Electromyographic Identification of Spinal Oscillator Patterns and Recouplings in a Patient with Incomplete Spinal Cord Lesion: Oscillator Formation Training as a Method to Improve Motor Activities

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Abstract. A patient with a strongly lesioned spinal cord, sub C5, relearned running, besides improving other movements, by an oscillator formation training (rhythmic, dynamic, stereotyped exercise) After 45 days of jumping on a springboard and other rhythm trainings, the patient was able to run 90 m in 41s (7 9 km/h) (even 9 3 km/h 3 years after the lesion) besi des marching (5 7 km/h), cycling, playing tennis and skiing

FF-type (α_1) (f = 8 3-11 4 Hz) and FR-type (α_2) (f = 6 7 Hz) motor unit firings were identified by electromyography (EMG) with surface electrodes by their oscillatory firing patterns in this patient In EMG literature, the α_2-oscillatory firing is called „myokymic discharging"

Alternating long and short oscillation periods were measured in FF-type motor units, with changing focus (change from long/short to short/long oscillation periods) The alternating mean period durations differred by approximately 10 ms

Transient synchronization of oscillatory firing FF-type motor units was observed with up to two phase relations per oscillation cycle

In recumbent position, the phase change in synchronization of two oscillatory firing motor units in the soleus muscle of one leg correlated with the change from alternating to symmetrical oscillatory firing of a third motor unit in the soleus muscle of the other leg This measurement indicates that the alternating oscillatory firing of premotor neuronal networks is correlated with synchronization of oscillatory firing neuronal subnetworks, i e with coupling changes of oscillators, and is not due to reciprocal inhibition of half-centre oscillators as suggested by the change from alternating to symmetrical oscillatory firing Coupling changes of oscillatory firing subnetworks to generate macroscopic (integrative) network functi ons are therefore a general organization form of the central nervous system (CNS), and are not related to rhythmic movements like walking or running only

It is proposed that synchronization of spinal oscillators, phase changes in synchronization, changes from alternating to symmetrical firing and backwards, and changes in the focus of alternating oscillatory firing are, among others, physiologic coupling rules of the human CNS to generate, by ongoing coupling changes of oscillatory firing subnetworks, integrative functions such as rhythmic and non-rhythmic movements

One phase relation between two oscillatory firing α_1-motor units was preserved from one volitional leg muscle activation (isometric contraction) to the subsequent one Since running times improved upon successive runs for 90 m, the spinal cord seems to be able to store pattern organization for seconds up to minutes

Controlled and uncontrolled oscillatory firing of α_1-motor units in volitionally activated leg muscles were observed in this patient, which indicated that there still were pathologic recruitments of subnetworks after re-learning running and other movements

During walking, running, and jumping on a springboard, the activation patterns of the vastus lateralis, hamstrings, tibialis anterior, peronaeus longus, peronaeus brevis and soleus muscles were recorded (surface electromyography) to be still pathologic in accordance with partly still pathologic joint rotation angles measured kinematically Especially upon running, the left knee joint flexion was reduced in swing by a rather permanent activity of the rectus femoris combined with an extra burst of the vastus lateralis in mid-swing The recorded abnormalities are due to modification of the motor program rather than to muscle weakness per se A further improvement of the movements of the patient seems possible by improving the motor program, i e by improving the functioning of the spinal pattern generators

By comparing the phasic EMG activity upon walking, running and jumping on a springboard, the motor program turned out to be best for jumping and running, at least with respect to the activity of the left peronaeus longus muscle This indicates that during the more rhythmic, dynamic, stereotyped movements (like jumping or running) more physiologic spinal motor programs were activated by the remaining supraspinal drive Jumping on a springboard generated the most physiologic movement pattern, probably by „Mitbewegung" (co-movement) activated by the synchronization of both legs once per jumping cycle, which induced stronger synchronization of right and left movement pattern generators by a shared afferent input and cycle resettings of oscillatory firing subnetworks of the left and right pattern generators

It is proposed that at least partly, the spinal cord generates stereotyped movements by coupling changes of oscillatory firing subnetworks The main cause for the movement disorders (and spasticity) occurring following spinal cord lesion is the pathologic organization of the functionally deteriorated neuronal subunits below the lesion (because of nonuse as one reason) in combination with a lesion- and degeneration-induced unbalanced supraspinal and afferent drive, respectively, for self-organization of spinal networks

On the basis of our successful therapy trial and measurements on normal, brain-dead, completely (paraplegic) and incompletely spinal cord lesioned (tetraparetic) individuals, it is proposed that the training-induced plasticity of the human CNS to re-preformate neuronal networks for up to minutes and permanently has been underestimated The oscillator forma-

tion training was successful, since the rhythm training fitted the rhythmic organization of the CNS (at least with respect to the premotor α_1, α_2 and α_3-oscillators), as the rhythmic, stereotyped, dynamic leg movements are mainly located in the lumbosacral enlargement of the cord, which was not lesioned in this patient (lesion sub C5), and could be activated by the little remaining supraspinal drive, and since co-movement („Mitbewegung") was induced once per jumping cycle by the simultaneous afferent input This improvement in movements was made possible by re-preformation of spinal neuronal networks for improved self-organization by rhythmic movement-induced afferent input, and by rebalanced lesion-adapted drive of supraspinal networks (by lesion-adapted reorganization)

The type-related single motor axon firing patterns were partly verified by telemetrically obtained rhythmic EMG patterns The self-organization of spinal oscillators, including coupling rules between oscillators, was compared with mathematically derived coupling features of populations of interacting nonlinear biological oscillators, and is discussed with respect to generation of spinal pattern generators in man and animals Spasticity, „Mitbewegungen" (co-movement), „reafference principle", supraspinal control and putative descending systems are analysed with respect to the pathologic organization of the human nervous system following incomplete spinal cord lesion The oscillator formation training is compared with the Bobath therapy, reinforcement learning and treadmill walking

Eight 0 to 5 days old naked infants, born in week 36 to 41 of gestation, showed primary automatic stepping with a mean frequency of 0 2 Hz upon natural stimulation of the soles of their feet The incompletely spinal cord lesioned patient was walking, jumping and running with frequencies of 0 8 Hz, 0 9 Hz and 1 5 Hz respectively It is discussed that the genetically predetermined preformation of spinal neuronal networks in the infants was immature It seems that the early movements of infants are precursors of later locomotion Since preformations of neuronal networks are not fixed, the primary stepping with its variations is a system designed to learn to walk or run from interactions with the periphery

Based on the similarities between the innervation during ontogenesis and lesion-induced reinnervation of muscle fibres by different types of motor axons in the frog, the neural maturation model and the system theory of infant motor development are compared to the reorganization of the CNS following spinal cord lesions especially with respect to micturition and stepping

In comparison to the Vojta physiotherapy, the oscillator formation training puts emphasis on the human-specific bipedal locomotion which is genetically predetermined The rhythm training fits the self-organization of spinal neuronal networks for intergrative functions by changing rhythm couplings of oscillatory firing functional subnetworks (biological oscillators) Only little supraspinal drive is needed for the rhythmic stereotyped dynamic movements Tetrapedal locomotion, not prominent after the birth, seems to be overstressed in the physiotherapy of spinal cord lesioned adult patients

Key words: Man – Spinal cord injury – Oscillator formation training – Entrainment – Rhythmicity – Motor unit type – Premotor spinal oscillators – Alternating oscillatory firing

– Phase relation – Synchronization – Right-left coupling – Pathologic pattern – Pattern storage – Re-preformation – Electrophysiological kinesiology – Newborn infants – Primary stepping

Introduction

While significant progress has been made in elucidating cellular and synaptic properties, projections and neurotransmitters of individual nerve cells and systems, there exists a large gap in our understanding of how these properties are integrated to produce complex behaviors The impulse activity of a single motoneuron does not produce a meaningful movement, complex spatiotemporal discharge patterns of many groups of motoneurons are required, these are driven by a large number of interneurons Thus, in order to unravel the mechanisms underlying the production of movements, the collective interactions of many neurons must be understood Likewise, knowledge of the manner in which the activity of large collections of neurons is orchestrated is necessary to understand homeostatic regulation [30]

In human neurophysiology a new development has started to improve treatment in patients with incomplete spinal cord lesion on the basis of a new understanding of the functioning of the human central nervous system (CNS) derived from human measurements with basic methods

A classification scheme for the human peripheral nervous system has been developed, in which nerve fibre groups are characterized by group conduction velocities and group nerve fibre diameters [93,94] Further, it has been shown that it is possible to extract simultaneous natural impulse patterns of identified single afferent and efferent nerve fibres from summed impulse traffic conducted in thin sacral nerve roots [94]

By analyzing interspike interval and phase relation distributions [95,99], it is possible to partly derive self-organized connectivity of the human spinal cord from the natural discharge patterns [90] Oscillatory firing motoneuron axons were observed [84] Since there is indication that the motoneurons are a part of oscillatory firing networks [90] and since these oscillatory firing networks are activated to fire oscillatory for continence functions [95] and non-rhythmic volitional contraction (nearly isometric) (Figs 7-10,19), it is concluded that spinal oscillators can be divided into premotor spinal oscillators and propriospinal oscillators In a first approximation, for high activation these premotor spinal oscillators are the output mechanism of spinal cord somatic networks Impulse patterns of premotor spinal oscillators were obtained by recording from motoneuron axons [96-99] and from motor units (Fig 7) of different muscles The premotor spinal oscillators are self-organized and driven by supraspinal input patterns and afferent patterns from muscle spindles and skin, and other receptors Premotor spinal oscillators fire rhythmically with impulse trains according to their motoneuron type (α_1(FF), α_2(FR), α_3(S)) [95], and interact with other coupled, rhythmically firing interneuronal subnetworks (propriospinal oscillators) to produce integrative functions by ongoing changes of rhythm couplings [90,95] The general rules of rhythm coupling or coordination (sliding coordination according to v Holst [45]) may show many transitions

between full independence to strict synchronization [53] There seems to be no basic difference in the mechanisms of coordination between different motor rhythms, different vegetative rhythms, and, finally, between vegetative and somato-motor rhythms [53]

The neuronal networks of the human spinal cord seem to show all transitions from special connections (monosynaptic connection between primary spindle afferents and α_1-motoneurons (FF) [97]) to the complex self-organization of preformated neuronal networks [96] The ongoing self-organization and re-organization by rhythm coupling upon input patterns from the periphery and supraspinal centres are probably of much higher functional importance than special reflex connexions, at least with respect to treatment of patients According to W R Hess [42], a reflex is a response to a sensible stimulus in the form of a facilitated involuntary successful action of a certain organ It gives no or only little information concerning the functioning of the human CNS

Following spinal cord lesion it has been measured that premotor spinal oscillators (and probably also propriospinal oscillators) fire less rhythmically (strongly broadened frequency band) [90,96] and probably give rise to pathologic organization and functioning of the spinal cord below the lesion Since there probably is a certain frequency range of entrainment [53,72] around endogenous frequencies, in which the rhythm of a subnetwork can be synchronized by a superimposed rhythm of stimulation, a rhythm training is used here to improve rhythmic functioning of subnetworks and their coupling to macroscopic functions A tetraparetic patient participated in an oscillator formation training, which is something like a rhythmic reinforcement training [10] With the improvement of rhythmicity, when jumping on a springboard, the patient relearned running and other rhythmic and not rhythmic movements

In EMG recordings from single motor units of this patient obtained with surface electrodes, similar or identical impulse patterns were found as those recorded intraoperatively from FF and FR-type motoneuron axons Physiologic and pathophysiologic recruitments of motor units were found in our patient which are probably the cause for the still rather pathologic movements The oscillator formation training is a treatment in spinal cord lesion, which has been derived from theory of human neurophysiology by multi-method studies in man

Since newborn infants can perform automatic stepping, which is most likely the precursor of later bipedal locomotion in man, there is indication that bipedal locomotion is genetically predetermined in the spinal cord and should be practicized in the therapy of spinal cord lesioned patients In similarity to the reflex theory and the oscillator theory in man, the model of neural maturation and the system theory [73] compete when infant motor development is considered

Materials and Methods

Training program of the patient with an incomplete spinal cord lesion sub C5

A 57-year-old patient suffered injury during a traffic accident After the injury the pati-

ent could move his head, 3 months later he could move his toes, and 9 months later he was able to leave the wheelchair without any reliance on wheelchair mobility The left leg showed poor, while the right leg showed reasonable volitional movement The results of manual muscle tests are shown in Fig 1 Thirteen months after the accident this therapy trial was started to make the patient run again The patient was trained by a research worker (GS)

Muscle state

Right leg											Left leg									
5	4-5	5	5	4-5	4-5	4-5	4-5	4-5	4-5	M iliopsoas	2	2	2-3	2-3	2-3	2-3	2-3	2-3	2-3	2-3
5	5	5	5	4-5	4-5	4-5	4-5	4-5	4	M sartonus	2	2	2-3	2-3	2-3	2-3	2-3	2-3	2-3	2-3
5	5	5	5-5	4-5	4-5	4-5	4-5	4-5	4	Mm adductores	2	2-3	2-3	3	3-4	4	4-5	4-5	4-5	4-5
5	5	5	5	5	4-5	4-5	5	5	4-5	M quadriceps femoris	4	4-5	4-5	4-5	4-5	5	5	5	4-5	5
-	-		-	-	-	4	3-4	3	2-3	M tensor fasciae latae	2	2	2	2-3	-	-	-	-	-	-
5	5	5	5	5	5	5	5	5	5	M tibialis anterior	3	4	4-5	4	4-5	4-5	4-5	4-5	4 5	5
5	4 5	5	5	4-5	3-4	3-4	3-4	3	1-2	M extensor hallucis longus	1-2	2-3	2-3	3	3-4	4-5	5	4-5	4 5	4-5
5	5	5	5	4-5	4	4	4	3-4	1-2	Mm extensores digitorum	1-2	2 3	3	3	3-4	4-5	5	5	5	5
4-5	4	4	3-4	3-4	3-4	3	2-3	2-3	2-3	M gluteus medius	1	1-2	2	2-3	2-3	3	3	3	2-3	3-4
5	5	5	5	4-5	4-5	4	4	4	4	Mm semitend et -membr	2-3	2-3	3	3	3-4	3-4	3-4	4	4	4
5	5	5	5	5	4-5	4-5	4	4	4	M biceps femoris	2 3	2-3	2-3	2-3	3-4	3	3-4	3-4	3-4	4
4	3	3	2-3	2-3	2-3	2-3	3	3	2	M triceps surae	2	3	3	2-3	2-3	2-3	2-3	2-3	2-3	2-3
5	5	5	5	5	5	5	5	5	5	M tibialis posterior	1-2	3	3	3-4	3-4	3-4	4	4	4-5	4-5
5	5	5	5	5	4-5	4-5	4	3	2	Mm peronei	2-3	3	3	4	4-5	4-5	5	5	5	5
5	5	5	4-5	4-5	4	4	4	4	3	M gluteus maximus	2	2-3	2-3	2-3	2-3	3	3	4	4	4
5	5	5	5	5	5	5	5	5	5	M flexor digitorum	1-2	2	4	4	4	4	4-5	5	4 5	4 5
5	5	5	5	5	5	5	5	5	4-5	M flexor hallucis	1 2	1-2	3-4	3-4	4	4	4-5	5	4-5	5
21	17	16	15	11	9	7	5	4	3	Months after accident	3	4	5	7	9	11	15	16	17	21
	← Training →																← Training →			

