skin enhanced the anal reflex, activated already by the positioned anal catheter. The neuronal network's state to secure anal continence was varied only a little, and little time was needed to enhance the anal reflex. Pin-pricking of the perianal skin, on the other hand, stimulated the protection reaction of the body which is fulfilled by a different neuronal network state. The change of the network's organization from the continence state to the

Figure 38

Relative phase and frequency coordination (Ae and Be) between α and γ-motoneurons and secondary muscle spindle afferents due to touching and pin-pricking sacral dermatomes as in Fig. 37. A. Interspike interval distribution of spindle afferents SP2(1) and SP2(2), α_2 (FR) and α_3-motoneurons (S) and the dynamic fusimotor γ_1 for different time intervals upon touch, pin-prick and anal catheter pulling. Interspike intervals (IIs) were collected from several sweeps of 0.8 s duration per second. External loop generation and frequency coordination of α and γ-motoneurons and secondary muscle spindle affeprotection state took more than 100 ms, which is in the range of one oscillation period of an α_1-oscillator or less than one oscillation period of an α_2-oscillator. The change of the neuronal network state therefore took more time than a slight variation of the existing network state.

That pin-pricking resulted in a longer response time of motoneurons than touching of the perianal skin is not obvious and cannot be explained based on the reflex theory. Being a stronger stimulus, pin pricking (touch plus pain afferent activity, Fig. 29A,F) would be expected to have the same or slightly shorter rather than a much longer response time than touching of the perianal skin (touch afferent activity only, Fig. 29Ea,b).

20. Similarities between the organization of the human spinal cord and the dog reticular formation of the lower brainstem

The rostral and very important CNS structure for the spinal cord to communicate with is the brainstem reticular formation. Similarly as the spinal cord, also the brainstem seems to undergo genetically determined repair (see regeneration). It is therefore interesting to compare the organization of the brainstem system with that of the spinal cord to see how the lower brainstem can be reorganized by re-learning together with the spinal cord.

Neurons in the reticular formation of the dog lower brainstem contribute to the coordination of the visceral, respiratory, somatosensory, and central nervous system functions. These reticular neurons constitute the common brainstem system (CBS) for basic regulation and integration of visceral and somatomotor systems and vigilance. Under the influence of afferents from somatomotor receptors, visceral receptors (cardiovascular, respiratory, and continence system) and from higher brain structures, the neurons of the CBS produce activity patterns which lead to cooperation with the spinal cord and other CNS structures to adequate patterns of behavior [72,99,181-185]. As these neurons always receive afferents also from those systems to which their afferents are directed, the CBS is a system with manifold feedback loops, in similarity to the spinal cord which has manifold feedback loops to the periphery (for example, the γ-loop).

Characteristic features of the dynamic organization of the neurons of the CBS include their level of excitation, their dynamic organization into local subpopulations as well as differing modulating rhythms with their temporal and spatial interactions within the neuronal networks [72]. In the spinal cord the level of excitation of a motoneuron is correlated with the organization into subpopulations of neurons, namely the spinal oscillators. For weak excitation, the motoneurons fire occasionally and for strong excitation the motoneurons fire oscillatory in cooperation with interneurons.

Under the dominating influence of somatosensory afferents, the CBS is organized dynamically into subpopulations of neurons. The functional organization can be changed by changing the afferent activity patterns. The changing coupling phenomenon is due to the permanently changing influences of somatomotor afferents. In periods in which discharge patterns of the CBS neurons are dominated by visceral afferents, the CBS is organized more as a single entity [72]. In the spinal cord, the functions of the somatic nervous system and the parasym-

rents are marked by the semi-circle and the full circle. The large arrows point to the increase and decrease of the mean II of the distribution. Unsafe identification of α_2 and α_3-motoneurons (or vice versa) because of loss of specific oscillator properties. B. Histograms of the phases between afferent and efferent fibres for the time intervals indicated, upon different stimulation. Phases were collected from several sweeps of 0.8 s duration per second. The small arrows indicate phase relations. Phase coordination is indicated in a,e. Para 9; vS4.

pathetic division are more separated, even though influencing each other. It seems as if parasympathetic efferents also fire oscillatory [125]. With the activation of the parasympathetic nervous system in addition to the activation of the somatic one, oscillatory firing α_2-motoneurons are influenced by the parasympathetic division. The α_2-motoneurons switch from a 2-phase coordination between motoneurons and afferents to a 3-phase coordination (Fig. 3 of [126]). For the clinically important coordination between the detrusor (parasympathetic) and the external urinary bladder sphincter (somatic) it is not clear whether sufficient coordination is already achieved at the spinal cord level or whether the brainstem level is needed. Clinically, it seems as if the integrative functions of the brainstem are needed for the physiologic coordination of detrusor and external sphincter (detrusor-sphincter-synergy).

The types of organization between oscillatory firing functional systems in the common brainstem system include mutual non-influence, sliding coordination of phase relations and frequencies, and tight coupling of phases and frequencies. In the spinal cord and for a weak activation, the motoneurons are recruited to fire in the occasional firing mode according to the size principle in each motoneuron group. Their firing is partly mutually non-influenced and partly in relative coordination with the spinal oscillators (the oscillatory firing motoneurons). For strong activation, the α_2-motoneurons fire oscillatory with sliding coordination of phase relations and frequencies among the α_2-motoneurons. The α_2-motoneurons subserving same or similar functions in a muscle fire in relative negative correlation (out of phase) (Fig. 39B). Such firing is meaningful, because synchronized firing of neighboring motor units (in-phase) would cause muscles or parts of them to vibrate. Tight coupling of phases and frequencies occurs between α_1-motoneurons and primary spindle afferents (SP1) (Fig. 25C).

The influence of various rhythms from different functional systems on common effector systems are particularly strong in cases when the different rhythms partly overlap within certain frequency ranges, and this leads to resonance

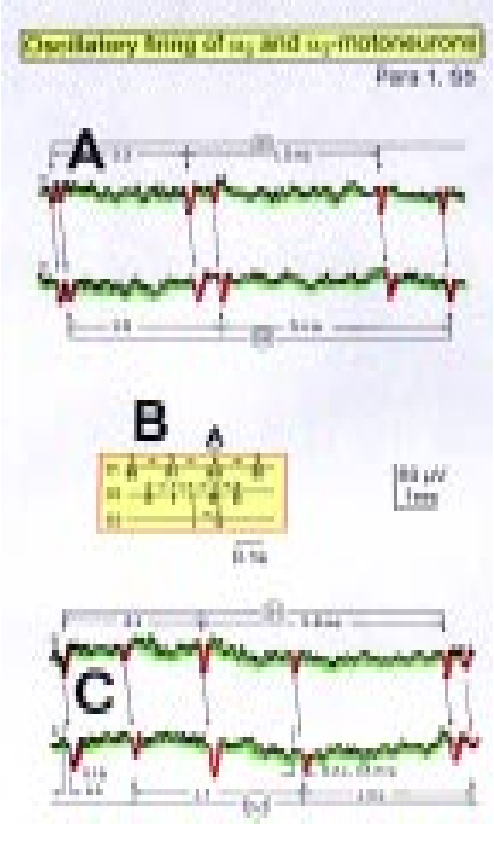

Figure 39
Natural impulse patterns of several firing motoneurons. No phase synchronization exists between the firing patterns to give rise to tremor. Records of impulse trains of oscillatory motoneurons for paraplegic 1. A. Impulse train of the continuously oscillatory firing α_2-motoneurons O1 (3 of the 4 APs are shown) together with the impulse train of the transiently oscillatory firing a_2-motoneuron O2. Interspike intervals are indicated. B. Impulse patterns of the 3 oscillatory firing α_2-motoneurons O1, O2 and O3: O1 continuously oscillatory firing, O2 and O3 transiently oscillatory firing. A marks the sweep piece shown in A. C. Impulse train of the α_2-motoneuron O1 together with a part of the impulse train of an oscillatory firing α_3-motoneuron Oα_3 (not shown in B). Interspike intervals, conduction times and conduction velocities are indicated. Para 1, S5.

phenomena. These phenomena are not restricted to the basic frequencies of the rhythms but also concern their harmonics [72]. This property will partly be used in the reorganization of the lesioned CNS (see below). Simultaneous inputs from several stimulating sources (central commands, visual coordination, auditory coordinated commands, movement induced afferent input, ...) on a common neuronal network to reorganize a certain rhythmic motor task seem to be especially effective in motor re-learning of the lesioned CNS (see below).

The influence of the rhythmically changed faster patterns on effector systems again result in changes in the slowlier rhythmic events. The connections between slow and fast components are essential for the high dynamics of the functional organization of the organism. In an altered internal or external situation, the participation of discharge patterns with higher frequency components enables a more rapid adjustment of the partial system concerned to their current necessary coordination in the course of regulatory procedures [72].

The correlation between slow and fast patterns (generated by subnetworks) for a rapid adjustment of subnetworks is used in the reorganization of the lesioned CNS by training dynamic (rhythmic) movements. For the regulation of movements, the firings of the three premotor spinal networks driving S, FR and FF muscle fibres (Fig. 21) should be correlated. Coordination between α_2 and α_3 and between α_1 and α_2-oscillatory firing subnetworks has been observed in the isolated spinal cord (Fig. 38, [127]).

The appearance and disappearance of differing rhythms, their changing phase relations in 'relative coordination', the appearance of harmonics and the simultaneous resonances within several frequency ranges are both (1) the expression of a steadily new coordination of partial systems of the body, and (2) a means of functional coupling and decoupling of the structures concerned [72].

21. Coordination and effects of rhythmic inputs on rhythmic motor pattern generating networks (MPN) in animals and humans

For a number of behaviors there are peripheral reflexes, automatisms or parts of movement cycles which supply input to the pattern generating networks at particular phases in each cycle of the rhythmic activity. For instance, passively bending the body of a fish into the position it assumes during one phase of swimming produces stretch responses which would by themselves produce the alternate swim cycle phase, even though the fish swimming pattern can be elicited from the deafferented spinal cord [43]. Coordination of the limbs in walking cats [90] is accomplished by phasic interactions between central pattern generating networks for the individual appendages. The phasic interactions between arms and leg pattern generating networks will be used (see below) in the coordination dynamic therapy to improve the coordinated rhythmic movements of arms and legs.

A way to measure the effects of inputs on a rhythmic pattern generator or network is illustrated in Fig. 40 [71]. Each of the two squares at the top represents either a single cell or a group of cells. The 'driven square' represents a spinal oscillator, rhythmic pattern generator or motor pattern generating network. The driver either excites or inhibits the driven pattern generator. The effect of the driver on the driven pattern generator is determined by activating the driver in short bursts presented at different phases in the driven cycle. If the driver has no effect, the period of the driven cycle in which a driver burst is delivered will be the same length as the previous period, as shown in the top trace in Fig. 40. Alternatively, the driver may lengthen or shorten the driven period, as shown in the next two, partial traces; these effects are termed positive phase change or phase delay (+DP), and negative phase change, or phase advance (-DP), respectively. The results of many such tests

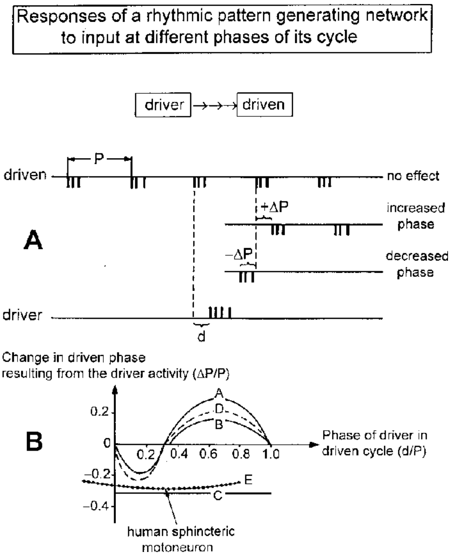

Figure 40
Responses of a rhythmic pattern generating neuronal network to input at different phases of its cycle. A. Three possible responses of a pattern generating network, indicated by the rectangle labeled 'driven', to a burst of impulses from a separate neuron or group of neurons, labeled 'driver'. The schematized recording from the driven pattern generating network indicates that, with no external input, it produces an impulse burst pattern that has a regular repetition period with a single phase. When a burst of impulses is produced in the driver, the pattern generating network may continue uninterrupted (recording labeled 'no effect') or its next burst may be delayed ('increased phase') or occur prematurely ('decreased phase'). P = period; d = delay from the start of the last driven burst to the start of the driver burst. The dotted line indicates the time at which the next driven burst is expected, on the basis of the length of the two previous periods. +DP, -DP = the amounts by which the period is increased or decreased, respectively. The horizontal axis represents time, in unspecified units. B. Phase-response diagram for the driven pattern generating network obtained by measuring the proportionate increase or decrease in period of the driven generating network (DP/P) as a function of the driven cycle in which the driver burst is delivered (d/P). The five lines labeled A, B, C, D and E are possible responses of a pattern generator to driver bursts delivered at all possible cycle phases. Curve A shows a case in which driver activity shortens the period of the driven network when presented early in the cycle, has no effect when presented at about a third of the way through the cycle, and lengthens the period when presented during the last two thirds of the cycle (inhibitory inputs onto Aplysia endogenous bursters and lobster pyloric network). Curve B illustrates a case in which driver input lengthens the period of the driven cycle but is effective only during the last half of the cycle (cat and cockroach walking, in which restraining the movement of a leg can slow down the step cycle only during the time when the foot is on the ground; during the swing phase, such restraint is ineffective). Curve C illustrates the case in which the driver shortens the cycle period of the driven network no matter when it occurs during the driven cycle (tonic excitatory input onto the pattern generating network shortens the cycle period, no matter when it occurs during the driven cycle; holds for all proposed pattern generating models). Curve D approximately illustrates the case, when the forefoot of a patient is skin-simulated by knocking onto the forefoot (to enhance the 'lift-off' afferent input) before and after the 'lift-off' phase of the forefoot (Fig. 42). Around the 'lift-off' phase, the cycle period is shortened (the foot forward movement enhanced), after the 'lift-off' phase, the cycle period is lengthened (the foot forward movement is inhibited or strained). Curve E illustrates the case, when the anal reflex zone of a patient is touched; the oscillatory firing sphincteric motoneurons shorten the cycle period throughout the cyle, but the dependence seems not to be a straight line (data extrapolated from Figs. 2-5 of [129], only stimulations are used, with only the first period following stimulation shortened (40%)).

at a number of phases in the driven cycle can be summarized efficiently in a phase response curve [92], as shown in Fig. 40B.

Three effects of input onto pattern generators are shown in Fig. 40B. Curve A shows a case in which driver activity shortens the period of the driven network when presented early in the cycle, has no effect when presented at about a third of the way through the cycle, and lengthens the period when presented during the last two-thirds of the cycle. Such effects have been shown for inhibitory inputs onto Aplysia endogenous bursters [92,93] and for inhibitory input onto the lobster pyloric network [6]. In addition, a similar curve was found for interappendage coordination in several animals [148,149] as well as for sensory input onto locust flight pattern generators [163].

The function of such an input can be understood by considering the effect of the driver on the driven patterns generator if the driver were producing rhythmic bursts. If the driver were going somewhat slowlier than the driven network, the two rhythms would start off at different frequencies. If the first driver burst occurred early in the driven cycle, the next cycle would be shortened so that the following driver burst would effectively occur somewhat later during the next driven cycle but would still shorten that cycle. This shortening would continue until the driver burst occurs during the last two-thirds of the driven cycle, at which point the next driven cycle would be lengthened. There is some phase at which the lengthening is just sufficient to make the driven period equal to the driver period. When this phase is achieved, the pattern then repeats continuously, with the driver burst always occurring at the same phase in the driven network cycle.

This fact or logic is used when applying rhythmic afferent input to the motor pattern generating network in man (induced by movement (walking or exercising on a device) or manually applied input from the trainer) to reorganize the lesioned CNS by an oscillator formation and coordination dynamic therapy. The rhythm training entrains the unrhythmically firing oscillators to fire more regularly again.

By similar considerations, it can be shown that this kind of coordination is stable in that small fluctuations in either a driver or driven cycle period would produce a change in the driven network that would restore the maintained phase relationship within a few cycles [7,148,163]. In addition, the opposite kind of phase response curve - with lengthening when the driver burst is delivered early in the driven cycle and shortening when it is delivered late in the cycle - also produces stable phase relations. In both cases the driver ‘entrains’ the driven cell with the driver rhythm. Line A in Fig. 40B describes the relation between two oscillatory networks that produces a stable phase relation of the type required to produce coordination between two pattern generators, as is e.g. necessary to keep the phase relationship between walking legs constant.

Such knowledge is used to enhance coordination between the pattern generators of arms and legs, and between arms and between legs in man following CNS lesion, if for example one arm is not moving any more. By exactly coordinating the pattern generators of arms and legs through ‘air-walking’ or exercising on the special coordination dynamic therapy device, the CNS is supervised to re-learn to move the arm in coordination with the other arm and the leg again (see also reorganization of the CNS).

What is the mechanism for the entrainment of oscillators? In the best understood cases, endogenous bursters are the driven cells [6,92,93]. The length of the interburst interval in these neurons is thought to be proportional to the amount of Ca^{++} that enters the cell during its depolarization and burst of impulses [26]. If the cell is inhibited during the impulse burst (i.e., ‘early’ in the cycle), it produces an abbreviated depolarization, less Ca^{++} enters, and the interburst interval is shortened. If the cell is inhibited during the hyperpolarized phase of the cycle (i.e., ‘late’ in the cycle), the imposed hyperpolarization does not affect the Ca^{++} accumulation or removal but simply sums with the endogenous hyperpolarization to lengthen the cycle. If the inhibition is delivered so as to overlap with the end of the burst and the start of the interburst period, both shortening and lengthening are produced, and the net effect is no change in period.

Curve B in Fig. 40B illustrates a case in which the driver input lengthens the period of the driver cycle but is effective only during the second half of the cycle. This effect has been described in cat walking [36], in which restraining the movement of a leg can slow down the step cycle only during the time when the foot is on the ground; during the swing phase, such

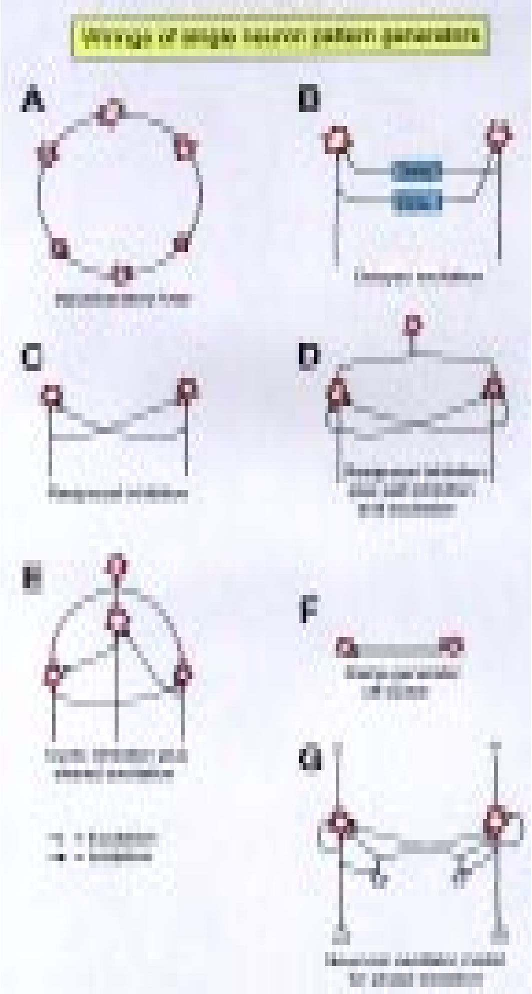

Figure 41
Theoretical modeling of rhythmic motor output. A. In the reverberatory loop, impulses in any element cause impulses in the next element in the chain. If the activity in the original element dies away before the excitation traverses the loop, the original elements are re-excited and the network continues to produce rhythmic bursts. B. Delayed excitation. C. In the reciprocal inhibition network, each element fires when the other element is not firing. The switch from firing in one element to firing in the other one is accomplished by some fatiguing property in the active element, e.g. accommodation, waning of postinhibitory rebound, or synaptic depression. D. Reciprocal inhibition plus self-inhibition and shared excitation from a third neuron. E. Cyclic inhibition plus shared excitation from a fourth neuron. F. The ‘ramp generator’ consists of an element (left neuron), whose impulse rate increases in time; this property could be due to endogenous properties or to a positive feedback network. The ‘off-switch’ is an element (right neuron), which has such a high threshold that a high rate of impulses of the left neuron are needed to trigger impulses in the right neuron. Once it fires, however, the left neuron effectively inhibits the right neuron, thereby resetting the right neuron to a low firing rate, which turns off impulse production in the right neuron. G. Neuronal oscillator model for phase transition.

restraint is ineffective. Assuming that the extrinsic inputs are weak relative to the intrinsic effects, then if, for instance, a sensory input weakly inhibits only the left cell group in reciprocal inhibiting network (Fig. 41) it would prolong the cycle period if it arrives during the impulse bursts in the left cell group but would have a negligible effect if arriving during the strong inhibition from the right cell group.

Alternating long and short oscillation periods, T, have been observed in α_1 and α_2-oscillator firings, indicating that there is some kind of a reciprocal inhibition between some spinal oscillatory firing networks in the human sacral spinal cord (Fig. 14, p. 32 of [127]). Increasing the afferent input from the forefoot in patients with CNS lesion when walking on the treadmill by pressing the forefoot onto the ground or even knocking the forefoot (Fig. 42), it can be seen that this increased afferent input speeds up the moving leg only if an additional afferent input is administered at the ‘lift-off’ time period of the forefoot. At other times of the stepping cycle of the foot, the increased afferent input from the forefoot has no effect or inhibits the stepping cycle. It seems therefore that curve A (dashed line curve D) better than curve B describes the effect of the rhythmic increased afferent input into the motor pattern generating network of

Figure 42
A patient with brain lesion during treadmill walking. The movements of the legs are supported by two therapists. One therapist is knocking with the hand on the forefoot of the patient to induce the stepping automatism and to enhance in this way the walking performance of the patient.

man. Actually, in patients with strong rigidity of the legs, the legs can only be made to move if the afferent input at the forefoot is administered at the ‘lift-off’ time.

Curve C in Fig. 40B illustrates a case in which the driver shortens the cycle period of the driven network no matter when it occurs during the driven cycle. This corresponds to the effect of tonic excitatory input onto the pattern generator, which shortens the cycle period in all the proposed models.

Rhythmic touching or pin-pricking with a needle the anal reflex area shortens the oscillation periods, T, of the oscillatory firing sphincteric motoneurons, independent of when the stimulus is applied with respect to the cycle phase (curve E of Fig. 40B). A rather constant shortening of the cycle period can therefore not only be achieved by tonic excitatory input to oscillatory firing networks, but the properties of oscillator response curves also depend on the function of the oscillators in the pattern generating networks. Whereas during the walking or running, the generating networks response curves will show increased and decreased phases, the premotor spinal oscillators driving external sphincters, where no coordination is needed, may not show inhibition.

22. Pattern generating neuronal networks

Rhythmic motor patterns can be generated by rhythmic changes of membrane properties of single cells (endogenous properties), by the rhythmic firing of neuronal networks (network properties) or by the rhythmic firing of neurons induced by phasic sensory feedback of arms or legs (clonus of arms and legs in man) or by a combination of the three. Motor neurons produce bursts of impulses at regular intervals. In some cases, the bursts consist of one or two impulses, or the bursts contain 10 to 50 impulses. The impulse patterns within bursts differ, some having an essentially constant impulse frequency, others showing either an increasing or a decreasing rate, or even an increase and a decrease within each burst [71]. The human α_2-oscillators showed a decreasing intraburst frequency (Fig. 34B,C), and an α_3-oscillator a decreasing and (for longer bursts) a decreasing and increasing rate (Figs. 22,23). Fig. 39 shows schematically impulse patterns of several oscillators measured simultaneously in man.

The mechanism of endogenous burst production involves changes in membrane conductances that are slow relative to the course of a single action potential. A decreased potassium conductance or increased sodium conductance [8] produce membrane depolarization; at some threshold voltage, active inward sodium and calcium currents are triggered, thereby producing an impulse burst. The inward calcium current increases the intracellular free calcium concentration which activates a slow potassium current, which in turn hyperpolarizes the membrane and turns off the impulse burst. As the free intracellular calcium concentration returns to normal by expulsion of the accumulated Ca++, the slow potassium current decreases and the cycle repeats itself.

The wirings of the proposed central pattern generating networks are summarized in Fig. 41. None of these pattern generating networks can explain the occasional firing of spinal oscillators in man, but these pattern generator models represent possible physiological instances of schematized network states.

In animal research, three classes of the proposed mechanisms have been reported for activating, maintaining, and inactivating a rhythmic pattern generator: neurons outside the pattern generator, properties of neurons within the pattern generator, and interactions between the neurons outside and those within the pattern generator [71]. Since in human spinal α_2 and α_3-oscillators, the reverberatory network loop, consisting of excitatory and inhibitory connections, progressively spreads with the increasing excitation (Figs. 26-28), the classes of neurons inside the pattern generating network, outside and at the functional fringe of the oscillator, vary with the changing afferent input. The neurons inside and outside the oscillator network loop or pattern generating network will have the same properties. The recruitment for taking part in the self-organization to generate certain movements depends on the space-time distribution of the afferent input patterns from the periphery and supraspinal centres.

The term ‘command neurons’ has been applied to those neurons completely external to the pattern generating network which, when stimulated tonically, turn on a rhythmic motor pattern. The activity of endogenous bursters can be turned on and off by membrane polarization or by ionic and hormonal influences that affect the expression of the slow potassium conductance [8].

Once active, the reverberatory loop does not require tonic input to maintain its activity. Hence, this network can, in principle, be quickly switched on (i.e., ‘triggered’) and off by excitatory input and by inhibitory input respectively to any or all of its member neurons. The positive feedback network produces a single burst of impulses at their maximal firing rate once some minimal activity in the network is achieved; however, for sustained activity, a tonic level of excitation must be maintained (i.e., the network activity is ‘gated’ on and off). This tonic excitation might be supplied by excitatory synaptic input (extrinsic) or spontaneous, regular impulse production in the individual elements (intrinsic), but activity from neurons outside the pattern generator is required to either gate on or off the pattern.

Network pattern generators with only inhibitory connections also require a source of tonic excitation. If the pattern-generating neurons exhibit postinhibitory rebound, however, the network can be triggered into activity by a short burst of excitatory or inhibitory synaptic input. Therefore, an exclusively inhibitory network can be either triggered or gated on and off, depending on the properties inherent to the neurons in the pattern generators [71].

A combination of endogenous and network oscillators may serve to produce reliability by true redundancy, or it may provide the means to produce a combination of pattern generator features that would be impossible to achieve in either a purely endogenous or a purely network type of pattern generator.

Probably, the human premotor spinal oscillators consist of an α-motoneuron and excitatory and inhibitory interneurons. The networks of the oscillators are interlaced. The natural firing patterns of the receptors activate motoneurons and interneurons. Waves of excitation possibly spread along self-organized reverberatory excitatory network loops sharpened by lateral field inhibition. With the increasing afferent (or descending) excitation, the equilibrium between excitatory and inhibitory connections shifts toward excitation, so that the network loop spreads further out into the neuropil for α_2 and α_3-oscillators. Delay elements at dendrites may contribute to the length of the oscillation period of more than 100 ms. Membrane properties may be neurally controlled and could make a substantial contribution to the features of spinal oscillators.

23. Entrainment of oscillators by external inputs: mathematical considerations

When a nonlinear oscillatory system is driven by an external periodic input z_k, its response contains both frequency components. If however the external frequency is close to the characteristic frequency 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 for biological oscillators as 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.

Mathematically, nonlinear oscillators can be entrained by periodic external input z_k. The entrainment can be harmonic (z_k itself has the period T of the oscillator), subharmonic (z_k has a period which is an integer multiple of T, mT) or superharmonic (z_k has a period which is an integer fraction of T, T/m) [89]. With the increasing order of subharmonic entrainment, the entrainment strength reduces for the same coupling strength. In α_2-oscillators, two entrainment phases per oscillation period were observed which correspond to ‘in-phase’ and ‘antiphase’ coordination of arms and legs.

If in a group of oscillators with an oscillation period T all units are in phase, then the individual oscillators as summed oscillators are entrainable by z_k to the common period T. If the oscillators form two groups with half a period phase difference, then the sum of oscillators will oscillate with a fundamental period equal to T/2. The external input can cause subharmonic entrainment (second order) of the individual units. If the second case is generalized that the oscillators form m groups which have phase differences T/m, they are entrained by z_k to m times their period. All three cases are called mth-order synchronization of the group of oscillators, where m is the number of groups which the oscillators are split into. Small phase differences are allowed around T/m.

Populations of interacting oscillators may have the following features:

(1) They may have more than one stable state of synchronization, each one with its own frequency of oscillations. Thus, after a disturbance, the system may return to a different limit cycle than it was on before.

(2) The possibility of multifrequency oscillations exists (human α_2-oscillators show multifrequency oscillation). If the coupling is weak, one expects that the states of stable synchronization may not be reachable from arbitrary initial conditions or after a disturbance has moved the system away

from a limit cycle. With the multiplicity of stable solutions it may be predicted that possibly a minor disturbance can result in a drastic macroscopic dynamical behavior of the system.

(3) The macroscopic behavior of such systems depends on the average value of its parameters rather than on the values of the individual units. Thus, they are usually quite insensitive to small variations of the latter. However, the opposite tends to be true for variations of the average values.

(4) Frequencies of oscillations may depend significantly on the coupling strength, and therefore the frequency of synchronization in a population may be quite different from the individual frequencies of the oscillators. With this feature of interacting oscillators it is understandable that the premotor spinal oscillators may have frequencies different from that of the rhythmic movement.

In the case of pathologic organization of the neuronal networks of the CNS, as for example in tremor or when a patient with a very severe brain lesion is in permanent coma, premotor spinal or other oscillators may not sufficiently inhibit each other any more, so that oscillators partly synchronize (in their functional group) and in turn, different motor units are partly activated in synchrony, with the macroscopic consequence that fingers, hands, arms, legs, mouth, eyes and eyelids may move rhythmically.

From the properties of populations of biological oscillators, many actual behaviors can be understood when performing rhythmic, dynamic, stereotyped, symmetric movements to improve CNS functions after a lesion using oscillator formation and coordination dynamic therapy. On the other hand, the occasional firing of motoneurons cannot be understood with pure oscillator theories. For the reorganization of the human CNS after a lesion, it seems useful to use that level of approximation of CNS functions which best explains the network states to be trained.

24. Self-organization of the spinal cord

If behavioral functions such as percieving, acting, learning, and developing are really due to self-organizing processes in the nervous system, it seems likely that relevant information is specified by coherent relations between neuronal events rather than by the oscillatory components per se. But since synchronization of discharges is a particularly efficient mechanism to increase with great selectivity the saliency of only those response episodes that contain coincidental discharges, synchronization of neuronal responses at a time scale of milliseconds may be used in CNS processing [145,146]. Synchronization can be used to select, with high spatial and temporal precision, those constellations of responses that should be considered for further joint processing. In this way, network oscillators may be organized. Through varying synfire chains [1] generated by coincidental discharges, recurrent excitatory and inhibitory network loops could be one possibility to self-organize premotor network oscillators. Long-term potentiation (LTP) [15] and long term depression (LTD) [76], whithin the range of hundreds of milliseconds, and therefore oscillator periods, may contribute to the self-organization of spinal α_2 and α_3-oscillators. Values of ± 100 ms have been observed for homosynaptic potentiation and depression induced by pairing test input with intracellular depolarizing and hyperpolarizing pulses, respectively [39]. Time intervals of 20 ms enabling associative LTP [73] were found in a study of the crossed (weak) and uncrossed (strong) enthorinal cortex projection to the dentate gyrus. These values lie in the time range of the building blocks of spinal oscillators, but data for the human spinal cord are needed. Recurrent inhibition or lateral inhibition is thought to provide an antagonistic organization that sharpens responsiveness to an area far smaller than would be predicted from the anatomical funneling of inputs. The loss of supraspinal or propriospinal inhibition following CNS lesion could account for muscle mass contractions and loss of specific responding of the critical two-joint muscles (e.g., m. rectus femoris). The generation of rhythmic, dynamic, stereotyped leg movements may arise as metastable spatio-temporal patterns of CNS activity, mainly from the motor pattern generating network (MPN) of the intumescentia lumbosacralis. The premotor and propriospinal oscillators will make a substantial contribution to the generation of these patterns by relative rhythm coupling. The phases between the impulse trains of different oscillators (and the spikes of motoneurons and interneurons which are firing not oscillatory) and between the oscillator impulse trains and afferent action potentials (especially from muscle spindles) specify the space and time ordering of the oscillators.