Figure 1. Muscle test according to V Paeslack (the strength of each muscle is graded on a six-point scale) 0 = total paralysis, 1 = palpable or visible contraction, 2 = active movement full range of motion (ROM) with gravity elimi nated, 3 = active movement, full ROM against gravity, 4 = active movement, full ROM against moderate resistan ce, 5 = (normal) active movement, full ROM against full resistance NT = not testable

The training was performed 5 days a week and had the following schedule Passive stretching of leg, arm and trunk muscles at 7 30 in the morning for 15 to 30min Between 10 00 and 12 00 a m , there was oscillator formation training (1 jumping on a springboard, 2 running (at the beginning under weight reduction)), marching, walking (for active recreation) and swimming (such exercises are only partly included in the regular rehabilitation program) The swimming exercise included several times crossing the distance of 25 m in a swimming pool (28 °C), and training (for example, flexion of legs) and relaxation in a therapeutic pool (34 °C) The same exercise training was performed in the afternoon between 2 00 and 5 00 p m Stretching and sometimes massage was performed for 0 5 hour between 8 00 and 9 00 p m Additionally, stretching and massage were applied in between the exercises, especially between each series of jumping on the springboard, to reduce the concentration of lactate in overactivated muscle parts

The exercises included jumping on a springboard (jumping „left forward"-"right backward" to „left backward"-"right forward" and backwards, Fig 2A) and free running (Fig 2C) During non-free running the patient was supported by a mountain climbing har-

ness suspended from a guide-rail fastened to the ceiling (available in the gymnasium; Fig.2G). The guide-rail, securing the patient while running, allowed rhythmic movements of arms and legs and visual recognition (the most important bio-feed-back system in patients with spinal cord lesions) that distance is covered (normal running situation).

Since the patient had not enough voluntary power in the legs, especially in the left one, elastic soles were positioned under the shoes to win back energy while jumping on the springboard (also the patient, himself a research worker in physics, reported it). The jumping on the springboard was performed in series with 1 min rest intervals. In each series the patient was jumping as long as he could. The limit was appearing spasticity. With this form of spasticity or stiffness due to supposed co-contraction, the patient could not move the left leg any more. The left knee joint was felt to be clamped (permanent activity of the rectus femoris (Figs.14,18), other muscles probably contributed). For a discussion concerning the defi-

Figure 2. A. Patient with an incomplete lesion sub C5 under oscillator formation training at a standard gymnasium. Heart rate (before exercise 80; during exercise up to 120-150/min, see Fig. 3), and oxygen saturation (96-98%) were monitored.

B,C. The patient walking and running with EMG surface electrodes in place.

D,E,F. The patient cycling, playing tennis and skiing again. Even though the patient can hardly hold the racket (cervical lesion), he hits the ball.

G,H. The patient running under weight reduction. An 8 days old infant, Juliane, when performing primary automatic stepping (see also Fig.22). Note that there is some similarity between the running shape of our incompletely spinal cord lesioned patient and the primary automatic stepping of Juliane, when she was manually supported in a slightly forward position.

nition of spasticity, see the Discussion section The research worker also jumped on a parallel springboard, and counted the jumps, and tried to stimulate the patient if necessary The number of jumps did not exceed 1,000 to 1,500 per day

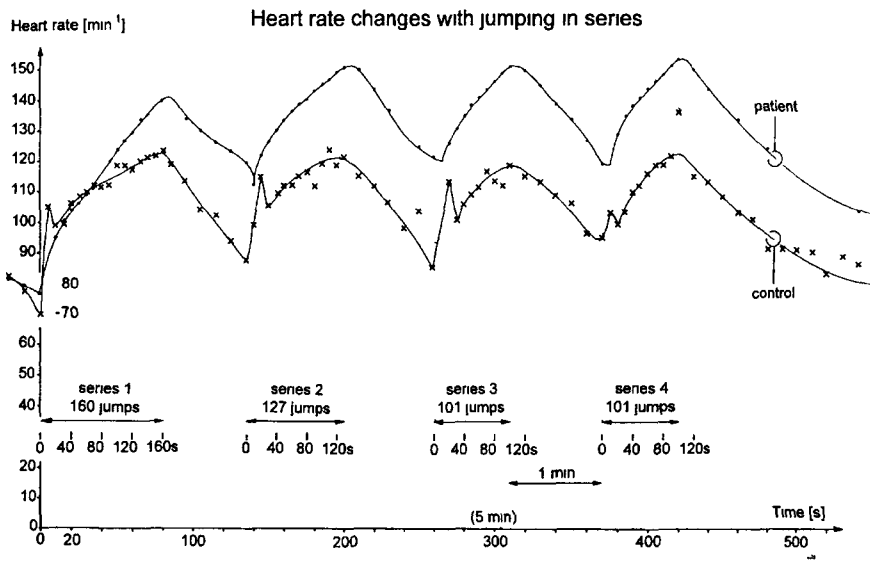

Figure 3. Heart rate vs time when jumping 4 series on a springboard at 1 min intervals The series number and the number of jumps per series are indicated Upper trace, patient (dots, age 57 years), lower curve control (crosses trainer (GS), 53 years) Control measurement not made at the same time Day 29 of training Note the saw tooth like dependence of the heart rate

With a few exceptions, the patient did not participate in the regular rehabilitation program provided at the clinic

Occasionally the heart rate was monitored (Hewlett Packard M1275A) during jumping on the springboard (Fig 3)

Degree of spinal lesion

The degree of the spinal cord injury could not exactly be measured It was assumed that 10% of the tract fibres had survived An estimate in animals made this assumption likely [29] The severity of the spinal cord lesion is emphasized by the experience the patient made 3 years after the spinal lesion He transiently (for 12 to 24 hours) lost the ability to walk and stand up as well as both continence functions upon having suffered from usual influenza lasting for approx 4 days The other members of the family with the same virus infection showed no disturbances of the nervous system This indicates how critically the remaining functions were regulated with the remaining tract fibres in this patient When once the patient

was sitting for 0.5 hours on cold ground (reduction of activities of the skin anal canal and other receptors) he transiently (for one hour) lost his rectal continence. In normal individuals, transient cooling of the anal sphincter with cold water (approx. 5 to 10°C) will relax the anal sphincter and disturb rectal continence for fractions of a second up to a few seconds only. The important two-point discrimination on the patients' foot sole was 8 cm (control person: 1 cm). Since there are approximately 7 to 8 receptors of myelinated afferents between the two points of the two-point discrimination [87], approximately 2% of the touch receptors of the sole were still connected to supraspinal centres (control: 8x8/1cm^2=64 innervated receptors/cm^2; patient: 8x8/8x8 cm^2 =64/64= 1 innervated receptor/cm^2). So far, shoe pads were not used to more strongly stimulate the skin afferent receptors in the foot sole because they reduced stability. Since patients with spinal cord injuries can best walk on deformable irregular ground (beach sand), shoe pads should have lumps to deform the foot sole. In this way, receptors of the T4 skin afferents which are very sensitive to touching alongside the skin, are activated.

Electromyography and Kinesiology

Fifteen-channel telemetry set (Biomes 80, Glonner GmbH ,Germany) was used to record dynamic EMG and temporal aspects of the gait and running strides. EMG was recorded with miniature skin electrodes (Sensor Medics, USA, ref. 650 414) with a pick-up surface of 2.5 mm in diameter, placed 15 mm apart, in the direction of the muscle fibers, on the area of minimal cross-talk between adjacent muscles. The bandwith of each channel was 1 kHz. After filtering (Butterworth 2nd order), the bandwith of each EMG channel was 34 Hz to 1000 Hz - 3dB. The signals were recorded on a strip chart recorder with a bandwith of DC to 10 kHz -3dB per channel (TA 4000 Gould Electonics, USA). In parallel, they were sampled at 2 kHz per channel and stored on an opto-electronic disk for off-line analysis.

Roll-over of the foot was measured with foot-switches [14] placed under the shoe at the level of the heel, 5th, 1st metatarsal heads, and the big toe.

Mean walking and running speeds were measured in a corridor 39m long, 2.8 m wide, with 2 photo cells spaced 5.8 m apart. At the same time, the foot-switches allowed calculation of the mean stride length.

Kinematics of the pelvis and lower extremities were captured by a Vicon system using VCM software (Oxford Metrics Ltd, England) with 5 cameras tracking reflective markers placed on anatomical landmarks. The volume of measurement was 18 m^3 (6 m long, 2 m wide and 1.5 m high).

The patient wore his usual jogging shoes and was asked to walk at a comfortable speed or run all along the corridor or to jump on a springboard.

Results

Oscillator formation training Jumping on a springboard

This training was performed during 45 days of re-rehabilitation (Fig 1) The research worker was leading the exercise by jumping on a parallel springboard, and counted the number of jumps per series and measured the time needed When the patient could not keep the rhythm of jumping, he was encouraged vocally The trainer always felt irregularities in the patient's rhythm because he often had to reduce his own rhythm to give the patient the right drive (phase) for jumping The results of jumping of the first day of training are shown in Fig 4A, and those of day 21 in Fig 4B It can be seen in Fig 4 that the number of jumps per series (mean of the first three series) increased from 53 to 117, and the variation of the jumping frequency (Δ2f) decreased from 0 18 to 0 05 Hz At least the improvement of the rhythmicity in jumping has to be attributed to an improvement of the organization of CNS neuronal networks, and cannot be explained by an improvement of physical fitness

With the ongoing exercise the number of jumps per series increased (Fig 5A) and the regularity of the rhythm improved (decrease in frequency variation, Fig 5B) Also, the frequency of jumping increased slightly with the training (Fig 5C) At the beginning of the tra-

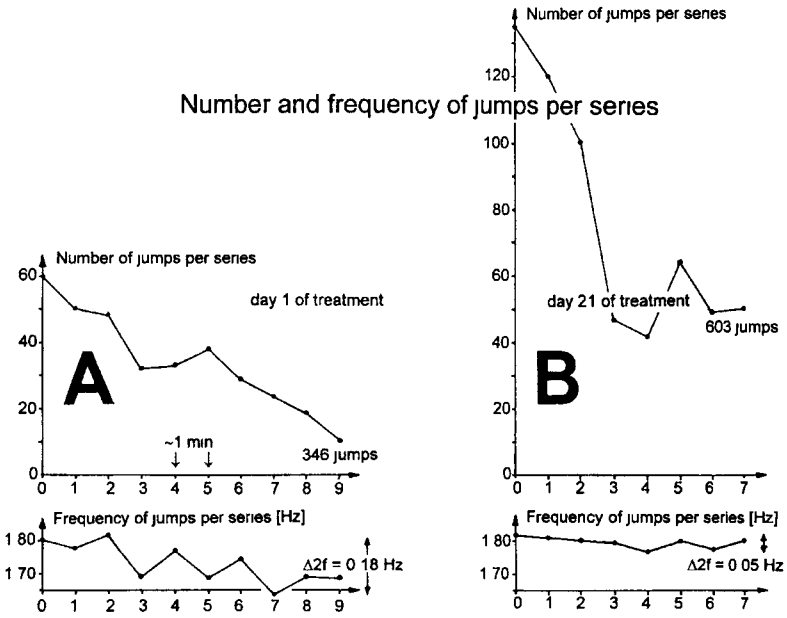

Figure 4 Number of jumps per series (upper part) and mean jumping frequency in a series (lower part)

A. First day of training (afternoon)

B. Day 21 (morning) Note the narrower variation of jumping frequency (Δ2f) in the lower part of B

ining, the patient was not able to volitionally lift the left heel However, when jumping on the springboard, he also lifted the left heel as a result of „Mitbewegungen" „Mitbewegungen" is the mechanism by which the movable leg makes the more seriously spinal lesion-affected leg to perform rhythmic stereotyped movements (see section „Mitbewegungen" of Discussion)

The number of jumps first decreased before increasing (Fig 5A) With the start of the free running exercise (second type of oscillator formation training), the number of jumps per series increased stronger Since jumping was limited by the appearance of spasticity (block of the left knee, for definition see Discussion), the increase in the number of jumps was a measure of the reduction of spasticity and a measure of the increase of useful movements With the free running exercise the spasticity further decreased

It seemed during the morning sessions of stretching that extensor spasticity decreased while flexor spasticity increased and the overall spasticity decreased It further seemed as if the extensor and flexor spasticity became more balanced and useful movements further increased

The improvement of natural movements (Figs 5A, 6) went in parallel with an improvement of rhythmicity (Fig 5B) The natural adaptable pacer (trainer and author G S) was important for the increase of useful movements and decrease of spasticity A comparable control patient who had more power in the legs, was involved in oscillator formation training for 2 days only This patient jumped so unrhythmically that the trainer had problems to adapt his rhythm to that of the patient The control patient still spends most of his time in a wheelchair, whereas our patient does not need any wheelchair any more

During the first 30 days of treatment, the volitional power of the left gluteus maximus increased from grade 3 to grade 4 (Fig 1)

Two months after the end of the re-rehabilitation, (the patient was running and performing other exercises at home 3 times a week), the general volitional power had further risen, but the speed of running had not increased because the appearing spasticity limited fast running

Oscillator formation training Free running

At the beginning the patient was running with a weight reduction of 20 kp, this was achieved through supporting by a guide-rail (does not belong to a regular rehabilitation program) Then, the patient was running without weight reduction but was still secured by the guide-rail After 30 days the first free running was possible The improvement in free running achievement was measured by the time the patient needed to cover a distance of 90 m The patient preferred running on grass, because it was slippery If the poorly innervated left leg could not be lifted (for kinematic diagnosis, see below), the slippery wet grass helped the forward movement (when the forefoot touched the ground during the swing phase) Also, when the patient fell, the grass was soft enough to avoid fractures Falling down was trained on a mat Again, the speed was mainly limited by the appearance of spasticity rather than by volitional power in the legs If the patient started the 90 m run with a first strong step, when

transforming potential energy of standing into kinetic energy of running, spasticity appeared quickly and blocked the running after a few steps. The start of the running had to be gentle. If the start was insufficiently gentle, spasticity frequently appeared after running a distance of approximately 40 m. To reach the goal at 90 m, running had to be started gently and the patient had to try to put as much as possible rhythmicity into his movements. For the sake of safety, the research worker was always running beside the patient and pushed him into rhythm by vocal stimulation.

If for example, the patient ran 90 m 8 times at intervals of approximately 10 seconds, the running time decreased with each 90 m distance (straight line) before increasing again. Repeated running seemed to increase the transient regularity of rhythmicity in the CNS, and thus allowed faster running before the running time started increasing again due to the loss of volitional power. To obtain short running times, the patient with the assistance from his trainer, had to get into a good rhythm.

The shortest 90 m running times decreased with the ongoing exercise (Fig. 6). The highest running speed, reached after 11 days of running, was 8 km/h (90 m • 3.6/41 s = 7.9 km/h). With home physiotherapy and exercise, the patient could run 90 m in 35s (9.3 km/h) 3 years after the accident. The left fingers and the left musculus psoas further recovered 2.5 years and 3 years respectively after the accident.

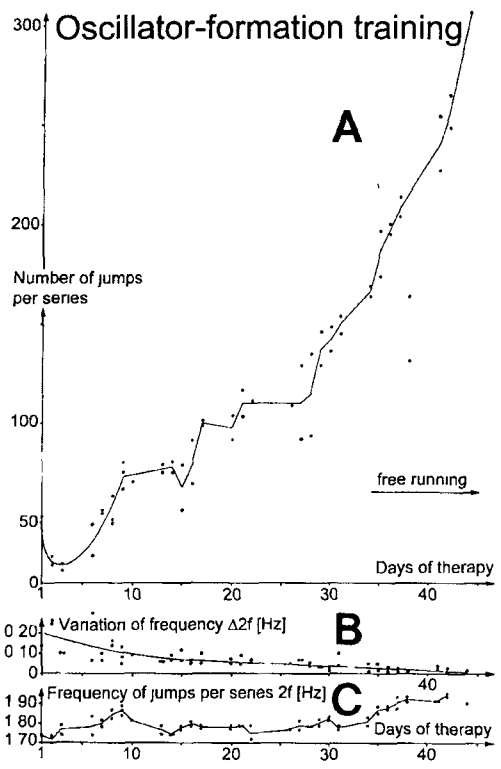

Figure 5. A., B., C. Quantified oscillator formation training

A. Number of jumps per series (mean of the first 3 series (Fig 4)) vs therapy time

B. Variation of jumping frequency Δ2f with ongoing therapy

C. Frequency of jumps per series Normally, 3 to 8 series were performed at 1 min intervals during the morning and afternoon session each The reduced number of jumps on day 38 was due to alcohol consumption (1 l of wine) the evening before Note that the frequency variation decreased with the increasing time of therapy, while the number of jumps per series increased

Oscillator formation training Marching

Marching was the mode of locomotion to cover longer distances quickly The patient could march 1,500 m or more with no problem The fastest marching speed achieved was 5 7 km/h (304 m/192 s = 90 m/57 s = 5 7 km/h) If marching was started too quickly, spasticity appeared after approximately 200 m Actually, spasticity was the limiting factor for speed again, although to a lesser degree than it was the case with running

The patient reported that the mode of locomotion while marching was different from that while running When marching was the first exercise, the patient had more problems with running Jumping on a springboard, on the other hand, seemed to be beneficial for running in that spasticity was slightly reduced while running

Swimming

The times for 25 m breast-stroke decreased from 75 s to 50 s If the legs touched each other, the left leg also moved but not otherwise (Mitbewegung - co-movement) After 45 days of training, the left leg also moved, even when the legs did not touch each other The swimming times were comparatively long Due to an injury to the cervical intumescentia (lesion sub C5), the arms had only little power, normally, they contribute approximately 60% to the swimming power The rhythm training of marching and swimming were used to measure (by the speed) the improvement of movements with the ongoing training, and to induce co-movements in different ways

Therapy pool

Different kinds of trainings were performed in the therapy pool In particular, the power of flexion was trained The flexion power of the left leg, measured with a spring balance, increased from 4 5 to 8 5 kp The right leg developed approximately 25 kp during flexion

Cycle, tennis, skiing

The patient relearned quickly to ride a normal lady's bicycle At the beginning, the problem was to mount or to dismount the bicycle The keeping of equilibrium presented no problem At the end of re-rehabilitation the patient was able to cycle in the countryside Due to the weakness of the patient's hands special brakes were mounted on his own bicycle later on One year after this treatment, the patient is again able to ride a bicycle to and from his workplace

The patient relearned to play tennis even though at the beginning he had problems to hold the racket At the completion of the training cycle he still had problems to simultaneously concentrate on two movements the coming of the ball and the running towards the ball

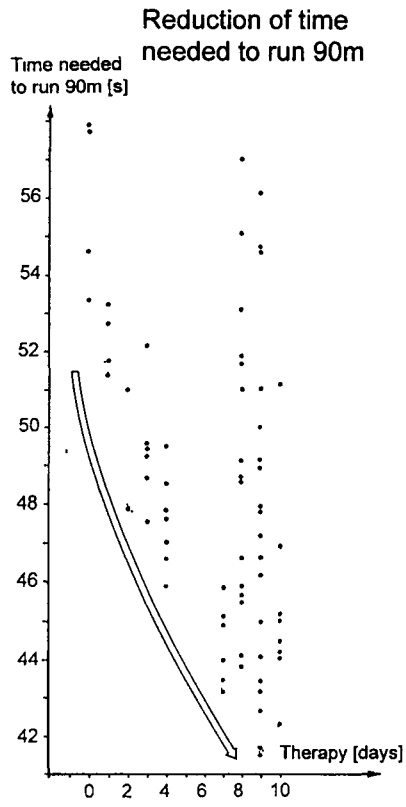

Figure 6. Running times for 90m in dependence on the duration of therapy (days) The shortest times are connected by the dotted line

Now the patient can easily perform cross-country skiing. The patient started downhill skiing 2 years after the accident; presently he can cover a difference (snow-plough) in altitude of 1,000 m and can use a ski tow.

Electromyographic identification of single oscillatory firing motor units

In the preceeding Results sections it was shown that useful movements increased (and spasticity decreased) in our patient with an incomplete spinal cord lesion with the increase of rhythmicity when performing rhythmic, stereotyped, dynamic movements. In the following sections, results of electromyographic measurements of basic neuronal network and macroscopic network functions in this patient will be presented to firstly get more knowledge on neuronal network organizations and functions, and secondly, to see what could be further improved to return the patient more useful neuronal functions. An interpretation of electromyographic (EMG) and kinematic recordings of the patient's state of walking, running and jumping will be given. The recording with surface electrodes is a non-invasive and painless method. The obtained impulse patterns of neuronal network functions were still more or less pathologic, but they can be expected to improve with an improved motor performance.

The EMG recording layout is given in Fig. 7. Single motor unit activity can be identified in the recording traces. The identified impulse patterns of rhythmically firing α_1 (FF) and α_2 (FR) motor units (Fig.3 of [96]) are marked. At that time period, two FF-type motor units fired at that time period in the biceps femoris and soleus muscles, every 120 ms (f = 8.3 Hz) with an impulse train consisting of one action potential (AP). In the peronaeus longus muscle, another FF-type motor unit fired with 10 Hz. In the biceps femoris muscle, an FR-type motor unit fired every 150 ms (f = 6.7 Hz) with a 2 AP impulse train, with an impulse train interspike interval of 10 ms. The identification of α_3-motor units (S) is unsafe (Fig.9, soleus muscle). As motor unit AP wavelengths are around 5 ms ([3], Fig.7), a safe identification of α_3-impulse trains is difficult, since the first interspike intervals of their impulse trains are also around 5 ms [84]. The motor unit AP amplitudes (on the average, AP amplitudes decrease with the increasing distance from the recording electrodes) seemed to decrease from FF-type (Fig.7) to FR (Fig.7) to S-type (α_3) (Fig.9) motor units, in similarity to the APs of the corresponding motor axons (Fig.1A of [97]). The identification of the impulse trains of oscillatory firing α_3-motoneurons will therefore be most difficult in EMG recordings.

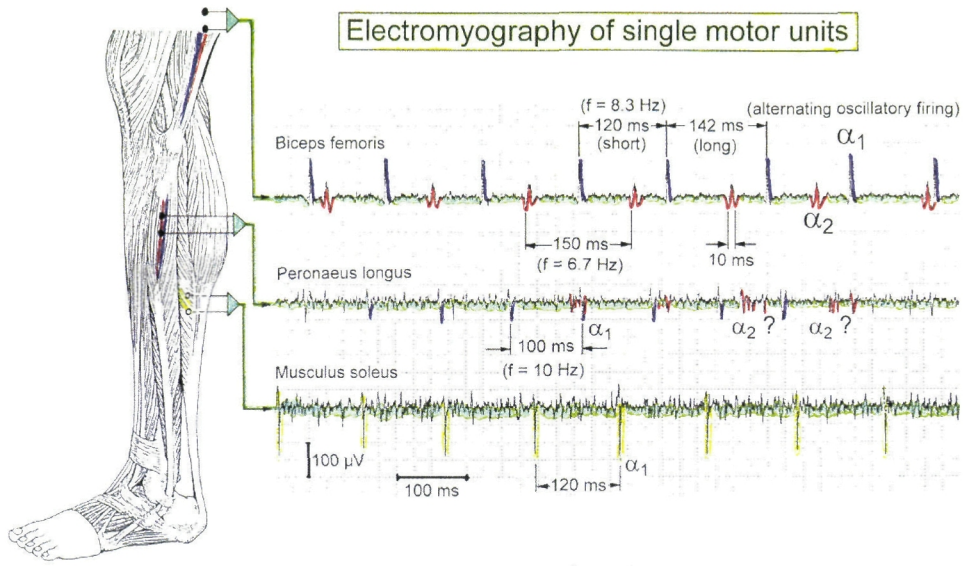

Figure 7. Extracellular electromyographic recordings with surface electrodes from the musculi biceps femoris, peronaeus longus and soleus. Impulse patterns of oscillatory firing α_1 and α_2-motor units can be identified in the recordings of the three muscles, and they are partly marked. A safe identification of α_2-motor units in the recording 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.

The natural impulse patterns of the different oscillatory firing motor axons could partly be verified in the motor unit activity For a safe identification of the motor unit type, it should be tried to differentiate between the different muscle fibre types by different group conduction velocities in similarity to the differentiation of the corresponding motor axons (see Discussion)

Alternating long and short oscillation period durations

Alternating long and short oscillation period durations were recorded from an α_1-motor unit of the biceps femoris muscle (Fig 7) The FF-type motor unit fired first with alternating short and long oscillation cycle periods of 142 ms and 155 ms (average) and then changed to periods of 136 and 126 ms (n = 14) We shall term the change in alternating firing of long/short oscillation period durations to short/long a change of „focus" For the sake of clarity, a change of focus of alternating firing means that the oscillation periods change from long/short durations through 2 identical intervals to short/long durations

The other α_1 (soleus muscle) and α_2-motor units in Fig 7 (left leg) showed no alternating firing No alternating oscillation period changes means that there was no alternating firing or that the focus changed so often that no longer term alternation in the periods could be observed

Alternating oscillation periods (134 ms and 124 ms, standard deviation < 10 ms) were also observed in the FF-type motor unit α_1^1 of the soleus muscle (Fig 8) of the right leg (for further details see below) The difference between long and short oscillation periods was approx 10 ms

Transient synchronization of oscillatory firing α_1-motor units, and memory of the state of spinal pattern generator

Fig 8 and 9 show transient synchronization of motor units from the soleus muscles of the right and left leg In Figs 8B and 9B it can be seen that the FF-type motor units α_1^2 and α_1^3 of the left soleus muscle, and α_1^1 of the right soleus muscle fired oscillatory when the patient activated the soleus (and other) muscles by volitional plantar flexion against resistance (hands of the examiner) The motor units fired slightly more regularly upon the second plantar flexion (Fig 9B, begin of activation included) Upon the first plantar flexion, all 3 α_1-motor units started to fire oscillatory The phases between the motor unit firings of the left and right soleus muscle were not or only little phase related The firings between the α_1^3 and α_1^2-motor units of the left soleus muscle had a phase relation of approx 85 ms (Fig 8C, left side of Fig 8A) At the middle of the sweep (Fig 8A), the two motoneurons of the left soleus muscle changed their mutual phase to fire simultaneously (phase 2 $\approx$ 5 ms, right side of Fig 8A) With the second plantar flexion a few seconds later (Fig 9), all 3 motoneurons started to fire oscillatory again, but the firings of all 3 units were phase related (Fig 9C) The nearly simultaneous oscillatory firing of the α_1^2 and α_1^3-motor units (phase of synchronization

≈5 ms) was preserved from the end of the first plantar flexion (right side of Fig 8A) over the period of no movement to the second plantar flexion The spinal cord thus seems to have kept the network organization state of synchronous firing of the α_1^2 and α_1^3-motor units from the first to the second plantar flexion

A somehow similar memory phenomenon with respect to macroscopic functions was observed during running, jumping and marching When running 90 m repeatedly, the running times of the patient became first shorter before becoming longer again The CNS (probably the spinal cord) seemed to have retained some information concerning the rhythmicity of the running state from one running to the next, and improved in this way the rhythmicity of the successive runnings Further, when marching before running or in between, the running was not as good (longer running times for 90 m) However, jumping on a springboard before running seemed to be beneficial for running (shorter running times), and also the patient felt so The CNS (probably the spinal cord) seemed to be able to keep the information of pattern organization, especially the rhythmicity, for seconds up to minutes

Correlation between the phase change in synchronization of motor units in the left soleus muscle, and changes in alternating firing of motor units in the right soleus muscle

Upon the first plantar flexion, the FF-type motor unit α_1^2 and α_1^3 of the left soleus muscle fired oscillatory (Fig 8B) synchronized by a phase of approx 85 ms (see phase 1 in Fig 8C and trace soleus muscle of the left leg (Fig 8A)) The FF type motor unit α_1^1 of the right soleus muscle fired simultaneously with alternating oscillation periods with mean durations of 134 ms and 124 ms (Fig 8B, dashed vertical lines) There was no clear phase relation of oscillatory firing between the α_1^1-motor unit of the right soleus muscle and the α_1^2 and α_1^3-units of the left soleus muscle The patient was recumbent and performed volitional plantar flexion of both legs against the hands of the examiner With ongoing first plantar flexion, the phase between the oscillatory firing α_1^2 and α_1^3-units of the left soleus muscle changed to phase 2 of approx 5 ms (Fig 8C, and trace soleus muscle of the left leg (Fig 8A)) Simultaneously, the α_1^1-motor unit of the right soleus muscle changed transiently from alternating to symmetrical oscillation Upon the second plantar flexion, all three motor units of the left and right soleus muscles fired synchronously oscillatory with no alternation of the oscillation periods (Figs 8,9)