25. Reorganization of neuronal networks

Reorganization of neuronal networks induced by motor learning and motor control learning will include changes of synapse efficacy (Hebbian learning [3,49,37]), migration of synapses, variation of neurotransmitters and postsynaptic receptors, branching of dendrites, change of membrane properties, development of new functions of neurons through the loss of input or target or both, which frees the neurons of their previous functional constraints (with respect to muscle cells, see [78]), and proliferation of neurons from stem cells [166,167].

In computational neurosciences [3], the extension of the Hebb rule is the covariance rule. The strength of a synapse is expected to increase if the firing of the presynaptic and postsynaptic elements are positively correlated; it should decrease if they are negatively correlated; and it remains unchanged if they are uncorrelated. The covariance rule is of importance because of the mixing of the influences of polysynaptic excitatory and inhibitory circuits linking the two cells, modulated by the diffuse network background activation (composite interaction).

26. Oscillators of the CNS

In the human neurophysiology research project [103-140], recording could be done from premotor spinal oscillators in the premotor neuronal network of the spinal cord. Premotor spinal oscillators are important because: 1) natural firing patterns can be recorded from undissected nerve roots of human CNS; 2) the oscillatory firing can be related to the natural afferent input patterns, and regulation units can be identified; 3) movement information runs through the premotor network, its functions must be known if one wants to deduce brain functions from movements. ‘Looking through colored spectacles, you can only judge upon the colors of a picture if you know the color of the spectacles you are looking through’.

The α_1, α_2 and α_3-oscillators have different oscillation frequencies and show different degrees of oscillatory network properties. The α_1-oscillators innervating FF-type muscle fibres are firing time-locked with primary muscle spindle afferents [128], and therefore show little oscillatory property, which is in accordance with the monosynaptic stretch reflex. Different kinds of network oscillators may exist from rather hard-wired to self-organizing ones, and mixtures of cell and network oscillators may exist. A neuron capable of firing spontaneously is also open to network oscillatory control. Synaptic stimulation could always catch the cell in a period between absolute refractory state and time of spontaneous discharge. With a frequent rhythmic arrival of impulses at the synapses, the cell does not reach the point of spontaneous action and stays under network control [49]. The rhythmic membrane changes would appear for low network activity only. Rhythmic firing has been recorded in animals [16,17,72,99,142,144]. For the suggested different kinds of hard-wired network oscillators, see Fig. 41 and [16,63,144].

27. Spinal oscillators and tremor

The α_1, α_2 and α_3-motoneurons fire oscillatory for continuous isometric contraction (of the external anal sphincter and functionally associated pelvic floor muscles, induced by the positioning of an anal catheter (Figs. 31-36, [128])). If physiologic tremor occurs by random synchronization of motor units or rhythmically firing subneuronal networks, then the tremor frequencies may be expected to be similar to those of spinal oscillators. From the relative coupling of spinal oscillators further tremor frequencies [60] can be expected from the addition and subtraction of the oscillator frequencies. Accounting for muscle-limb mechanics, there will be further differences between tremor frequencies and oscillator frequencies. Stiffness of the contracting muscles and inertia of the moving parts may act as a mechanical filter [80], influencing the frequencies of the random synchronization of spinal oscillators. Agarwal and Gottlieb [2] found resonance frequencies of the active gastrocnemius-soleus muscles of 6.25 Hz and near 8 Hz. Since the gastrocnemius-soleus muscles consist of slow (S), fatigue resistant (FR) and fast fatigue (FF) muscle fibres, which are innervated by α_3, α_2 and α_1-motoneurons, premotor spinal oscillator frequencies are ~1 Hz (with a wide range) (α_3), 6.25-8.7 Hz (α_2) and 8-12 Hz (α_1). When patients with tremor exercise on the special coordination dynamic therapy device, rhythmic changes of movements (turning) can also be observed in the frequency range of 0.15 Hz. The tremor frequencies are therefore similar to those of the premotor spinal oscillators. Alpha and theta rhythms of the brain and slow oscillations in the thalamus with frequency ranges of 7-12 Hz, 4-10 Hz and < 1 Hz respectively (page 246 of [63]) are very similar to the frequency ranges of the oscillatory firing α_1, α_2 and α_3-motoneurons of the spinal cord (see above under similar frequencies of premotor spinal oscillators and field potential oscillations in the cortex). Premotor spinal oscillators are likely to underly physiologic tremor since firstly, the frequencies are similar and secondly, the spinal oscillators show a similar coupling phenomenon as can be seen in tremor, i.e. change of the leading (tremor) rhythm [60] (see 'Magnet-Effect' and Fig. 38).

B. Relationship between human and animal research and theory of neurosciences

28. Self-organizing neuronal networks and attractors

An open system such as the neuronal network, in which many neurons communicate with one another, shows a remarkable feature. When the network is fed with patterned afferent input (e.g. Fig. 29), it will show ordered structures which were not formerly apparent. Such self-organized neuronal network organization induced by afferent input is totally different from the characteristics of the neurons that constitute the network. The afferent input patterns induce communication (cooperation and competition) among the neurons so that space ordered structures and time regularities occur.

The difference between self-organization of neuronal networks and that of physical systems is that the change in self-organization (interactions of the internal components) is induced by the changing natural adequate afferent input patterns (sensitivity to external conditions) and not necessarily by the energy pumped into the system; in other words, the neurons are not simple components as in physics, and they may change their properties with the ongoing change in self-organization. Information on how the nucleons cluster in an atomic nucleus [100,101] provides practically no help for the understanding of the organization of the human CNS.

When systems self-organize under the influence of an order parameter (collective actions of the individual elements that govern the behavior of the systemic collective variable(s)), they ‘settle into’ one or a few modes of behavior (which may be very complex) that the system prefers over all possible modes. This behavioral mode is an attractor state as, under certain conditions, the system has affinity for that state. The system prefers a certain topology in its state space.

The state space of a dynamic system is an abstract construct of a space whose coordinates define the components of the system; they define the degrees of freedom of the system’s behavior.

The behavior of a simple mechanical system such as a pendulum can be described completely in a two-dimensional state space where the coordinates are position and velocity. The circular orbit of the frictionless pendulum and the resting point of the pendulum with friction are the attractors of this system: a limit cycle attractor and a point attractor.

The state spaces of neuronal networks are abstractions of the possible values of the elements in n-dimensional space, where n is the number of components necessary to characterize the system.

An atractor is commonly pictured as a ball within a potential well. If the ball is in a deep potential well then the system is in a very stable attractor state. While some attractor states are so unstable as to almost never be observed, other attractor states are so stable that it is easy to believe that they are generated by hard-wired structures or programs within the system. To be moved from their preferred positions, very stable attractors need to be pushed rather strongly, but they are dynamic and changeable nonetheless. Complex systems may have two or more attractors with different basins of attraction coexisting. In this case, the same system may have multi-stable modes, which are discrete areas in the stable space [154] (see also definitions in coordination dynamics).

With respect to the change of the organization of the CNS after a lesion to stabilize and destabilize preferred attractor states, spastic attractor states have to be destabilized and desirable attractors like walking or other physiologic movements have to be stabilized (Fig. 107).

Especially when training on the special coordination dynamic therapy device (see below), it is possible to stabilize a physiologic movement attractor state very close to a very stable spastic attractor state with the consequence that the attractor state ‘spasticity’ reduces its stability. In practical terms, physiologic movement can be build in patients with cerebral palsy and very strong spasticity (for example, extensor spasticity), when exercising on the special coordination dynamic therapy device (by creeping into the movement) (Fig. 107), even if rather severe spasticity seems to block all movements.

Walking and running are behavioral attractors. When switching from one gait attractor to another one, there is no stable intermediate pattern for healthy humans. Patients with a lesioned CNS and strong deficits in locomotion may show a half running and half walking pattern, when changing the gait on a treadmill with increasing speed. With respect to the movement of one leg (pattern generating network of one leg), the limit cycle attractor may show several subattractors for the different false movements. When exercising on a treadmill for reorganizing the lesioned CNS, those attractor states have to be stabilized which are most physiologic, by varying the afferent input patterns.

Running is a stable and deep attractor and quite automatic, and it will ‘suck in’ other organizations of the system; it is therefore very suitable to reorganize the lesioned CNS by evolving a more physiologic state-space landscape. In the CNS reorganization section which follows, we shall show how further behavioral attractors can be stabilized to establish a more physiologic state-space landscape of the lesioned CNS. Stabilization of former stable steep behavioral attractors like walking, running and crawling will be used as external boundary conditions to develop a more physiologic state-space landscape. Further, in similarity to the human bimanual coordination in the ‘in-phase’ and ‘anti-phase’ condition, time-locked jumping in ‘anti-phase’ on a springboard can be used to stabilize the attractor state ‘jumping in ‘anti-phase’’ and destabilize the attractor state ‘extensor spasticity’. With the deepening of the attractor ‘jumping in ‘anti-phase’’, the occurring fluctuation of noise in the CNS organization becomes relatively reduced enough, so that a switching between the ‘attractors jumping ‘in-phase’’ and ‘jumping in ‘antiphase’’ occurs relatively less often and the attractor ‘extensor spasticity’ also occurs less often. Parts of the human state-space landscape can be studied in patients with a lesioned CNS since such patients only show details of the landscape. In healthy humans, some attractors are so deep that certain movements always occur and other attractor states are so unstable that other movements are nearly never observed, so that the state-space landscape in a certain movement range seems to be very simple, even if it is not as unbalanced CNS lesions CNS show (see the Section Reorganisation and unmasking of attractors).

29. Verification of self-organization of premotor spinal oscillators

It has been stated that, according to neuroanatomical studies, the premotor network for controlling goal-directed movements is represented by extensive interconnections between the motor cortex, the red nucleus and the cerebellum [56]. Even though there is little doubt that the integrated functions of limb movements are distributed throughout the CNS, the premotor network for the maintenance of rhythmic dynamic stereotyped movements is mainly located in the spinal cord since rhythmic firing of motoneurons has been observed in patients with complete spinal cord lesion [118] and in brain-dead individuals [107], and because newborn babies [35] (Fig. 43) and anencephalic babies [91] can step automatically. Moreover, brain-dead individuals whose brains were dead for one to two weeks, during which time their spinal cord became automated, are sometimes able to move their legs in a coordinated way when touched.

To verify the self-organization of the human spinal cord networks, it is first necessary to demonstrate the self-organization of the premotor spinal oscillators as described in [63], namely the spontaneous occurrences of spinal oscillators, their flexibility, and their changing involvement as participating subsystems.

1. *Spontaneous occurrence of spinal oscillators*. With increasing bladder filling, the α_2-motoneuron driving the external bladder sphincter for securing continence started to fire oscillatory (in the demonstrated case, starting at 600 ml volume of bladder filling (Fig. 14D)) due to adequate afferent input from stretch (S) and tension (ST) receptor afferents (Fig.14E). Therefore, at a critical point when adequate afferent input was reached, the neuronal network contributing to this α_2-oscillation changed its pattern from not firing oscillatory to firing oscillatory. The intermediate region of transient oscillatory firing (560-600 ml volume of bladder filling) was probably due to fluctuations in the adequate afferent input and/or tonic background drive. The inhibition of the spinal oscillator can be seen in Fig.14F for bladder filling volumes exceding 750 ml. Due to a strong increase in flow receptor afferent activity (S2 in Fig.14E), the activity of the oscillator reduced again. Probably, the bladder became overfilled and urine was passing through the urethra and stimulated flow receptors. Continence was lost because of overfilling.

2. *Flexibility of spinal oscillators*. These premotor spinal oscillators are flexible as they can be organized and de-organized according to the activity needed ((Figs. 18B,19B) and page 64 (Fig. 4) of [128]). α_2-Oscillators, often firing with 3 APs every 160 ms (18.8 APs/s) can even switch their oscillatory firing mode for changing activity, to fire very approximately with 2 APs every 130 ms (15.4 APs/s) or with 4 APs every 190 ms (21 APs/s); the oscillatory firing network (assembly [49]) can thus probably shrink or grow (Fig. 28). Stimulus-mediated phase and/or frequency synchronization (Figs. 2,3,5 of [129] and Fig. 3 of [130]) is only transient, so that under physiologic conditions the oscillators do not enter a resonant mode-locked state.

3. *Changing involvement of oscillators as participating subsystems*. Probably, the premotor spinal oscillators are participating subsystems to generate macroscopic function by flexible engaging and disengaging in coupling, since the number of phase relations between oscillatory firing systems changes according to the stimulation, and therefore network organization (Fig. 7 of [130]).

4. *Coherent relations between neuronal events rather than oscillators*

If, according to Kelso [63], behavioral functions such as perceiving, acting, learning, remembering, and developing are really due to self-organizing processes in the nervous system, it seems likely that relevant information is specified by coherent relations between neuronal events rather than by the oscillatory firing components per se. In a patient with a paretic cervical spinal cord lesion, the relative phase between rhythmic firings (coordinated firing) was preserved from one plantar flexion to the next one, indicating some storage in the short-term memory of phase relations between oscillatory firing subnetworks (Figs. 8,9 of [130]). Still, it seems that the information is more specified by the coherent relations between the neuronal events, since especially the α_2 and α_3-oscillators are very flexible. With increasing afferent input (adequate for α_2 and polymodal for α_3-oscillators), the activity per time unit increases (higher network activation) with the increasing oscillation frequency. As if the Renshaw-inhibition became reduced with the increasing afferent input, so that the activity can spread further out into the neuropil. Moreover, only a part of the motoneurons fire oscillatory; many motoneurons are recruited to fire only occasionally (Figs. 9-13, 16-19).

For low network activation, the motoneurons in each motoneuron group fired occasionally approximately every 3s (0.33 Hz) according to the Henneman's size principle [9] (Fig. 9-13).

The motoneurons' firing therefore was not completely chaotic. For very low network activation, the firing of motoneurons and interneurons may be chaotic. Kelso [63] argues that the brain immediately manifests coherent spatio-temporal pattern from relatively incoherent or rest state if it is confronted with a meaningful task. Being chaotic at rest allows the brain access any of these unstable orbits (of pattern states) to satisfy functional requirements.

As can be seen from Fig. 14B, motoneurons O2 and O1 of the brain-dead human HT6 fired repeatedly with impulse trains consisting of 3 APs or 1 to 2 APs respectively, but they did not fire in synchrony. For the distributed (not synchronized) firing of spinal oscillators, subserving same or similar function, see Fig. 39. The random synchronization of spinal oscillators may give rise to tremor (see above). As can be seen further from Figs. 31-36, the premotor network of α_2-motoneuron O2 (innervating the external striated urinary bladder sphincter) is organized by the drive of secondary muscle spindle afferent fibre SP2(2) and other afferents, and the network of α_2-motoneuron O1 is organized by the afferent activity of stretch receptor S1(1) and other bladder stretch or tension receptor afferents (Fig. 14E,F). These two oscillatory firing subnetworks therefore fired rather independently of each other (Fig.14F) according to their adequate afferent input.

30. Self-organization of the human spinal cord

The CNS is fundamentally a pattern forming self-organizing system governed by potentially discoverable, nonlinear dynamics laws. Behaviors such as perceiving, intending, acting, learning, and remembering arise as metastable spatio-temporal patterns of CNS activity that themselves are produced by cooperative and competitive interactions among neural clusters [63] (as e.g., oscillators).

The CNS is a neuronal network unit which communicates via receptors with the external environment. Separating a part from the CNS will change the network functions of that part (e.g., the spinal cord), and will change the network functions of the remaining CNS. After some time, the CNS parts will adapt to the lesion, which means that the CNS parts will change their properties. The functional isolated human spinal cord, following complete spinal cord lesion, becomes automated and will take over, to a certain extent, functions which were previously mainly activated in supraspinal centres, such as urinary bladder function (so-called bladder reflex), temperature regulation, and some motor performances. With respect to the spinal cord functions, the difference between a rostral traumatic spinal cord lesion and slowly occurring brain death is unclear. In spite of the not clearly specified condition of separated CNS parts, some properties concerning the self-organization of the spinal cord can be explained.

Since the premotor spinal oscillators and the whole CNS are self-organizing networks, we can expect the same from the spinal cord. It remains unclear how the premotor spinal oscillators cooperate with other neural clusters or assemblies like propriospinal oscillators to generate macroscopic function. We shall try to check the self-organization of the human spinal cord with respect to macroscopic pattern states.

1. *Spontaneous occurrence*. The patient shown in Fig. 52, willingly jumping on a springboard in the 'anti-phase' mode, often switched spontaneously into the 'in-phase' mode (when not supported manually) and backwards into the 'anti-phase' mode with ongoing jumping series and progressing exhaustion; the patient was not aware of this. The macroscopic pattern states jumping 'in-phase' and jumping in 'anti-phase' can spontaneously occur and change, unnoticed by the patient. The patient in Fig. 55 switched between the jumping modes spontaneously, even though he intended to jump abduction-adduction.

2. *Flexibility*. When walking on a treadmill with approximately 30 kg weight reduction (Fig. 51, paretic lesion sub C5), extensor spasticity of the right leg could be broken by increasing the afferent input from the right forefoot just before ‘lift-off’, by pressing the forefoot transiently onto the ground. Different afferent inputs to the spinal cord, therefore changed the way the leg moved, in other words, changed the network state. The flexibility of the changing pattern states of the CNS (in this case especially the spinal cord) makes behavioral functions possible.

3. *Changing involvement of participating subsystems*. When the right leg was manually supported to keep it in the ‘anti-phase’ jumping mode when jumping on springboard, the left leg of the patient mentioned above switched itself transiently into the ‘in-phase’ jumping mode with sometimes even loosing the phase to the right (supported) foot. A healthy man can hardly jump with one leg in ‘anti-phase’ and the other one in ‘in-phase’ mode. In the lesioned CNS it turns out that subsystems of the pattern generating network can engage and disengage. Different jumping modes of the right and left leg are shown schematically in Figure 55.

31. Unsupervised learning: Recovery of functions not induced by training

A newborn infant can step automatically (Fig. 43). How did the neuronal network of the CNS learned to self-organize itself to induce automatic stepping? If there is further some similarity between the human ontogenesis and reorganization following CNS lesion, then there might be some recovery contribution of locomotor function from unsupervised learning. The patient shown in Fig. 44 (with a paretic lesion of the spinal cord sub TH12 with most likely lesioned motor pattern generating network) re-learned walking and other movements 14 years following the accident. She thought she would never run again, and did not try it. Then, after 14 years she tried it with the author (G.S.) and she could run again immediately with no balance problems, even though she had nearly no feeling in her feet. She could run better than walk. It seems therefore that some motor functions can recover without being directly trained. A possible explanation comes from animal experimentation.

An intrinsic synchronous bursting activity which arises prenatally from the retina before rodes and cones are even formed (‘dark discharge’) exerts a structuring influence on the developing retinofugal pathway. Similar activity-dependent changes might apply to the development of CNS connectivity: the Hebbian rules of synaptic plasticity seem to hold throughout

Figure 43:
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. Note that there is some similarity of the shape of the automatic stepping in A and B to the shape of walking and running of the patients shown in Fig. 44.

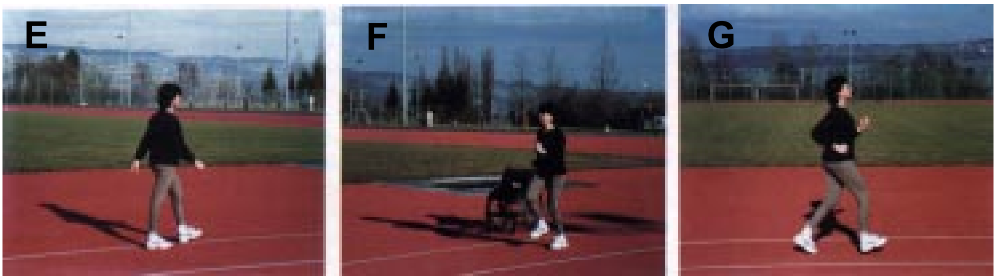

Figure 44:
A 39-year-old female paraparetic patient re-learned running in one minute 14 years after the accident. E. A 39-year-old female paraparetic patient (lesion sub Th12, injury 14 years ago caused by falling down a staircase) during walking. The heel of the left foot strikes the ground first, in some similarity to automatic stepping (Fig. 43A). The walking is still pathologic; the right knee, e.g., sometimes overstretches. The patient had little sensibility in the legs. F. Same patient as in E. The running performance is rather physiologic. Note the similarity of the running shape to automatic stepping of the 8-day-old infant (Fig. 43B). G. Same patient as in E,F. Also in this part of the running cycle, the running performance looks physiologic. The patient is running with the heel touching the ground first (compare with Fig. 43A). It seems as if she is using stepping automatism for running.

the ontogenesis, if one does not restrict the choice of the postsynaptic control variable to spike activity. Subthreshold calcium activity and electrical coupling could act prenatally as a substitute for synaptic transmission to ensure assembly (and oscillator) formation in the absence of conventional fast Na^+ APs [37].

With respect to patients, unsupervised learning of the lesioned CNS (especially the spinal cord) will only be of benefit if the muscles did not undergo inactivity-induced atrophy. For supervised learning, see below (reorganization of the CNS)

32. Models of genotype-to-phenotype matching during an individual’s lifetime

The nervous system and other phenotypic traits form during the ontogeny based on the genetic information stored in the cells (genotype). The information specified in the genotype determines aspects of the nervous system which are expressed as innate behavioral tendencies and predispositions to learn. The inherited genotype can completely specify the phenotypic network; i.e. both the network’s architecture and connection weights are genetically determined. In this case, the behavior of the network is entirely innate and there is no learning [85]. Or the genotype specifies the network’s architecture, but the weights are learned [79]. In still other cases, what has been selected during the evolution are good initial weights for learning or good learning rates and momentums [10].

To apply genetic algorithms to model neural networks, it is necessary to codify the neuronal network (phenotype) into a string (genotype). The way in which this encoding should be realized is not straightforward. A direct genotype-to-phenotype mapping is biologically implausible. In real life, we cannot predict which phenotype will emerge from a given genotype because of the large nonlinearities present in the mapping process. If the genotype is viewed as a set of instructions, it is not the case that each of these instructions will result in a single network property. Rather, the properties of the network emerge as the result of many interactions among the various instructions and their products [81] (for similar argument, see Fig. 61; only the similarity between ontogeny and reorganization/regeneration is needed (see below)).

Neuronal network models of the nervous system (aside from the inevitable simplifications of simulation) must enable the study of both the functioning of the adult nervous system and neural evolution and neural development. For this purpose, what is needed are distinct representations for inherited genotypes and for phenotypic networks, and some models of the complex genotype to phenotype mapping (development).

Models have been developed of genotypes for neuronal networks and of the genotype-to-phenotype mapping. Genotypes can directly incorporate innate behaviors that require no learning, or they can incorporate innate predispositions to learn some behaviors. Innate behaviors can be present at birth (congenital) or they can develop during the life under the control of genetically specified information. Already in simple models, neural architectures progressively structure themselves into functional subnetworks or neural modules [81], which is an important feature to model because of the measured spinal oscillators. But subnetworks responsible for coupling the 'angle of turn' are always more complex than subnetworks responsible for computing the amplitude of the motor step.

Other important processes involved in the genotype-to-phenotype mapping include cell division, cell proliferation from stem cells, and migration of neurons to reach their terminal position in the brain, especially because these processes may take place in the adult human CNS [45,166,167]. Another crucial property of the genotype/phenotype mapping in biological individuals is its temporal character. Biological development (or maturation) does not simply yield an 'individual'; rather, the phenotypic individual is a succession of different phenotypic forms which are sequentially generated by the genotype in interaction with the environment. A model in which the genotype/phenotype mapping (i.e., ontogeny) takes place during the individual's lifetime and is influenced both by the genotype and by the external environment has been described by Nolfi, Miglino, and Parisi [82].

33. Cooperative behavior in networks of chaotic elements [61]

In the search for the understanding of self-organization, re-organization and de-organization of premotor spinal oscillators (especially α_2 and α_3), their transient synchronization, for example, by repeated afferent inputs from the skin, networks of chaotic elements are helpful when mean-field contributions and feedback are included. The cooperative behavior of these networks can partly explain the integrative organization of premotor spinal oscillators to generate macroscopic function by the formation of a coherent structure. The spontaneous switching between attractor states (switching from 'anti-phase' to 'in-phase' jumping or the interaction between walking movement pattern and spastic states) in the lesioned CNS (measured by the deterioration of premotor spinal oscillator function or false motor program (loss of specific spinal cord functions)) can partly be explained by the globally coupled map of chaotic elements as shown below.

Chaos is an irregular motion appearing in a deterministic system. Chaotic dynamics is the only scientific mechanism to connect deterministic and probabilistic views at a macroscopic level. Partial synchronization of nonlinear oscillators has been discovered in the visual cortex [27] and in the spinal cord [107,130] (Fig. 38) and other parts of the CNS. The dynamics of nonlinear oscillation suggest the existence of chaos. Both the synchronization and the desynchronization mechanism are necessary for the processing of external inputs, by some balance between chaos and entrainment. Synchronization and desynchronization of premotor spinal oscillators have been observed during the processing of skin and mucosal afferent inputs (Figs. 37,38).

A dynamical system with discrete time ('map'), discrete space ('lattice'), and a continuous state (coupled map lattice (CML)) consists of dynamical elements on a lattice, each interacting ('coupled') with suitable chosen sets of other elements.

Because of the sensitive dependence on initial conditions that is typical of chaos, a homogeneous state becomes unstable in the coupled map lattice with chaotic components. In the model with the logistic map with weak nonlinearity, domains of various sizes are spontaneously formed in which the oscillations are highly correlated. Oscillations of elements are out of phase between the neighbouring domains, while they are in phase for elements in the same domain, although they cannot be completely synchronized because of chaos. The nature of the dynamics of a site depends on the domain size it belongs to (a feature called spatial bifurcation). In a large domain, the motion is chaotic, while in the smaller domains it is periodic, with the periods depending on the domain sizes.

In a frozen random state, domain positions are frozen in space. With increasing nonlinearity in each element, domains 'melt', and a transition to fully developed spatio-temporal chaos begins. In this spatio-temporal intermittency transition, ordered motion and turbulent bursts coexist in space-time (which could explain the bursts of spasticity during ordered walking in patients). The ordered region forms a large cluster whose size ditribution obeys the power-law distribution, leading to a wide-range correlation in space-time.

In the CNS, the interaction among neurons is not only local, rather, it is global with a complex structure. The model of the simplest case is given by the globally coupled map of chaotic elements. The model is a mean-field theory type of extension of the coupled map lattice. The dynamics consists of parallel nonlinear transformation and a feedback from the 'mean-field'. Through the interactions, some elements oscillate synchronously, while chaotic instability leads to the destruction of coherence. Attractors in globally coupled map are classified by the number of synchronized clusters k, and the number of elements for each cluster N_k.

In a globally coupled chaotic system in general, the following phases appear successively with the increasing nonlinearity in the system:

1. Coherent phase. A coherent attractor (k=1) is obtained from almost all initial conditions.
2. Ordered phase. All initial conditions lead to attractors with few clusters.
3. Partially ordered phase. Coexistence of attractors with many clusters and attractors with few clusters.
4. Turbulent phase. All attractors have many clusters.

In the partially ordered phase, state orbits visit several ordered states successively via highly chaotic states. In the ordered states, elements split into a few 'effective' clusters, whose elements are almost synchronized, i.e., they take the same value up to a given level of precision. The system exhibits intermittent switches between self-organization towards a coherent structure and its collapse to a high-dimensional disordered motion. The total dynamics consists of residences at ordered states interspaced with a high-dimensional chaotic state. The dynamics is called chaotic itinerancy.

The relevance of chaos to neural information processing is given by the capabilities of a network of chaotic elements and the neural dynamics.

1. *Hierarchical memory storage at many attractors and switching.* In the frozen random states and the partly ordered states as mentioned above, huge numbers of attractors (c^N with c>2) coexist, and they are hierarchically organized as a tree or a domain structure. Chaos is essential to this hierarchical complexity, since it leads to successive splittings of clusters. These attractors can serve as basic hierarchical memory units, and they can be related to dynamical categorization in the brain. By applying an input to a single element, one can make

a switch from one attractor to another. Depending on the inputs, different attractors are retrieved as different memories. During the course of switching, intermittent chaos is observed, which may be useful: the system partially retains its previous history, but a search for a novel state is also possible through the destruction of the structure by chaos.

2. *Spontaneous transition among local structures with spatio-temporal intermittency or chaotic itinerancy.* Spontaneous switching among ordered states is possible through chaotic states. The switch is deterministic, but because of the chaotic motion of the system it is not rigidly fixed.

3. *Generation of information and its transmission by chaotic travelling wave.* Through chaotic dynamics, microscopic information is amplified to a macroscopic level. In the chaotic travelling in the coupled map lattice, attractors with different velocities coexist. Switching among attractors by single (local) inputs is again possible, to change the speed of transmission. By means of the travelling wave, some information is transmitted to the whole space. Thus, transformation from local to global information is possible through this switching.

4. *Partial coherence as a mechanism of grouping and feature detection.* In a globally coupled map, partitions into clusters are spontaneously created, while domains of partial synchronization are formed in coupled map lattice. In information processing, grouping of many inputs is required, based on some conditions such as continuity [27]. The network of chaotic elements can provide such a capability, since the coupling term leads to the grouping of elements with (partial) coherent oscillations. In neural processing, a partially synchronized cluster changes its members according to inputs to the system. In a globally coupled map, this request is attained by the orbital instability of chaos.

Change of coherence is important in epilepsy. An ensemble of neurons exhibits a large spike because of oversynchronized firing of neurons, and the information processing ability is often lost [61]. It has to be measured whether in spasticity there is also too much sychronization of premotor spinal oscillators and many other not oscillatory firing neurons so that specific information processing is lost. An increase of the inhibition of these spinal oscillators (increasing descending inhibition) with entraining of also chaotic states (for example, handshaking) seems to enable physiologic information processing again.

The main drawback of the chaos theory is that it has not been applied to human reality. No hard human data have been incorporated to see whether certain predictions on, for example motor functions in patients can be made, which can be measured by the coordination dynamics in patients (Fig. 103F, 86L, , 110, 112, 114, 117-119).

34. Regeneration and neurogenesis in the human CNS

Spinal cord functions may recover up to 10 years or even longer following a lesion. It will be difficult to explain such long recovery times of the CNS by a repair of damaged nerve cell somas only. Most likely, sprouting in the CNS also occurs in humans [157]. But there might still be a more of growing capacity in the human CNS as suggested by the improvement of functions shown in a patient during rhythmic impact training of the feet in a weelchair (Fig. 45).

In this patient, a rather strong increase of muscle power function due to the regained volitional control in the functional improvement of the CNS was observed during period I (Fig. 45B). During period II, only little improvement was achieved as a result of the coordination dynamic therapy, since all previous recovery was used and the little increase came from the slow further recovery. The strong increase in functional output in period III was due to the rhythmic impact training. Such dependences have been observed for different rhythm training

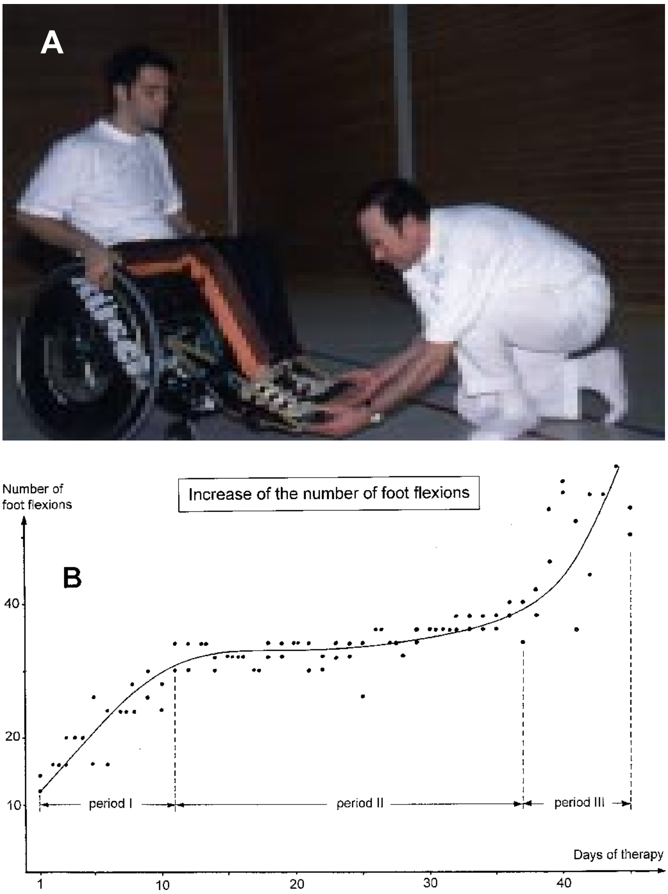

Figure 45: Three-stage improvement of foot flexion
A. Patient in a weelchair with a device for training dorsal and plantar flexions. The power needed for flexion can be adjusted. B. Increase of the number of foot flexions per training session in dependence on the days of therapy. Note that there are three periods of dependence with a plateau phase in period II.

methods in different patients. It might seem therefore that with strong impact training, some regeneration may occur with a delay of approx. 30 days. Probably, this lesion-induced reorganization or regeneration [45,157] takes place via the interneurons in the gray matter, since 30 days might be too short a time for the tract fibres to grow. The neurons of the gray matter in the area of the lesion may have been used as neuronal relays.