Important for the understanding of the functioning of neuronal networks of the human spinal cord are the following

1 Premotor neuronal networks fired oscillatory also upon no rhythmic movements
2 Two phase relations were also electromyographically observed between oscillatory firing motor units, as for motor axons (Figs 5B 7 of [99])
3 Alternating oscillatory firing was also observed electromyographically as for motor axons (Fig 14 of [96])

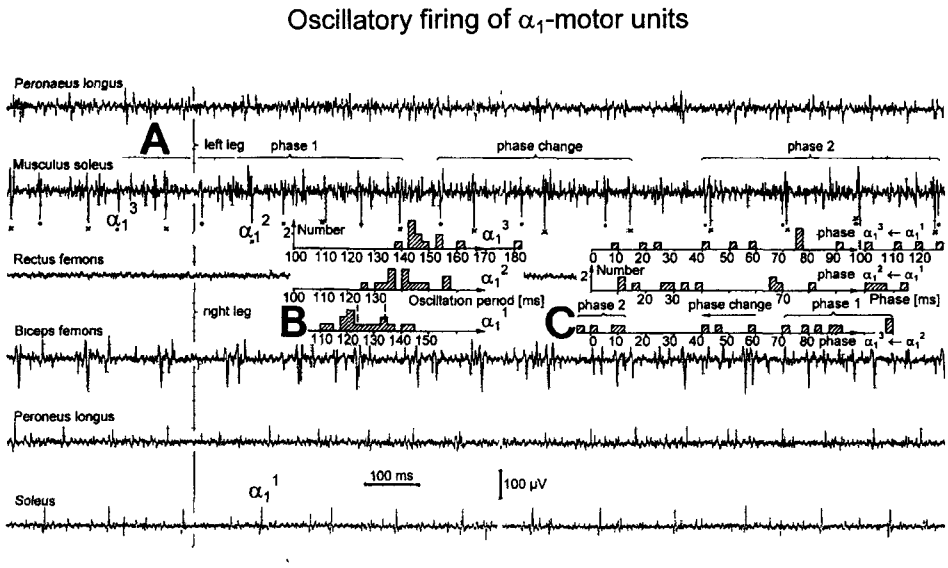

Figure 8. Electromyographic recordings from the peronaeus longus and soleus muscles of the left leg and the rectus femoris, biceps femoris, peronaeus longus and soleus muscles of the right leg (A) The α_1-motor unit potentials α_1^1 (soleus, right leg,), α_1^2 (cross) and α_1^3 (soleus, left leg, dot) are marked and oscillation period duration (B), and mutual phase distributions (C) are constructed For definition of phases, see Fig 9 Note that there is nearly no correlation between the firings of the α_1^1-motor unit and the α_1^2 and α_1^3-units and that the phase relation changed from phase 1 (≈ 85 ms) to phase 2 (≈ 5 ms) in the oscillatory firings of the α_1^2 and α_1^3-motor units (C) The α_1^3-oscillation period durations of 160 and 180 ms (upper part of B) occurred with the phase change just before the domain of phase 2 The different muscles were activated by voluntary plantar flexion. The two mean oscillation periods for the alternating oscillatory firing α_1^1-motoneuron (at that time) are indicated by the two dashed lines

4. Spinal oscillators changed from alternating to symmetrical oscillatory firing simultaneously with the phase change of two other synchronized oscillatory firing oscillators. Consequently, (a) alternating oscillatory firing is generated by ongoing coupling changes of different spinal oscillators rather than being due to reciprocal inhibition of half-centre oscillators. (b) Changes from alternating to symmetrical oscillatory firing and phase changes in synchronization of oscillators are indicators for coupling changes in a population of coupled oscillators.
5. Alternating oscillatory firing changed in the right soleus muscle simultaneously with the phase change of synchronization in the left soleus muscle. It is concluded that there is a correlation between right and left-sided neuronal networks, even for non-rhythmic movements (the patient was recumbent).

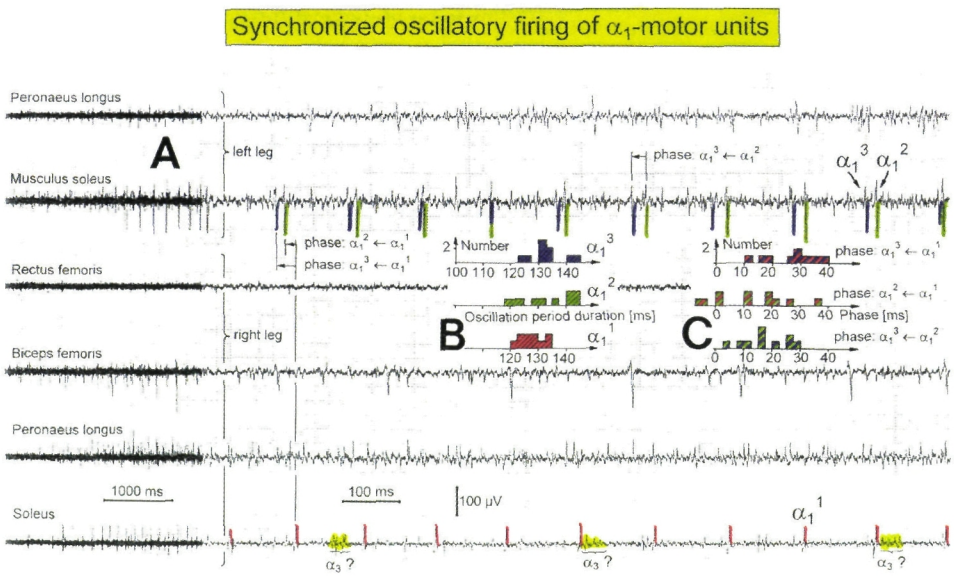

Figure 9. Same recording layout as in Fig.8. The different muscles were activated by a second plantar flexion (A). The marked oscillatory firing α_1^1, α_1^2 and α_1^3-motor units (B), same as in Fig.8, all fired now in a synchronized manner (C). Note that the mutual phase ($\approx$ 5 ms (phase 2)) between the α_1^2 and α_1^3-motor unit firings (right side of Fig.8) was approximately preserved from the first plantar flexion (Fig.8) to the second one (Fig.9). Possible α_3-motor unit impulse trains are marked at the recording trace of the right-sided soleus muscle.

Controlled and uncontrolled oscillatory firing of α_1-motor units for volitional non-rhythmic muscle activation

In Fig. 10, the activation of oscillatory firing of α_1-motor units is shown for our patient (solid lines) and a control person (author Y.B., dashed line). The control person activated single motor units (Mot 1, Mot 2) by switching them on (and off) for a few seconds of activation time. With the activation, the frequency of firing increased and decreased (Fig.10B). Similar activation shapes were recorded from secondary muscle spindle afferents of the brain-dead individual HT6 (Fig.4 of [91]). In our patient, with some disorders in the movements and the neuronal network organizations still present (see below), pathologic recruitment of motor units occurred. In comparison to the control person (Fig.10B), normal activation shapes also occurred. Some motor units were switched on and off for oscillatory firing (Mot 2, Fig.10A) as in the control person. These motor units were fully volitionally controlled by the patient. But then, motor units were found (Mot 1, Mot 4, Fig.10A) activated at the general activation time (when a majority of other motor units were activated), but not switched off again at the end of the general activation time. The motor units went on in oscillatory firing for longer times, even when the patient relaxed his leg. Whereas the oscillatory firing of mo-

tor unit Mot 4 (Fig 10A) could be switched off by the end of the subsequent activation time, motor unit Mot 1 continued its oscillatory firing for 1 min, i e motor unit Mot 4 but not motor unit Mot 1 was under control again with subsequent muscle activation

Even though our patient relearned running and other modes of movement, there still remained some poorly controlled motor units

EMG and foot switch signals when jumping on a springboard

Fig 11 shows the EMG activity of the musculi rectus femoris, biceps femoris, peronaeus longus and soleus of the right and left leg, and the foot switch signals for providing temporal information about foot contact when jumping on a springboard

Interpretation of foot switch (alternating pattern) and EMG signals
Left foot switches
-- Foot forward (FW) Always contact of the fore foot (GT(big toe)) and ball of the foot (M5 + M1 (5th and 1st metatarsal head)) The fore foot is the initial contact
-- Foot backward (BW) It is the heel that makes contact Initial contact is by the lateral side of the shoe (M5), at almost the same time contact of the medial side of the fore shoe (M1) Then contact of the heel and the fore foot
Left EMG signals, when compared to the right
-- Rectus femoris Shows permanent activity
-- Biceps femoris Bursts in stance forward (FW) and in swing between backward (BW) and forward (FW)
-- Peronaeus longus Permanent activity, burst in stance when the foot is backward
-- Soleus Permanent activity, but burst in mid-stance, when the foot is backward, but sets on before peronaeus longus Burst is of low amplitude and low spike density Burst delayed in mid-stance No breaking activity between the ball and the heel contact No push off when the foot is forward and is about to move backwards Thus the patient can be assumed to use his hip extensors for backward swing of the lower extremity The burst of EMG activity of the biceps femoris during the early swing from forward to backward can confirm this assumption
Right foot switches
-- When the foot is backward Initial contact on the heel (opposite to the control subject), no fore foot contact, only ball of the foot
-- When the foot is forward Initial contact on the big toe and then M1, sometimes briefly the heel is in contact at mid-stance The contact of the lateral side of the shoe (M5) is very irregular between forward strides This is a sign of medio-lateral instability
Right EMG signals
-- Rectus femoris Phasic activity, burst in each stance
-- Biceps femoris Permanent activity, with a burst during the swing from backward to forward and during the second half of the stance when the foot is forward

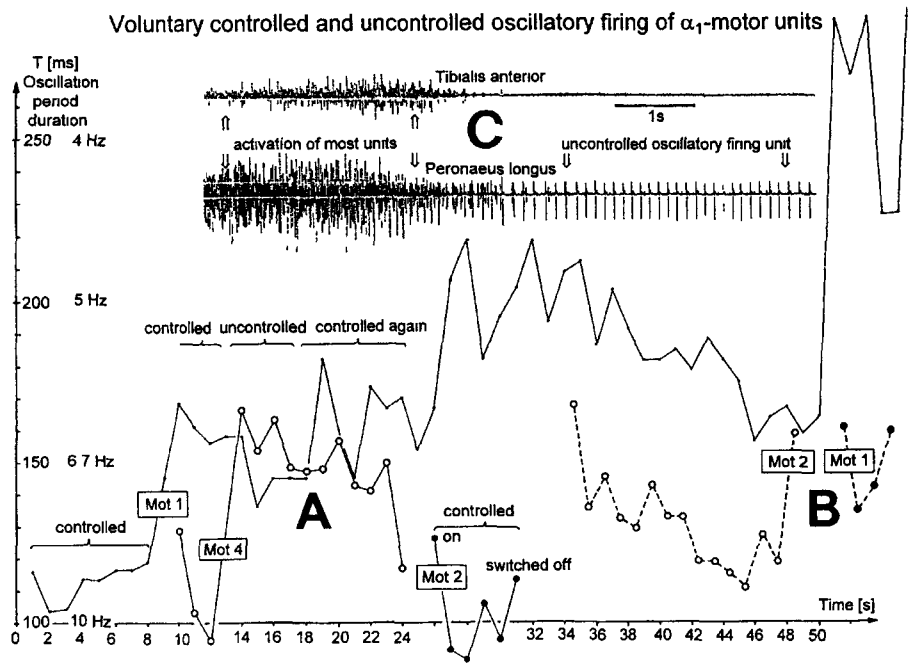

Figure 10. Voluntarily controlled and uncontrolled oscillatory firing α_1-motor units Solid lines (Mot 1,2,4) connect oscillation period durations measured in the tetraparetic patient (A), the dashed lines (Mot 1,2) refer to a healthy individual (author Y B) (B) Note that the control motor units are fully controlled (switched on and off) (B), whereas the motor units of the patient are controlled (Mot 2), controlled and uncontrolled (Mot 4), and mainly uncontrolled (Mot 1) (A) Each value of oscillation period duration shown represents the mean of 5 to 10 measurements The motor units of the patient (dashed line) were activated in the peronaeus longus muscle by knee extension, the motor units in the control person were activated in the tibialis anterior and the soleus muscles (C) Original registration of the uncontrolled oscillatory firing motor unit Mot 1

-- Peronaeus longus: Permanent activity, but bursts can be recognized in stance with noticeable difference if the foot is forward or backward. When the foot is backward, the activity is denser.

-- Soleus: Phasic activity in stance. The activity is higher for the backward stance phase.

Generally, the activity levels of the rectus femoris, peronaeus longus and soleus of the left leg are much lower than those of the right leg. This was also observed in voluntary contraction. Further, the overall patterns of activity of the left rectus femoris and the soleus are different from those of the right sided muscles. The characteristic EMG pattern is nearly lost in the left rectus femoris.

After a full cycle of jumping, there is always synchronization of the feet, namely the stance phase of the right leg backward and the left leg forward are always exactly the same in timing and duration as indicated in Fig.11 by dotted lines and „syn" (synchronization).

An obvious feature in Fig.11 is that the left peronaeus longus and soleus had very little activity in comparison to the right sided muscles. The right leg of the patient was the „better" leg in that it generated more power and was more movable (see also Fig.1 (muscle status) and below). In the left leg, spasticity occurred when the patient jumped long series on a

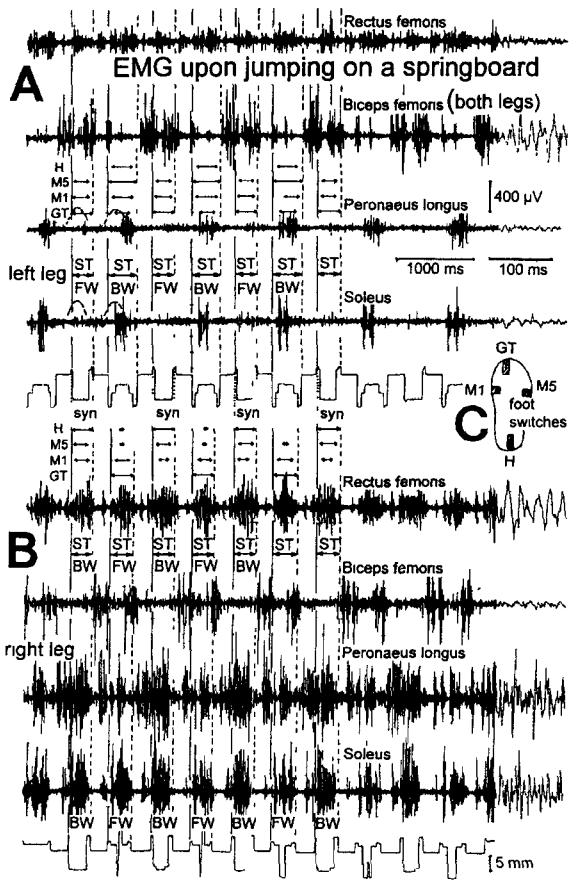

Figure 11. Electromyography during jumping on a springboard The recording traces of the musculi rectus femoris, biceps femoris, peronaeus longus and soleus and the potential changes of the foot switches (C) of the left (A) and right leg (B) of the tetraparetic patient Note the difference in activity level and the patterns of the right and left-sided muscles On the average, the patient had more voluntary power in his right leg (Fig 1) ST = stance phase, swing phase in between stance, not marked, BW = foot backward, FW = foot forward, syn = synchronization of right and left leg, while jumping, indicated by dotted lines Foot switch layout GT = big toe, M1 = 1st metatarsal head, M5 = 5th metatarsal head, H = heel Code for the foot switch trace Change in mm, when switched on or off H = 5 mm, M5 = 10 mm, M1 = 1 mm, GT = 3 mm

springboard (not shown here, as no spasticity occurred during ongoing jumping). Even though the patient was aware of that his left leg was the poor one, he did not feel much difference between the right and the left leg when jumping on a springboard. Partly, this can be understood because of his strongly reduced sensibility (with variations) below the level of the lesion. Once, the patient hurt the skin of one leg upon leaving the swimming therapy pool. It was bleeding, but the patient did not notice it, because of a reduced sensitivity. The skin sensitivity for myelinated fibres thicker than 3.5 µm was calculated to be reduced by more than 95% in the soles of the feet (see Method); the reduction was even stronger on the left. It may also be that more motor units increased in size in the left leg (see Discussion) or

that FR and S-type motor units with motor unit potentials of low amplitude were more activated.

From the research perspective it is obvious that it is easier to record with surface electrodes single motor units from lesioned spinal cord than from normal individuals because of the reduced activity in cord-lesioned patients. If for high muscle activation only few motor units are activated then they can easily be identified because the few units fire rhythmically (oscillatory), as shown in Figs.7-9. For activity levels like those shown in Fig.11, single motor unit impulse patterns can only sometimes be identified in healthy individuals.

EMG and foot switch signals for a control person jumping on a springboard

Fig.12 shows the movement-induced rhythmic activity of a control person (author G.S.) when jumping on a springboard. The EMG activities of the peronaeus longus and soleus are always weaker in the forward stance phase than in the backward stance phase for both legs. Synchronization of the stance phase occurred once per full cycle, when the left foot was backward and the right foot forward. On that day, the control person reported some pain in his right foot.

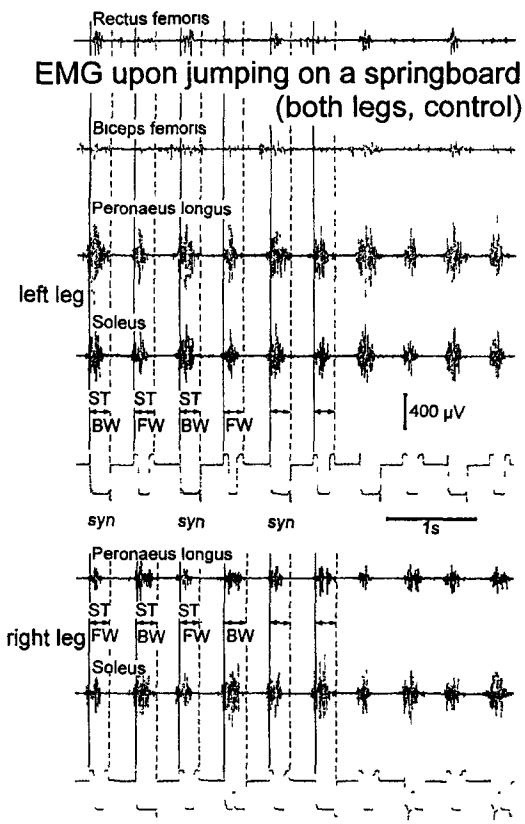

Figure 12. Electromyography upon jumping on a springboard, normal individual (author G S)

Electromyographic and kinematic interpretation of walking and running based on left leg EMG and on 3D kinematics of both legs

Standing at ease, walking barefoot on a level ground, and jogging while wearing shoes have been studied here using three-dimensional (3D) kinematic and kinesiological electromyography.

The *standing* position showed a preferential weight bearing on the right which is actually the less affected side. In the sagittal plane, a triple flexion of 5° is observed at hip, knee and ankle level. Also, the left hip was in slight abduction, while the right one was in neutral position. Permanent EMG activity of the vastus lateralis muscle controls the knee flexion.

Kinematic, walking (Fig.15): Walking was characterized by a greater than normal knee flexion at initial contact followed by an exaggerated dorsiflexion of the left foot in stance and lack of plantar flexion in pre-swing.

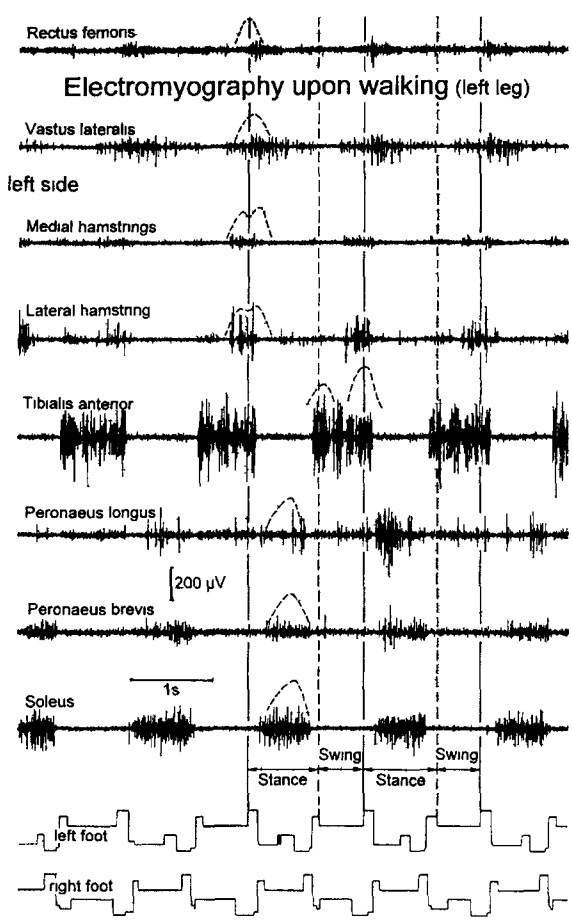

Figure 13. EMG of the left leg, upon the walking at comfortable speed on an even ground (mean velocity 0 91 m/s, mean stride length 1 37 m) wearing jogging shoes
Normal burst of EMG activity is represented by the dotted line
When based on timing error, the data can be interpreted as follows

- rectus femoris permanent activity which decreases and delays the peak of knee flexion during pre-swing and mid-swing (see Fig 15, kinematics)
- vastus lateralis premature and prolonged
- hamstrings (medial hamstrings = semimembranosus plus semitendinosus, lateral hamstring = biceps femoris) premature activity and poor inter-cycle repeatability of the biceps femoris
- tibialis anterior overall normal timing of the activity but abnormal shape of the burst
- peronei permanent activity
- soleus overall normal timing of the activity, but no increased amplitude in late stance corresponding to the push off sub phase

EMG, walking (Fig.13): EMG activity of the soleus was premature in stance and did not show the usual burst at push off. The left rectus femoris presented, in late stance and pre-swing, a burst which limited the knee flexion in swing and impeded toe clearance.

The left peronaeus longus was even more premature than the soleus. This may explain the abnormal medio-lateral roll-over of the foot. No sign of phasic activity has been recorded except for one stride where it was premature and curtailed. These abnormalities are due to a modification of the motor program rather than to muscle weakness per se.

Kinematic (Fig.16) *and EMG* (Fig.14), running: While jogging, the left knee was permanently flexed (mean 25° range 10°). No marked flexion occurred either in pre-swing or in swing to facilitate foot clearance. This corresponds to a severe stiff knee pattern. The knee joint was locked by a permanent activity of the rectus femoris with an extra burst of the vastus lateralis in late stance combined to premature activity of both hamstrings in swing. The soleus presented a weak premature activity without push off. 3D kinematic and EMG de-

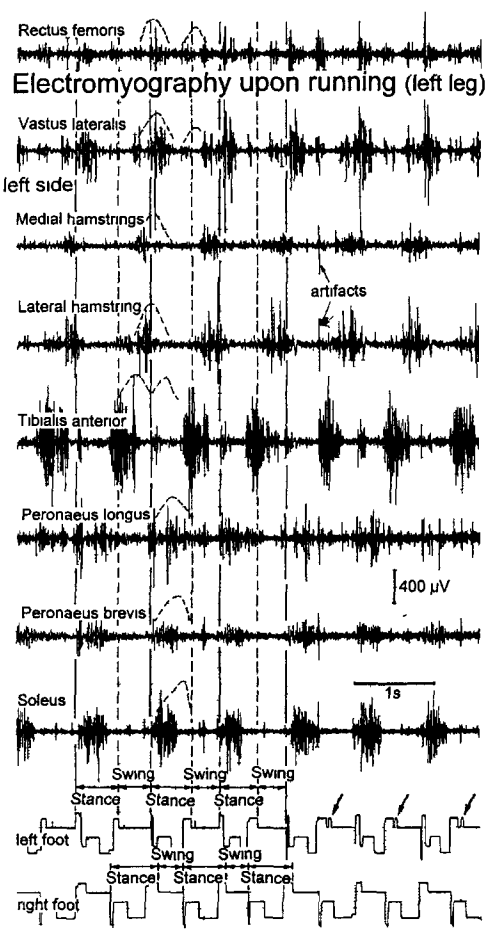

Figure 14. EMG of the left leg upon running, wearing jogging shoes (mean velocity 1 71 m/s, mean stride length 1 16 m). Normal bursts of EMG activity is represented by the dotted line

Interpretation of the data based on timing errors

The rectus femoris is permanently active while the hamstring is premature in swing As a result of this co-activity, the knee is locked in flexion throughout the cycle (see Fig 16, kinematics)

The second burst of the tibialis anterior from late swing to early stance is missing The peroneI have a premature and prolonged activity in stance

The soleus is premature and does not exhibit the typical high amplitude burst, corresponding to push off

The roll-over of the left foot shows two patterns. the first 3 strides have an initial contact on the heel, for the following it is on M5 (5th metatarsal head) The arrows point to dragging of the fore foot at very early swing

On the right side, the contact of M1 (1st metatarsal head) is often delayed or missing. For definition of the foot switches, see Fig 11.

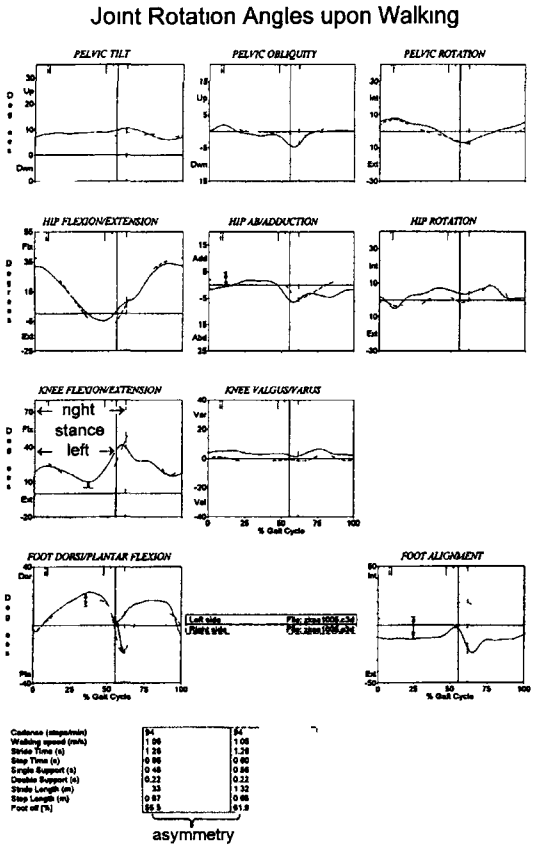

Figure 15. 3D Kinematic data of a representative cycle while walking The main peculiarities include a decreased flexion of the left knee in swing due to the permanent activity of the rectus femoris, and an increased dorsiflexion of the left foot in stance corresponding to an insufficient net moment of the plantar flexor muscles

monstrated asymmetrical patterns between the right and the left side They were primarily due to abnormal motor programs and/or decreased sensory inputs

EMG and foot switch signal comparisons between the right and the left side upon jumping on a springboard, upon walking or upon running

By comparing the EMG activities between the right-sided and the left-sided muscles upon jumping (Fig 11), walking (Fig 17) and running (Fig 18), the activities of the left leg muscles were always smaller Very little activity occurred upon walking in the muscles of the left leg in comparison to the right leg muscles Even though all muscle activation patterns were pathologic, the patterns were better for running than for walking, and those for jumping were better than those for running (when taking the peronaeus as a measure) This indicates that during the more rhythmic, stereotyped, dynamic movements such as running or jumping, more spinal cord functions were recruited (see Discussion) This conclusion is in accordance with what the patient reported himself The faster and the more rhythmically

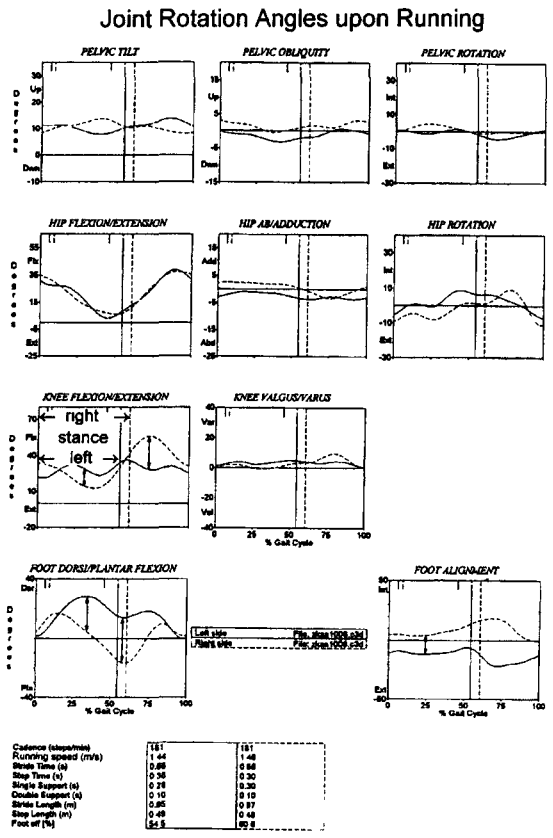

Figure 16. 3D Kinematic data of a representative cycle during running. The left knee remains in permanent flexion, locked by the co-contraction (Figure 2). This stiff knee pattern impedes foot clearance in early swing and shortens the stride length compared to walking.

he was running the better it went by itself, which probably means that he got more support than from the spinal cord networks. Always when asked to walk slowly controlled, he claimed it was becoming difficult, most likely because he needed more supraspinal control then, which was limited by the remaining tract fibres following the cervical spinal cord lesion.