Even if the adult brain has been claimed to be unable to produce new neurons, multipotent, self-renewing stem cells in the adult mammalian CNS (including man) have been identified in the adult forebrain lateral ventricles and spinal cord [166,167]. When isolated in vitro, the adult forebrain stem cells proliferate in response to epidermal growth factor (EFG), renew and expand themselves, and produce neurons, astrocytes and oligodendrocytes. In vivo, adult spinal cord neural stem cells prolefirate in response to epidermal growth factor and basic fibroblast growths factor, and renew, expand and show multipotency [45]. Spinal cord neural stem cells have the capacity to produce cholinergic neurons. It has been suggested that the regulation of neural stem cells of the adult human CNS may be part of new strategies for cell replacement and/or axonal regeneration following CNS injury or disease [167].

The proliferation of stem cells to neurons needs very roughly 6 weeks (personal information). The somehow stepwise improvement of motor functions mentioned above took approximately 4 to 6 weeks. It seems possible that training-induced neurogenesis [157] contributed to the re-learning of motor functions. In animal research, pharmacological methods are under development to manipulate the rate and fate of neurogenesis in the intact and damaged adult brain and spinal cord [5,45,157]. Neurogenesis in adult man has been detected by histochemical methods in the hippocampus [31]. There is no morphological and no functional evidence to suggest that there is no neurogenesis in other parts of the CNS if an adequate intensive therapy is applied to patients with CNS lesion. The enormous extent of repair achieved in patients with severe CNS lesions (see case reports and cell death of motoneurons) makes it very likely that new neurons can also be made functioning in the desirable way if a proper neurorehabilitation therapy is applied. The new cells in the hippocampus originated from the remnant pluripotential stem cells situated in the subgranular zone of the dentate gyrus (enlargement) [31,95,28]. Stimulation of neurogenesis and enhancement of neurogenesis are tried by going with the oscillator formation and coordination dynamic therapy to the limits (see below).

Functional improvement in adult rats with transsection lesions on one side of their spinal cords were observed following the repair of the corticospinal tract by transplants of olfactory ensheating cells [75], and after treatment with antibody IN-1 that neutralizes the myelin-associated nerve growths inhibitors [151]. From clinical point of view, it is not impossible to bring a patient out of the wheelchair if as much as 50% of the spinal cord survived the injury.

Electrophysiologically and morphometrically, nucleotides (a combination of uridine monophosphate and cytidine monophosphate) have been shown to enhance nerve fibre regeneration in the rat PNS [161,162] and probably also in the CNS. In the frog, the thicker axons regenerate faster than the thinner ones [78,102]. In the human PNS, the regeneration rate of 1-2 mm/day is slowlier than in the rat. If fibres do regenerate in the human CNS, one can expect similar or slowlier regeneration rates. If a spinal cord lesion occurred in the cervical range and the distance between the intumescentia cervicalis and lumbosacralis lies in the range of 300 mm (Fig. 49), one can expect recovery times due to axonal regeneration in the range of one to two years (the slow recovery of a patient with poliomyelitis (see case report), getting an intensive coordination dynamic therapy, is in accordance with the slow process of neurogenesis and cell proliferation including axonal regeneration). For longer application times, side effects of drugs would also have to be taken into account.

It has been argued that following CNS lesion the vacant synapses of neurons are reinnervated by input afferents (due to sprouting) and that the target for re-innervation is lost in this way. Also, neurons without sufficient input are dying. It has been shown that denervated slow muscle fibres of the frog are first re-innervated by the false quickly regenerating thick axons, innervating normally the twitch muscle fibres. But when the proper slowly regenerating axons reach the muscle, they take over control of the slow muscle fibres and they push away the false innervation at the synaptic sites [78,102,197-199]. Therefore, occupied synapses may not stop a proper re-innervation. The dying of neurons in the lesioned CNS may be critical (also human muscle fibres start to die when denervated for longer than 1 year). We emphasize in the present paper that the coordination dynamic therapy has to be started as early as possible, i.e. the therapy has to be started at the intensive care unit, to prevent the severely lesiond CNS to deteriorate in its functioning where neuron cell death is contributing to. The practical experience is that the deterioration of CNS functions in very severe lesions can be stopped if an intensive coordination dynamic therapy is applied. In humans, atrophy and dieing of distant muscle fibres is delayed if the muscles are stimulated electrically. Frog slow muscle fibres change their membrane properties following denervation, because of lack of activity and trophic substance. The change of the membrane properties is delayed if the muscles are supplied longer with the trophic substance [201] or when activated repeatedly [200]. The data from the peripheral nervous system support the finding that the deterioration of CNS functions can be stopped if an intensive coordination dynamic therapy is applied. Further, if a frog slow muscle fibre is only partially denervated, then only parts of the slow muscle fibre change their membrane properties [202]. It may therfore be that, in partially denervated CNS neurons, the denervated parts of the neuron change their membrane properties. Such possible complicated membrane structures will be difficult to measure electrophysiologically in the CNS, but they are important for CNS organization, because changes of membrane properties change the timing of firing of neurons.

In a preliminary study to the above mentioned experiments dealing with enhancement of the regeneration rate in the rat PNS by the application of nucleotides (unpublished observation) the regeneration in the control group was found to reach the same level after a few months as in the experimental rat group which received nucleotides. Enhancement of the rate of nerve fibres regeneration by, e.g. 20% in the human PNS is beneficial for the patient, because the regeneration times are in the range of one year and the muscles may atrophy during that time period. The muscles may disappear before regenerating motoneuron axons reach them. When it comes to drug-enhanced regeneration in the human CNS, the outcome of the enhanced regeneration will have to be assessed after many months or even a few years, to see whether the beneficial effect of enhanced regeneration overrides the side effects of long-term drug administration. To be of clinical relevance therefore, animal regeneration experiments must be discussed in detail with respect to the human application including different regeneration rates, regeneration power and regeneration lengths in humans.

Vertical cooperation is needed to bring animal regeneration data to clinical setting. But since regeneration is unspecific in man, therapy-induced reorganization of the CNS is nevertheless necessary [24]. ‘Until recently, clinical pessimism was so rampant that medical personnel often did not treat spinal cord injuries as true medical emergencies’ (Editorial (page 1907) to [75]).

35. Motoneuron cell death

An essential limitation to re-learning of somatic and autonomous functions is cell death of somatic and autonomous efferents. Surviving motoneurons can increase their motor unit by approximately 50% only. Muscle fibres (effector organ) can only benefit from reorganization of CNS networks if sufficient amount of motoneurons have survived. Patients with a lesion of the intumescentia cervicalis may achieve full muscle power in the legs, because the intumescentia lumbosacralis is not injured; they however cannot gain full muscle power in the arms and hands because of motoneuron cell death in the intumescentia cervicalis.

Similar holds for brain stem lesions due to virus infections, in which the motoneurons of the phrenic nerve (the most important breathing nerve) often die, as an unpublished morphometric study and clinical experience indicated. In such cases, nerve anastomosis is performed from the intercostal nerves to the phrenic nerves to reinnervate the diaphragm. The intercostal nerve axons are then electrically stimulated to activate the diaphragm for breathing.

If spinal cord stem cells could actually be activated on a large scale to proliferate into interneurons and motoneurons, then invasive treatments would have to be reconsidered. If motoneuron axons grow out of the CNS in the direction of muscles (1-2 mm/day), form functioning synapses and become integrated in the functioning of the CNS, delay times of a year or more have to be expected until a function appears.

As the case report on the poliomyelitis patient suggests (see case reports), there may also be neurogenesis of motoneurons in the spinal cord of adult man. A 37-year old patient was striken by severe poliomyelitis (which is believed to destroy the motoneuron cell somas) 36 years ago with no sign of remaining muscle activity for the subsequent 36 years. After two months of coordination dynamic therapy, leg muscle functions started to recover. Further recovery of leg muscle functions after 7.5 months of therapy could be evidenced by electromyographic recordings which showed reinnervation of muscles (Fig. 95A-F). After 17 months of intensive coordination dynamic therapy, the strength of the leg muscles further improved. The patient is now able to turn the pedals of the special coordination dynamic therapy device against 6 kp without arms and without auxiliary muscles, indicating that quite a lot of motoneurons are already activating leg muscles again, since human motor units cannot be increased by more than 50% (rat 1000%). The regaining of leg muscle functions in caudal spinal cord and conus medullaris lesions (see case reports) supports the possibility that new motoneurons can be built in humans besides substantial reorganization by coordination dynamic therapy.

Actually, the functional data presented herein, suggesting neurogenesis, support the reports on neurogenesis, where only morphologic data were presented to document neurogenesis and cell proliferation [31,45,157,166,167]. So far, evidence for the functioning of the new nerve cells and neurites following neurogensis and cell proliferation in the adult CNS by electrophysiologic methods has not been provided. For the frog peripheral nervous system it could always be proved electrophysiologically that newly built synapses (motor endplates) were also functioning, since during (re)innervation (following denervation [78,197-199] or during development [102]) the function of the membrane (the contracture and the Ca-transients) of slow muscle fibres were controlled by the kind of innervating motoneurons; Na-channels for generating action potentials may not have been incorporated or channels could be blocked by certain molecules [200]. It is conceivable that the membranes of newly formed nerve cells and their functional contacts (synapses) may not have been incorporated into certain channels for excitation or that certain channels are blocked. There is no reason to believe that the structure of the human CNS is simplier than that of the peripheral nervous system of the frog.

36. Genotypes for adapting neural networks

There exists some capacity for neurogenesis in the adult CNS, which may be induced pharmacologically or by an intensive coordination dynamic therapy [45,157,166]. This opens up another temporal dimension in the process of adaptation. Migration of neurons into a new position is a widespread phenomenon in the developing brain, and can also be expected to take place in the adapting CNS. It is not understood so far what initiates, guides and arrests such migration [45]. The positioning of the de novo neurons (hopefully in the place needed to function, e.g. a relay neuron) will be correlated with the formation of novel inputs. Difficult to explain is how the dendrites and the cell bodies of the novel neurons are reached by axons from supralesion levels, and what guides the axon of the new neuron to grow towards the more caudal neurons. Or is the growing of neurites and the formation of synapses completely random, and the learning network only makes ‘sense’ of the connections?

Principally, after stem cell proliferation some neurons of the identical population could assume a different function by reaching a different target or by segregating their perikarya and dendrites (and thus input) through differential migration or both. How this identity could be achieved is still unclear. Can selector genes be influenced by excessive training to achieve different phenotypes of neurons [62]?

Another possibility for the adaptation of neuronal network functions following CNS lesions could be a change of the commitment of neurons. The lesion-induced loss of input or target or both, which eliminates the constraints normally acting on the neurons, could allow them to develop a new function [42]. Such a property change could be much more powerful with respect to neuronal network reorganization than changing the efficacies of synapses, when leaving out collective effects. Frog slow muscle fibres change their membrane properties (action potential generating mechanism present or not) and excitation-contraction coupling according to the motoneuron type they are innervated [78,102]. The neural control of the specialization of synapse formation and membrane properties (and excitation-contraction coupling) seems to be more powerful than the changes of synapses achieved by activity changes. This frog model is of special interest in this connection as it shows similarities in the neural control of membrane properties between ontogenesis and readaptation following neural lesion. The power of this animal model lies in its safety to identify membrane property changes.

C. Basis for neuronal network reorganization

37. Identification of oscillator firing patterns in EMG recordings

By measuring single nerve-fibre action potentials of afferent and efferent nerve root fibres, regulatory mechanisms of the spinal cord and partly of supraspinal centres can be analyzed [130]. The disadvantage of this recording method lies in its invasive nature. Recordings can be obtained only during surgery for e.g. implantation of anterior nerve root stimulators to paraplegic patients for urinary bladder control (the anaesthesia is very shallow during the operation, the paraplegic patients feel no pain). Intraoperative diagnosis is performed during the surgery to identify the representation of the bladder and somatic functions in the nerve roots to de-afferentate the bladder and to subsequently stimulate preganglionic parasympathetic efferents with the implanted electrodes to empty the bladder.

In EMG recordings with surface electrodes on the other hand, it is possible to record the rhythmic firing of single motor units (Fig. 46), especially in individuals with lesioned CNS when oscillators are not fully under volitional control any more (Fig. 48, see below). Oscillation period distributions for oscillators and phase distributions between them, as well as synchronization and desynchronization of spinal oscillators can be measured non-invasively by means of single motor unit recordings with surface electrodes [131].

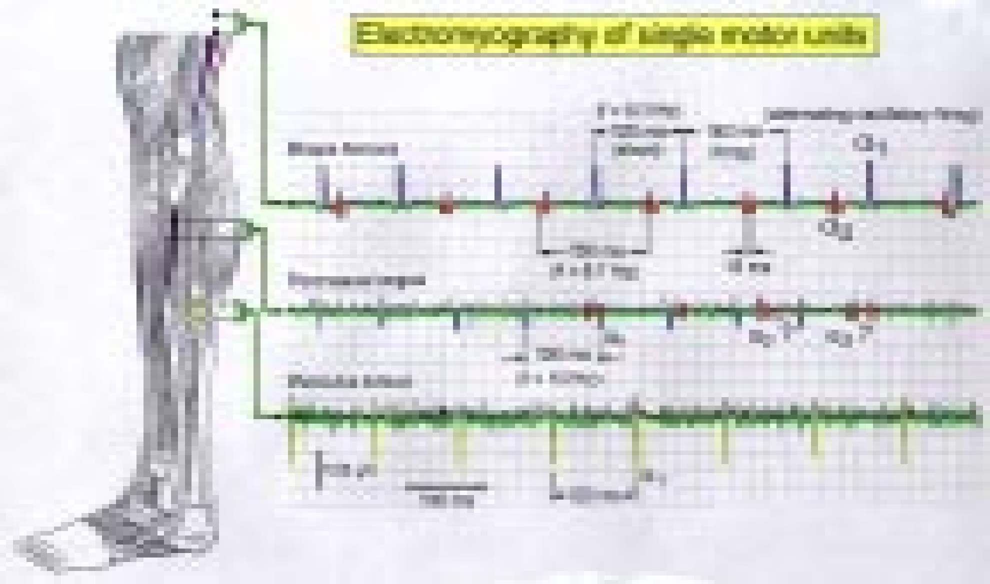

Figure 46
Extracellular electromyographic recordings with surface electrodes from the musculi biceps femoris, peronaeus longus and soleus. Impulse patterns of oscillatory firing α_1 and α_2-motor units can be identified in the recordings of the three muscles, and are partly marked. A safe identification of α_2-motor units in the record traces of the peronaeus longus and soleus muscles is not possible because of the high activity. Note that on the average, the α_1-motor unit potentials have a higher amplitude than the α_2-motor unit potentials. Note further the long and short oscillation periods of the alternating oscillatory firing α_1-motoneuron of the biceps femoris muscle.

38. Electromyographic kinesiology

Electromyographic kinesiology was also performed in patients with paretic spinal cord lesions [131]. It is a standard method which is used world-wide and provides details about the pathology of the motor program. Electromyographic kinesiology offers however no information how to reorganize the lesioned CNS to improve the motor program. Still, electromyographic kinesiology diagnosis is used to improve motor functions in patients along the orthopedic line (see under 'A new start after Bobath therapy').

For research reasons the analysis of pathologic motor programs is of interest, especially if recordings of single motor unit firings are included, because it would be of interest to see how relative coordination of premotor spinal oscillators takes place in different muscles (Figs. 8,9 of [131]). It is of interest to find out how the motor program is self-organized. Activity levels in the electromyographic recordings are only of little interest for research because single unit firing patterns offer more information concerning the self-organization of neuronal networks.

39. Dynamic memory of the spinal cord

Since it was observed electromyographically that spinal oscillators can switch back to the same phase relation in relation to other oscillators from one muscle activation to the next one, there is indication that the spinal cord has a memory (Figs. 8,9 of [131]). The short-term

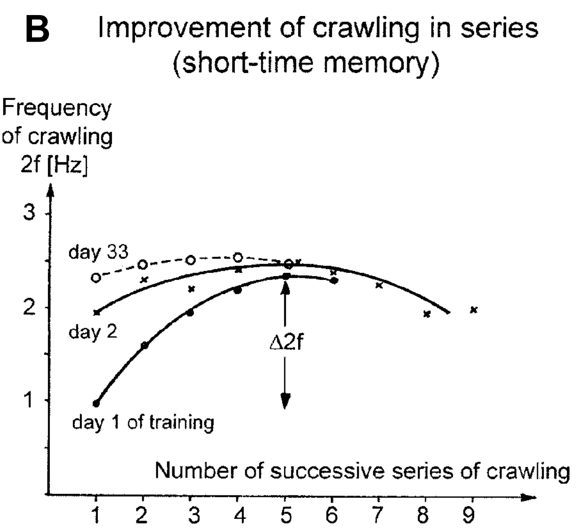

Figure 47A, B
A. A female paraparetic patient (sub L1) crawling, accompanied by the trainer (author G.S.) over a distance of 5 m. The trainer was slightly hindered in crawling because he had a stopwatch in his right hand, and therefore did not crawl cross-like. The patient's weelchair used for training rhythmically dorsal and plantar flexion is seen in the background; the strength of the rubber strings was 0 to 1 kp in neutral position. B. Improvement of neuronal network organization measured by the absolute crawling frequency 2f and the variation of the crawling frequency Δ2f. As can be seen from the 3 curves of successive crawlings, the absolute frequency increased from the first to the second to the 33rd day of training; 2f increased from 2.3 Hz to 2.4 to 2.55 Hz. The variation in frequency reduced from Δ2f = 1.4 Hz to 0.5 to 0.2 Hz, suggesting an improvement of neuronal network organization. On day 33, the patient was only crawling on her elbows and not on her hands, to reduce the burden on the wrist joints; the frequency crawling on hands would have been slightly higher.

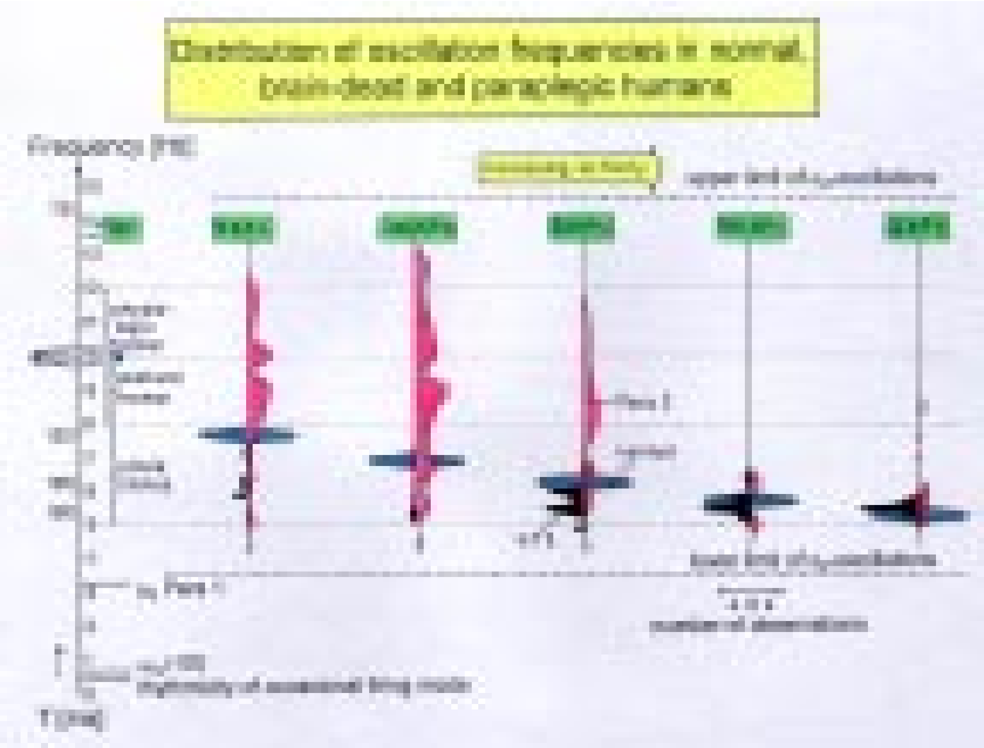

Figure 47C
Frequency distributions of oscillation frequencies of continuously oscillatory firing α_2-motoneurons with increasing number of APs per impulse train (increased activity) in paraplegic 2 (open), in brain-dead HT5 (filled), and probably normal human (cross-hatched). Frequencies and rhythmic activity changes in the occasional and oscillatory firing mode are indicated. Ranges of physiologic tremor, postural tremor and ankle clonus are also drawn. Note that frequencies for the brain-dead HT5 are too low, and the oscillation frequencies of the spinal cord isolated for a long time (Para 2) are too high and too spread as compared to the theoretically predicted frequency ranges (cross-hatched). T = oscillation frequency.

memory can also be measured clinically by the improvement of rhythmic movements from one performance to the next one during an interval training (Fig. 47A, B). The updating of the stored movement state is quantified in Fig. 47A, B by the crawling frequency, which increases with successive crawlings over 5 m. With appearing exhaustion, the frequency reduces and the movement performance becomes poor.

If we believe that the repeated storage of a movement in the short-term memory leads to storage in the long-term memory, then it should be possible to quantify the efficacy of a therapy to reorganize the CNS with the outcome of more physiologic movements following CNS lesion, by the improvement of the movements in the short-term memory. The time consuming and expensive statistics, with still the problem that no CNS lesion is equal to any other and all distributions measured in human neurophysiology so far are asymmetrical ones (not of Poisson or Gaussian type (Figs. 1,25-28,35,36; [127])), would not be necessary then. Dynamic measures for quantifying reorganization would speed up the clinical research. Measuring the improvement of reorganization of the CNS by the rhythmicity of performed coordinated movements of arms and legs, when exercising on the special coordination dynamic therapy device (Figs. 103F, 86L, 110, 112, 114, 117-119), is a first step in the direction to directly quantify the improvement of CNS organization (see also under Summary of the theory of coordination dynamics of the lesioned human CNS). To measure the efficacy of therapeutical methods intended to reorganize the lesioned CNS by improvements in the short-term memory would be in the interest of the patients and would be more ethical, as patients with CNS lesion could benefit more quickly from the progress in human brain research.

40. Change of the functioning of premotor spinal oscillators and change of the neuronal network organization following spinal cord lesion - pathologic network organization

Following spinal cord lesions the spinal cord neuronal networks have been observed to change their organization, and this can be quantified by six changes of organization.

1. Following spinal cord lesion, the spinal oscillators strongly widen their oscillation frequency band [136], which means that their firing becomes unrhythmical (Fig. 47C). An increase of the more irregular oscillator firing can also be seen in the broadened distributions of the interspike intervals of the impulse trains of oscillatory firing α_2 and α_3-motoneurons [118].

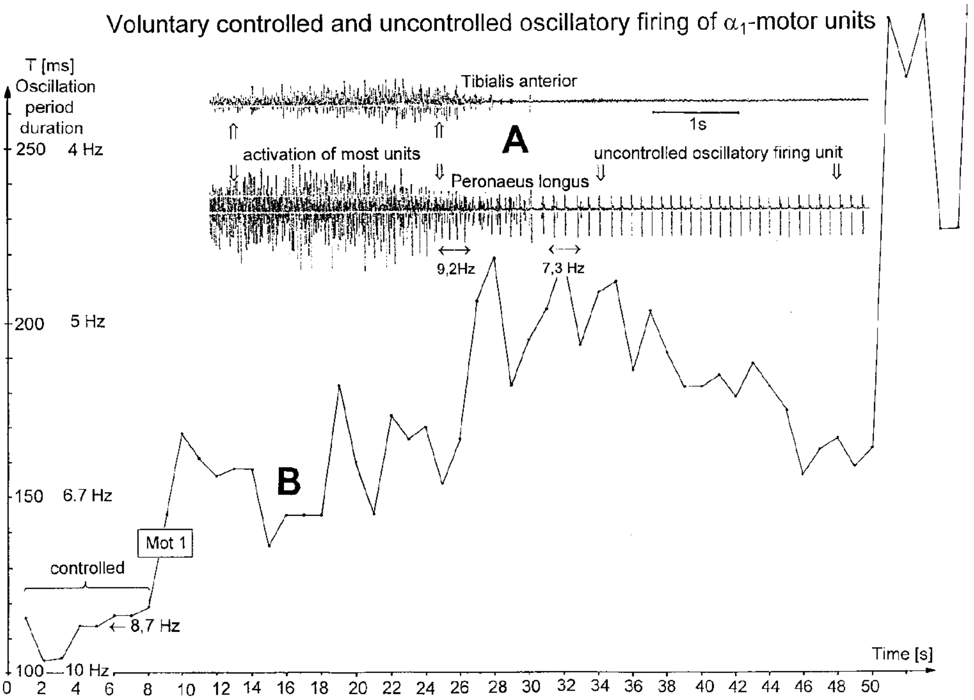

Figure 48

Volitionally controlled and uncontrolled firing of α_1-motor units in a patient with a paretic spinal cord lesion sub C5/6. A. Original electromyographic (EMG) registration of many volitionally controlled motor units in the tibialis anterior and peronaeus longus muscles and one uncontrolled oscillatory firing motor unit Mot 1 in the peronaeus longus muscle. B. The solid line of Mot 1 connects oscillation period durations; each value of oscillation period duration shown represents the mean of 5 to 10 measurements. The motor units were activated in the peroneus longus muscle by knee extension.

The loss of specificity of oscillatory properties will at least partly be due to the loss of supraspinal inhibition because muscles below the paretic spinal cord lesion are overactived.

2. Following the lesion, the phase relations among the oscillators and between oscillators and their driving afferents (for example, secondary muscle spindle afferents) become very instable (Fig. 6 of [130]).

3. Because of the widening of the frequency bands and the instability in phase coupling [130,136], the oscillators lose partly their rhythmicity and their coordination and cooperation properties. The rhythmicity of movements and their coordination and coupling of arms and legs is reduced. The loss of rhythmicity and the loss of coordination can be observed easily when training rhythmic coordinated movements with the patient (Fig. 86L).

4. The spinal oscillators are not under full volitional control by the patient any more (Fig. 48). Sometimes, paraparetic or tetraparetic patients can switch on motoneurons to fire oscillatory, but cannot switch them off again.

5. Following natural stimulation, the recruitment of motoneurons in the occasional firing mode (low activity mode of motoneuron firing) according to the size principle in each nerve fibre group changes [113,117]. The level of motoneuron activation increases following spinal cord lesion (probably due to loss of inhibition) and the slowly conducting α_3-motoneurons (S) are recruited before the faster conducting α_2-motoneurons (FR), which is pathologic (see above under recruitment in the occasional firing mode following spinal cord lesion).

6. The coupling of α and γ-motoneurons changes in strength following natural stimulation [117].

The loss of rhythmic oscillator properties and the change of motoneuron firing in the occasional firing mode (when the oscillators have not been self-organized because of low activation) indicate deterioration in the self-organization of the spinal cord neuronal networks below the lesion, and can at least partly explain the false CNS network organization called spasticity and increased clonus. The loss of stable properties of spinal oscillators can be compared to the weak character of some persons in a society when the system changes, and such oscillator behavior may be similarly called ‘to put one’s flag to the wind’ (the wind represents the afferent drive). The partly uncontrolled firing of spinal oscillators seems to correlate with the false motor program of the self-organized spinal pattern generators measured electromyographically [131]. Therapeutic intervention cannot be followed up on the basis of activity levels and phases of muscle activations of motor programs during locomotion only, but also based on the physiologic and pathophysiologic firing patterns and recruitment of spinal oscillators.

41. Entrainment of spinal oscillators and entrainment of coordinated motoneuron firing as means to treat patients with CNS lesions

At this point of research, there are clinical applications opening up before paraparetic, tetraparetic and brain-lesioned patients. If the neuronal networks of the spinal cord below the lesion are organizing pathologically as measured by the pathologic organization of subneuronal networks, namely the spinal oscillators and the motoneurons firing occasionally, then the spinal oscillators and the motoneurons have to be entrained for a better, i.e. more rhythmic, coordinated, specific functioning. The entrainment of the biological oscillators [89] is materialized by rhythm and coordination training methods. Effective energy saving rhythms can be felt by the trainer, and have been published in 1928 by Wacholder from Breslau [159]. Exact synchronized afferent input ‘in-phase’ and in ‘anti-phase’ (and other coordinations) in combination with the descending control (movement on volition, excitation and inhibition) should entrain the motoneurons and interneurons for an improved physiologic functioning. Dynamic movements should be trained to activate more extended network parts and to entrain the cooperation between fast and slow components of the network, to restore, for example, the physiologic recruitment of α_2 (medium fast) and α_3-motoneurons (slow). More generally, the neuronal networks of the spinal cord and supraspinal centres have to be trained to improve self-organization including cooperation and competition, so that more physiologic functions can be performed by the patient.

Rhythmic movements such as running or jumping have a frequency between 0.8 to 1 Hz, and the premotor α_1, α_2 and α_3-oscillators have frequencies ranging between 8-12 Hz, 6-9 Hz and around 1Hz respectively. It seems therefore that only α_3-oscillators could be entrained directly, but most oscillators would be entrained subharmonically and the entrainment energy would be rather small. But one has to remember that the afferent input patterns give rise to self-organization of the motor pattern generating network (MPN) and to the entrainment of the premotor spinal oscillators as subnetworks of the MPN. E.g., when the foot touches the ground, skin afferents fire with impulse trains (Fig. 29) with first interspike intervals of approx. 10 ms (corresponding to 100 Hz), so that oscillators may get many entrainment pulses per entrainment cycle. If the movement is dynamic, also the dynamic oscillators (α_1) and the dynamic muscle spindle afferents (primary) are fully included in the entrainment. The α_1-oscillators and the primary muscle spindle afferents fire in absolute coordination (time-locked) [128], and the primary spindle afferents can therefore entrain the premotor α_1-oscillators harmonically [131]. α_2 and α_3-, and possibly existing propriospinal oscillators of the MPN are not absolutely correlated with the afferent drive. Phases between the oscillation cycles are important for the relative coordination between spinal oscillators, and phases between the afferent action potentials and the oscillation cycles are important for the relatively coordinated entrainment of spinal oscillators by the afferent input patterns. Upon skin touch-induced phase resetting, secondary muscle spindle afferent and α and γ-motoneuron action potentials have been shown to become transiently relatively phase-coordinated [129,130] or even relatively coordinated in phase and frequency [130] (Figs. 37,38). With respect to coordination dynamics (see below), the required relative phases are relative constraints whereas frequencies are nonspecific constraints.

Synchronization of neuronal responses on a milliseconds time scale may be used in cortical processing, since synchronization of discharges is a particularly efficient mechanism to increase the saliency of responses [145,146], and may be used in the spinal cord to build up the network loops of oscillators. The coordinated afferent input from arms and legs during crawling, jumping on a springboard, ‘air-walking’ and exercising on the special coordination dynamic therapy device enhances the coupling of arm and leg movements (see below) by sharing of self-organized network loops of the spinal oscillators (see co-movement).

42. External loops of spinal oscillators as a means to entrain spinal oscillators by a rhythm training

Simultaneous interspike interval and phase relation distributions suggest that spinal oscillators can build up an external loop to the periphery by including the γ-loop into the oscillatory firing when interspike interval distributions of α and γ-motoneurons and spindle afferents become very similar at constant phase relations of the broad peak type [130] (Fig. 38). Muscle spindle and other afferents are driving spinal oscillators, but this does not necessarily mean that the γ-loop becomes an external loop of a spinal oscillator. Only the similarity of interspike interval distributions of α and γ-motoneurons and muscle spindle afferents at two rather constant phase relations (phase and frequency coordination) is a measure for the building up of an external loop.

The setting up by the self-organized spinal oscillators of an external loop to the periphery provides an opportunity to directly entrain spinal oscillators by a rhythm training, such as jumping on a springboard, running or exercising on the special coordination dynamic therapy device. Via the external loop drive and other drives, the organization of the neuronal networks of the lesioned CNS can be improved for a better lesion-adapted functioning as measured by the improvement of locomotion (quantified high impact power training). As will be shown below, coordinated, rhythmic, dynamic, stereotyped symmetric movements are especially powerful in reorganizing the lesioned CNS for re-learning of physiologically useful functions.