Comparison of EMG patterns upon jumping on a springboard, running or walking

By comparing the EMG patterns of the peronaeus longus and the soleus muscles between the left (the weak) and the right leg (the better leg, but still pathologic muscle activation), between pathologic (shown patterns) and normal (dashed shape curves), and between jumping (Fig.11), running (Fig.18) and walking (Fig.17), three main pathologic activation patterns could be distinguished in the muscles of the left leg. First, there was permanent activity in the EMG recordings. Second, mostly the burst of phasic EMG activity was reduced and its shape was changed. Thirdly, the muscles were activated at wrong times (pathologic motor program).

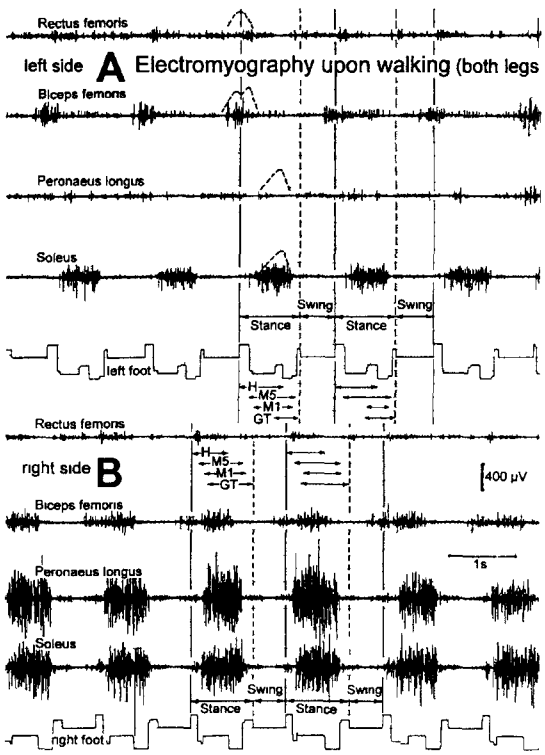

Figure 17. Usual walking, with jogging shoes on, on an even floor (mean velocity 0 93 m/s, mean stride length 1 41 m) Differences in EMG phasic activity between the left side (most involved) and the right side

The normal burst of EMG activity is represented by the dotted line H = heel M1 = 1st metatarsal head M5 = 5th metatarsal head GT = big toe

Interpretation of the data based on timing errors

- left side
- -- rectus femoris abnormal activity in swing
- -- biceps femoris premature activity in swing and in some cycles also prolonged activity in stance
- -- peroneus longus almost permanent trace of activity, no distinctive burst
- -- soleus normal timing but decreased push off

The foot switches show an abnormal timing pattern the 1st metatarsal head is often „on" after the big toe During pre-swing (roll-over of the fore part of the shoe) the 1st metatarsal head is abnormally „off" the ground before the 5th

- right side
- -- rectus femoris delayed activity in stance
- -- biceps femoris prolonged activity in stance
- -- peroneus longus and soleus premature activity and important inter-cycle variability

The foot switches show an abnormal timing pattern of the 1st metatarsal head which could be interpreted as a sign of unsteadiness

Permamanent activity mainly occurred in all muscles of the left leg measured and in some muscles of the right leg. Since it was predominantly low amplitude motor unit activity that contributed to permanent activity, the S-type motor units were permanently activated. We shall show in Discussion that probably, the permanent activity was caused by the loss of control on premotor S-type neuronal networks and by discoordination between FF, FR and S-type neuronal networks.

The left peronaeus muscle showed no phasic activity during walking, when compared to normal (dashed shape) and the right leg; there was some activity upon running, and clear phasic activity upon jumping on a springboard. It seems therefore that the EMG pattern for jumping was slightly superior to those for running and walking. With respect to muscle power generation, jumping on a springboard therefore seems to be the best approach to training. It will be shown in Discussion that probably, the activation of the peronaeus longus

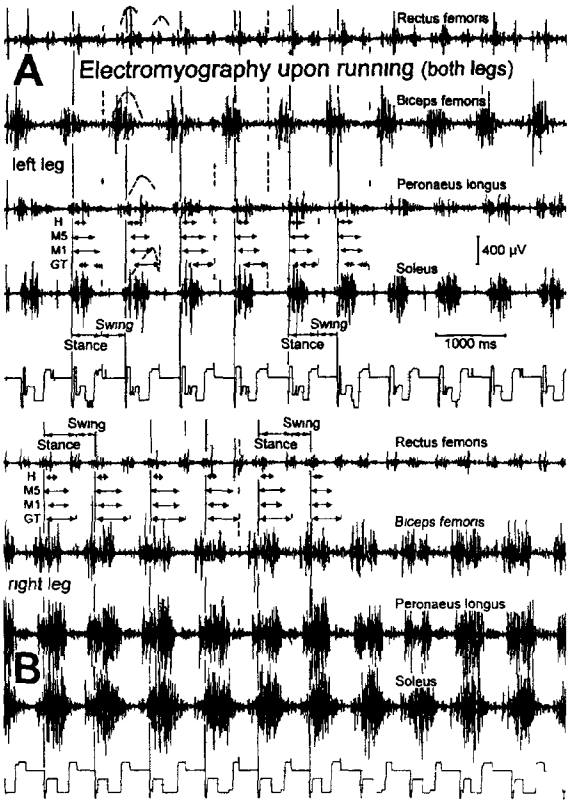

Figure 18 Comments on EMG and foot switch signals when the patient was running with jogging shoes on on an even floor approx 2 5 years after the accident and one year after the oscillator formation training

Shoes roll over

heel (= H)

lateral side of the shoe (5th metatarsal head = M5)

medial side of the shoe (1st metatarsal head = M1)

fore foot (big toe = GT)

left shoe

most of the time the initial contact is on the lateral side of the shoe

then the medial side the heel and the for ward foot touch the ground almost simultaneously while M5 is off for about 40 millise conds and then on again

3 fore foot drags have been recorded in early swing

right shoe

initial contact = lateral side of the shoe (M5)

then medial side of the shoe (= M1) heel and fore part of the shoe (= GT)

3 fore foot drags have been recorded in early swing

EMG

left side

rectus femoris permanent activity which contributes to the limited knee flexion in swing The isolated spikes after the initial contact are considered to be movement artifacts

biceps femoris phasic activity but anticipated in mid swing and continues until loading response The activity in late swing limited knee extension in swing and prevented normal positioning for initial contact This muscle certainly acted together with the medial hamstrings

peronaeus longus activity is decreased but the timing is correct

soleus phasic activity Each burst is too short when compared to heel M1 and M5 off and the timing of the EMG peak value is too early The push off is certainly decreased with a consequence such as propulsion diminution of the whole body We can hypothesize that the power to swing the left lower extremity is provided by the hip flexor muscles

right side

rectus femoris phasic activity double bursts within normal timing

biceps femoris a double burst pattern can be recognized in most strides Their overall duration goes from mid swing to the end of mid stance

peronaeus longus and soleus monophasic activity from mid swing to pre swing The peak value is slightly anticipated but we can postulate that the forward thrust is more efficient than that on the left side

muscle upon jumping on a springboard was caused by a transiently enhanced coupling between the right and the left movement pattern generators, inducing „Mitbewegungen“ The

synchronization of the leg movements once per jumping cycle (Figs 11,12) will have induced simultaneous afferent input patterns in both legs and a transient correlation of the right and the left pattern generators by shared afferent inputs for increased coupling

The appropriate muscle activation times were different from normal upon jumping, running and walking The activation times were best for running, since the peronaeus longus and the soleus were activated and the timing was not too much different from normal It will be shown in Discussion that running was quite good as it is a rhythmic, dynamic, stereotyped movement, learned (or genetically predetermined) before the spinal cord lesion occurred (old learned movement) Walking is also a rhythmic, dynamic, stereotyped movement, if the patient walks at a comfortable speed and is not trying to control his gait pattern Walking is an automatic rather than voluntary activity The only voluntary part of it is the decision and the best way to travel from A to B according to internal and/or external constraints

In conclusion, it seems that jumping was closest to normal followed by running and walking

Primary automatic stepping in newborn infants (genetically predetermined locomotion)

If rhythmic dynamic stereotyped movements are mainly generated in the spinal cord, then it is worthwhile to see how locomotion is organized in healthy newborn infants Since micturition is organized automatically during the first two years of infant development, it could be that some kind of locomotion is also automatically organized in the newborn, genetically predetermined by neuronal network preformation

Seven out of eight naked infants 0 to 5 days old, born in week 36 to 41 of gestation, showed primary automatic stepping One not healthy premature newborn (gestation week 36) with some temperature dysregulation, showed no full stepping cycle The mean duration of the full stepping cycle (left plus right strides) was 4 8 s (range 3 5 to 8 s), which corresponded to a stepping frequency of approximately 0 2 Hz The stepping frequency depended on the manual support given to the infant The touching of the ground (soft tissue) with one foot was the stimulus for the forward movement of the other foot (see also [129]) When the other foot touched the ground, then the first foot moved The touching of the ground was therefore the stimulus for one stride, i e for half a stepping cycle If the infant was helped to touch the ground quicker, then the stepping frequency increased Also the stride length of stepping influenced the stepping frequency The primary stepping was different from adult walking (see Discussion) The two most important differences were a slower stepping frequency than walking in the adult (see Discussion), and that the quickly lifting of a foot was followed by a rather slow forward movement Of 9 other infants with clothes on, only two showed primary stepping, the touch of the clothes and/or the missing touch of the supporting naked hands hindered or inhibited the stepping

The stepping automatism (generated by the spinal pattern generator for stepping, probably consisting of many coupled spinal oscillators) seemed to show similarity to the transient and continuous oscillatory firing of premotor spinal oscillators, which is the important

point here for describing the well-known automatic stepping. If neuronal networks of the spinal cord get only little afferent or supraspinal drive, then the premotor spinal oscillators will fire only occasionally. With the increasing adequate drive, they fire first transiently oscillatory for a few cycles and then continuously oscillatory for even higher drive [97]. When the infant's foot or feet touched the ground, no movement occurred at all or the infant started stepping. Sometimes the infants did only a few steps or they got into a continuous stepping rhythm, which was terminated by the end of the table (Fig.22A,F).

Not obvious was whether the stepping automatism was directly stimulated or whether the quick lifting foot was something like an avoidance reaction which triggered the stepping automatism. Tickling of the infant's foot sole stimulated an avoidance reaction of similar speed as the lifting of the foot during stepping. Tired infants or infants with a low muscle tone did not step as much as action-ready infants.

The response to the stimulation of the stepping cycle by touching the ground, mostly lasted only for half a stepping cycle (till the next foot stimulation), in similarity to „Mitbewegungen" (co-movement). There, the response to the additional simultaneous afferent input from both feet in the chest-swimming cycle in incompletely lesioned patients seemed not to support the „poor leg" for longer than a cycle period (see Discussion).

In some infants the stability of the stepping was poor. The legs easily became mixed up. Probably, stabilizing supraspinal control was missing.

Discussion

Activation of dynamic rhythmic stereotyped movements

We have shown that a tetraparetic patient could relearn running and other modes of locomotion; this has not been thought possible so far. At the end of the treatment period the patient still had problems with slow controlled walking, or with simultaneous running and walking while playing tennis. However, the patient had no problems with fast walking, marching and running (stereotyped locomotion). Therefore, it can be implied that the dynamic, rhythmic, stereotyped movement patterns could be activated in the spinal cord by the remaining volitional power which started, maintained and terminated locomotion.

The right - left inbalance, nearly always occurring in patients with incomplete spinal cord injuries, was slowing down the progress in the training of the nervous system. The poorly volitionally innervated left leg disturbed the rhythm of locomotion. The central pattern generators for both legs could not be activated optimally, because running was asymmetrical. However, as soon as the patient reached a somehow good rhythm of running he felt to get support from somewhere, namely the spinal cord. If he could not get into a good rhythm, there was only little support from the spinal cord. The mechanism of „Mitbewegungen" (i.e. with additional simultaneous afferent inputs from both legs, the stronger right leg improved the movements of the left leg, see below) helped to improve symmetrical running. According to Patla [71] four major classes of input to the central pattern generators are nee-

ded tonic input to initiate and maintain rhythmic movements, patterned sensory input from the periphery, patterned input from the CNS, and coordinating signals between pattern generators for different appendages

Because of the lesion, the connections to supraspinal centres were asymmetrical and not balanced with respect to different tract fibres An improvement of symmetrical running, marching and swimming will therefore be accompanied by some reorganization of supraspinal centres to partly „rewire" the tract fibres by CNS plasticity with respect to function The rehabilitation of patients with incomplete spinal cord lesions is therefore very similar to the rehabilitation of those with brain lesions [16,22] (see the final part of Discussion)

Rhythmic swinging of the arms improved rhythmic walking, marching and running Now the enlarged pattern generator for the four limbs also integrated the symmetrical afferent input from the arms, and probably became more symmetrical in general

In animal research, similar conclusions were drawn based on phylogenetic trends Cohen [23] stated that sensory or descending control systems can be responsible for including the changes in gait The coordinating system, especially in the cat (in comparison to phylogenetically lower animals), seems to be somewhat unstable in isolation, exquisitely sensitive to both descending and sensory control and is easily acted upon to produce a wide variety of other patterns It would appear that the major phylogenetic trend has been to increase separation and independence of the „limb oscillators" combined with an increased role to be played by the descending and sensory systems which lend considerably increased flexibility A possible conclusion could be that, during evolution, what is changing in the central pattern generator of the limbs is the access to and the need for extrinsic control and the general lability of the coordinating systems [23]

Improvement of neuronal network functions

The decrease in the variation of the jumping frequency (Fig 5B) is interpreted as re-preformation of neuronal networks of the human CNS The neuronal networks are the substrate of premotor spinal oscillators and of the spinal pattern generators, which are probably built up of propriospinal oscillators (Fig 20) This interpretation is supported by the muscle power tests The strong improvement in locomotion and other movements was not accompanied by an equal improvement in volitional power of certain muscles (see muscle tests during the training period, Fig 1) Also, the muscle activation patterns during walking and running (Figs 13,14,17,18) still indicate a pathologic and insufficient activation of the leg muscles after the training period With the given strength of muscle power in this patient after the training period, a further progress in movement would still be possible if the motor program for muscle activation could be further improved No such further training was tried since the patient was reluctant to stay at the clinic