43. The scientific basis and assumptions for network reorganization following CNS lesion

The scientific basis for the reorganization of the patient's CNS to re-learn useful movements (and autonomic and higher mental functions) derives from several facts:

I. With respect to coordination dynamics [44,63,172-176], the CNS of man organizes itself by changing rhythm couplings of oscillatory firing subneuronal networks and the tendency toward phase and frequency coordination of other neurons, not firing oscillatory [107]. The rhythm *training* fits therefore the organization principle of the CNS. 'Rhythmicity, or better *phase and frequency coordination*, is what the CNS understands well, because it fits its organization principle'.

II. The *training of coordinated, rhythmic, dynamic, stereotyped movements* in paraparetic and tetraparetic patients is especially effective for the reorganization (re-learning) of functions of the CNS, since the neuronal networks for the self-organization of those movements are mainly *located in the lower spinal cord,* which is not lesioned. Walking and running seem to be genetically predetermined in the preferences of neuronal network connections of the intumescentia lumbosacralis (they are deep attractors), and therefore very effective for reorganization, since newborn babies [152,153] and anencephalic infants [91] can step automatically (Fig. 43). It is suggested that innate neuronal networks of the spinal cord generate the infant stepping, and that the same networks are also utilized in adult age [35,153]). If there is neurogenesis from stem cells and regenerative repair capacity in the CNS (see above), then the walking pattern generating network in the intumescentia lumbosacralis should repair itself on the long-term. The clinical experience with lower spinal cord lesions supports the regenerative repair capacity theory. A 39 years old patient with a paraparetic lesion sub Th12 (running network in the spinal cord impaired) re-learned running 14 years after the accident within a minute [136] (Fig. 44).

Generally, reorganization of the lesioned CNS can efficiently be achieved by the following movements: 1. Genetically predetermined movements (running, walking, crawling), 2. Old-learned movements stored mainly in the spinal cord (climbing a staircase, playing tennis, skiing, ...). A long and frequently used movement pattern state, organized with long-established network assemblies, can be expected to have wide safety margins to injury, so that the long-established memory can be expected to be rather resistant to disruption [49], 3. Movements, which are efficient in reorganizing the network, such as jumping on a springboard, i.e. phase and frequency entrainment by synchronization of re-afferent input in antiphase movement, and 'air-walking on a strider (Figs. 66D;68B,C), i.e. phase entrainment by coordinating re-afferent input of arms and legs (forced coordination of arms and legs). Especially the entra-

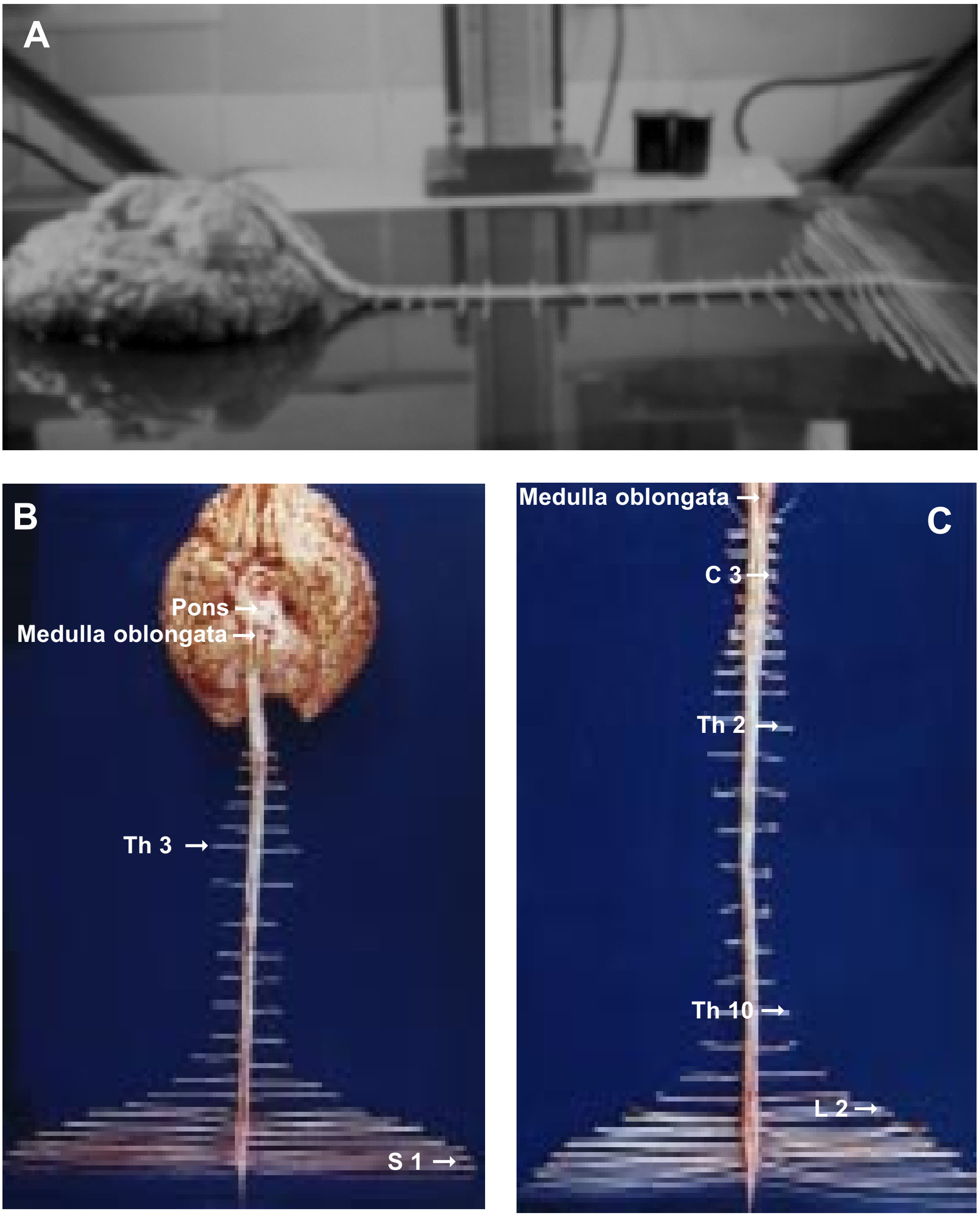

Figure 49
Original photographs of the human central nervous system (CNS). The long nerve roots in the lumbosacral range quantify the ascensus of the caudal spinal cord, mainly the lumbosacral one. The longer nerve roots in the range of Th2, Th3 (B,C) indicate a slight ascensus of the intumescentia cervicalis or a bigger variability with respect to the correlation between the spinal cord segments and the vertebrae segments in that range. The weight relationship (A,B) of the CNS rostral to the medulla oblongata to caudal including nerve roots = 30: 1. A,B. CNS of a 70-year-old lady; size = 167 cm. C. The spinal cord of another individual including medulla oblongata. The distance between the intumescentia lumbosacralis and cervicalis is approx. 30 cm. Identification of nerve roots by counting from rostral to caudal or from caudal to rostral with the characteristics that the ventral S1 root is the last thick root in caudal direction [103].

inment of phase and frequency coordination is efficient, when exercising on the special coordination dynamic therapy device. 4. Last but not least, movements which are needed for the everyday life (one has to re-learn what is needed).

III. Since rhythmic dynamic stereotyped movements are mainly organized in the spinal cord by the afferent input from the periphery, only *few ascending and descending tract fibres are necessary for their activation.* In monkeys, 5 to 10 % of tract fibres were sufficient for locomotion, without essential reorganization of the CNS [30]. In many spinal cord lesions, such fibre numbers may survive.

IV. Spinal movement patterns which are mainly localized in the *spinal cord* below the lesion (walking, running, crawling, jumping, ...) *can activate muscles rather physiologically* since they are only little affected by a brain lesion. Further, spinal cord networks may undergo more innate repair than phylogenetically younger structures (supraspinal or supra-brainstem centres) as the experience with patients indicate. This means that also those muscles can be activated which cannot be contracted on volition by the patient because of the lesion. When training rhythmic, dynamic, coordinated movements like running or jumping on a springboard, the volitionally not activable muscles will not undergo atrophy because of lacking activity, and the recovery of the CNS can fully be used to improve movements even 5 or 10 years after the injury.

V. Lesion-induced right-left inbalance (one leg (or arm) is mostly worse than the other one) can partly be compensated for by inducing ‘Mitbewegungen’ *(co-movements,* Fig. 53). By an exact simultaneous afferent input to the oscillators of the right and the left leg, the spinal oscillators and also the pattern generating networks will couple more strongly. In this way, the ‘poor’ leg couples more strongly to the ‘good’ leg, and *the functions of the poor leg improve,* as can nicely be observed during chest-swimming (see below). In hemiparetic patients, the ‘poor’ arm and hand can be coupled by symmetric movements to the ‘good’ arm and leg to reduce spasticity and improve volitional movements. The coupling between right and left side does not only hold for the activation of muscles, but also for the de-activation of muscles. A spastic hand of a tetraparetic patient can be easier relaxed, if the therapist takes both hands (simultaneous afferent input) and asks the patient to relax. Symmetrical shaking will help to relax, also when performed by the patient himself. Therefore, relaxation of muscles is partly an active process.

Coordination of arm and leg movements can be improved in infants and paraparetic patients (lesions in the range of sub Th12) by crawling (Fig. 47). The poorly functioning oscillators and in turn the pattern generators of the legs are coupled to the healthy functioning oscillators and pattern generators of the arms by propriospinal tracts and long propriospinal subnetworks, which connect the intumescences of the spinal cord.

VI. A quantified *high impact training* shows an improvement of the locomotion and motivates the patient for further training. A training in series at 1 min intervals (interval training) is especially beneficial since the neuronal networks can store the movement pattern from one running series to the next one (for minutes), whereas the muscles (and the CNS) can partly recover from the exercise. Successive rhythmic movements (running, walking, crawling) improve in performance and speed, probably by a successive improvement (updating) of the transiently stored network organization before worsening due to exhaustion (Fig. 47).

VII. From therapeutic point or view*, running is more important than walking,* since it can mostly be performed by the patient more physiologically and is faster in reorganizing neuronal networks. Because running is more rhythmically and dynamically stereotyped, more afferent input per unit time is used for a stronger neuronal network organization of the spinal cord, so that relatively less lesion-altered supraspinal drive is needed at the summing points (motoneurons, interneurons). Also, there is less burden on the joints during running on the long term because of the false movement pattern, generated by the false motor program activating the muscles. A slow controlled walking with walking stick is best to the joints, but less spinal networks are needed for locomotion, the networks are organized slowlier and less generally, and the walking stick can only be used in less severe lesions. If there is too little volitional muscle power, free running (and walking) can be helped by weight reduction by supporting the body (Fig. 95H,I,L).

VIII. The *reorganization* and changed self-organization of the lesioned CNS by the oscillator formation and coordination dynamic therapy *can be better understood in the framework of coordination dynamics* by the landscape changes of a potential function for asymmetric CNS lesions, intention, learning, reduction of spasticity and phase transition of the neuronal network states jumping 'in-phase' and in 'anti-phase' (see below). The theoretical model of Haken, Kelso and Bunz [44,63] describes experimental findings with respect to motor coordination of 'in-phase' and 'anti-phase' hand movements, which is applied here to jumping on the springboard 'in-phase' and 'anti-phase'.

IX. *Coordination* of neuronal responses *in the millisecond range to increase the saliency of responses by coincident discharges* [145,146] (Fig. 104) to establish relations between the neuronal responses for self-organizing motor pattern generators of arms and legs (and to increase the coordinated coupling of arm and leg movements), achieved by the absolute synchronized afferent inputs to the motor pattern generating networks during rhythmic movements (especially when exercising on the special coordination dynamic therapy device), may be a more basic principle of self-organization. During physiologic crawling, e.g. when the right hand (or right elbow) and the left knee touch the ground, the motor pattern generating networks of the right arm and left leg get synchronized afferent input from the skin, joints and muscle spindles for coupling, since coincident discharges will occur more often. During jumping in antiphase on a springboard, the pattern generating networks get synchronized afferent input from the forward and backward foot for coincident firing and therefore coupling. During air-walking on the strider, the pattern generating networks of arms and legs get coordinated afferent input for coupling. As can be seen from Fig. 49, the forced coupling of the pattern generating network for the rhythmic arm movement (intumescentia cervicalis) and for the rhythmic leg movements (intumescentia lumbosacralis) covers a distance of approximately 30 mm. Especially in striders (air-walkers) with no right-left coupling, so that the patient has to also exercise body balancing, the pattern generating networks for rhythmic leg movements are coupled via the intumescentia cervicalis to the brain stem and higher centres. The coupling of the arm movement to that of the leg is very important in hemiparetic patients, to release the spasticity in the plegic or paretic arm and to increase volitional power. During crawling, jumping, air-walking or exercising on the special coordination dynamic therapy device, absolute coordinated re-afferent input reorganizes the CNS networks by training the two coupling phases of premotor spinal oscillators (oscillator interpretation) or by selecting, through synchronization with high spatial and temporal precision, those constellations of responses [145,146] that should couple the pattern generating networks (synchronized neuronal response interpretation).

X. In brain lesions (cortex or brain stem), the coordinated, rhythmic, dynamic, stereotyped, symmetric movements of the spinal cord, which need little supraspinal drive, are used for supraspinal network re-learning. Running is especially very efficient in the reorganization of CNS structures as many anatomically distributed network parts are involved in the activation, and since *running is* also *an escape reaction; its attractor state* is innate (genetically determined). In spinal cord intumescentia lumbosacralis lesions, running can be re-learned, and seems therefore to get genetically restored. In cerebral palsy, in which the spinal cord is 'bombed' over maybe 10 or 20 years by false and unbalanced impulse patterns from the cortex and other supraspinal structures, the running gait is preserved quite well and not much changed by network plasticity, as if the genes preserve, by unsupervised learning, the running attractor. Running on a treadmill, or if possible, free running, is of high importance for reorganizing the CNS.

XI. With the maturing of the CNS during child's development (during the first 5 years), movements become more varied and differentiated, and smaller segments of the body are moved independently due to the development of inhibitory control. The total flexor and extensor synergies are broken up and resynthesized with many variations of parts of the former total patterns [11].

In *similarity to ontogenesis,* in neuronal network reorganization one may *start with symmetric movements,* synergetic movements such as hopping like a sparrow, jumping 'in-phase', and then include more and more differentiated movements like jumping in 'antiphase' or walking and running to enhance the regeneration, reorganization and differentiation of the inhibitory control.

XII. *Tools or equipment for reorganization.*

When training rhythmic, dynamic, stereotyped, symmetric, coordinated movements, the CNS is expected to be reorganized by the patient performing the respective movement as well as possible, so that the physiologic movement-induced re-afferent inputs guide the movement and update the movement pattern in the dynamic memory (reinforcement learning), counteract the lesion-rendered pathophysiologic supraspinal drive at the spinal level, and instruct supraspinal centres to re-learn by reorganization.

To enable physiologic movements, different kinds of manual help are given and facilities are used like springboard, treadmill, rail-suspended running equipment (Fig. 95H,I,L), air-walker or crawling device. The treadmill, with its variations for different purposes, allows the patient to perform rhythmic, dynamic stereotyped symmetric movements in a controlled way, and is therefore of high therapeutic value. For the use of treadmill in neurorehabilitation, see [22,24,74,164]. The disadvantage of the treadmill is that, for high speeds, the backward acelleration increases substantially and that the eyes don't see the moving surrounding (the trunk and the head do not move), but after a few trials patients with a CNS lesion seem not to be disturbed by the slightly unphysiologic performance of walking or running. When running under weight reduction using a rail-suspended running equipment, the running is physiologic and the eyes get the right input (Fig. 95H, L, I). The disadvantage of this running equipment is that there is no support of the movement possible. The trained movements have to be adapted to the movement capabilities of the patient resulting from the lesion and the stage of re-learned motor patterns.

Interestingly, re-afferent input from direct manual help (touch afferents) does not disturb the patient, whereas patients complain when it comes to artificial devices. As if the human CNS were familiar with getting touch afferent input from touching other humans but would mind skin afferent input from mechanical devices. Newborn infants seem to be happy to get touch (and 'Streicheleinheiten' (stroke units)) from human hands, but they are hindered strongly during automatic stepping, e.g. when an EMG cable touches their legs.

The methods for training rhythmic, dynamic coordinated movements, to reorganize the CNS rely on two principles. One strategy was to use mainly complex automatisms activated in the spinal cord (genetically supported repair, if the spinal cord itself is lesioned) like walking and running to reorganize the lesioned CNS to re-establish physiologic movements necessary for everyday life. Network instructions (by interlacing networks, see below) and movement induced re-afferent input and visual and auditory input were used to ‘tell’ what the CNS has to re-learn. Instructions and interpersonal coordination were used for supervised learning, including higher and lower centres (interpersonal coordination) of integration. The training mainly used treadmill for walking and running in combination with airwalker to coordinate arm and leg movements. The other strategy was primarily to train rhythmicity, rhythm coupling and coordination, which means phase and frequency coordination of up to milliseconds if possible. The exactly synchronized (more generally coordinated) afferent input (activating more strongly coincidence detectors than e.g. motoneurons or networks which favour and enhance in their processing simultaneous events) when jumping on the springboard should re-establish the coordination dynamics of the CNS, partly destroyed by the lesion. Therefore, one strategy used rather permanent network organizations to reorganize the CNS and the other strategy tried to re-establish the organization principle of the CNS, giving less emphasis on important network states. In a way, the training of complex automatic movements like running can be seen as a further development of the Bobath therapy, whereas the training of the coordination dynamics of limb movements, neuronal subnetworks (oscillatory firing assemblies) and single neurons is completely new and is based on the new developments in neuroscience, namely the dynamic self-organization of neuronal networks and relative rhythm coupling to generate macroscopic functions.

A new device was developed to train more generally and exactly the coordination dynamics of the CNS. The patient moves with the legs and feet pedals as if riding a bicycle and turns cranks, while movements of the legs, hands and arms are coordinated. In this way, arms, hands, fingers, legs and feet can be moved in a very coordinated way, and at the same time the trunk performs rotational movements (anti-spasticity movement) in coordination with the arm and leg movements (Fig. 50). The set of the training instruments allows quite a variability of coordinated rhythmic movements. Importantly, using the coordination dynamic therapy device mentioned, movements can be performed with no or only little load on the joints (and little power is needed). It is actually argued that this movement therapy is beneficial for joints.

Details of the device for training the coordination dynamics of the CNS will be provided in the next paragraph. It will be shown that the therapy principle is in accordance with the measured neuronal network properties of the human CNS.

Figure 50
The 5-year-old Katarina with a slight disorganization of the CNS during coordination dynamic therapy for prevention of scoliosis. She watches her coordination dynamics on the computer display and tries to improve her present coordination dynamics (bio-feedback).

44. Special device for training the coordination dynamics of the CNS

For the restoration of the coordination dynamics of the CNS, a new device was used which simultaneously coordinates finger, hand, arm, toe, foot, leg and trunk movements during the exercise [137,128] (Figs. 50, 109, 113). The important point is that, in addition to coupled arm and leg movements, the patient performs coordinated three-directional trunk movements, which continuously involve more rostral to caudal segments and vice versa. The forced coordination of arms, legs and trunk is in accordance with the coupling possibilities of α_1 (8-12 Hz), α_2 (6-9 Hz) and α_3-oscillators (0.4 (may be down to 0.1) -4 Hz), even though the frequency is only a relative coordination parameter, whereas the phase is an absolute coordination parameter.

When the hand levers are turned (~ 0.4-1.5Hz), the resulting frequency difference in turnings between arms and legs is 8.5 Hz (low α_1-oscillator frequency or high α_2-frequency) for low hand frequency turning of 0.5 Hz (low α_3-frequency). A slowlier turning of the hand levers would train directly more the premotor α_2-oscillators ($f < 8.5$ Hz). Faster turning of the hand levers (higher α_3-frequency) would train directly the α_1-oscillators in the higher frequency range ($f > 8.5$ Hz).

Turning the levers steadily with medium or high strength entrains the premotor spinal oscillators; the turning is therefore an oscillator formation therapy. The members of the self-organized oscillator assembly (motoneuron and interneurons) are entrained to cooperate better by adjusting, for example, the efficacies of the corresponding activated synapses to improve the timing of firing of the neurons. By turning the levers with little strength at approx. 0.4 Hz (releasing the power-setting knob), the motoneurons are only partly organized into premotor spinal oscillators (Fig. 14D). The motoneurons are firing mainly in the occasional firing mode (Figs. 9,12,13) and are trained for a better recruitment according to the size principle (recruitment rhythmicity ~ 0.4 Hz (Fig. 15)). Between the motoneuron firing in the occasional and oscillatory firing modes, a better coordination of both firing modes is entrained (Fig. 15).

Further, by turning the levers steadily, the coordination of the movements of fingers, hands, arms, toes, feet, legs and the trunk can be trained, and in turn the premotor spinal oscillators driving the muscles are entrained for a better coordination. Because premotor spinal oscillators build up an external loop to the periphery [130], all the phases of firing between the α and γ-motoneurons, the muscle spindle afferents (Figs. 30-38), the interneurons and supraspinal cell assemblies are trained (phase entrainment). This phase and frequency entrainment is necessary because of deterioration of phase and frequency coordination between α and γ-motoneurons, spindle afferents and parasympathetic neurons [130,126] following CNS lesion. If we think of a motoneuron (and other neurons) as a coincidence detector (Fig. 104) [137], the motoneuron detects coordinated input much more efficiently. The simplest type of coordinated input is simultaneous input from many synapses. During the forced coordination of the different muscle activations during exercising, different motoneurons and interneurons get afferent input exactly timed up to milliseconds. The forced coincidence becomes more successful with the increase of the synaptic strength of the synapses firing in coincidence. A patient with a lesioned CNS and false organization of the CNS can often feel the improved self-organization in the short-term memory already after a few minutes of exercising. But the coordination includes either excitatory and inhibitory membrane conductances within the same neuron and/or network architectures comprising inhibitory neurons and feedback connections, since the premotor spinal oscillators fire coordinatedly but not in synchrony (Fig. 39B). Transient synchronization of oscillatory firing motoneurons (as members of different oscillatory firing assemblies (premotor spinal oscillator = motoneuron plus interneurons)) only occurs when forced by repetitive afferent input (response synchronization, Figs. 37,38). The instruction to the lesioned CNS during the process of reorganization by training the forced coordination using the device (stimulus configuration) is by response synchronization or coordination. The feature of the response coordination is given by the coordinated movements.

Lesioned neuronal networks can be repaired by genetic repair mechanisms and by functional reorganization. A repair by reorganization is only possible if the lesioned networks are activated. To instruct the lesioned networks what to re-learn one has to offer physiologic afferent input (for example, movement-induced afferent input), and (considered in a first approximation) interlaced network activation of other extended healthy network parts to teach the lesioned network parts what they have to re-learn. The lesioned network parts have to be forced to cooperate with activated healthy network parts for re-learning. But to ensure that the healthy network parts instruct the lesioned ones and not vice versa, large areas of 'healthy' networks have to be activated to predominate the activated lesioned network parts. The trained network states of the lesioned CNS have therefore to be as integrative as possible, including, if possible, sensory-motor functions, vegetative functions and higher mental functions. To increase the movement induced re-afferent input and to enhance the integrativity of the activated network states integrative motor functions, including finger, hand, arm, toe, foot, leg, trunk and head movements have to be coordinated and activated in coordination with auditory and visual functions and higher mental functions (Fig. 111). The touch afferent input can be enhanced by placing the exercising patient (using the special coordination dynamic therapy device) in water (Fig. 106).

Different training conditions during the coordination dynamic therapy are shown in Figures 89 and 109. The variability of the training positions makes it possible to include many muscle groups in the training therapy. By performing coordination dynamic therapy also in water (Fig. 106), in addition to the proprioception and exteroception, further exteroception is included in the re-afferent input, induced by the relative coordinated movements of water. Extreme training positions can be used, because of the weight reduction in water by buoyancy. If tap water is replaced by warm saline solutions further unspecific spastic-releasing effects can be achieved.

Visual functions can be improved during the coordination dynamic therapy since the turning levers are in the patient's field of vision. When having additionally coordinated rhythmically flashing light in the field of vision (Fig. 101C), also the adaptation to light intensity can be trained in coordination with other visual and motor functions. Additional coordinated accoustic stimuli will further increase the integrativity of the coordinated re-afferent input.

Following CNS lesion the coordination dynamics is impaired. The re-learning of the impaired phase and frequency coordination between the firings of the neurons of the CNS is partly achieved by moving, at a certain frequency, on the special coordination dynamic therapy device. Energetically optimal frequencies of moving have been given by Wachholder [159]. The patient moves with a frequency he likes best. Important is not whether he makes 1.5 or 2 turnings per second, but that he turns at a certain steady frequency. The turning has to be relearned to be rhythmic. By adapting the movements to the device the arms and legs move in coordination up to milliseconds. But because the patient cannot hold a fixed frequency during the whole cycle, he is turning unrhythmically. By re-learning to move rhythmically on the special coordination dynamic therapy device, he re-learns phase and frequency coordination of arm and leg movements and re-learns phase and frequency coordination of the neurons (and self-organized spinal oscillators) of the activated neuronal networks. The correlation between the timed firing of the neurons and the coordinated arm and leg movements are the spaciotemporal impulse patterns from the periphery and supraspinal centres and the existing coordination tendencies of the activated neuronal network. But how the frequencies of the premotor spinal oscillators are correlated with the moving frequencies depends on the phase of coordination between arms and legs, and remains to be studied. The pace gait coordination of arms and legs is easily performed and may be generated by premotor spinal oscillators rather easily (rather simple coordinations). Other coordinations between arms and legs are more difficult to perform. This may indicate that more complicated coordinations (higher order couplings of frequencies) have to be achieved between premotor spinal oscillators, which may only be possible if the self-organized oscillators fire rather specifically, that means have a rather specific eigenfrequency. So, re-learning of frequency coordination means not so much to re-learn to move at certain frequencies, but to move at certain frequencies throughout the whole cycle. The correlation between the coordinated firings of premotor spinal oscillators and the coordinated movements of arms and legs may be studied in the future by correlating measurements of coordination dynamics on the special coordination dynamic therapy device (Fig. 110) and single motor unit electropmyography with surface electrodes (Fig. 46).

44 A. Measuring coordination dynamics in patients

Improvements of the organization of the lesioned CNS can be quantified by measuring the improvement of performing movements. The time for running a certain distance with ongoing therapy can be used, e.g. as a measure of the improvement of CNS functioning (Fig. 78H). In patients who cannot run or move any more (coma patients) other means are needed to measure the reorganization of the lesioned CNS. Direct measurement of the present coordination dynamic tendencies (Fig. 108) of the CNS in patients would be better than indirect measuring (in terms of improved movements), because of a better understanding of the changes in the CNS in the process of reorganization. The special coordination dynamic therapy device offers a possibility not only to improve phase and frequency coordination during exercising, but also to directly measure average coordination dynamics between arm and leg movements. If the patient cannot move the levers him/herself, the therapist turns the levers (Fig. 103F) and the device measures the rhythmicity of the patient/therapist ‘team’.

Kelso, Zanone and Schöner [63,172-176] (see below) measured the coordination dynamics in man during a bimanual coordinations task (synchronization to a visually specified phasing relation) including the phase transition (loss of stability) from the more difficult anti-phase movements to the easier in-phase movement. With the special coordination dynamic therapy device phase transitions of neuronal network states can be evaluated by the change of rhythmicity over time (coordination dynamics), when changing from the pace gait (arm and leg on one side move together) to the trot gait moving (arm and leg move in diagonal pairs) and backwards (Figs. 86L, 103F, 110, 112, 114, 117-119).

45. Spastic syndromes and modulation of the walking pattern and clonus

In spinal cord lesion, spasticity is due to a lesion of the neuronal network of the spinal cord, especially affecting the ascending and descending tracts. The integrative functions of the neuronal networks caudal to the lesion are pathological, due to the lesion-changed self-organization induced by the remaining descending and peripheral afferent inputs. The complexity of disorganization in different cases will be enormous due to different lesion possibilities. The imbalance of excitatory and inhibitory synaptic events results in a net increase of excitability and loss of specificity (with the result of mass contractions) of the functions subserved by the premotor spinal neuronal networks [84].

The clinical components of spastic syndromes [94] (in the language of clinicians) include increased muscle tone (not clearly defined), exaggerated proprioceptive reflex activity, exaggerated polysynaptic ('cutaneous') reflex activity, postural abnormalities, and disorders of voluntary movements. Increased proprioceptive (tonic and phasic (velocity-dependent)) and polysynaptic reflex activity in spastic syndromes can be looked upon as 'positive' symptoms, since patients may retain the ability to stand and to walk ('spastic crutch'). A typical gait pattern where the legs have to be thrown forward from the pelvis, and the extended leg circumducts to clear the sole from the ground was called by Babinski 'chicken gait' [96]. 'Negative' symptoms are weakness and loss of coordination and dexterity in the same muscles. The disorders of voluntary movements in spastic syndromes are the 'negative' symptoms (weakness and loss of dexterity), lack of reciprocal inhibition (co-activitation of opposing muscles and 'spastic gait') and synkinetic movements (flexor synergy (arm) and extensor synergy (leg)). The synkinetic activation of synergistic muscles to the prime movers may also contribute to the mass responses seen in spastic movement disorders [96]. Voluntary effort induces widespread muscular activity with simultaneous contraction of opposing muscles, and the resulting movement depends on the relative power of the muscles involved [23]. Pure spasticity is rare, more commonly it is associated with paresis. Therefore, the ratio between paresis ('negative' symptoms) and positive symptoms becomes an important factor.

The time course and the pattern of the clinical findings depend on the localization of the lesion and the subneuronal networks of the CNS involved. We have to distinguish at least between spasticity of spinal, mesencephalic and cerebral origin.

The aim of the therapy is to correct, at least partially, the disorganization of the CNS by network plasticity, i.e. by re-learning motor and vegetative functions. The patient has to be brought into a rather physiologic movement pattern, by manipulating the supraspinal (see under learning) and peripheral afferent inputs, to bring the spinal cord network (and supraspinal network) into a dynamic pattern so that physiologic movement is generated. If for example, the patient walks under weight support on a treadmill, the walking is quickly limited by increasing extensor spasticity. The spasticity (the abrupt melting away of the resistance is called 'clasp-knife' phenomenon) can repeatedly be manually broken until the dynamic memory is updated to a pattern, so that extensor spasticity does not occur any more for the next, say 30 steps. The sudden drop in muscle force depends on joint angle and muscle length. Another possibility to get rid of extensor spasticity is to push the forefoot onto the ground, so that flexor reflex is partly induced, which counteracts (breaks) the extensor spasticity. By manipulation it is possible to achieve a balance between the different reflexes or automatisms. If we think in terms of the partially released stepping automatism, a stronger heel strike or manually supported stronger push at 'lift-off' when changing from the stance to the swing phase, will enhance the partially released stepping automatism. The reduction of spasticity on one side can partly reduce spasticity on the other side by relative coordination between the left and right side (co-movement). By bringing the neuronal networks of the sponal cord and supraspinal networks into a dynamic network state which generates physiologic locomotion, it is believed that with training over months, the short-term memory will become long-term memory, which means that the neuronal networks of the lesioned CNS have reorganized to generate rather physiologic movements. The increase in muscle force (reduction of 'negative' spastic symptoms) will be due to reorganization and to some capacity for regeneration (see above).