In brain lesions, the principal cause of movement disability is the loss of muscle strength and control resulting from the lesion [22] The emphasis on training there is to train the individual to gain control over the muscles required for different volitional tasks [16,22], on the

contrary, rhythmic stereotyped movements such as jumping or running have to be trained with injuries mainly located in the spinal cord, for which probably only little supraspinal drive is necessary (see final part of Discussion) How much drive is needed and what pathways are most important has to be shown by further research in man This will be extremely difficult and also requires further knowledge concerning the extent of plasticity of the human nervous system

Electromyographic recordings from leg muscles of similar patients showed an improvement of the pathologic activation patterns simultaneously with improved walking, when training walking on a treadmill [26,116] The new aspect is that it was possible to a patient to relearn running, a fact not thought to be possible so far This improvement in locomotion was possible because of a new understanding of the functioning of the human spinal cord (based on new measurements in man), namely the self-organization of neuronal subnetworks to spinal oscillators and their coupling in turn to generate macroscopic function Since treadmill walking becomes very pathologic when higher speeds are used (acceleration of legs backwards, see below), a more physiologic way of free running under weight reduction was used for the first time Single motor unit recording with surface electrodes was first used to non-invasively identify oscillatory firing and function disorders The improvement in function of the premotor spinal oscillators recruited by the pattern generators still needs to be studied electromyographically, and can be expected to provide further data on neuronal network functions

Recovery of spinal cord tract fibres one year after injury

Even though, the volitional power of certain muscles increased more than expected during the 6 weeks of training, its extent cannot explain the running itself The left gluteus maximus increased its volitional power from „active movement against gravity" to active movement against moderate resistance (Fig 1) An increase of muscle power was also visible It seems that one year after the injury still a substantial number of tract fibres had recovered in the lesioned spinal cord The patient did not notice this recovery however, since the muscle fibres of the corresponding motor units were probably strongly decreased in size because of lack of usage The patient behaved therefore in a way as if there were no recovery of tract fibres The exercise training most likely made the recovery of nerve (and muscle) fibres obvious The quantified daily controls (Figs 5,6) were a biofeedback, which motivated the patient to continue his efforts

Two-and-a-half years after the accident, the patient noticed further increase in the volitional control of the fingers of his left hand Substantial recovery has to be expected therefore even 2 5 years after a spinal lesion The cause could be a further recovery of tract fibres or „reconnection" of gray spinal matter interneurons for ascending and descending control to be substituted for the lost tract fibres A minor regeneration cannot be excluded

Conclusions on the rhythm training

The training which enabled the patient to run again, probably made use of the fact that (1) „Mitbewegungen" (co-movement, see below) also exist in man (2) By activating rhythmic dynamic stereotyped spinal cord movement patterns, such as marching, jumping and running, the patient could partly move by recruiting spinal cord functions, which probably need only little supraspinal tonic (or patterned) drive (3) Training can strongly enhance the plasticity of the human CNS (4) Oscillatory firing neuronal circuitries can be made to re-organize themselves by a rhythm training (jumping on a springboard, marching, running) to generate more physiologically useful movement and reduce spasticity

Identification of the oscillatory firing patterns of FF, FR and S-type of motor units

Oscillatory firing FF and FR-type motor units were identified by the firing patterns of α_1 (FF) and α_2-motoneurons (FR) Oscillatory firing of FF-type motor units with frequencies ranging between 8 and 12 Hz were easily recognized in the EMG recordings Tremor rates of between 8 and 12 Hz (probably generated by α_1-oscillators (FF)) and 6 5 and 7 Hz (probably generated by α_2-oscillators (FR)) have been observed since long [49] Oscillatory firing of FR-type motor units has been documented in EMG literature [3], but has not been recognized as oscillatory firing Aminoff [3] called the α_2-oscillatory firing „myokymic discharges" The myokymic discharges represent spontaneous repetitive motor unit activity, showing grouped (double, triple or multiple) discharges (Fig 9 7 of [3]) The fact that the α_2-oscillatory firing, called in EMG literature myokymic discharging, can easily be observed in CNS disorders such as multiple sclerosis is not surprising, since recruitment for firing in the occasional and oscillatory firing mode (see below) becomes pathologic for these conditions Physiologically, for low activation most motor units fire in the occasional firing mode [88] With increasing activation more units fire oscillatory [97] In disorders, some motor units may fire oscillatory already for very low activations and can easily be recognized then (see below) In EMG recordings it is sometimes difficult to distinguish which firing originates in the nervous system and which in the muscle fibres There is no such problem with recordings from motor axons [93-99]

The firing patterns of α_3-motoneurons could not be identified safely from EMG recordings as yet, since the first interspike intervals of their impulse trains (5-10 ms) lie in the range of the duration of the motor unit action potential (MUAP) ($\approx$ 5 ms (Fig 7 and [3])) Also, the S-type MUAP amplitudes seemed to be very small, which makes identification difficult (Fig 9) (see below) The narrow bandwith of each EMG channel (34 Hz-1kHz, see Methods) was not the reason for the long duration of the AP, since recording with the single nerve-fibre AP recording equipment with a broader bandwith (100 Hz-20kHz) [93,96] also gave an AP duration of the FF and FR-type motor units in the range of 5 ms

In the present study, the FF and FR-type motor units were identified by their characteristic oscillatory firing patterns [96] Since following spinal cord lesion the patterns of oscil-

latory firing more or less change [90,96], it has to be tried to additionally identify the different motor unit types, hopefully, by different group conduction velocities, when recording with 2 pairs of surface electrodes, in similarity to the identification of the motor axon type The velocities will be in the range of 2 to 4 m/s [75,100,106] Several problems will arise First, the motor unit AP is a summation of a few hundred APs of single muscle fibres (the size of the motor unit depends on the type of the muscle) Second, the conduction velocity depends strongly on the muscle fibre diameter $\varnothing$ ($V \sim \varnothing^{1/2}$), and the muscle fibre diameter varies, e g with age, sex, muscle type and muscle exercise The muscle fibre diameters are in the range between 40 and 70 µm [74], and type II fibres are only slightly thicker than type I fibres At the surface of the soleus, type I muscle fibres (S) have a mean diameter of 66µm and type II muscle fibres (IIA (FR) plus IIB (FF)) a mean diameter of 68µm [74] Also, the conduction velocity of a muscle fibre strongly depends on membrane properties such as specific membrane resistance E g , in frog the membrane properties of slow and twitch muscle fibres are very different Slow muscle fibres (Fig 21) have a passive membrane resistance more than 10 times higher than that of twitch fibres [62] Differentiation between the 3 major muscle fibre types seems only possible if their membrane properties are very different

Another problem arises from the velocity measurement itself The innervating motoneurons should not synapse between the recording electrodes, since this makes velocity measurements impossible A similar complication occurs with respect to the measurement of motor axon velocities When the axons dry up, artificially evoked APs are also generated between the electrode pairs (by the increasing electrolyte concentration), and mirror picture potentials will be recorded, wetting of the roots re-establishes physiologic conduction again Similar phenomena may be found among MUAPs when recording with two pairs of surface electrodes, if the motor endplate lies between the two recording electrode pairs It may however be possible to find leg muscle areas where there are no motor endplates [103], so that motor unit conduction velocities can be measured [75,100] At least with the noninvasive multi-electrode array EMG [75,100] it should be possible to locate the motor endplates

In normal individuals, it is not so easy to record with surface electrodes a single motor unit firing because many units fire simultaneously For low activation, most motoneurons fire in the occasional firing mode [88,89], according to the thickness (and velocity) of the motoneuron axons in each group (Henneman's size principle [11,88]) The validity of the size principle only within certain groups of motoneurons is often disregarded and not always obvious to see, since mostly the static S-type motoneurons are activated before the more dynamic FR and FF-type motoneurons, because e g , we can run (activation of large dynamic motoneurons) only when we were able to stand before (activation of small static motoneurons) Also with respect to energy expenditure, the S-type motoneurons (slow oxidative [95,96]) will be activated first Separate motoneuron supply of slow (red) and fast muscle fibres (white) is also found in animals, e g in frogs [62] or mackerels and herrings [38] But if the size principle were to hold for motoneurons regardless of their grouping, then for example, the preganglionic parasympathetic fibres would be recruited before the fusimotors before the α_3, α_2 and α_1-motoneurons, which has not been observed so far

Following spinal cord lesion, the recruitment order in the occasional firing mode was preserved in each group of motoneurons, but the group recruitment changed [89] For higher activation, the motoneurons switch from the occasional firing mode via the transient oscillatory firing mode into the continous oscillatory firing mode [84,97] When recording with surface electrodes in normal individuals, oscillatory firing motor unit patterns will be mixed with patterns of other oscillatory firing motor units and with patterns of occasionally firing motor units In our patient with a partial spinal cord lesion, the remaining volitionally activable motor units were already highly activated for rather small muscle power, i e, they fired in the oscillatory firing mode Additionally, the few activable motor units may have increased in size by some kind of sprouting (the other, non-volitionally activable motor units were still innervated but they were only sometimes activated by spinal networks) Single motor unit activity patterns can therefore more easily be identified in spinal cord lesioned patients Only the patterns may have changed following the lesion [96]

Amplitude of the motor unit action potential (MUAP)

It seems in Figs 7 and 9 as if the MUAP amplitudes decrease from FF to FR to S-type motor units This is to be expected, since the motor axons decrease in diameter from α_1 (FF) to α_2 (FR) to α_3-motoneurons (S) [93,96] The motor unit type dependence will be disturbed by the different size of motor units (number of muscle fibres, innervated by one motor axon) in different muscles and by the decline of the amplitude of the motor unit AP, when the unit is distant from the recording surface electrodes [33,106]

Alternating and symmetrical oscillatory firing and phase changes in synchronization

Alternating long and short oscillation period durations were observed in FF-type motor units in leg muscles (biceps femoris, soleus) The difference in alternation was approximately 10 ms Earlier, alternating oscillatory firing with a mean differerence of 5 ms was recorded from α_1 and α_2-motor axons in striated continence muscles [96] We do not know yet whether this alternation in oscillatory firing is physiologic or pathophysiologic in nature

Alternation however is the only interlimb coordination pattern observed innervating all intact, reduced, or spinal animals [23] On this basis, Cohen [23] has concluded that it is the primitive or „default" coordination pattern for the vertebrate locomotor central pattern generator

Obviously, alternation in muscle activation was observed during walking, running or jumping on a springboard (Figs 11-14,17,18), even though the motor programs were pathologic (see below) However, alternation in oscillatory firing was also observed in striated continence muscles of individuals with a complete spinal cord lesion, and in the present paper in leg muscles during plantar flexion of both feet in a patient with an incomplete spinal lesion during non-rhythmic movement Alternation is therefore most likely a basic coordination pattern for changing couplings of spinal oscillators for changing neuronal network orga-

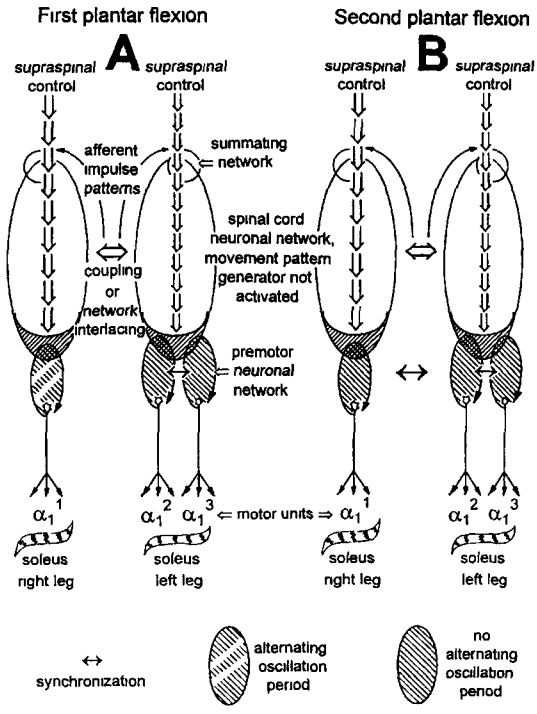

Figure 19. Possible neuronal network states for the activation of three α_1-motor units located in the right and left soleus muscles upon two plantar flexions, pictured from Figs 8 and 9 Note that premotor neuronal networks fire oscillatory upon no rhythmic movement (no spinal pattern generators are organized for rhythmic movements) Note further that from first to second plantar flexion, the synchronization of the motor units α_1^2 and α_1^3 of the left soleus is preserved (also, the phase is preserved as can be seen in Figs 8 and 9)

nization rather than for only the organization of central pattern generators to rhythmically activate limb muscles on both sides of the body

In the present study this alternation in the duration of oscillation periods was observed to often change from long/short to short/long and vice versa If these changes in alternation occurred often, then alternation could not be measured any more In similarity to the change of synchronization in tremor frequencies, we shall term these changes in alternation „change of focus" and they will be taken to indicate coupling changes of spinal oscillators

A very important finding is that with the change of synchronization of two oscillatory firing motor units of the soleus of the left leg the alternating oscillatory firing of a motor unit of the right leg changed from alternating to symmetrical firing This measurement is shown in Figs 8 and 9 and is pictured in Fig 19 The question is, whether oscillatory firing premotor neuronal networks interact with each other or whether propriospinal oscillators of the pattern generators of both sides interact with each other, even though there is no rhythmic movement performed. A further question is, whether there is some rhythmic pattern generating network organized if there is no rhythmic movement performed (see also memory of the spinal cord) Actually, for low activation of striated continence muscles, the motoneurons were activated occasionally approximately every 3 seconds This means that if the premotor

neuronal networks do not fire oscillatory then the motoneurons are integrated into another rhythmically firing neuronal network organization Therefore, neuronal network properties such as coupling of oscillatory subneuronal networks (propriospinal and premotor spinal oscillators), synchronization, phase changes in coupling, focus changes in alternating oscillatory firing and changes from alternating firing to symmetrical and backwards are organizational network function tools to generate integrative network functions Further, the neuronal network can include receptors of the periphery in its organization Skin stimulation induces phase-related afferent input [66,70] and synchronization of spinal oscillators [98] The movement-induced afferent inputs include, via the reafference principle (see below), receptors of the periphery in their network regulation and organization Muscle spindles can be integrated via the γ-loop rather directly into the organization of premotor spinal oscillators [99], and therefore into spinal network organization

Further research has to show what rhythm coupling is physiologic and what is pathophysiologic If synchronized discharging of large cell masses becomes exessive in the cerebral cortex an epileptic attack occurs [49] (see below) It may well be that „network wiring" is more prominent and can be better studied when the network is functioning pathologically

Memory of the spinal cord

An additional interesting feature was that a certain phase of coupling of two oscillatory firing motor units was preserved from one plantar flexion to the subsequent one One possibility is that accidentally the same phase (of two possible phases) built up again The more likely possibility is that phase relations between spinal oscillators are fundamental for pattern organization and that they can be stored for seconds up to minutes The improved running (more rhythmic and shorter running times) when running several times over 90 m (see Results) supports the view that the CNS can store neuronal network states of movement patterns from one running performance to a subsequent one

When the patient performed old learned movements such as running, cycling or playing tennis, he felt the performances as a „Wiedererwachen alter Lebensgeister" (revival of old spirits of life) The spinal cord may be expected to be able to store network functions (by preformation of networks) for up to years It is unclear, how much of learned movement performances is stored by the cord and how much is stored by supraspinal centres An essential storage site contribution seems to be made by the spinal cord So, the patient had problems holding the racket to play tennis (cervical spinal lesion), but he performed the old learned arm and hand movements nicely and hit the ball as in old times (Fig 2)

The improvement of automatic stepping in newborn infants in successive trials supports the view that the spinal cord has essential capabilities for memory With the repeated trials of the primary stepping (4 to 5 times), the primary stepping became more rhythmical (in similarity to the increase of rhythmicity with successive running trials in the spinal cord lesioned patient), and the stride length of the steps seemed to increase The limitation for further successive trials was mostly the beginning of the crying of the newborn, which could

at least in one case be stopped when giving the infant to drink, which may indicate that the newborns got exhausted with repeated primary stepping in similarity to the exhaustion with repeated running of the spinal cord lesioned patient.