The attractor state extensor spasticity very often competes with the attractor state 'walking', induced and maintained by intention, intensified by strong motivation and modulated by manual help. In a 25 year-old patient with a severe paretic lesion sub C6 (Fig. 51), walking

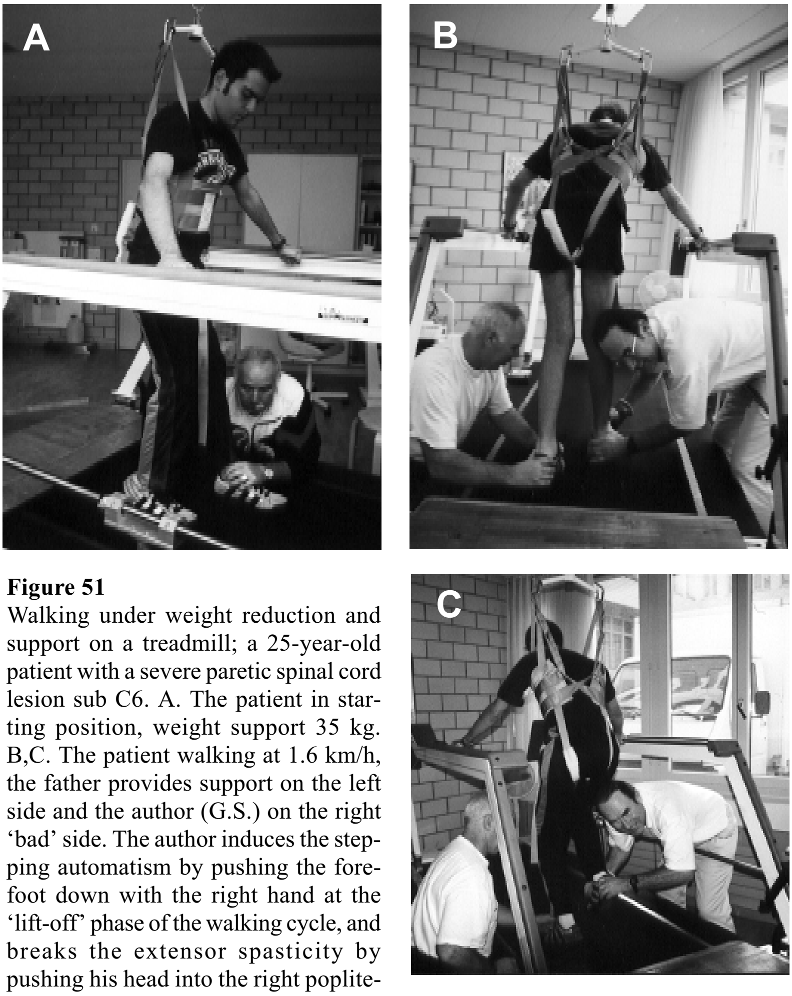

Figure 51
Walking under weight reduction and support on a treadmill; a 25-year-old patient with a severe paretic spinal cord lesion sub C6. A. The patient in starting position, weight support 35 kg. B,C. The patient walking at 1.6 km/h, the father provides support on the left side and the author (G.S.) on the right 'bad' side. The author induces the stepping automatism by pushing the forefoot down with the right hand at the 'lift-off' phase of the walking cycle, and breaks the extensor spasticity by pushing his head into the right popliteal space of the patient (to avoid hindering by the spectacles, the author was often not wearing them (B)). After breaking the extensor spasticity 10 to 20 times, the walking pattern of the patient improved often so much in the short-term memory that the breaking of the extensor spasticity was not necessary any more in that walking period.

on the treadmill at 1.6 km/h under weight support of 35 kg was improved by handling his extensor and flexor spasticity and by pushing his feet onto the ground to increase the peripheral afferent input, since body weight support of more than 30% may reduce the activity of the antigravity muscles [51]. The walking performance was further slightly improved by instruction commands 'right' and 'left' given before the swing phase, and thanks to a good interpersonal communication between two to three attending therapists and the patient.

With the increasing walking distance covered on the treadmill (progressing exhaustion of the patient and the therapists), spasticity and clonus (during walking and afterwards) increased. Extensor spasticity seemed to compete with the walking pattern, especially at a knee angle close to 180°, whereas the clonus seemed not to compete with the walking pattern. At least the clonus in one leg could not be influenced by the strength of the clonus of the other leg. It seems therefore that clonus represents dysregulation of α and γ-motoneurons with the muscle spindles in the periphery via the γ-loop. The human γ-loop does not only include primary spindle afferents and dynamic α and γ-motoneurons, but also α_2 (FR) and α_3-motoneurons, static γ-motoneurons (γ_{21}, γ_{22}) and secondary muscle spindle afferents with their different encoding sides, which may generate different impulse patterns on the same secondary spindle afferent fibre (see above). Clonus frequency ranges between 5.5 and 10.5 Hz [150] seem to suggest that not only primary spindle afferents and α_1-motoneurons (FF) are involved. According to Hagbarth et al. [47], clonus is maintained by reverberating stretch reflexes elicited by preceding relaxation discharges.

Upon jumping in 'anti-phase' on the springboard, there were similarities with respect to spasticity and clonus as compared to walking on the treadmill at comparable walking frequency (~ 4.4 km/h).

46. Oscillator formation and coordination dynamic therapy in the Haken-Kelso-Bunz model

From changes of oscillator and neuronal network properties following spinal cord lesion, such as enlargement of frequency bands, phase instability and false recruitment, it was followed above that coordinated, rhythmic, dynamic, stereotyped, symmetric movements should be included in neurorehabilitation because this is how space-time symmetries are trained, to improve the self-organization of the oscillators and their coupling to contribute to the generation of macroscopic functions like movements. The step from the oscillator properties to the integrative CNS functions (bottom-up approach) is at least partly in accordance with the predictions of the Haken-Kelso-Bunz (HKB) model (top-down approach), including intention and learning. In the HKB model, integrative functions are characterized by a collective parameter, the phase difference (relative phase) between the left and the right leg. In the following sections, the HKB coordination model will be introduced and used to support the understanding of the oscillator formation and coordination dynamic therapy.

47. The HKB model and its consequences for the therapy

The HKB model [44,63] describes interlimb motor coordination upon moving the index fingers 'in-phase' or in 'anti-phase, and is applied here to 'in-phase' and 'anti-phase' jumping on the springboard (Fig. 52A).

The simplest mathematical function that can accommodate space-time symmetry ($V(\varphi) = V(-\varphi)$ and $V(\varphi + 2\pi) = V(\varphi)$) and bistability is a Fourier series of the potential function, V, which includes the first two terms only:

$$V(\varphi) = -a \cos\varphi - b \cos2\varphi$$

The single variable, φ, is the phase difference (relative phase) between the right and the left leg. The behavior of the system is easy to visualize by identifying φ with a black ball moving in an overdamped fashion in the landscape defined by the function, $V(\varphi)$ (Fig. 52). The ball will move to the attractor states at $\varphi = 0$, which corresponds to the jumping with closed legs (in-phase), and at $\varphi = \pm\pi$, which corresponds to the jumping in 'anti-phase' (Fig. 52). The ratio b/a determines the jumping frequency. If the value of b/a decreases, the jumping frequency increases. With the increasing frequency in the finger movements experiment and in the model, a phase transition occurs from the 'anti-phase' movement to the 'in-phase' movement. No spontaneous transition from the easier 'in-phase' movement to the more difficult 'anti-phase' movement occurs. Upon jumping on the springboard, the jumping frequency can only be changed little. But in patients with severe CNS lesions, a spontaneous transition from 'in-phase' to 'anti-phase' jumping also occurs for long jumping series with progressing exhaustion.

The significance of the HKB model for neurorehabilitation lies in its predictions for the coordination dynamics for rhythmic movements, if the model is extended with a symmetry-breaking term to simulate non-symmetrical CNS lesions or if it is extended by parametric changes to include intention (the will of the patient) and learning.

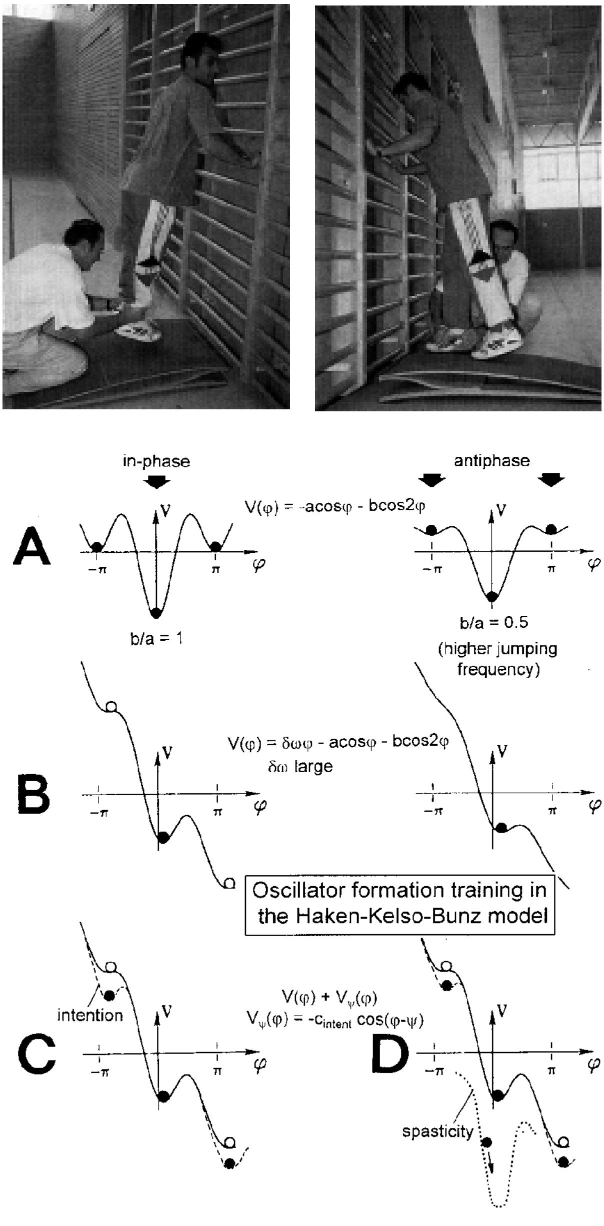

Figure 52

Potential, $V(\varphi)$, of the coordination dynamics in the Haken-Kelso-Bunz model of coordination dynamics when jumping on springboard (A, top, with manual help) in 'anti-phase' ($\varphi = \pm\pi$) and 'in-phase' ($\varphi = 0$) under physiologic conditions (A, CNS not injured), with broken symmetry (B, asymmetrical CNS injury), with additional intention or strong will (C), and with additional spasticity (D). The region around each local minimum acts like a well that weakly traps a system into a coordinated state. White balls are unstable coordinative states; black balls are stable states. Potential, $V(\varphi)$, is shown in A and B as b/a ratio. A decrease of b/a ratio is equivalent to an increase in jumping frequency. As $\delta\omega$ (term for broken symmetry) increases, there is a point at which the curve loses its stable fixed points (potential minima, B right), the system is no longer phase locked, synchronization is lost, and running or wrapping solutions predominate. In C, a single parameter, C_{intent}, determines the strength of the intention to produce 'in-phase' or 'anti-phase' pattern or stabilizes an unstable state (due to broken symmetry). In D, spasticity represents a rather stable state, in which the system is easily trapped. It remains unclear for the moment how spasticity fits into the potential landscape of coordination dynamics.

48. Broken symmetry and intention in the HKB model of coordination dynamics

In spinal cord and/or brain lesions, the lesion almost always affects one leg more seriously than the other one. The broken symmetry in the rhythmic movements of the legs can be accounted for in the HKB model by including a symmetry braking term, $\delta\omega$, in the potential function (Fig. 52B):

$$V(\varphi) = -\varphi\delta\omega - a \cos\varphi - b \cos2\varphi$$

With the increasing broken symmetry ($\delta\omega$ increasing), the neuronal network states at $\varphi = \pm\pi$ are not stable any more, the ball moves away (Fig. 52B). The system is no longer phase locked, but is running about as symbolized by the white ball or no ball in Fig. 52B. Intentionally or even more by strong will, the patient is able to get into the jumping in 'anti-phase' despite strong broken symmetry (Fig. 52B). Intentionally or through strong will, it should be possible to stabilize or destabilize movement pattern states. In the HKB model, the attractor states of the coordination dynamics can be stabilized by intention or strong will, and is included in the potential function by parameter c_{intent} (intended, i.e. 'in-phase' pattern represents $\psi = 0$ degree and the intended 'anti-phase' pattern represents $\psi = \pm 180$ degrees). The potential function with intentional force of a given strength, c_{intent}, is now a superposition of intrinsic and intentional contributions $V(\varphi) + V_\psi(\varphi)$ with:

$$V_\psi(\varphi) = -c_{intent} \cos(\varphi-\psi)$$

For even more broken symmetry and very little muscle power in the legs, strong will is not enough to get the patient into the jumping movement in 'anti-phase'. However, jumping can be achieved upon manual help from the therapist. The manual help will be supported by the movement induced re-afferent input for the self-organization of the movement pattern by the spinal cord and supraspinal centres. So far, no manual help has been contained in the HKB model.

49. Co-movements (Mitbewegung) and symmetric rhythm training

Self-organizing systems, such as the human CNS, respond very sensitively to broken symmetry [63]. The CNS will therefore try to correct the lost symmetry. The improvement in the functioning of the 'bad' leg by the 'good' leg during co-movements (Mitbewegung), through synchronized or coordinated afferent input to both legs (e.g. during swimming (Fig. 53A-F), jumping or exercising on the special coordination dynamic therapy device (Fig. 53G,H)), can also be understood as an attempt of the CNS to enhance symmetry during rhythmic movements rather than as a better rhythm coupling of premotor spinal oscillators in their two coupling phases of the right and left sides only. On the cell level, co-movement due to simultaneous afferent input can be understood in the way that the motoneurons or interneurons work as coincidence detectors, which means time-coordinated postsynaptic potentials reach faster the threshold for action potential induction than statistically distributed ones (increase of the saliency of responses by coincident discharges (see above)).

In-phase co-movement

In the case of in-phase co-movement demonstrated herein (see Fig. 53A-F), the co-movement was so strong that it was an 'all or non' phenomenon. Half an hour before the swimming, the patient performed treadmill running, he thus had trained the running (and walking) pattern

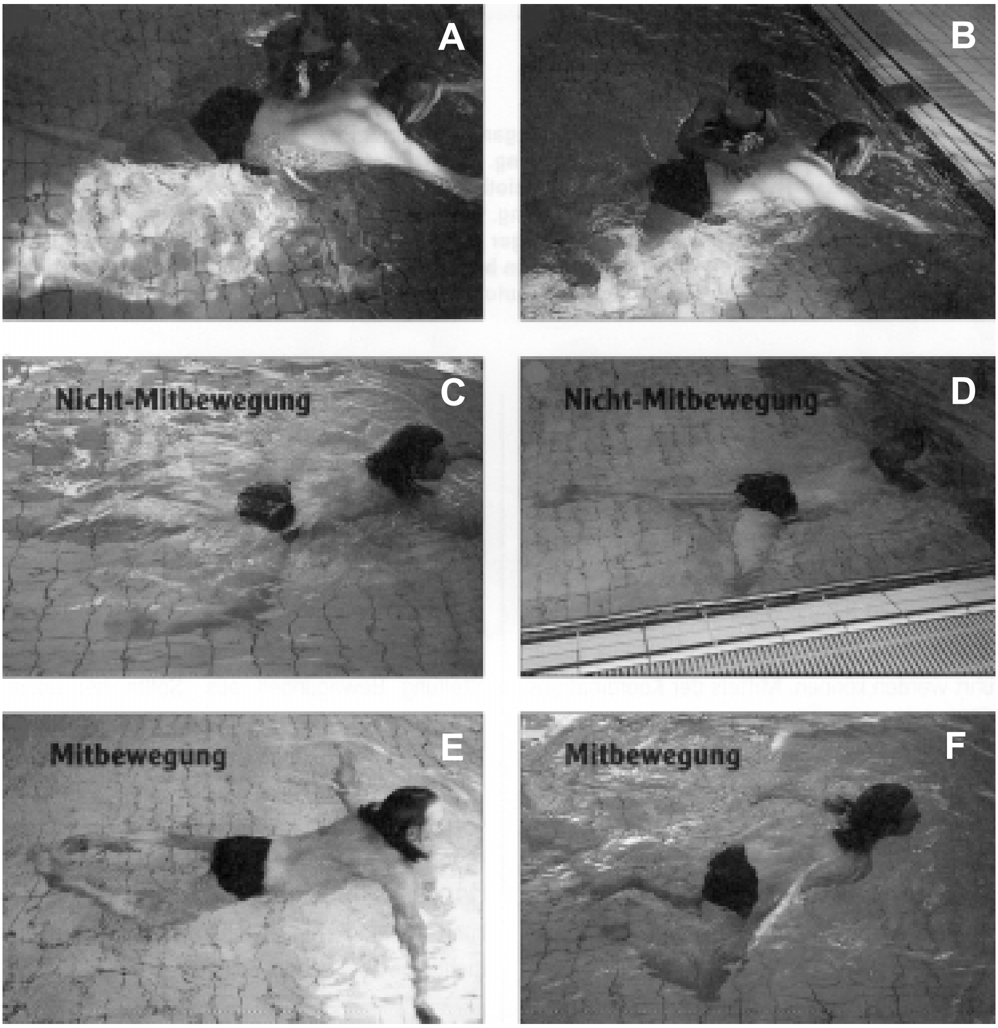

Figure 53A-F
In-phase co-movements (B,E,F) and non co-movements (A,C,D; 40-year-old male patient 5 years after a tetraparetic spinal cord lesion (a tree fell upon him during work). The patient used to swim during the following 5 years after the accident as in C,D, with one leg flexing and the other one kept straight because of not closing the legs (C) before flexion (D). When the legs touched each other before flexion (E), both legs flexed (B,F). In this case, this was an all-or- non phenomenon, i.e. flexion of the right leg or no flexion depending on whether the legs touched each other or not, during free swimming (C-F; arms and legs move) or when the moving was supported (A,B; only legs performed swimming movements). The co-movements during the swimming were therefore most likely induced in the pattern generating network of the intumescentia lumbosacralis.

generating network. But during swimming, he did not move the right leg at all (Fig. 53C,D). Following the instruction to close the legs before flexion, the right leg also flexed strongly, for the first time 5 years after the accident. After 10 to 20 leg flexions during swimming, a bit of flexion could be seen in the right leg, even when the right and left legs did not touch before flexion: the CNS learned quickly. The flexion and non-flexion of the right leg could be observed during free swimming (Fig. 53E,F;C,D) and during swimming performances of the legs only (Fig. 53A,B). This means that the co-movement was mainly induced in the pattern generating network for the leg movement in the intumescentia lumbosacralis. Interestingly enough, running, jumping and air-walking seemed to have enhanced the flexion of the right leg (when co-movement occurred), because the first flexion after 5 years was that pronounced. Exact synchronized input from both legs was necessary to start the flexion of the right leg. It seems therefore that similar movements use similar networks. But the network organizations of similar rhythmic movements are not identical. For retraining the CNS, many movements should be exersised. Children in their development like very much running and jumping and the training of the equilibrium (balance), but they try also all possible movements they can think of. The strategy of the above mentioned patient was that he always takes the 'bad' left foot with the 'good' foot. This, of course was only imagination to be sure to always close the legs. Another tetraparetic patient training with the above mentioned patient showed also co-movements during swimming, but the co-movements were not an 'all or non' phenomenon. Healthy individuals experience that upon closing the legs (with touching) before flexion during chest swimming the flexion becomes easier. The co-movements therefore work also in healthy subjects, but it is of importance in the clinical case.

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Anti-phase and higher-order co-movement

Anti-phase co-movement can be observed during jumping on the springboard in anti-phase: lifting of the heel of the 'bad' foot, which without co-movement lifts up only little or not at all. During training on the special coordination dynamic therapy device the abducted and supinate knee and leg of the 'bad' leg (Fig. 53G) can be brought into the middle position (Fig. 53H) (adduction and pronation) by inducing mainly higher-order (besides in-phase and anti-phase) co-movement during exercising.

Before exercising or after a pause in exercising the right 'bad' leg of a hemiparetic patient was outwardly directed and the 'good' left leg was in the middle position (Fig. 53G). With the movements on the device, the supinate leg came gradually, after 20 to 30 turnings, into the middle position (Fig. 53H). When stopping the movements, the 'bad' right leg went slowly back to the lateral position. The higher-order co-movement, to enhance the symmetry of the leg movements, can be seen also as gradually improving coordination dynamics of the neuronal networks of the CNS in the short-term memory. During the organization of the pattern generating networks, mainly located in the intumescentia lumbosacralis, by the pathologic descending drive impulse patterns and the rather physiologic movement induced re-afferent input, more symmetric movements are gradually generated. It can therefore also directly be seen that, when exercising on the special coordination dynamic therapy device, the coordination dynamics generating the rhythmic symmetric movements improves in the lesioned CNS in the way that the lost symmetry is restored in the short-term memory.

Symmetric coordinated rhythmic movements

In an experiment concerning anticipation and sensorimotor coordination patterns, the task for the subject was to synchronize peak flexion of the index finger with a metronome in two modes of coordination: on the beat (synchronization) and off the beat (syncopation). With the increasing pacing frequency there always occurred a phase transition from the more difficult syncopation to the behaviorally easier synchronization. As measured by magnetic field, using SQUIDS (superconducting quantum interference device), the brain activity was less coherent during synchronization than during syncopation. The less difficult syn-

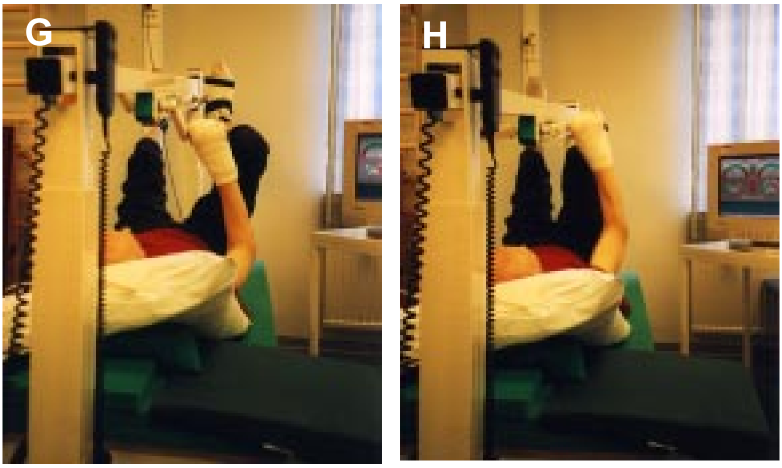


Figure 53G,H Anti-phase co-movement induced in the right paretic leg during exercising on the special coordination dynamic therapy device; a 60-year-old stroke patient with an occlusion of the cerebri media on the left side. The paretic right hand is fixed with a bandage to the lever, so that the patient can exercise alone. When the right hand was supported by a therapist, also the right hand showed co-movements so that transiently the right hand could nearly hold the lever. G. Patient at the beginning of the exercises or after a break. The right knee is in the lateral position (no co-movements). H. When turning approximately 30 times the levers, the knee could be hold by the patient in the middle position (co-movement in action). Interestingly, when the patient watched concentratedly at the right hand or leg, their functions further improved a bit, which means the right hand became a bit stronger in holding the lever and the right leg came faster into the middle (symmetrical) position. In the upper left of the computer display the momentary average coordination dynamics of the patient is shown when moving in coordination arms, legs and trunk.

chronization task puts the brain activity into a less coherent state, free, as it were to do other things (page 275 of [63]).

Moreover, amphetamine-mediated release of norepinephrine provides a condition of increased cortical excitability that facilitates plasticity after stroke injury, resolving functional diaschisis spared by the primary injury [18]. The cortical function areas of the injured side substituted by plasticity were larger than the functional area of the healthy side, as measured by functional magnetic resonance imaging. It seems therefore that rhythmic, dynamic, coordinated, symmetric movements are an easy begin for functional reorganization following brain injuries, because (1) those movements are mainly generated in the motor pattern generating networks (MPN) of the spinal cord with little supraspinal drive necessary, and (2) there is less coherence of cortical areas needed, when the efficient (and therefore small) cortical area for these movements is injured. The synchronization of the rhythmic movements with those of the trainer (social coordination, see below), further restricts the area needed for coherence, and may speed up reorganization.

50. Synchronization, rhythmicity in vision, re-connection of network parts, binding problem, and co-movement

Visual synchronization, performance and correction of movements seem to be important with respect to re-learning of movements [165]. The visual system has two kinds of tasks to perform. One function is to support visual cognition or perception, and the other, sensorimotor, function is to drive visually guided behavior. Phase synchronization has been proposed as a ‘binding’ mechanism in the visual cortex of cats and monkeys [29]. Relative phase and frequency synchronization occurred among the firings of α and γ-motoneurons and secondary muscle spindle afferents upon touching or pin-pricking repeatedly the anal reflex skin area [129,130]. There may be similarities in the organization of the visual cortex and the spinal cord when performing rhythmic, dynamic, coordinated movements. It may not only be that the visual system helps to improve the functioning of the motor system, but the sensorimotor system improves vision. Rhythmic, coordinated movements seem to reduce the number of dioptries needed by myopic individuals by one or two, probably by a better network focussing, and seem to enhance the reorganization of the lesioned CNS for a better adaption to light (see case reports). Unclear is whether the improvement in vision is accomplished indirectly by an improvement of the general coordination dynamics of the CNS due to coordination dynamic therapy or whether the improvement is due to use-dependent network modification under the condition that the dynamic visual afferent input, caused by rhythmic movements in the visual field, is absolutely correlated with the rhythmic exteroceptive and proprioceptive afferent input, caused by the moving of arms and legs. Generally, it has been so far assumed that the improvement in the sharpness of vision is not only achieved by lens corrections of the optical system of the eye, but that the dioptry number in myopic individuals can also be slightly reduced by vitamin A administration and focussing exercises with the eyes.

The binding problem: The fundamental question of how the visual system establishes the appropriate relationship among the large number of neurons that respond to the many features in any given visual scene is often referred to as the binding problem. The synchronization on a millisecond time scale may be exploited to link featural information that is represented in the different parts of the cortex. The identification of related features, for example those belonging to the same perceptual object, is achieved by the temporal coincidence of the neuronal discharges evoked by those features [145,146].

It has been suggested that binding between neuronal assemblies distributed over many cortical areas (formation of a horizontal assembly) is brought about by the integration (convergence) of activity mediated by afferent subsystems [87,88].

The essential advantage of assembly coding (an assembly consists of a large number of simultaneously active neurons which may be distributed over many cortical areas) is that individual cells can participate at different times in the representation of different objects. A particular neuron can participate at different times in different ‘assemblies’ of co-active neurons [145,146]. This is what Abeles [1] proposed for synfire chains. A particular neuron can participate at different times in different ‘synfire chains’, so a crossing of synfire chains is possible. In the human nervous system the maximum transmission frequency of motoneuron axons has been measured so far to be as high as 5260 Hz [125]. Textbooks of animal physiology give 1000 Hz as the highest transmission frequencies in nerve fibres. This may mean that a particular neuron in the human CNS can participate in more different assemblies per time (more crossings of synfire chains per time is possible) than in the CNS of animals, which could allow a higher organization complexity in the functioning of the human CNS.

Singer and Gray argue [146] that synchronous activity may arise in cortical networks without oscillatory firing, and the presence or absence of a regular oscillatory time structure in single-cell activity neither proves nor disproves that spatially segregated cells discharge in synchrony. Oscillations per se are thus of little diagnostic value for the testing of the temporal correlation hypothesis. The synchronization of activity is the relevant issue. But it seems not easy to distinguish between correlated activity of single cells and oscillatory firing of assemblies. It has been measured that premotor spinal oscillators in man (assemblies most likely organized by a motoneuron and many interneurons) undergo relative coordination during firing. In response to adequate afferent input they may transiently synchronize their firing for a few oscillation periods by phase resetting. Other motoneurons which are activated only little, fire only occasionally. But a part of the ocasionally firing motoneurons correlate their firing with those of the oscillatory firing motoneurons, and in the group of occasionally firing motoneurons the motoneurons are recruited for firing at approximately 3 Hz (see above). The motoneurons in the human spinal cord may fire differently from the neurons in the cortex. But in the cortex also those frequencies have been found which were recorded from the spinal cord (~1 Hz, 6-9 Hz, 8-12 Hz), and there is a close correlation found at the level of integration between vision and movements as indicated, for example, by interpersonal coordination. The real human brain (CNS) is very complex and it is not so easy to differentiate between synchronous activity with and without oscillatory firing.

Re-connection of network parts: Very important is the argument that synchronization (and coordination) may be a particularly efficient mechanism to increase the saliency of activity to functionally re-connect cell assemblies and network parts. Synchronization (or more generally coordination) can, in principle, be used to select with a high spatial and temporal resolution those activity patterns that belong together and to enhance the effect of this activity so that it can be evaluated for further processing. Following a CNS lesion there may be only a few synapses (out of 4000 on the the average) with a low efficacy remaining between neurons of a subnetwork or functionally disconnected network parts. With synchronized inputs as a special case of coordinated inputs, the threshold of action potential production can be reached faster with the same amount of postsynaptic potentials (Fig. 104) and the efficacy of the synapses can be increased. The enhancement of coordinated firing can occur between cells of the same cortical column, of different columns, of different cortical areas, between the two cerebral hemispheres, and between different CNS parts including the spinal cord. By increasing the extent of integrativity of the (to a few milliseconds) coordinated movement induced re-afferent input (due to coordinated movements of the whole body), very distributed assemblies or neuronal network parts can be reorganized and their cooperative functioning re-established.

Using a neuron as a coincidence detector, response saliency is achieved by synchronized or coordinated input, because the threshold for action potential generation is reached more quickly (Fig. 104).

The stimulus-dependent dynamic coupling and use-dependent synaptic modification, on the long term, among neurons in the CNS can be achieved in man (and animals) by a coordinated rhythm training (oscillator formation and coordination dynamic therapy). Jumping on springboard and running will already enhance stimulus-induced coupling (including vision) and use-dependent modification, since the rhythmic movements are performed over a long time. With such rhythmic movements alone improvement of vision can be observed. But with the special coordination dynamic therapy device, the efficacy of the improvement of vision and movements can be strongly enhanced. When moving the coupled hand and foot levers, a stimulus-induced dynamic coupling is achieved in the sensory-motor system. By moving levers in the field of vision, stimulus-induced dynamic coupling is also induced in the visual cortex (and lower parts of the brain), and stimulus-induced coupling is induced between neurons subserving vision and motor functions. With this synchronized stimulus-dependent dynamic coupling of vision and sensory-motor functions, co-movement of the legs could be achieved in the stroke patient (Figure 53G,H) after approx. 3 turnings; the right knee came to the intermediate position. Without watching the knee and without trying volitionally to bring the knee into the intermediate position, approx. 20 turnings were necessary. Without turning, the right knee could not be brought volitionally into the intermediate position. Co-movement of the right and left pupils (m. sphincter pupillae and m. dilator pupillae) could be achieved in a brain-lesioned patient (Figure 101C) after approximately 1000 turns, when using additionally flashing light.

Co-movement: In paraparetic patients who can move only one leg during chest swimming, the touching of both legs is sufficient to induce in-phase co-movement of the plegic or paretic leg. The response correlation is achieved by one burst of touch afferent input induced by the touching of the legs. To induce higher-order co-movement on the special coordination dynamic therapy device 20 to 30 turns were necessary. Many correlated stimuli were necessary to induce co-movement of the pupils. In another patient (Fig. 111), co-movement of the pupils occurred immediately due to flashing light. But the sympathetic and parasympathetic nervous system divisions do, however, contribute more directly to the opening and closing of the pupils than do leg movements.

The rhythmic coordinated stimulation seemed to be a particularly effective way to enhance response saliency in improving vision. In the cases referred to above, the 4 levers were moved rhythmically in the field of vision. There was a frequency difference between the hand and foot levers in the range of those of α_1 and α_2-oscillators. Since human premotor spinal oscillators build up an external loop to the periphery via the γ-loop also the secondary muscle spindle afferent input was rhythmic in addition to the rhythmic input from the skin. The continuous activation of correlated rhythmic activities induced in the retina, correlated up to milliseconds with the coordinated rhythmic activities of proprio- and exteroceptors, seems to be a very efficient way to increase the saliency of functions and features, i.e. of supervised learning. Coordination was also observed between the movements of limbs of different animals (see interpersonal coordination).

51. Air-walking in the Haken-Kelso-Bunz (HKB) model

In cerebral palsy and in other brain lesions, we encounter missing coordination between right and left arms and legs and missing coordination between arms and legs. By increasing the time-locked afferent input, for example from both legs upon jumping on springboard, it was possible to couple the poorly functioning leg to the good functioning one (co-movements). But how to re-learn the coordination between arm and leg movements? During the ontogenesis, a child exercises the coordination between arms and legs by e.g. crawling. After CNS lesions, the crawling performance is often that poor or not possible at all (one arm is not moving) that this coordination dynamics cannot be trained. To get more movement in the poor arm of a hemiparetic patient and to reduce spasticity, devices are needed which force coordination of arms and legs to get coordinated movement induced afferent input from arms and legs to reorganize the lesioned CNS in the way that the volitional central command impulse patterns are coordinated with the coordinated movement induced afferent input from the skin, joints, muscle spindles, Golgi tendon organs and other receptors of arms and legs to restore the integrative functions. Functionally, only few or no communicating sub-networks of the supraspinal CNS have to re-learn coordination (cooperation and competition).

With a strider (air-walker) it is possible to train the coordination of arms and legs. In difficult cases, feet or hands can be fixed to the moving parts. During air-walking, a coherent neuronal network state builds up in the spinal cord (and partially more rostral centres) from the intumescentia lumbosacralis to the intumescentia cervicalis (Fig. 49), which generates the coordinated, rhythmic movements and which improves through the short-term memory.

Rhythmic finger, arm and leg movements can be described in the HKB-model separately. The coupled arm and leg movements are not described by the HKB-model. An approximation is tried here for the mechanically coordinated arm and leg movements by using the same potential form (Fig. 54A). By the mechanical connection between the left and the right side of the strider, only the movement in antiphase ($\varphi = \pm\pi$) is possible. The potential well for the in-phase movement at $\varphi = 0$ disappears (the dotted line in Fig. 54). Even when the in-phase movement is possible, the movement state does not occur when the patient is exhausted. By the mechanically coupled arm and leg movements on the strider, it is possible to couple the arm movement to the leg movement with respect to the movement induced afferent input and intention (Fig. 54A,B; coupling is marked by the dashed line). In a spinal cord lesion caudal to the intumescentia cervicalis or a corresponding brain lesion, the poor leg movement ($\delta\omega \neq 0$)

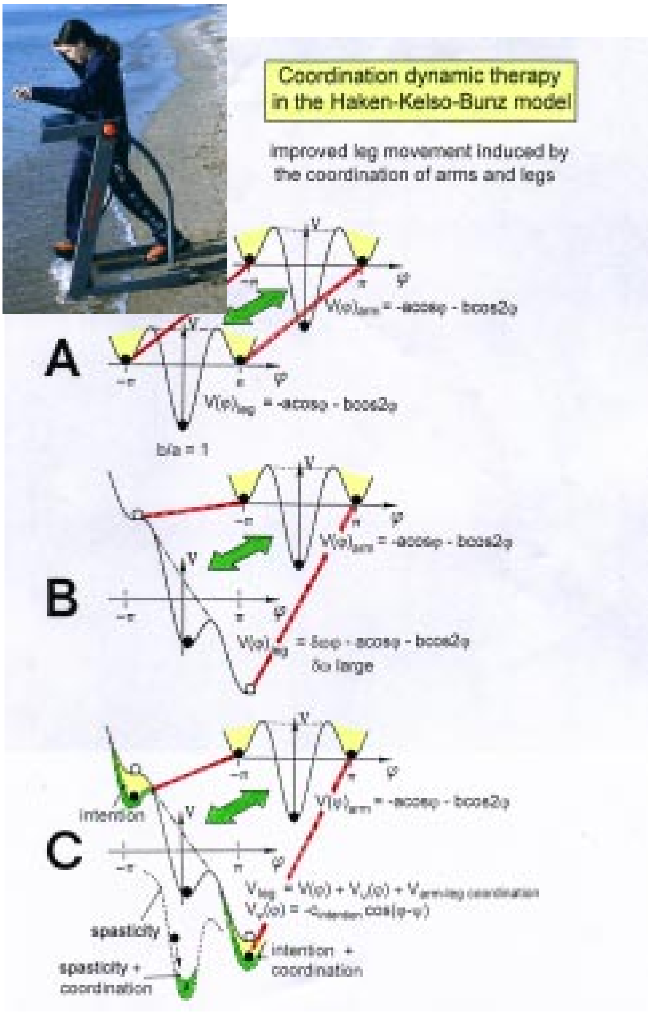


Figure 54
An effort to describe the coordination dynamic training of arms and legs in the Haken-Kelso-Bunz model, when performing air-walking (A top, anti-phase movement). The potential V(φ) for arms and legs for the coordination dynamics in the HKB coordination dynamics model during air-walking in 'anti-phase' ($\varphi = \pm\pi$) under physiologic conditions (A, CNS not lesioned), for lost symmetry of leg movement (B, CNS asymmetrically lesioned with respect to leg movement ($\delta\omega \neq 0$)), and with additional strong will and intention and spasticity (C). For additional description, see legend to Fig. 52. Because of transmission shafts of the right and left side of the strider, the movement 'in-phase' is not possible with this strider, which is indicated by the dotted line in the potential form V(φ). The movement of the arms in 'anti-phase' forces the legs into an exact coordination with the arms, indicated by the dashed lines between the potential for the arms and legs in the physiologic case (A) and in the broken symmetry case (B). If there is no mechanical right-left coupling at the strider then the term $V_{arm\text{-}leg\text{-}coordination}$ is included in the potential. A reduction of leg spasticity (for an assumed lesion of the intumescentia cervicalis and lumbosacralis) as a result of the leg movements in coordination with the arms is schematically indicated by the dotted line in C. For another description of physiologic movement and spasticity, see Fig. 107.

can be coupled to the physiologic arm movement (Fig. 54B). With intention and a lot of will, the little remaining leg movement forces can be fully used and improved, which is indicated in Fig. 54C by a deepening of the potential well for the legs at $\varphi = \pm\pi$. An additional effect of the absolute coordination by the improved leg movement is indicated in Fig. 54C by an additional deepening of the potential well at $\varphi = \pm\pi$ (dashed-dotted line) and a shallowing of the spastic potential well. Extensor spasticity of the legs can be easier reduced on the strider than with the treadmill or the springboard, probably because the coordinated movement 'air-walking' state is more extended in the neuronal networks, needs less power for its generation, and the movements are less dynamic.

A patient with large deficits in motor function and intelligence had strong rigidity, so that it was very hard to perform supported treadmill walking with her. After a few stepping performances, the therapists got exhausted and could not support the patient any more. However, when treadmill walking was preceded by air walking (mostly passive), the rigidity reduced, so that treadmill walking could be performed more easily and for longer time periods. The movement induced afferent input with nearly no descending motor control impulse patterns (no volitional movement contribution) brought the neuronal network into an organizational state, so that subsequent treadmill walking could be more easily performed.

A patient who lost large parts of the motor cortex for hand, arm and leg movements, and with a concentration capacity of 3 s was just able to grasp with one hand the handle of the strider (the coherent activity of large brain areas was just sufficient for the group movement of one but not two hands) could – if the stereotyped strider movement was achieved – nearly normally perform air-walking, to reorganize the brain for an improved leg movement, improved arm-leg coordination and improved arm movement. Already after 3 days, the patient who had suffered an extensive brain lesion felt that the strider training (in conjunction with treadmill and free walking) was easier to perform.

52. Unmasking of attractors, limitations of the Haken-Kelso-Bunz model, and large numbers of coexisting attractors in networks of chaotic elements

In adults, movements are initiated, maintained and terminated by supraspinal control. In adult man movements are performed by the descending motor command impulse patterns, the movement induced re-afferent input patterns, and corrections at spinal and supraspinal levels.

If the supraspinal control is reduced and changed by a CNS lesion, the movements become less controlled and less stabilized. Some movement attractors become less stable (less deep potential well), other attractors become so unstable (a very shallow potential well) so as they are observed extremely seldom. Still other attractors become more stable, so that they are observed. This means that, following a CNS lesion, the state-space landscape does not change very much in principle, but new attractors seem to appear. Attractor states are observed following CNS lesions which were not observed before the lesion. The CNS lesion and the loss of supraspinal control unmasks more of the existing spinal cord neuronal network state-space landscape. Lesion studies are therefore important to learn about the capabilities and complexity of the CNS state-space landscape, including network states necessary for the ontogenesis or states phylogenetically not needed any more, and their combinations.

An 18-year-old hemiparetic patient could jump in the abduction-adduction mode (Fig. 55A,Ba). Due to fluctuations in the attractor state 'abduction-adduction jumping', the patient made many mistakes (Fig. 55Bb-d), which the trainer (author G.S.), jumping in coordination, could only follow on intention or not at all (Fig. 55Bc). Fig. 55Bb shows the patient performing

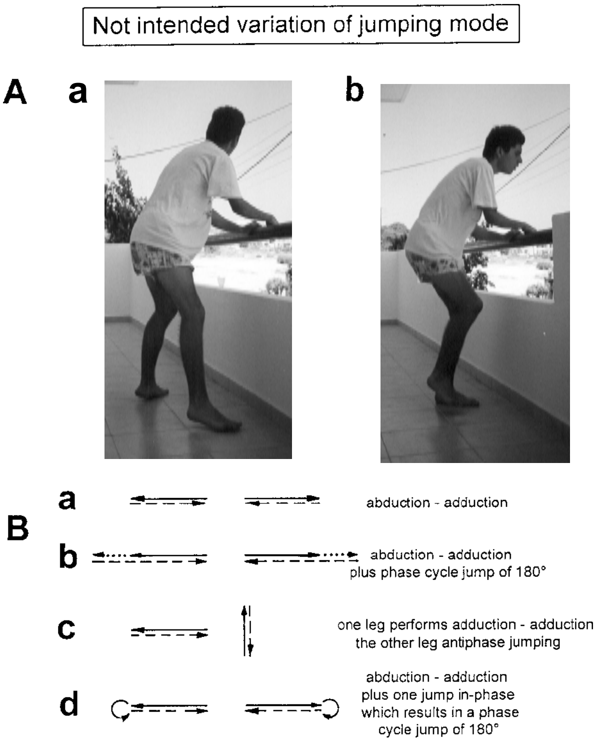


Figure 55
Jumping mistakes (B,b-d) by a 19-year-old hemiparetic patient with a CNS lesion suffered at birth, when jumping abduction-adduction (A). Note that the patient is looking around during jumping, which indicates that he does not concentrate very much on his jumping task. B.a. Physiologic jumping scheme. b. Jumping of an extra abduction, which represents a phase jump of 180° (π). c. The right leg (right-sided hemiparesis) is transiently in the anti-phase jumping mode, while the left leg (good side) goes unaffected on with the abduction-adduction performance. d. Performance of one extra in-phase jumping cycle in the abducted position, which represents a phase jump of 180° (π).

an extra abduction, which results in a phase cycle jump of 180°. The phase change of 180° is not included in the HKB-Model, even though such phase jump can also be observed in 'anti-phase' jumping or in hand movements performed by a patient with a hemiparesis. The phase jump of 180° can be explained based on human data mentioned above, because the premotor spinal oscillators have two windows for being driven per oscillation cycle (for somatic activation), 180° apart (Fig. 5 of [126]). The attractor state 'jumping with one leg in abduction-adduction and with the other leg in the anti-phase mode' (as in Fig. 55Bc) is not possible in a healthy individual without being trained. An extra jump in the 'in-phase' jumping mode (as in Fig. 55Bb) when performing abduction-adduction jumping could be performed by the healthy author.

Interestingly, the author jumping in coordination with the patient (see below) could easily follow the patient when he varied the frequency or amplitude of jumping (unspecific network constraints) but he needed a few jumping cycles to concentrate on jumping an extra abduction (Fig. 55Bb) or for performing an extra in-phase jumping (Fig. 55Bd). The change of the phase cycle (specific network constraint) probably needed an essential descending network 'activity' burst to achieve this 180° phase jump.

The relative increase of the fluctuation in the patient's attractor state 'abduction-adduction jumping' can be explained by a relatively decreased stabilizing descending control impulse pattern in relation to the impulse patterns from the periphery at the summing network (or a decreased stabilized descending control). This relative reduced descending impulse pattern, including motivation (see below), is in accordance with the reduced concentration of this and other CNS lesioned patients during therapy.

The shift in the relative contributions from the periphery and the supraspinal centres can be experienced by healthy individuals. If for example, there is a rather constant pain afferent input from a joint (partial inhibition of the movement), then this extra afferent input from the periphery shifts the relative contribution towards the input from the periphery, so that the influence from the periphery is relatively enhanced. With this extra pain input, movement performances like walking become more unstable, i.e. the dependence on the periphery is increased. Hitting a small stone during walking may result in falling or nearly falling, which means in the destruction of the whole movement pattern. This would not occur without the additional pain afferent input.

Realizing the complexity of attractors in the state-space landscape of the lesioned CNS and the easy switching among the attractor states makes the chaos theory attractive to explain the observed phenomena. The network of chaotic elements can provide, for example, large numbers of coexisting attractors, which are hierarchically organized, and small input changes can cause a switch from one attractor to another (see above, networks of chaotic elements). In neural processing, partially synchronized clusters of chaotic elements change their members according to the inputs to the system, which explains the changes in self-organization and grouping of spinal oscillators in the spinal cord.

53. A new start after the Bobath therapy: the importance of the hand function

The Bobath´s neurorehabilitation method rests on the facilitation of physiologic righting, equilibrium, coordinated posture and movement reactions by simultaneously trying to normalize the postural tonus and to inhibit pathologic reflex patterns [11].

It was the merit of B. Bobath that spasticity has not been regarded any more as a local phenomenon affecting individual muscles and showing itself in exaggerated stretch reflexes; spasticity started to be seen as manifesting itself in patterns of hypertonus involving the entire affected parts of the body in widespread patterns of posture and movement rather than affecting individual muscles. The former view led to local treatment for muscle spasticity, such as physiotherapy along orthopedic lines, i.e. exercises to strengthen weak antagonists of spastic muscles, as well as some surgery and bracing. The testing for individual tonic reflexes has led to ‘the treatment of reflexes’ rather than of children [11].

Moreover, B. Bobath pointed out (apart from the detailed account on righting, equilibrium and posture reactions) that it was a mistake to apply neuro-physiological observations derived from animal experiments to human beings who have a much higher developed CNS. In contrast to the animal for example, whose righting reactions are present at birth and enable it to get on its feet at once, righting in man is incompletely developed at birth. Only the neck and labyrinthine reflexes are active. Righting reflexes in their unmodified form do not persist, but become modified and partly abandoned [11].

The limitation of the Bobath therapy becomes apparent with the argument of Kennier Wilson [66] who tried to differentiate movement from posture and kinetic from static contraction. According to B. Bobath, ‘movement is in reality a series of changes of posture’. B. Bobath writes further (page 3 of [12]): ‘Abnormal tonus and co-ordination are due to the release of postural reflexes’. This statement is not in accordance with the new developments in neurosciences and human neurophysiology. Abnormal tonus and co-ordination in movements is due to the lesion of the CNS with a false self-organization of the intergrated functions of the neuronal networks of the spinal cord and supraspinal centres for the generation of movements. But because postural reflexes are generated in the same networks as movements, the postural reflexes are also abnormal. This is a fundamental difference in the understanding of the functioning of the CNS, which has consequences for the treatment. If the abnormal postural reflexes were the reason for pathologic movements, then the postural reflexes would have to be trained. But if it is false self-organization of the lesioned CNS that is the reason for the pathologic movements, then movements have to be trained which reorganize the CNS to bring self-organization to generate more physiologic movements again. Many suitable movements can be used, like rhythmic, dynamic, stereotyped, coordinated ones. Since human subneuronal networks (e.g. oscillators), and in turn large network parts have been shown to change their self-organization following a CNS lesion (arrhythmic firing of oscillators, phase instability, false recruitment in the occasional firing mode, see human neurophysiology (above)), the latter statement is right, and Bobath's statement is not valid any more. This does not mean that the training of postural reflexes is wrong. It just means that movenments have to be trained which reorganize the CNS most integratively and efficiently and which are adapted to the special lesion suffered by the patient and the movements learned before the accident (history of the CNS).

Bobath's therapy lead to the treatment of righting, equilibrium and postural reactions rather than to the treatment of patients. The author (G.S.) has seen grown up children with cerebral palsy who were walking something like robots, that means with stops in between parts of the movement cycle. Theoretically, the attractor walking is not the summation of the attractors 'right leg forward and left leg forward'. The continuous movement is a different network state than the succession of righting, equilibrium and posture reactions, even though these reactions are somehow incorporated in the movement, as can nicely be seen when a newborn baby steps automatically. If the adequate afferent input for automatic stepping (heel strike) is not strong enough then only one leg is moved forward and the stepping automatism ceases. If the afferent starting push is strong enough to reach the next heel strike, then automatic stepping goes on and becomes continuous. On the other hand, it is much easier to keep equilibrium during fast walking and running than during very slow controlled walking. There are a lot of patients with cerebral palsy who cannot keep equilibrium when standing, but they can walk without support, and this not only because the kinetic energy is larger for higher speed. The whole complexity of the regulation and coordination processes is only activated when dynamic movements are performed. Dynamic movements are needed for the coordination of static and dynamic subnetworks (see above). Further, healthy children move all the day round, especially running, jumping and balance training they do like, to optimize the organization of their CNS. When B. Bobath tried to treat children with cerebral palsy, she forgot to observe what the healthy ones are doing. Patients with CNS lesions have a 'good feeling' in their CNS when performing coordinated movements. They enjoy the movement. Spasticity reduces strongly if they exercise on the special coordination dynamic therapy device (rhythmic, dynamic, coordinated movements), sometimes even only for minutes. On the other hand, the training of rhythmic, dynamic, coordinated movements is much more efficient for the reorganization of the CNS than the training of postural reactions because much more movements are performed per therapy time (see below) and the coordination of the movements is up to milliseconds. Apart from a low rate of learning using the Bobath therapy, continuous and rhythmic movements are missing and the level of the training of the coordination dynamics of the neuronal networks is low.

A misunderstanding of the Bobath therapy is introduced with the argument to normalize the postural tonus. In the foreword to [12], P.W. Nathan expressed it in the following way: 'Excessive effort is worse than useless in spastic conditions, for it reinforces the abnormal patterns of posture and movement and increases spasticity'. All therapeutic means which transiently increase the tonus or spasticity were disqualified with this argument to run the patient into increased spasticity. A 'good physiotherapist' then has to work for weeks with the patient to reduce the spasticity again.

From the point of view of human neurophysiology, the main task is not to normalize the postural tonus or to reduce spasticity, but to reorganize the lesioned CNS to make physiologic movements like walking possible. If the attractor state 'walking' is stabilized, the attractor state 'spasticity' (e.g. extensor spasticity) will destabilize at the same time; spasticity reduces (see also Fig. 107). The genetic repair (innate repair) may even help a bit to stabilize the attractors 'walking' and 'running'. The release of spasticity in the short-term memory by the physiologic movement walking is shown in Fig. 56.

A 19-year-old hemiparetic patient with cerebral palsy from birth could reasonably walk, but kept his right arm in a spastic position, which could be recognized by the palmar flexion of the right hand. When the patient was not active, then often as a habit, he was resting on his good left leg and tried to reduce the spasticity of the fingers of the right hand by manipulating on them with the left hand (Fig. 56A). Probably, he has done such finger stretching for many years without success. When riding on a donkey (without feet support), he was also sitting on the left 'good' side (Fig. 56C), i.e. the trunk was also turned to the left side, as expected in hemiparesis. To improve the physiologic functioning of the right hand, i.e. to release the spastic palmar flexion of the hand and the spasticity of the fingers, the integrated functions of the whole CNS had to be improved. During fast walking, the patient moved mostly only the left 'good' arm. But when also the right 'bad' arm moved in coordination, the spasticity of the hand released, which can be seen in Fig. 56D,E (release of the palmar flexion). Therefore, when the right arm was integrated in the movement pattern 'fast walking', spasticity was

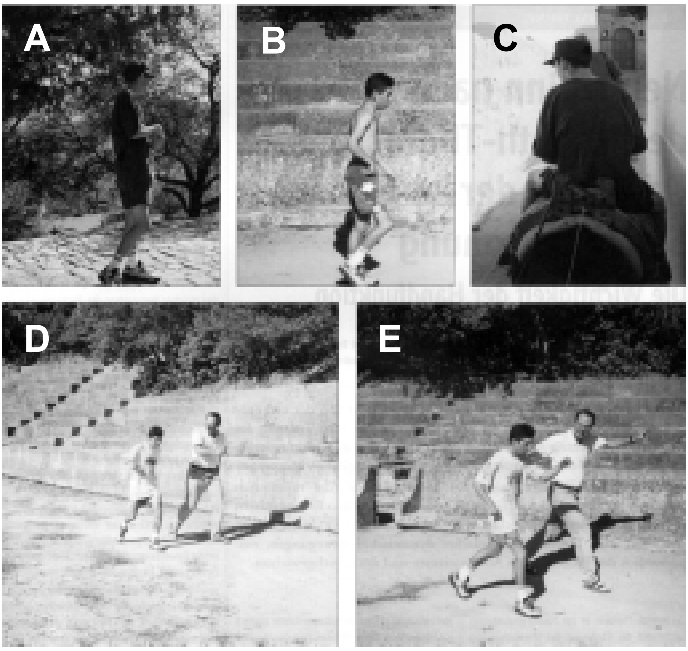


Figure 56
Release of spasticity of the right hand (release of palmar flexion) in a 19-year-old patient with cerebral palsy, when the right arm moves in coordination during fast walking. A. The patient tries, without success, to release the spasticity of the right hand by stretching it with the good left hand. B. When the right arm is not moved during fast walking, the right hand is in spastic position (palmar flexion). C. The patient with right-sided hemiparesis is sitting on a donkey on the left good side (feet not in stirrups). D,E. When walking in coordination with the therapist (author G.S.), the right arm moves in coordination and the spasticity of the right hand is released (no palmar flexion). In the background of B,D,E the stadium (close to Acropolis) of the ancient Rhodes in Rhode (a work most probably of the 2nd century B.C., which is 200 m long and 35 m wide) can be seen, where Diagoras, the first winner of the Olympic games in wrestling and boxing, most likely trained. The use of the 'taxi of Lindos' in C to get up to the Acropolis of Lindos (Rhodos) can be used to train trunk stability.

released (Fig. 56D,E) and when the right arm was not moving in coordination, spasticity was present (Fig. 56B).

An interesting point concerns the contribution of the descending impulse patterns from supraspinal centres in relation to the movement induced afferent input patterns, both contributing to the self-organization of the motor pattern generating network to generate ‘fast walking’. From Fig. 56D it can be seen that the patient is moving in full coordination with the trainer (author G.S.). The right arm is forward and the left one backward. In Fig. 56E, the other movement cycle is shown. The left arm is forward and the right arm is backward. In comparison to the trainer walking (in exact interpersonal coordination, see below), the right arm was not in backward position. The reason for the missing backward swinging of the right arm was the limited rotational angle of the shoulder joint, because of non-use during early childhood. The motor pattern generating network in the attractor state ‘fast walking’ most likely produced the motor patterns for the backward swinging of the arm but it was not taking place because of the limited excursion capacity of the shoulder joint angle. The non physiologic swinging of the right arm produced a non physiologic re-afferent input to the pattern generating network of the spinal cord. But this movement-induced slightly pathologic afferent input did not destroy the coordinated movements of arms and legs during the walking, started and maintained by probably the descending pathologic control (because of the lesion). Since automatic stepping in newborn babies (induced mainly by the stepping induced afferent input) includes only the leg movements, it is probable that the leg movements make a stronger contribution to the coordinated movements of arms and legs than do the arms. Descending control and re-afferent input contribute to the self-organization of the neuronal network state ‘fast walking’. Because of the higher developed CNS of humans in comparison to animals, and the more interlacing of spinal and supraspinal neuronal networks, it seems that in man unlike in animals, the network state ‘fast walking’ cannot be self-organized by the afferent input of arms and legs alone or the descending impulse patterns alone. It was argued with respect to newborn babies that the network state ‘automatic stepping’ gets some descending control [131]. With respect to reorganization of CNS functions following spinal cord lesion in man, at least a bit of descending volitional control besides afferent input to supraspinal centres or a bit of afferent input besides volitional descending control is necessary to make walking possible again.

In the patient mentioned above, the improvement of fast walking and the release of spasticity in the right hand was measured by the number of successive movements of the right arm in coordination with the other arm and the legs. During one week of training it was possible to increase the number of coordinated successive right arm movements from 10 to 100. But when the patient was not in interpersonal coordination with the trainer, his walking network state changed more often between the attractor states ‘walking without the right arm movements’ (Fig. 58D) and ‘walking with coordinated right arm movements’.

The training of non-rhythmic movements in the countryside was too early for this patient, because it was too difficult for him. He used, again, too much the good body side, and the right hand became spastic again (Fig. 58C). Only with further improvement of the functions of the impaired side, arrhythmic movements are helpful in reorganizing the CNS (see below under reorganization).

To improve the functions of the right hand of the above patient, also the volitional movements have to be improved. It was reported [135] that, when giving the right hand (Fig. 57A), the spasticity in the right hand grew quickly that strong that it was impossible to the patient to reach the right hand. But by reaching the left ‘good’ hand first and then the ‘bad’ right hand, the spasticity of the right hand released or did not appear when the hand shaking included both the left and the right hand [135]. After months of training, it was now possible for the patient to reach only the right hand without strong spasticity appearing (Fig. 57B). By comparing the angle between the hand and the arm of the trainer (author G.S.) and the patient (Fig. 57B), it can be seen that the hand of the patient was still a bit in palmar flexion, so that there was still some spasticity left. An additional reaching of the left 'good' hand released also the last bit of spasticity of the 'bad' hand, which can be seen from the alignment of the arm and that hand (Fig. 56E). Symmetric coordinated shaking of both hands released the spasticity in this patient with cerebral palsy and in patients with tetraparetic spinal cord lesions. The reason for the release of spasticity in the hands upon shaking both hands is not clear. One reason could be that one has to start with symmetric movements before training the one-sided movements to couple the bad spastic hand to the good, not spastic hand, as was done in that patient. Another reason could be that shaking of both hands is related to phylogenetic or ontogenetic automatisms. The importance of hand shaking, hand reaching or hand holding (see Fig. 80B,C) has not been realized sufficiently in neurorehabilitation and has been underestimated with respect to spasticity relief. Hand reaching gives support and the feeling of safety. The importance of the hand function is obvious, if one realizes how many hands of patients a physician is shaking per day (to give a bit of safety to the patient), how many hands an everage person is shaking per day (in dependence on the culture) and how often humans walk with their children holding their hands. The touching of the hands is a gesture of love, and the poet Schiller described the beauty of the hand. Species specific for man are the upright position and the hand function; some species of monkeys take an intermediate position.

It is known from sports (e.g. tennis) that the clenched fist is very effective for self-encouraging or enhancing one's own motivation. This also holds for patients with CNS lesions. Even a 28-year-old patient with cerebral palsy and an IQ = 30(!) understood the clenched fist for self-encouraging for high impact power therapy. For our above mentioned hemiparetic patient, this means that he has to use the right and left clenched fist for self-encouragement (Fig. 58A) for coordinated power therapy to also improve the function of the 'bad' side. When showing himself and others both clenched fists, no spasticity occurred in the 'bad' right hand, even though not being normal, as compared to the good side (Fig. 58A). But when jumping from a big stone (Fig. 58B), with a similar position of the arms and hands in comparison to the clenched fist position (Fig. 58A), spasticity appeared in the 'bad' right hand, as can be seen

Figure 57
After 3 months of coordination dynamic training, the 19-year-old patient with cerebral palsy is able to reach the right hand (A, hand in spastic position) and to shake the hand of the trainer (B) with only little spasticity (palmar flexion) present. In the background a relief of a ship engraved in the rock outside the acropolis of Lindos, Greece. The ship was used as the base of the statue of Hagesandros. Lindos probably contributed most Greek ships to the Trojan war.

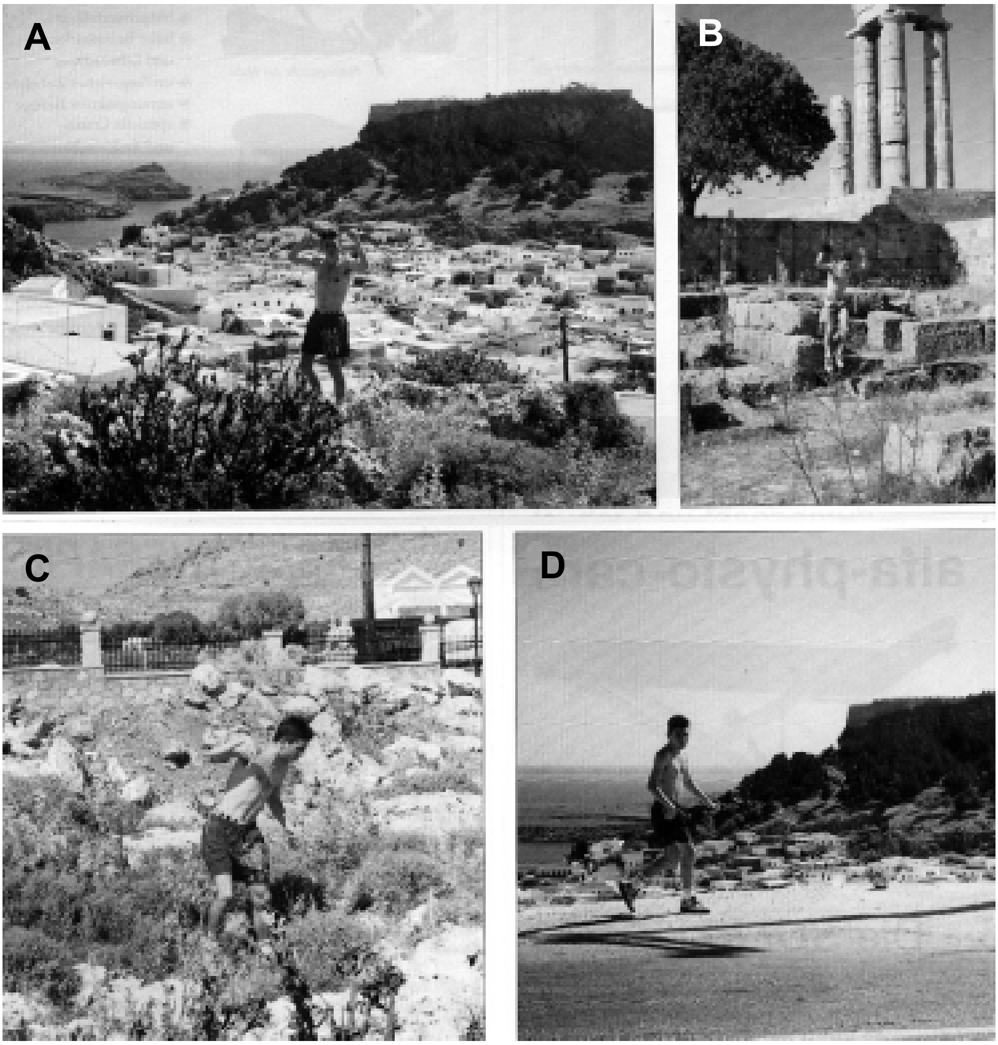


Figure 58
Hand spasticity in the 19-year-old hemiparetic patient with cerebral palsy. A. The patient shows himself and the trainer the right and left clenched fists for self-encouragement. No spasticity occurred in the 'bad' right hand (no palmar flexion), probably because of symmetric motivation for both hand movements. B. The patient jumps from a stone. The arms are in a similar position as in A, but spasticity occurred in the right hand, as can be judged from the palmar flexion of the right hand. C. The patient climbing in the countryside. The patient used primarily the left 'good' side and spasticity occurred in the right hand; the patient became angry because of the difficult task. The training of volitional non-rhythmic movements is too early in the course of his therapy, because the CNS of the patient sticks to the false organization. D. The patient walking with a non-coordinated right arm; spasticity occurred in the right hand (palmar flexion). In the background of A, the Acropolis and the bigger natural harbour of Lindos (Rhodos, Greece) can be seen. The background of B shows the acropolis of Rhode (Rhodos, Greece).

Figure 59
Relief of hand spasticity in a severe case. A. A patient with cerebral palsy, walking with her mother. Note the extreme hand and finger spasticity and the hard work the mother has to do to make her child moving. B. Relief of hand spasticity when taking both hands for stretch exercises. C. The transient partial relief of hand spasticity made it easier to fix the hands of the patient to the treadmill railing for improved treadmill walking.

from the flexion of the right hand. Therefore, in this case of CNS lesion, the symmetric motivation was maybe primarily the reason for spasticity not occurring in the right hand. A state-space landscape similar as for locomotion has been reported to build up for motivation [154] (see below).

The release of the spastic hand may not just be a coupling of the ‘bad’ spastic hand to the ‘good’ hand, as seen in Fig. 59. The patient with cerebral palsy and strongly impaired motor and mental functions had two spastic hands (Fig.59A). The spasticity was so prominent that during stretch exercises (in similarity to Fig. 59B) the therapist took the patient at the wrists, because she thought it would not be possible to take the hands for stretching. On the advise of the author (G.S.) she tried to use the hands for that exerxise. Apart from some difficulties at the beginning to get her hands into the spastic hands, she was astonished and amazed that the spasticity of the patient’s hands released. Holding the hands during the stretch exercises not only released spasticity of the hands but also trunk spasticity released better.

The use of both hands is of obvious importance for the personal and professional life. In this case, the improvement of the hand function made it possible to improve the treadmill training (Fig. 59C) in the way that the patient could hold herself better. An improved walking will reduce the burden on patient mother’s spine when walking with her child (Fig. 59A). In Athens, where these pictures were made, it is very difficult to use a wheelchair, because the pavements are not adjusted for wheelchairs. For mobility reasons, the child has to learn to walk.

It has been reasoned herein that, for spasticity to be released in a localized area, the integrated functions of arms and legs have to be trained on the basis of exercising coordination dynamics, and that it is not justified from theory and practice to train arms and legs separately, as recommended by B. Bobath. To emphasize it once more, to release spasticity in a thumb or index finger, coordinated movements of arms and legs have to be trained! Only by coupling the network organization for thumb and index finger movement to the integrated functions of the body (Fig. 102), spasticity will reduce.

In accordance with B. Bobath, it is helpful in the reorganization of the lesioned CNS to use righting, equilibrium, posture and other reactions. But the training of rhythmic, dynamic, stereotyped, symmetric, coordinated movements, including coordination dynamic therapy methods, is a start to reorganize the lesioned CNS; it reorganizes the CNS more generally (rather than special reactions only) and is much more efficient than training of posture, righting and equlibrium reactions (see below).

On the basis of neurology, Bobath made a step away from the orthopedic line and from the training of reflexes towards the training of righting, equilibrium, and coordinated posture reactions. On the basis of human neuroelectrophysiologic measurements and the new knowledge derived from theoretical neurosciences, the step was made from the Bobath therapy towards the training of rhythmic, dynamic, stereotyped, symmetric, coordinated movements, including the training of automatisms like the stepping automatism and the exercise of balance.

54. Interpersonal (social) coordination

Interpersonal coordination, i.e. coordination of movements of two or three or more persons, has been observed to be similar to the relative coordination in man [141,142]. Therefore, the trainer (author G. S.) has always ben trying to perform exaggerated movements in parallel to the patient to show how the patient has to coordinate his movements and what he has to learn or re-learn. In addition to visual coordination, auditory, synchronized stimulation was tried by counting the steps or by shouting ‘right – left’. The trainer adapted his rhythm to that of the patient, but always tried to draw the patient into a steady physiologic rhythm. If, for example, the right leg was always behind the left leg, the shouting ‘right’ was made more suggestive (emphasized).

With the direct touch, an additional strong interpersonal coordination of rhythmic movements is possible (see, for example Fig. 66E,F), because touch is a more direct ‘input’ for the movement than light. If one helps a child during ‘swinging on a swing’, it can be experienced that the timing of the push one has to give to keep the swing going is easier to adapt by feeling than by watching (see below).

Interpersonal coordination between patients motivates the patients for a stronger training. On the treadmill, a 9-year-old girl synchronized her walking with those of the patient in front of her and succeeded in this way to perform longer walking series. In addition to interpersonal coordination between patients, the trainer could alternately support the right feet for a better walking position for supervised learning (Fig. 32 of [135]).

Fig. 60A,B shows a 38-year-old patient with a tetraparetic spinal cord lesion who coordinated his running on the treadmill with the running of his healthy son in front of him. Two tetraparetic patients coordinated their air-walking, even though the air-walker properties were quite different. Since one patient slipped several times from one pedal (the ‘bad’ foot),

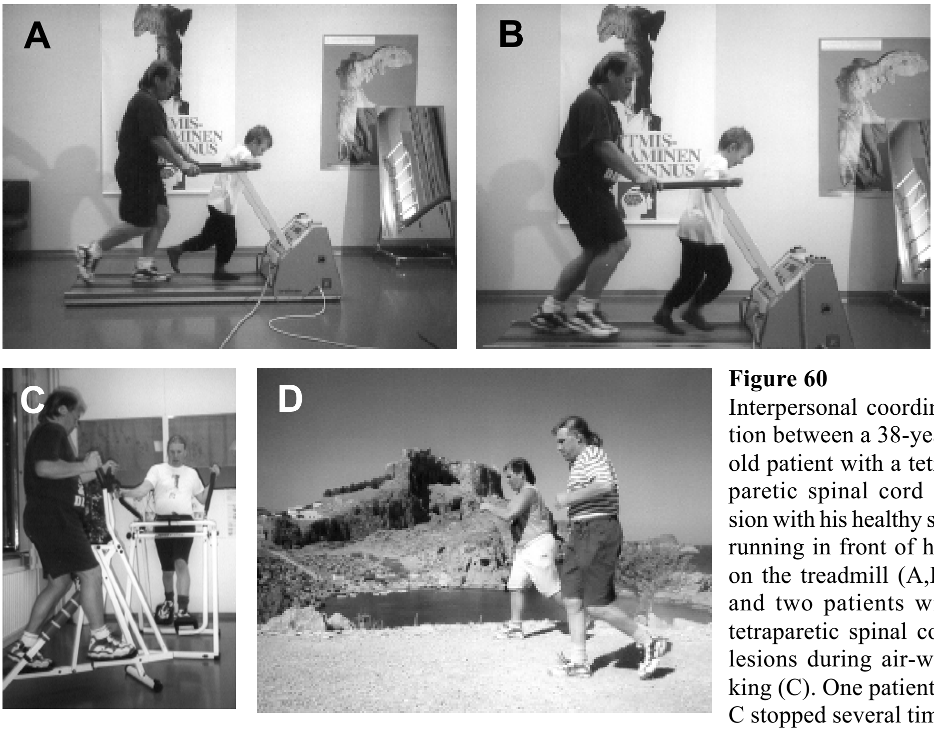


Figure 60 Interpersonal coordination between a 38-year-old patient with a tetraparetic spinal cord lesion with his healthy son running in front of him on the treadmill (A,B), and two patients with tetraparetic spinal cord lesions during air-walking (C). One patient in C stopped several times the air-walking exercise, after a few seconds he reached the synchronized air-walking with the other patient again. D. Interpersonal coordination during running: two tetraparetic patients with a cervical spinal cord lesion 5 and 10 years after the accident. The running was performed in coordination, even although it was not correlated at the start. In one patient the right leg was lagging, and in the other one the left leg was lagging due to the lesion, which means that by interpersonal coordination the leg movements should become more symmetric, because in each patient the 'good' leg should be hindered and the 'bad' leg accelerated. In the background the Acropolis and the second natural harbour of Lindos (Rhodos, Greece).

he had to stop his air-walking several times to position the foot again. After a few seconds of air-walking, he could match the rhythm of the other patient again each time (Fig. 60C). If the air-walkers were positioned in a way that the patients could not see each other, no synchronization of the air-walking took place. When the tetraparetic patients were running beside each other, they were running in coordination, probably because it was easier for them due to interpersonal coordination (Fig. 60D).

Movement coordination among man and animals has been used frequently. When soldiers were marching, they did it in coordination. Interanimal coordination can be found frequently throughout the animal kingdom for safety reasons (fishes in a flock) as well as for food supply. Lions often match stride length with their prey before attacking. The found parallel tracks of a carnivore and a herbivore dinosaur seem to indicate that the carnivore could have come into rhythm with the herbivore (maybe to attack) by adjusting the length of its stride, just as mammals do today [155].

In patients running on a treadmill at 8 to 9 km/h, rhythmicity was found to slightly improve when the rhythm of running was drummed on a drum in coordination: the bad right leg improved a bit. Shouting 'right - left' in rhythmic coordination before the 'lift-off' phase improved the movement of the bad leg (rhythmic supervised learning) so that the lagging phase was more shortened.

When the trainer (author G.S.) was running in parallel and in coordination with the patient, an additional rhythmic supervised learning with respect to the right bad leg was possible by shouting ‘right - right’. But an interesting unexpected problem of rhythmic supervised teaching occurred. When the trainer was only running in coordination, he could run rhythmically and symmetrically with both legs. But when he concentrated additionally on the lagging right leg of the patient and shouted ‘right - right’ before the lift-off phase, then the lagging phase (in relation to the physiologic timing) of the patient’s right leg shortened, but the trainer (author G.S.) also started to run arrhythmically in the way that his right leg also lagged. In other words, when concentrating on the patient’s lagging right leg, the interpersonal coordination between the patient and the trainer became that strong that the trainer could not hold his own physiologic rhythm, but was partly drawn into the unphysiologic rhythm of the patient, and also his right leg lagged.

Such a strong interpersonal coordination may be explained by firstly projections from the optic nerve to the thalamus and the brainstem, and secondly by the oscillation in the visual cortex which may fit especially the running frequency. A further optimization of interperonal coordination seems possible to further enhance the reorganization speed of the lesioned CNS, for example by using the technique of virtual reality.

55. Efficacy (rate of learning) and strategy of the oscillator formation and coordination dynamic therapy

Since the injured CNS can improve its functioning over many years after the injury and the training-induced reorganization progresses only slowly, the efficacy of therapy methods for the reorganization of the CNS is essential.

The efficacy of the reorganization is determined by genetic mechanisms of repair (and their possible (pharmacological) enhancement), therapy time and therapy methods.

The genetic repair mechanisms are a.o. induced following compression, hit or pressure trauma, direct brain injury and infections. The recovery of the CNS seems to be fastest following compressions lasting only shortly. The training should be two times per day (for a few hours altogether), five to six days per week. A break of 8 days in the daily training (Fig. 67), in the case of a spinal compression by ependymoma, resulted in the training success being brought back by about 4 days in addition to the lost 8 days of therapy. Efficacy considerations are therefore very important in the process of reorganization of the CNS, even though difficult to judge upon because of the very different nature of CNS lesions. The training should follow the same principles as fitness training or sports. It is unclear so far, which therapy methods are most effective to most quickly result in CNS reorganization: many movements per time with little power or less movements with more power. During air-walking, many movements can be performed with little power. When jumping on the springboard (or without it) in anti-phase, much power is needed. When walking on a treadmill, the patient is able to walk longer at low speeds than at high speeds. In a first approximation, probably the efficacy of reorganization depends on the number of movements performed per therapy session for medium power movements. With a certain amount of power in the patient, most movements can be performed on the special coordination dynamic therapy device in recumbent position. Treadmill walking, air-walking and exercising on the special coordination dynamic therapy device will be much more efficient than training postural reactions according to Bobath, at least because many more movements are performed per therapy time.

The re-learning of movements, vegetative and higher mental functions is accomplished by

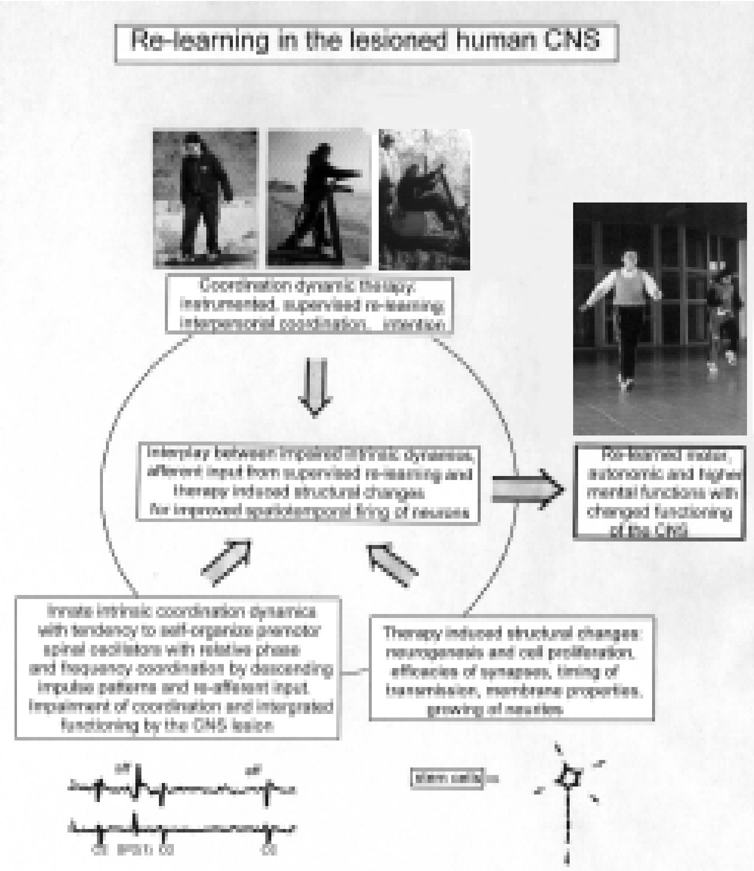


Figure 61
Re-learning of physiologic movements and autonomic functions by exercising rhythmic, dynamic, coordinated movements to restore the impaired coordination dynamics, the rhythmicity of subnetworks and the rhythm coupling between subnetworks by forcing the CNS of the patient into network states in which rhythmic firing subnetworks are coupled in relative coordination again. The movement induced exteroceptive and interoceptive afferent patterns (including those induced by interpersonal coordination and motivation) supervise the neuronal networks to change their functional organization under the support of the genetic repair mechanisms. The interrelationship between coordination dynamic therapy, the coordination dynamic organization tendencies (properties) of the networks and the genetic repair mechanisms is suggested to be responsible for changes in the network functioning of the lesioned CNS so that physiologic functions of the CNS get restored. The CNS functioning is not the same as before the lesion; only the outcome of somatic, autonomous and mental functions are very similar to those before the lesion. For another scheme of re-learning, see Fig. 108.

inter-correlation between (1) the internal coordination dynamic tendencies of the CNS, how the neurons self-organize among themselves under the influence of the afferent input patterns, central command patterns (including impulse patterns induced by motivation) and network instructions, (2) the rhythmic external coordination dynamics, i.e. the training of coordinated, rhythmic movements including intention, supervised learning (by manual, visual and auditory instructions) and interpersonal coordination, and (3) the different genetic repair mechanisms of the lesioned network including neurogenesis (Fig. 61, see also summary of the coordination dynamics (Fig. 108)).

The self-organization of the lesioned pathologically functioning CNS can be changed by internal and external coordination dynamics, the genetic repair mechanisms and their mutual interactions.

The inner coordination dynamics of the CNS can be improved by offering the network physiologic afferent input patterns from physiologically performed movements, improved central command impulse patterns by visually realizing what has to be re-learned, and strong network instructions from the more physiologic functioning networks to the pathologically functioning ones. Running is an innate spinal cord movement which needs little supraspinal drive. When a patient with a lesion of mainly the leg motor cortex runs on a treadmill, then the neuronal networks of the spinal cord ‘tell’, by network instruction, the lesioned motor cortex to reorganize for sending caudally better adapted drive impulse patterns. Such network instructions include network components which use feedforward working networks (occasionally firing mode of neurons not correlated with the firing of oscillators with the internal state not defined by reverberating activity) and rhythm coupling between oscillators of different network parts (oscillatory firing mode; coupling may be in similarity to the building up of an external loop of the premotor spinal oscillators).

If a patient with a supraspinal CNS lesion walks and runs on a treadmill at a speed increasing from 2 km/h to 8 km/h, one can observe the different network contributions made by the spinal cord and the supraspinal CNS (Fig. 62). For low speeds (2 to 3 km/h), the contribution from supraspinal centres with pathologic command patterns is strong, the movement performance of the patient is poor; the feet in this case rotate outwards at the moment of the ‘lift-off’. At medium treadmill speed (4 to 5 km/h), the patient walks fast and the feet do not rotate any more outwards; the network contributions from the rather physiologically functioning spinal cord are relatively large in comparison to the pathologic central commands so that the movement becomes rather physiologic. At high speed (7 to 8 km/h), when the patient walks very fast or runs on the treadmill, the contributions from

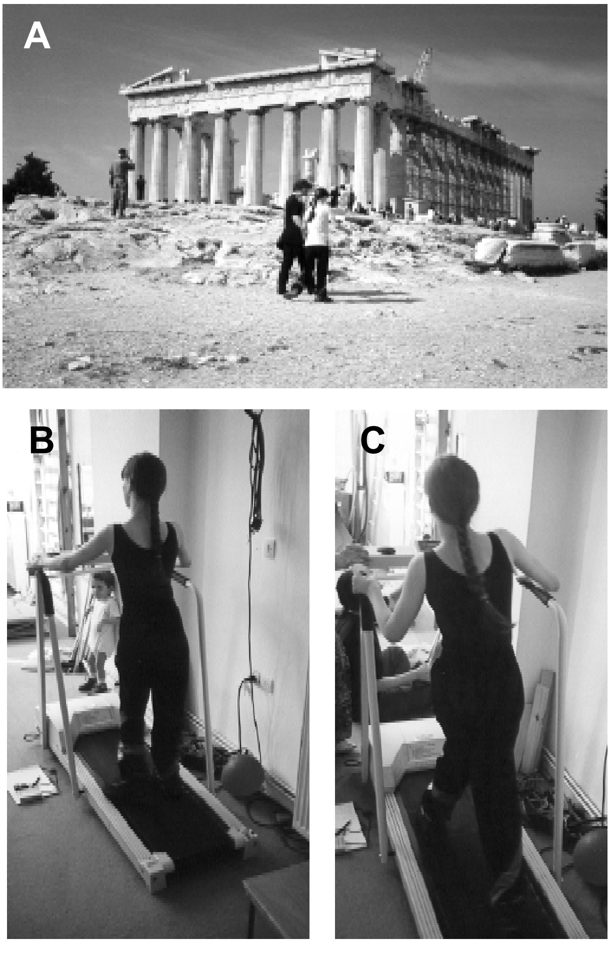


Figure 62
Improved walking and running performances with increasing treadmill and running speed in an 18-year-old woman with cerbral palsy (see also Fig. 63). For low walking and treadmill speeds, the walking performance was poor, as can be seen by the outward rotation of the (left) foot at the ‘lift-off’ phase of the walking cycle (A,B); see also Fig. 63A. At higher speeds, the walking and running performance on the treadmill was better, as can be seen from the little outward rotation of the feet (C); see also Fig. 63C,E. In the background of Fig. 62A the Acropolis of Athens can be seen.

the spinal cord networks are obviously very large and the feet of the patient go slightly into inward rotation at the lift-off point; it seems therefore as if now the spinal networks are overcompensating the false central command patterns for little (pathologic) descending control. Running as a phylogenetically old movement (escape automatism, innate) seems not be changed very much by 18 years of receiving pathologic central command firing patterns from lesioned supraspinal centres (Fig. 62).

The external coordination dynamics has to offer those movements with respect to time and network location (space) so that the reorganization of the lesioned CNS can be optimized. Healthy functioning networks have to be recruited to teach damaged networks what to relearn by certain movements. Movements have to be performed which recruit many healthy network parts, are integrative and include limb dynamics and kinetics, i.e are rhythmic. The training of reflexes and parts of movement cycles may result in non-continuous movements like those of poor robots. The deep potential well limit cycle attractor ‘walking’ should have small subwells at the bottom of the well for parts of the movement cycle. A better description may come from the chaos theory. In a network of chaotic elements for partly ordered states, huge numbers of attractors coexist, and they are hierarchically organized as a tree or a domain structure (see above, cooperative behavior in networks of chaotic elements). If the attractor layout has the form of a tree, then parts of movement cycles could be represented by the branches of the tree, whereas continuous movement is represented by the trunk.

Non-rhythmic movements should be trained to a larger extent only when the main coordination dynamics is restored, i.e. when the rhythmic, dynamic, coordinated movements of arms and legs have been re-learned, because firstly, in similarity to ontogenesis, the automatisms and simple functions have to be re-learned first, and secondly, to avoid spasticity in functionally disconnected arms or legs. It has been shown in an 18-year-old patient with cerebral palsy and hemiparesis (see above under Bobath therapy) that spasticity in the right arm and leg could be released upon integrating the arm into the movement during fast walking (Fig. 56).

The oscillator formation therapy concentrates primarily on the improvement of the organization of the spinal oscillators and their coupling. Coordination dynamic therapy tries to integrate primarily functionally disconnected network parts (on the oscillator level of description) to make, for example, an immovable arm in hemiplegia to move again in coordination with the other arm or the legs. The coherence of the organizing neurons should be strong in the horizontal and rostro-caudal direction during the coordination dynamic therapy to tell, using integrated functions, the more damaged contributing network part what has to be re-learned. Training a child to crawl by setting each arm or foot separately is not in accordance with coordination dynamics, because the arm and the leg have always to move in coordination. Also, the movement cycles have to be run through continuously. Crawling machines with an exact timing (forced coordination) of the leg and arm movements are better for re-learning crawling.

56. Going to the limits

Genetic repair mechanisms can be complex, from neurogenesis of destroyed neurons in functionally critical network parts to changes of functions of neurons to restore integrative network functions. An important point would be how the regenerative capacity can be enhanced. In animal experimentation, regenerative capacity is induced or increased by applying epidermal growth factors. With respect to our new method it is hoped or believed that the small regenerative capacity can be increased by going to the limits, i.e. the patient performs a movement until getting exhausted (Fig. 63). It can nicely be seen in Fig. 63 how concentration and motivation increased in the patient when going to the limits. The fight against spasticity with the volitional available power and when going to the limits is nicely sculptured by the Laokoon group (Fig. 63K). It can also be seen in Fig. 63 that the movement performance improved, as judged by the reduction of the outward rotation of the feet with the increasing treadmill speed. For higher speeds of the rhythmic, dynamic movements walking and running, the contribution from the spinal cord increased and that from the lesioned supraspinal centres decreased, so that the movement performance became better.

Pharmacological enhancement of the regenerative capacity in man would be of great value. If there is some similarity between ontogenesis and regeneration in lesioned network parts (see below), then reorganization of CNS parts has to be seen under the aspect of ontogenesis of locomotion, where crawling is an important movement.

If we look at the CNS more generally as an 'adaptive machine' which has to be forced to adapt, then it seems likely that, when going to the limits of the movement power (without drugs), many mechanisms of adaptation will be recruited for adaptation to the desired movements.

57. Rhythm training for medium strong network activation and relaxation

It has been shown that motoneurons fire occasionally for low activation (Figs. 9-14) and oscillatory for high activation (see, for example Figs. 14, 21, 31-34). Neurons in the dog brainstem also show different firing modes [72]. It has been further shown that also the occasional firing mode of motoneurons, recruited according to the size principle in each motoneuron group, has changed following spinal cord lesion (Figs.12,13).

Therefore, also the self-organization of the neuronal networks following a lesion has to be improved for low and medium strong activation to repair the organization of occasionally firing neurons and their interaction with oscillatory firing neurons. Further, if we model the human neuronal networks on the basis of the chaos theory, then the network organization has also to call upon chaotic states (see above).

Rhythmic movements for medium activation can be accomplished by air-walking with little power strength. Rhythmic coordinated movements of arms, legs and trunk can be trained for low, medium and strong activation with the special coordination dynamic therapy device, where arms, legs and trunk do perform forced coordination by turning coupled levers and pedals. Active relaxation may be achieved with this device by turning slowly (low dynamicity) and with little power. By freely shaking the trunk, the arms, the hands, legs or feet, it may be possible to reach, from a rather spastic state, a chaotic state and in turn then a non spastic state.

58. Similarity between ontogenesis and regeneration

It has been shown in frog experiments that there is similarity in the peripheral nervous system between ontogenesis and regeneration following nerve lesion [78,102].

Membrane properties, calcium transients and muscle contracture of adult frog slow muscle fibres are under neural control, and change during regeneration following denervation in the same way as the innervation of the pyriformis muscle during the ontogenesis. Non-denervated adult frog muscle fibres do not change their muscle properties [78,102]. It may therefore be that, in severe brain damage in adult individuals or in delayed development following brain damage at birth, there are similarities between regeneration and recovery induced by training exercise (motor learning) and supported by the regenerative capacity of the brain.

A 9-year-old female patient suffered, among other injuries, a lesion of the dorsal brainstem

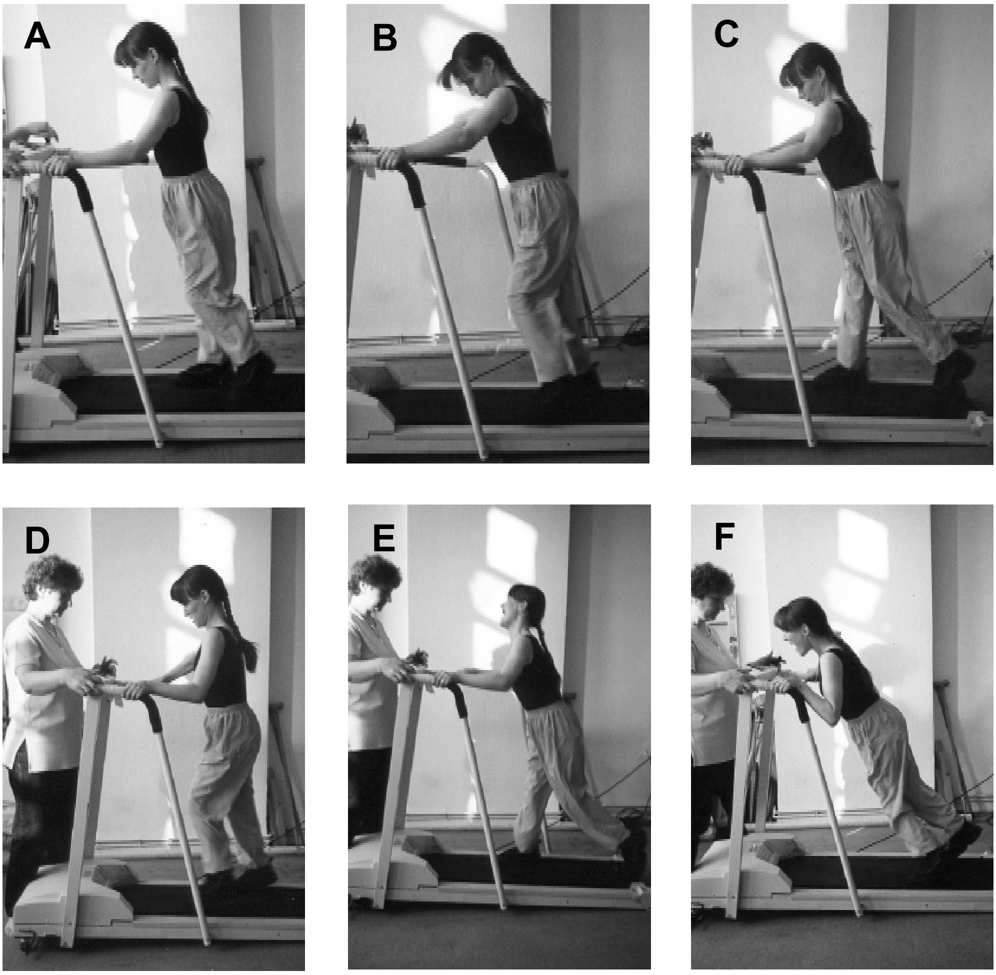
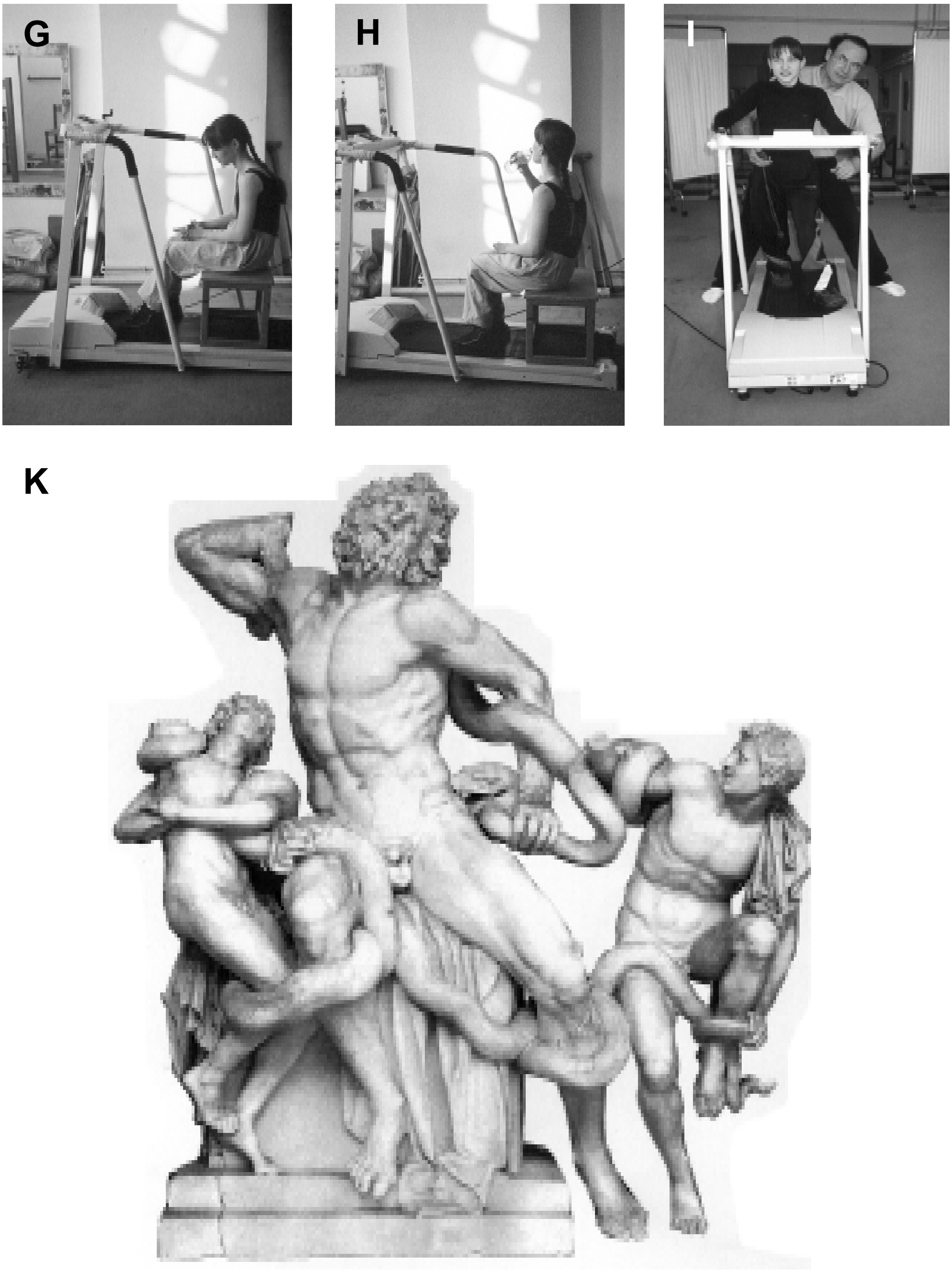


Figure 63
Going to the limits when running on a treadmill. An 18-year-old patient with cerebral palsy walking and running on a treadmill, at speeds increasing from 2 to 7 km/h. The walking interval lasted approx. 10 s and the running interval 15 s (the patient was running when the speed exceeded approx. 6 km/h). The increased concentration of the patient can be seen in her face. Note that with treadmill speeds increasing from 3 to 7 km/h (A,C,E) the locomotion performance improved as measured by the reduction of the outward rotation of the left foot at the lift-off phase.
A. Relaxed walking at 2 to 3 km/h. Note the outward rotation of the left foot at the 'lift-off' phase of the walking cycle. B. Walking at approx. 4 km/h with little concentration. C. Concentrated walking at approx. 5 km/h. Less outward rotation of the left foot. D. Running at 6 to 7 km/h. Strong to very strong concentration of the patient. She just manages to cope with the speed of the treadmill and fights exhaustion. E. Running at 7 km/h. She is at the limit of her locomotor power; she starts to cry. Nearly no outward rotation of the left foot. F. The patient has exceeded her limit, when running for approx. 15 s at 7km/h on the treadmill. Her feet slip from the treadmill. She is crying. G. The patient in the recovery phase between two series of running. H. The patient is drinking water to recover lost liquid. No energy replenishing agents or drugs in the water. I. Safety posture during the therapy (author G.S.) to give more safety to the patient and to reduce her fear to exceed the locomotor limit. It is more a psychological safety support. K.The patient fights with the left volitional power, following a CNS lesion, against



gravity forces and pathologic organization of the CNS (spasticity) when going to the limits: a beautiful representation in the sculpture The Laocoon group. Compare the face of the patient in D,E,F with the faces of Laocoon and his sons. The Laocoon group was made by the Rhodian sculptors Agesandros, Athenodoros and Pylodoros.

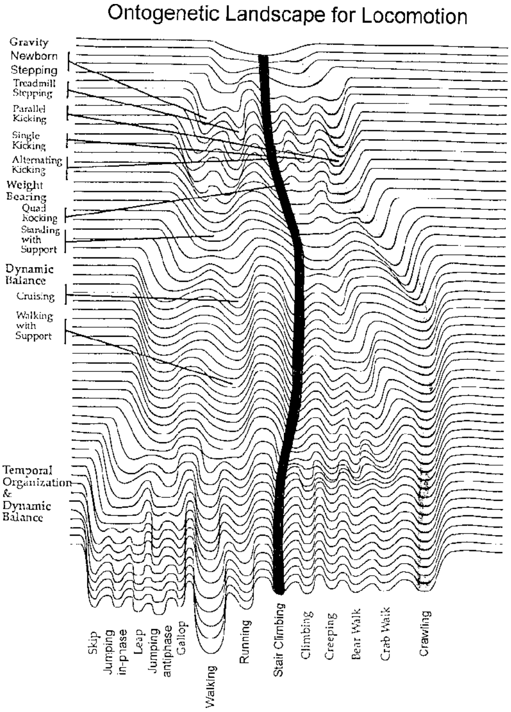


Figure 64
The ontogenetic landscape of locomotion. With permission of Esther Thelen [154].

at birth (forceps). After the birth, she could not breathe (she was ventilated by a respirator), could not speak, not really walk and not drink, and was incontinent because of artificial nutrition. Now, after 9 years she can sufficiently well eat and drink (no artificial nutrition is needed any more), is continent, can speak and attends school. The coordination dynamic therapy was partly used to reorganize the respiratory centre. With respect to the similarity between ontogenesis and reorganization, it is interesting that many functions were learned by the girl with a delay of 6 to 8 years. When, for example, she just learned swallowing with 9 years, she enjoyed it being fed by a patient known to her.

A 30-year-old female patient (having a child of 6 years) suffered a spinal cord lesion sub Th12, which improved with the training to a lesion sub L3. Two years after the accident, when she could perform the first free walking steps, she had the impression of having the ‘grasp reflex’ (well known to her from her child) manifested in her again.

When reorganizing the lesioned CNS, it seems therefore meaningful to consider similarities to ontogenesis. In CNS lesions suffered at birth, the development of certain brain functions may be delayed, and for CNS lesions suffered at a later point of time, periods of ontogenesis may be repeated with respect to functions lost due to the lesion. Very close similarity to ontogenesis cannot be expected since the maturing of the CNS differs in both cases from the normal one, and also experiences in childhood are different in normal and lesioned individuals.

When a cortex lesion is suffered at birth, automatisms and postural patterns may go on to exist. The shadow of the influence of primitive phylogentic patterns may last longer before higher centres mature and modify these early patterns. When tonus increases under stress shadows of patterns of lower integration may appear transiently [11]. In lesions suffered at later times or during adult life, postural reactions or shadows of lower integration or influences of primitive phylogenetic patterns may reappear.

Also, movements should therefore be used in the reorganization of the lesioned CNS that a healthy child would use to develop from automatisms to walking and running. Fig. 64 shows the ontogenetic landscape for locomotion. Crawling, walking, running and jumping seem to represent a representative set of movements of the ontogenetic landscape.

59. Learning in the injured self-organizing CNS

Following spinal cord or brain lesion resulting in paraparesis, the integrative functions of the CNS change due to loss of neural tissue and to destruction of connecting tracts between subnetworks. Re-learning by motor training is a modification of the existing movement patterns, changed by the lesion, in the direction of the tasks to be re-learned. In the HKB model, with respect to jumping on the springboard, re-learning of physiologic movement patterns can be understood as a gradual change of the potential landscape of V(φ) from the pathologic patterns (Fig. 52B-D) in the direction of the physiologic potential landscape (Fig. 52A). Reorganization of the CNS is achieved by cooperative and competitive interplay between intrinsic coordination dynamic tendencies, extrinsic training related inputs (including intention and instruction), with re-afferent input during rhythmic and non-rhythmic movements and genetic repair mechanisms (Fig. 61). The genetic repair strategies include de novo formation of a set of neurons by stem cell proliferation ([166], see above) and could include the allowance to adopt a new commitment for neurons through the loss of input or target or both, which frees neurons of their previous functional constraints. Significantly more new neurons exist in the dentate gyrus of adult mice exposed to an enriched environment compared with littermates housed in standard cages [64]. The learning process is only efficient if the intrinsic tendencies of self-organization are known beforehand. Whether some tasks are re-learned more easily than others in terms of the rate of learning and performance efficiency will depend on the extent to which the patterns to be learned cooperate or compete with existing organizational tendencies following the injury. Each patient must be viewed as a special case, because he/she brings his/her personal CNS lesion and personal history and experience (such as old learned movements) into the learning and training environment. Learning does not change just one thing, it changes the entire system. Not just one association or connection is being strengthened, other connections are being altered at the same time. Learning may take the form of instabilities or phase transitions of movement patterns depending on the relation between what is to be learned and the existing coordination tendencies of the CNS. Even intrinsically stable patterns may show signs of destabilization. The learned patterns become stable attractor states of the underlying coordination dynamics [63]. What is to be re-learned are most likely phase and frequency coordination of neuron firing, i.e. the timing of firing dependent on the neuronal network organization.

If with the re-learning of movement patterns the whole CNS is changed in its integrative functions, then also the entire attractor layout (the state a dynamical system settles into is called an attractor), including spasticity attractors, changes. Indeed, during interval training (repeated movement series at approximately one minute intervals), spasticity which mostly is the limiting factor for a faster achievement of a better movement performance reduces in the short term memory. With the long-term improvement of the movement, also spasticity reduces in the long-term. Spasticity attractors are not included in the landscape of the potential function of the HKB model (Fig. 52). In healthy man, different patterns exist in the same network as a consequence of multistability in a complex system possessing several attractive states (multifunctionality). With respect to spasticity this means that the latter is generated in roughly the same network as e.g. walking. This is what the patients complain about: they have to use their volitional power to fight against fluctuating spasticity as sculptured by the Laokoon group (Fig. 63K).

In the competition between volitional power and spasticity, manifesting 'itself' or in response to minor afferent input, volition and motivation have to be strengthened to get them through the network to the premotor network to perform the rhythmic movements. But it may be even more important to improve the coordination dynamics of the lesioned CNS. The patient has to learn to adapt and differentiate his will to the coordinated movements of, for example, arms and legs during air-walking (motor control and motor learning). The re-learning of the coordination dynamics is the way to reduce spasticity by integrating large network parts in the coordination process of neurons and oscillators by relative cooperation and competition. The perception of the supervising is mainly on a lower integration level; in other words, the patient has not specially to concentrate on the coordination with the trainer (see also interpersonal coordination). The patients express their feeling in the CNS when they get into a rhythmic, dynamic, coordinated movement by saying that the moving is not sticky, viscous, intricate and troublesome anymore, but it becomes easy as if they were lifting up from the ground. The coordinated, rhythmic, dynamic, stereotyped, symmetric movements are the 'wings' (see the cover, Nike of Samothrace) to lift from the ground, to 'win' against the false self-organization of the CNS (spasticity).

The therapy-induced learning process is a combination of unsupervised (self-organization) and supervised learning. The patient performs the movements with intention and will. The injured neuronal networks self-organize the movement according to the injury. Oral, visual and manual help is coming from the trainer who instructs the patient what to do, and who performs the movements in parallel (visual instruction and/or manual help) to improve the movements to enhance the physiologic movement-induced re-afferent input (by helping interneurons to respond to the desired input and to block undesired input to cells) for an improved self-organization of the CNS, the outcome of which has to be a physiologic movement. It is especially the parallel performing of the movements by the trainer (visual supervising) supported by instructions which provides a strong interpersonal 'in-phase' coordination. Interpersonal coordination of rhythmic movements (social coordination) [141] between the trainer and the patient also uses the order parameter with respect to phase between arms and legs of the trainer and the patient to increase, by a constant small phase drive, the cooperative behavior of the patient through visual and auditory instructions.

Aspects of motor learning: Several aspects of motor learning have been given in models [56]: 1. It is essential to identify precisely what is being learned in the information processing sense. 2. Network models need to adopt a rule for modifying synaptic efficacy. The rule should be motivated by the cellular mechanisms that underlie neuronal plasticity. But if one includes realistically membrane property changes of dendrites and axons and regenerative processes in the cellular mechanisms, then such networks might be too complex to be modeled. 3. The credit assignment problem, which concerns the difficulty of directing training signals to appropriate sites in the network and at appropriate moments in the training process, in order for learning to be adaptive. If human neuronal networks can only process natural spatio-temporal impulse patterns for physiologic self-organization and adapted learning, models for human motor learning need neuronal circuitry which is adjusted to such natural impulse patterns. 4. The training information should be known which is provided to the model. It should be justified in terms of the information that is likely to be available for guiding the learning process in the body.

Relationships between motor capabilities and formation of higher-level categorization: The relationship between the learning and the development has already been emphasized [154]. If there is some similarity between the development of normal children and recovery of patients with a lesioned CNS, then one can expect limitations in the development of patients, especially those with lesions suffered at birth, because of the limited motor capabilities (and others) of the patients which reduced the previous opportunities to explore and form perceptual categories and higher-level categorization. The gaining of new motor capabilities when reorganizing the CNS in patients with cerebral palsy may therefore also increase the mental variability of these patients. This is what persons close to patients with brain lesion report: With the improvement of dynamic motor functions also their behavior or intelligence improves.

Because infants' experience of acting and thinking in many different contexts – a necessity for moving from perceptual categories to higher level concepts – is limited primarily by their motor skills, what infants remember should be tied closely to the perceptual-motor situation in which the associations were established. This context defines the initial attractor, and the system will be stuck in that attractor – a motor-experience habit, so to speak – until new mappings can be established through different 'takes' on the situation. Thus, the appearance of a new motor skill acts as a control parameter. It shakes up the stable system, it provides the needed variability, the quasi-stability that allows the system to explore new ways of grouping the components (with respect to the premotor network, the spinal oscillators). With this freedom from context-boundness, this system can aquire enough disjunctive input to categorize, to form higher-level concepts and access memories from both convergent and divergent pathways [154].

Most importantly, however, the theory predicts that perceptual categories and re-categorizations (memories and concepts) should be most easily established in modalities where the opportunity for exploration exists, as exploration provides the rich, disjunctive mappings that facilitate the formation and stabilization of neuronal groups. This means that, in an experimental situation, where perceptual-motor 'knowledge' is assessed, infants will demonstrate a more sophisticated understanding in domains where they have had the opportunity to make these multimodal maps and where the experimental situation particularly taps on their previous experience. In other words, what any test of infant ability taps is not just current knowledge, but the strength of the attractor formed by the infant's previous opportunities to explore and form perceptual categories and higher-level categorizations. These are individually acquired and reflect absolutely infant's interactions in the world [154].

Patients with very limited motor capabilities during their childhood may show limited variability in certain behaviors. Indeed, the variability of higher functions in connection with motor functions seemed to be limited in three patients (18 years and older). The increase in the range of movements (rhythmic, dynamic, symmetric, stereotyped, coordinated movements and non-rhythmic volitional movements) may therefore support the intelligence by increasing the freedom from motor capability restrictions and because integrating the brain parts partly functionally disconnected. The functional use of the whole brain capacity may be important in severe CNS lesions.

60. Motivation

When performing rhythmic, dynamic, coordinated movements in parallel with the patient, for example, during crawling or jumping, the interpersonal coordination, to draw the patient's movement into a more rhythmic movement with a better performance, on a lower level of perception, is only one part of the social coordination. When giving instructions 'left - right' or 'one - two - three - four' in the language of the patient and making them sounding more suggestive when the poor leg has to be moved, with the right timing in the movement cycle or when the patient wants to stop the series of movements because of exhaustion, it was tried to enhance the motivation of the patient or push him on the emotional level to go to his limits of motor power and coordination.

Motivation and emotions can be quantified during crawling in series. Normally, with successive series crawling times over 5m for patients with CNS lesions become shorter (updating of the movement patterns in the CNS) before becoming longer again because of exhaustion (Fig. 47). But when a patient with a brain and a spinal cord lesion generated some extra motivation (and he said that he got more courage by hearing his own voice (self-instruction)), he could achieve shorter crawling times, even when already in the exhaustion phase. When a person he did not like watched his crawling, then the crawling times were longer and the performance poorer. When a beautiful woman watched his crawling, he achieved the best crawling times. It has been argued that part of the oscillator formation and coordination dynamic therapy results from motivation and emotion-bound interrelationship between the trainer and the patient, when training movements in social coordination.

The motivation landscape - potentials for percieving and acting - lives in the same space as the behavioral state spaces [154]. It is part of the same dynamics, as the walking pattern can mainly be induced by the afferent input from the legs (autonomic stepping in newborn babies) or mainly by the descending control impulse patterns (adults). In animals (e.g. cats), locomotion can be induced only by the afferent input (spinalized cat) or only by the descending control (deafferentiated spinal cord). The cause for the descending volitional impulse patterns is motivation. The motivation landscape may thus be similar to that for locomotion. The hills and valleys do not represent particular leg configurations; rather, they represent the relative strength and stability of the forces encouraging or discouraging the infant with respect to various stimuli or tasks [154].

If there is close similarity between the landscape potentials for locomotion and motivation, it may be successful for reorganizing associative centres of the motor cortex and other supraspinal centres in similarity to rhythmic, dynamic, coordinated movements by rhythmic, dynamic, coordinated motivation exerted by the corresponding volitional movements. Hand shaking with both hands or repeated fist clenching (see above under Bobath) are rather rhythmic, dynamic, stereotyped, symmetric volitional movements. It was argued above that making the clenched fist without spasticity occurring in the right hand was probably due to a symmetric motivation (Fig. 58A), since a similar movement without motivation was associated with spasticity (Fig. 58B, jumping from a stone); in another patient (Fig. 86A, left) an emotional condition was observed to reduce spasticity. A strategy in neurorehabilitation may therefore be to start with rhythmic, dynamic, coordinated, symmetric automatisms (walking running), and then go on with the therapy using rhythmic, dynamic, coordinated, symmetric volitional movements (movements of arms and legs) before training non-symmetric volitional movements. The coordination dynamic training has to be performed in parallel. Imagined movements may also be helpful to train, because this may change the motivation landscape.

In psychology, it was postulated that emotion is not felt experience alone, nor a pattern of neural firing, nor an action such as smiling. Emotion is the process that emerges from the dynamic interaction among these components as they occur in relation to changes in the social and physical context [34]. The standpoint of human neurophysiology is different. Emotions are certain feelings in the CNS, which are materialized by neuronal network states. These network states are generated by the space-time distributed natural impulse patterns among very many neurons. On the average, each neuron is connected with 4000 other neurons. The integrative action of these neurons contributing to the feeling of emotion are in communication with the periphery and other network states of the CNS. When a child with cerebral palsy or a stroke patient is walking for the first time for a few minutes on the air-walker (or exercising on the special coordination dynamic therapy device), they mostly feel strongly the improvement in the organization of the CNS, and they start to smile or to laugh. The emotion 'joyfullness' motivates them to go on in the rhythm training, even though it is a hard locomotor work. When a patient with a tetraparetic spinal cord lesion (lesion in the intumescentia cervicalis) is running on a treadmill, it is hard work. But when he gets, by movement induced network updating and external stimulation from the therapist or other patients (interpersonal coordination), into a better rhythmic running mode, he is emotionally affected by the improved running. Even though exhausted, sweating and being red in the face, he smiles, indicating that he is in an emotional state of being happy. One part of the feeling is that it is easier to run when he is getting into the rhythm. He somehow ‘gets wings for lifting partly off the ground’. These wings for running easier are represented by the wings of the ‘Nike of Samothrace’ placed close to him when running on the treadmill (Fig. 60A,B) (cultural stimulation). By seeing the wings of Nike, the induced feeling should motivate the patient to run more rhythmically and smoothly on the treadmill. To improve the attractor state ‘running’ on the treadmill, all possible inputs should be used including rhythmic visual (simulating the leg movements with the arms) and acoustic drive (shouting ‘right-left’), motivation (the sound of the trainer´s voice) and emotional drive (association made by the sound of the voice or by certain hand movements) and, if necessary, rhythmic leg support (Fig. 51).

Emotional network states are not only induced by the afferent input patterns in many thousands of afferent fibres via the supported movement, they also get feedback via the movement induced afferent input. For the re-organization of the lesioned CNS, also activity patterns from emotional network states are used.

The principal problem of describing emotional states by communicating impulse patterns between neurons of the CNS can be explained by the simpler emotional feeling, when the skin is being caressed, gently touched.

When caressing the skin, changing space-time distributed impulse patterns of the kind shown in Fig. 29 will be generated in the receptors of the skin which give rise to the emotional state ‘caress-feeling’ in a large number of neurons communicating for a certain function in the CNS. Touching repeatedly the skin gives rise to similar changing impulse patterns in the skin receptors, but will not induce the emotional state ‘touch-feeling’ in the CNS. In other words, the emotional state ‘caress-feeling’, generated in a large number of neurons in the CNS depends very critically on the space-time distribution of the natural impulse patterns conducted in thousands of skin afferent fibres to the neuronal network. It is therefore not possible to mimic such complex pattern distributions by electrostimulation (no natural impulse patterns in nerve fibres, no space-time distribution of different patterns).

The problem how to arrive from the impulse patterns to the feeling which appears already in the feeling of certain afferent firings remains unresolved. The terms ‘touch-feeling’ or ‘caress-feeling’ are easily understandable characterizations of tremendous complex communications between nerve cells. But why then worrying about impulse patterns if a nice term is doing it already? One of the most important problems in human brain research is, how the neuronal networks of the human CNS generate certain functions and not what (artificial) network states can produce a certain function. With respect to neurorehabilitation, the finding of the rhythmic firing of motoneurons and its regulation by the afferent input patterns and the changes in rhythmic firing led to the oscillator formation and coordination dynamic therapy with which it is possible to get patients with CNS lesions ‘on the feet’ (not possible so far when the spinal cord is anatomically separated).

It is believed that the gate from the somatosensory to the mental functions are the autonomic functions of the CNS. At least in spinal cord lesions, the repair of the vegetative functions is most important. Patients with spinal cord lesions and continence, sexual, somatosensory and pain problems put the control of the urinary bladder and colon (continence) on the first place, followed by sexual, somatosensory and pain problems.

In a CNS lesion, the patient has not only to reorganize the CNS by re-learning, but he also has to re-learn to communicate with the external world by an essentially reduced and unbalanced afferent input. How to experience the external world and the states of the body is not a theory, it is reality for patients with CNS lesions. When in a spinal cord lesion, the stretch, tension and flow receptor afferents (Fig. 14) are cut due to the spinal cord lesion, then the patient has lost the feeling of 'urinary bladder filling'. Interoceptive afferents, running through the sympathetic chain or through the connections of the plexuus, may signal a very full urinary bladder through sweating, heart rate increase or some kind of pain. The patients have to learn to substitute these unspecific feelings for the proper bladder filling feeling to become continent and to manage in the society. In older times, patients with spinal cord lesions died of repeated bladder infections destroying the kidneys. Pregnant women experience that an infection in the bladder more strongly activates the bladder stretch, tension and flow receptors, simulating a too full bladder; so that they have to run continuously to the toilet, even though there is nearly no fluid in the bladder.

Psychology operates with logic and nice definitions, and in theoretical neurosciences we may select behaviors which may be described nicely by a few order parameters. In human neurophysiology and neurorehabilitation we are faced with the reality. We have to work with the details of afferent inputs to the CNS, the functional organization of the CNS and its functional changes following a lesion to find a strategy to re-learn physiologic movements by a changed self-organization of the integrated functions of the lesioned CNS.

61. Reorganization of autonomic functions

Improvement of the urinary bladder function

With the single-nerve fibre action potential recording method [106] it has so far been possible to record single-nerve fibre action potentials from undissected thin long nerve root fascicles down to approximately 3.5 μm in diameter. It is therefore possible to record natural impulse patterns from parasympathetic efferents (par), urinary bladder stretch and tension receptor afferents (S1, ST), mucosa afferents from mechanoreceptors of the bladder, the urethra and the anal canal (M), from afferents responding to fluid movement (S2), and from α_2, α_3 and γ-motoneurons and muscle spindle afferents innervating the external striated urinary bladder and anal sphincters (or functionally associated pelvic floor muscles) (Fig. 2), and to analyze regulatory and organizational mechanisms of parasympathetic neurons and motoneurons in the human CNS.

The self-organization of a premotor spinal oscillator innervating the urinary bladder sphincter has been measured in detail (Fig.14). In response to retrograde urinary bladder filling, the bladder afferents (S1, S2, ST) increased their firing (Fig. 14E), and sphincteric α_2-motoneuron O1 switched from the occasionally firing mode to the oscillatory firing mode (Fig. 14D,F). Phase relations between the firing patterns of bladder afferent fibre S1(1) and oscillatory firing urinary bladder sphincteric motoneuron O1 can be seen in the schematized firing patterns in Fig. 14B. Further phase relations can be directly seen between the firing patterns of secondary muscle spindle afferent fibre SP2(2) and oscillatory firing motoneuron O2. But no synchronized firing can be seen between the sphincteric α_2-motoneurons, innervating the external bladder sphincter and anal sphincters, probably to avoid an increased physiologic tremor (macroscopic rhythmic activation of muscles, due to sub-optimal regulation).

Important for the application of human neurophysiology to neurorehabilitation is the duality of the functions of the sphincteric motoneurons and secondary muscle spindle afferents, subserving somatosensory and autonomic (parasympathetic) functions. In animals it was found that also sympathetic fibres innervate muscle spindles [86]. It could therefore be (and seems to be so) that also parasympathetic fibres innervate muscle spindles in the parasympathetic innervation area (S2-S5). The doublet firing of secondary muscle spindle afferents (Figs. 14B, 32) and γ-motoneurons (Fig. 30) may be due to parasympathetic activation of muscle spindles by parasympathetic efferents [126].

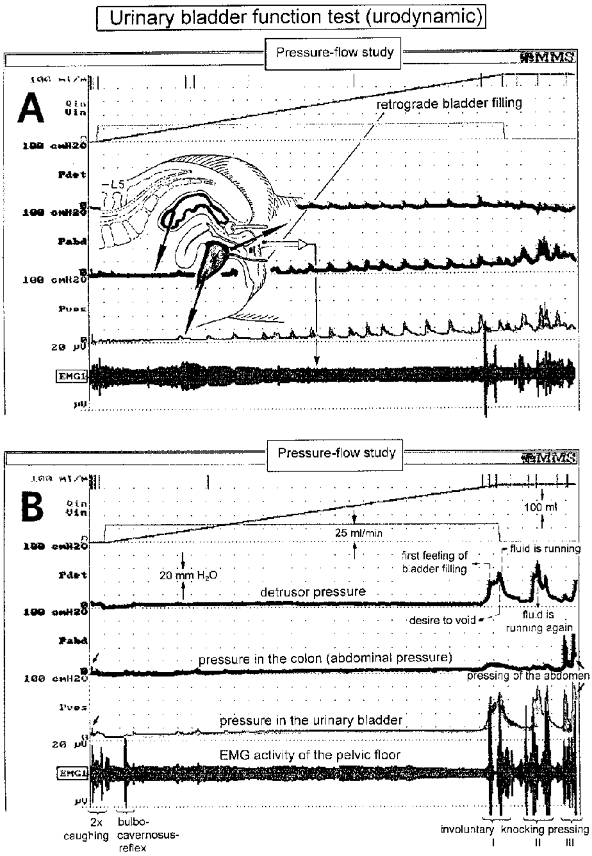


Figure 65
Improvement of the urinary bladder function mainly due to therapy, quantified by urodynamics in a 30-year-old female patient. A. 3 months after the accident in the mountains with resulting paraplegia sub Th12 following spinal cord lesion. B. 12 months after the accident (lesion level lowered to sub L3). In A, the detrusor pressure (P_{det}) is generated by the contracture of the bladder wall, as the pressure difference between abdominal pressure (P_{abd}, measured in the colon) and the bladder pressure (P_{ves}, measured in the bladder). Electromyographic recording obtained with surface electrodes from the sphincters and the pelvic floor (EMG) is shown; the external sphincters and the functionally correlated pelvic floor muscles show similar EMG activity (the rhythmic pressure peaks in A do not originate in the bladder). In A, the detrusor shows nearly no activity with retrograde bladder filling at 25 ml/min; in B, the detrusor shows first activity at 360 ml bladder filling. A detrusor-sphincteric-dyssynergy occurs, because the detrusor pressure peaks occur at the same time as the sphincter EMG activity peaks (B) (bladder and sphincter contract at the same time, so that fluid can only emerge from the bladder at high bladder pressure; there is a danger of reflux through the ureter into the kidneys). The EMG peaks are a bit irregular, probably because the fluid, leaving the bladder, shunts transiently the EMG electrodes. Exact functional description of B: 2x caughing (B below) increases the EMG activity and passively the pressure in the abdomen and in the bladder (marked by the small arrows, physiologic). The bulbocavernosus reflex (induced by pressure applied to the clitoris) increased the EMG activity of the sphincters (physiologic). Conclusion: The reflex arch is in order; sacral nerve roots and nerves have not been damaged in the accident. I (bottom right): The patient feels an increase of unvolitional detrusor pressure (first feeling of bladder pressure at 360 ml). She tries to contract the sphincters to stop the bladder emptying. Shortly after the desire to empty the bladder, as the detrusor pressure decreases, fluid is leaving the bladder. II: Due to tapping onto the bladder, the bladder reflex is activated (detrusor activated, nearly no abdominal pressure); fluid is leaving the bladder. III: Due to the abdominal muscular pressure the pressure in the abdomen increases as does passively the pressure in the bladder (the detrusor is not activated); fluid left the bladder. With a delay, the detrusor was activated by the bladder reflex. - The urinary bladder of the patient is partly functioning. It has to be further improved by therapy induced reorganization of the CNS: (1) An earlier feeling of bladder filling, (2) an increase of the time difference between the feeling of the first bladder filling and the unvolitionally emptying of the bladder (for the time being, approx. 10 min, in dependence on whether the patient is physically active (such as walking) or not, (3) further learning how to activate the detrusor on volition, and (4) the physiologic coordination between the bladder and the external sphincter functioning (to stop the detrusor-sphincter-dyssynergy). In cooperation with U. Bersch, Urology, SPZ Nottwil.

Motoneurons innervating the external sphincters of the bladder and the anal canal subserve somatic functions (contraction of the sphincters on volition or for protection reaction) and parasympathetic functions for the coordination of the detrusor function (parasympathetic) and the external sphincter function. The motoneurons build up two phase relations per oscillation cycle with other motoneurons and secondary spindle afferents for somatic activation (Figs. 3,7 of [130]), and build up 3 phase relations per oscillation cycle when also the parasympathetic division is activated (Figs. 4,7 of [130]). The neuronal networks of the somatic and the parasympathetic nervous systems are interlaced and interact with each other. It should therefore be possible to improve parasympathetic functions when improving somatic functions by a coordination and rhythm therapy, especially as there is indication that also parasympathetic efferents fire rhythmically [125].

If we want to implant, in a paraplegic patient with a spinal cord lesion, an electrical bladder stimulator for bladder control or perform a nerve anastomosis for bladder control [108-111], then the afferents and efferents have to be identified during the surgery (very light anaesthesia) in the cauda equina of the opened spinal canal. By stimulating electrically the lower sacral ventral roots and measuring the detrusor pressure, it can be identified through which roots the parasympathetic efferents are running, which innervate the detrusor. There is no method so far to identify in which dorsal or ventral roots (ventral root afferents) the bladder afferents are represented, even though the bladder afferents can be identified in the summed impulse traffic recorded from the root, after the operation, when analyzing the summed impulse patterns in detail. A natural stimulation of the bladder afferents by a quick bladder pressure increase and the measurement of the natural induced compound action potential should be possible.

Reorganization of disregulated blood vessel microcirculation

It has been shown that in patients with cerebral palsy, spasticity of the arms and hands can be released by rhythmically shaking both hands [135] (see also Fig. 57). A training of coordinated, rhythmic, dynamic, symmetric movements released transiently spasticity (disorganization in the somatic nervous system). Since there is a close relationship between the autonomic and the somatic nervous system, the neurogenic control of the blood vessel microcirculation might also be improved by a rhythm training.

A hemiparetic patient with a spastic arm and hand showed additionally blood vessel disregulation of that arm obvious by the red-blue color in comparison to the ‘healthy’ arm. A rhythmic symmetric shaking of both hands released spasticity as expected. But in parallel, also the disregulation of the blood vessel microcirculation by the autonomic division of that arm improved, visible by color change of the arm. The color of that arm and hand became the same as in the ‘healthy’ arm. Shortly after the termination of the rhythm training (when the short-term memory became also cleared), spasticity in the arms returned and also disregulation of the blood supply of the arm (re-appearance of the red-blue color) re-appeared. A coordinated, rhythmic training in series of the arms released spasticity in the somatic and autonomic nervous systems repeatedly. Since there is indication that, in rhesus monkeys, cerebral microcirculation is directly regulated by CNS activity [70], training of rhythmic, dynamic, coordinated movements may not only improve the functioning of the CNS directly but also indirectly via improvement of the regulation of the cerebral blood supply.

Breathing

In a pilot study, reorganisation of the breathing centre for better breathing was attempted (in an 8-year-old girl with a hypoxic CNS lesion suffered at birth). The girl needed an electrical phrenicus stimulator to be able to breathe during the night, but not during the day (Ondine's Curse). An interval training of running seemed to be beneficial with respect to the improvement of breathing during day and night. It was shown in dog experiments that certain functions of lesioned parts of the respiratory centre of the reticular formation can be taken over by other brainstem parts [68]. The beneficial effect of rhythmic movements on improvement of autonomic function is likely, since rhythmicity is also the organization principle of the autonomous nervous system, and autonomous and somatic networks are certainly interlaced [69,72,99,182-185].

Temperature regulation

An 18-year-old lady suffered brain lesion at birth, including brainstem lesion. Among other deficiencies of the somatic and autonomic nervous systems, she had no temperature regulation. She could not sweat. During hot days her temperature went up to 38 or 39 °C. Manual cooling (taking, for example, a cold shower) helps to reduce her inner temperature. During the 18 years of her life, she gained a bit of temperature regulation. When running repeatedly on the treadmill, slight sweating could be recognized. Apart from an indirect training of the temperature regulation via rhythm training of the somatic nervous system, a direct rhythmic warming and cooling, for example, in a sauna should be tried.

Since somatic and autonomic functions of the CNS can be improved, it seems likely that also mental functions can be improved in patients with brain lesions. This is what the relatives of patients report: also the mental functions improve over the years. An essential enhancement of the recovery of mental functions by re-learning rhythmicity and coordination (integrative organization) should be possible in similarity to ontogenesis.

Sexual functions

It is generally known that fitness training improves sexual potency in men. Since the fittness training program mostly includes rhythmic dynamic coordinated movements like jogging, it is likely that an intensive oscillator formation and coordination dynamic therapy further enhances sexual potency in men. There is indication that relative coordination of rhythms is also a basis for self-organization in the autonomic nervous system divisions [72,99,124-126,142]. In patients with spinal cord lesions urinary bladder and bowel functions also slightly improve during oscillator formation and coordination dynamic therapy. In one case (case report 1), the urinary bladder function improved substantially, which was at least partly due to the coordination dynamic therapy. It is therefore likely that sexual functions, mainly generated by the autonomic nervous system, will also improve during coordination dynamic therapy.

An improvement of sexual potency in men by coordination dynamic therapy including running will be healthier than taking drugs to transiently enhance potency because training makes the whole body more fit including breathing, and does not only work with respect to the sexual function complex.

Stress

If it is possible to improve the functioning of the lesioned CNS, then it should also be possible to regulate the activation of the CNS if there is continuously a too strong input from the autonomic nervous system division (sympathicus). Stress-induced overactivation of the CNS can even persist if the stress factors involved are eliminated as in chronic pain. The overactivated CNS will act on the heart, the stomach or other parts of the body. A causative therapy would be to eliminate the stress factors and to regulate the overactivated CNS. It is well known that overactivation of the CNS before an examination can be reduced by walking up and down. The rhythmic movements (mainly somatic nervous system division) partly reduce overactivation in the sympathetic nervous system division (interlacing networks). A more efficient regulation of overactivated CNS can be achieved by exercising daily using a special coordination dynamic training device (Fig. 109). After having turned the levers 500 - 1000 times, the author (G.S.) himself feels to calm down (short-term memory).

62. Descending drive for locomotion and speech

In a 58-year old patient with a cerebellar lesion on both sides slowly walking was irregular with some stops in between, even though he wanted to walk continuously. In addition, the patient spoke slowly and irregularly (syllabic speach due to a poor coordination of muscles for speaking due to a lesion of the neocerebellum [25]). The patient often stopped talking, even though he claimed to have no problems in finding the words. It was thought therefore that the reasons for the transient stopping of walking and speaking in this patient were the same. To prove this assumption, the patient was put on the device to move arms and legs in a coordinated way, while speaking (Fig. 92C).

First, the patient could count the turns of the hand levers without stopping in between. Second, when the author (G.S.) was talking to the patient while the latter was turning the levers, the speech of the patient became more fluent as long as the hand and leg movements were continuous and the speech arrested at the same time when the movements stopped. When the movements became irregular also the speech became irregular. Two conclusions may be drawn from these observations. First the continuous drives for speech and locomotion are at least partly materialized by the same activation system; and second, speech can be improved when training talking in parallel with rhythmic, coordinated integrated movements. The descending control system may be improved in its regularity by training complex integrated rhythmic coordinated movements, probably because the activation system for speech and movements gets, on the average, more continuous feedback from several simultaneously ongoing functions. The activating system may be an integrated action of the CNS, and when parts of the CNS are lesioned, irregularity occurs in a somehow similar way as rhythmic shaking occurs when the premotor spinal oscillators are partly out of control because of a lesion of the CNS. The speech control may therefore be improved in its regularity by coupling speech to integrated movements, including many submovements.