With the first sweating following exercise after a break of more than a year, the spinal lesioned patient became euphoric to be able to sweat again. The process of learning of somatic and autonomic functions seems to have similarities to learning by heart. If the learning of the spinal cord is a very simplified (primitive) form of supraspinal learning, then one may better understand the process of learning by understanding how the spinal cord learns.

Since there is indication that the spinal cord can even store the state of pattern organization to a certain extent (see Results), we have to expect that slightest inputs to the cord will have consequences on its network organization. Effects of the Jendrassik manoeuvre on reflexes or muscle spindle activity [39] have to be expected, since such strong maintained voluntary muscle activation must have some general influence on the network organization of the entire cord and the higher centres.

Two phase relations per oscillation cycle for coupling of somatic spinal oscillators

Two phase relations were observed (Fig.8) for the coupling of two oscillatory firing FF-type motor units. In a brain-dead individual, also two phase relations were observed for the coupling of oscillatory firing motoneurons [95], and two phase relations per oscillation cycle were observed in a patient with a complete spinal cord lesion [99].

In lampreys which have no paired fins the phase delays between any two ipsilateral „oscillators" are very nearly invariant or have two possible phase relations [23]. In limbed mammals, including man, the axial muscles serve to support, stabilize, and bend the back dorsally and ventrally during locomotion. Their activity in man [109] and walking cats [20] has two components per step-cycle, one to coincide with the ipsilateral stance phase and one to coincide with the contralateral stance phase. Thus, in mammals the „oscillators" to the axial muscles are 2:1 phase-locked with their ipsolateral limb muscle oscillators [23]; 2:1 activity can be observed under abnormal conditions in the lamprey [76].

Two phase relations per oscillation cycle may therefore have a phylogenetic origin. One has to be careful though, at least with respect to man. Three phase relations per oscillation cycle have been shown to occur when the autonomic nervous system interacted with the somatic nervous system [95,99].

Synchronization of motor units

Transient synchronization is a basic mechanism for organization and reorganization of neuronal networks to generate coordinated action of many muscles. Further research has to show which synchronization changes are, and which are not physiologic. If in the cerebral cortex synchronized discharge of large masses of cells becomes excessive then an epileptic attack occurs; the smaller cell groups lose their individuality of differentiated function [49].

The probably increased synchronized firing of motor units may not be physiologic but it may also not just be pathologic either Because the motor unit size cannot be increased sufficiently, it could be that the CNS tries to increase motor output of the few volitionally activable motor units by synchronizing them with other ones, which cannot be activated to partly compensate for the partial spinal cord lesion and therefore loss of motor control

Controlled and uncontrolled oscillatory firing motor units and the lability of the coordinating system

Fig 10C clearly shows that the patient could not switch off again a motor unit (Mot 1) He lost the volitional control of that motor unit Generally, it was shown in Fig 10 that the patient lost more or less volitional motor control over the FF-type motor units, whereas the control person fully controlled his motor units Instabilities in the control system of movements must have occurred following incomplete spinal lesion Such instabilities in the control and coordinating system may partly explain the pathologic activation patterns for walking, running and jumping (Figs 11,13,14,17,18) This is what Cohen [23] proposed, namely that what is changing in the central pattern generator control of the limbs during evolution is the access to, and the need for intrinsic control and the general lability of the coordinating systems

In young otherwise healthy brain-dead individuals it is sometimes observed that within a week after brain death, the remaining spinal cord automatizes itself and takes over functions from supraspinal centres, e g the temperature regulation Re-increase of the body temperature is not so much an indication that the patient is recovering from brain death but that the spinal cord took over the temperature regulation because of the loss of supraspinal centres Even coordinated movements are sometimes generated by the isolated spinal cord, such as taking a leg back into the bed when touching it! It seems as though surviving CNS parts stabilize at a phylogenetically earlier stage one or two weeks after brain death

It may therefore be that with training-induced CNS reorganization the loss of supraspinal control in incomplete spinal cord lesion can be compensated for on a phylogenetically lower stage of central pattern generator control with more stereotyped movements and less extrinsic control, but a more stable control system

In other words, the CNS has been reorganized in such a way that the remaining tract fibres are now used for important simple nervous system functions such as stereotyped movements To be clarified in the future is how few tract fibres and which tracts are needed to activate basic important locomotor patterns

Reorganization of CNS networks to improve activation patterns for locomotion

It has been shown that by a rhythm training (jumping on a springboard, Fig 5A) an incomplete tetraplegic patient relearned running besides other movements With the improvement of rhythmic movements (jumping, running, marching), the jumping became more

rhythmic, the variation of the jumping frequency (Fig 5B) became reduced By EMG and electrophysiological kinesiology (Figs 10,11,13-18) it was further shown that after the treatment there were still essential disorders in motor control The disorganization of neuronal CNS networks showed three main features First, loss of control of motor units as demonstrated by uncontrolled oscillatory firing of motor units following volitional non-rhythmic activation of the peronaeus longus muscle (Fig 10) and by the permament activity (between the phasic activities) during rhythmic movement such as jumping, running and walking (Figs 11,13,14,17,18) Second, the muscles monitored electromyographically showed no full activity, and changed shape, which also depended on the kind of the rhythmic movement, this is obvious from a comparison of the activity strength of the left and the right leg muscles (Figs 11,17,18) Thirdly, the different muscles were still not activated at the appropriate time (wrong motor program) (Figs 11,13,14,17,18), also depending on the kind of locomotion

We believe that the neuronal networks of the CNS are an entity in which different subnetworks are more activated than others The different activation levels change over time according to the function to be performed The basic units of the networks are different kinds of oscillator populations which couple with each other to generate integrative functions

For simple stereotyped movements, the network is approximated by functional parts which interact with each other according to the movement to be performed The activated parts are approximated further by the premotor spinal oscillators and the propriospinal oscillators which couple to pattern generators (Fig 20) It is believed that, for principal different stereotyped rhythmic movements, different network patterns are generated which can be varied to a certain extent It is further believed that the activated networks for jumping running and walking are mainly located in the lumbosacral enlargement of the cord „A chicken runs away, when its head has been cut off", soldiers can march, while sleeping

It is clear from Fig 10 that some premotor spinal α_1-oscillators could not be controlled sufficiently The oscillatory firing could be switched on but its switching off was not sufficiently safe The descending tracts for volitional activation do not synapse on the α_1-motoneuron soma but onto the premotor networks (probably including the motoneuron) or on propriospinal oscillators which are coupled to the premotor oscillators The propriospinal oscillators however are not coupled to locomotor pattern generators (Figs 10,19) Since it was found mathematically (see below) that in populations of interacting biological oscillators certain states of stable synchronization may not be reached any more for weak oscillator coupling (page 156 of [72]), it is likely that the loss of volitional control of these premotor oscillators is due to a loss of strength of the descending control By training, it has to be tried to increase the descending control strength, e g by synapse enlargement or sprouting with additional synapses or by changing the program organization for the remaining tract fibres descending from supraspinal levels Permanent activity of low amplitude (and therefore mainly from premotor α_3-oscillators (S-type), and maybe a few FF and FR-type motor units positioned at a distance from the surface electrodes) was observed rather continuously

between the phasic activity during jumping, running or walking The too weak coupling of oscillators upon exerting descending control, as a possible reason for the loss of volitional motor unit control, was therefore not primarily related to the functioning of spinal pattern generators

The permanent activity of low amplitude might also be a disorder between the tonic α_3-neuronal network and the dynamic networks (α_1, α_2) in general or it could be a compensatory response of the lesioned CNS to secure posture or to better counteract the force of body weight, because the more dynamic neuronal network systems were altered and too weak in their functions

The reduced amplitude of the phasic activity, which results from a reduced number of activated motor units, can be explained by too weak coupling between the different spinal pattern generators and the premotor spinal oscillators At least the altered shape of the phasic activity and the false motor program however are caused by a pathologic organization of the different pattern generators It is interesting that muscles with similar function seem to have similar false activation times (see rectus femoris and vastus lateralis muscles activation on the left side, Fig 13) Additional limbs (with additional comparable muscles) in animals show identical movement functions [113], and supernumerary fingers in man perform senseful movements [114] It seems therefore that the basic motor program as a whole is organized in the spinal cord, and changes in the motor program affect also functionally close muscles During movement, groups of functionally related muscles are activated rather than single muscles This conclusion is in accordance with Bernstein's opinion [12] that joints and muscles never work in isolation (see later)

The question is why do the pattern generators function in a false way When patients with incomplete but extensively lesioned spinal cords lie in bed for months, the preformation of the neuronal networks below the lesion level probably changes because of nonuse and missing descending activation Disorganization of movement pattern generators can be expected because of a changed preformation of propriospinal oscillator networks in similarity to the changes in preformation of premotor spinal oscillator networks, indicated by an extension of the oscillation period and interspike interval distributions [90] Nevertheless, such a network deterioration cannot be expected to give rise to rather stereotyped movement patterns with fixed false activation phases for the different muscles It seems therefore that it is unbalanced activation from the remaining tract fibres (ascending and descending) which causes a pathologic movement pattern Even if the lumbosacral networks have preserved a physiologic preformation, the unbalanced descending control would probably initiate and maintain a false pattern of muscle activation A strongly rhythmically induced and once per jumping cycle synchronized (see below) afferent input, caused e g by jumping on a springboard, can probably only partly compensate for the unbalanced drive

The unbalanced tonic or patterned drive is caused by an unbalanced lesion of the descending tract fibres and by the changed impulse patterns in the descending fibres due to a false response of supraspinal centres secondary to a false movement-induced afferent input, caused in turn by the unbalanced lesion of the ascending tract fibres An unrhythmical pat-

hologic movement will additionally send pathologic movement-induced afferent input to supraspinal centres.

Neuronal networks have to be re-preformed with very rhythmical and physiological movements (with high activation to fully activate the premotor networks to fire oscillatory) to strongly force the lumbosacral networks to organize the desired pattern generator. A rhythmic physiologic movement is nicely achieved when jumping on a springboard with an exact strict correlation once per jumping cycle between the left and the right foot (opposite phase) to induce co-movement („Mitbewegung", see below). Hopping like a sparrow, but with closed legs (same cycle phase for both legs), was not used, but should also be beneficial, because of the simultaneous skin, and maybe other, afferent input to induce co-movement of the „poor" leg. In addition to the biological rhythm „pacer" (author G.S.), the mechanical properties of the springboard were further pushing the patient into a dynamic, stereotyped, rhythmic movement. The EMG for jumping seems to show, as expected, the best rhythmicity and therefore the best motor program (Fig.11) as compared to running and walking, as has partly been verified by the activation pattern of the peronaeus longus muscle.

The peronaeus longus of the left leg is probably activated by „Mitbewegung" (see below), most likely because of an exact synchronization of the right and the left leg once during a full jumping cycle (in Fig.11 indicated by „syn") which increased the coupling between left and right-sided pattern generators, so that the left pattern generator was pushed by the right pattern generator to better activate the left peronaeus longus muscle. The activation of the peronaeus longus only at the stance phase backward (and not or only little in the forward stance phase) has probably two reasons. First, the backward stance phase of the left leg probably generated normally a stronger activation of the peronaeus longus than the forward stance phase, which is physiological under the existing jumping conditions, as can be seen from the muscle activation pattern (Fig.12) of a control person (author G.S.). Second, the increase in the coupling of the left and right movement pattern generators („Mitbewegung") seems to have been induced by the synchronized half-jump, when the right leg had the stance phase backward and the left leg the stance phase forward. The synchronized jumping-induced afferent input probably lasted, after a delay, less than a cycle period and therefore also the shared afferent input to motoneurons and interneurons (and spinal oscillators) of both legs. Since synchronization occurred once during a jumping cycle (physiologically, Fig.12), increased coupling of right and left pattern generators was also achieved once during a jumping cycle. The same is applicable to „Mitbewegung" upon breast-swimming. In complete spinal cord lesion (paraplegics), the response for increased coupling (synchronization) of α and γ-motoneurons upon skin touch lasted, after a delay of 30 to 140 ms, approximately for a few hundred milliseconds (Figs.2,4 of [98]). Exact synchronization (phase 0° or 180°) of left and right pattern generators seems to be crucial to induce „Mitbewegungen" (see also below for mth-order synchronization).

A major further problem is the supply of the lumbosacral network with the necessary descending drive for physiologic movement. Since the remaining tract fibre population is unbalanced, supraspinal centres have to be reorganized to send different patterns down to the

lumbosacral networks The patient has to relearn the task of giving the appropriate drive through the remaining fibres by watching his and the trainer's movement and by „hearing the movements" The trainer always had keys in his pocket which produced movement-induced noise A large part of the reorganization concerns supraspinal centres, to compensate for the reduced and unbalanced drive caused by the unbalanced lesion Also, spinal networks have to adapt to the unbalanced descending drive, but more plasticity has to be expected from supraspinal centres

Mathematically derived features of populations of interacting biological nonlinear oscillators can partly explain human data on spinal oscillators

Probably, the most appropriate mathematical approach to calculate self-organizing neuronal networks is by synergetics, since the principles of self-organization are the central point of its study According to the definition, synergetics is concerned with systems that are composed of many parts that interact with each other and in this way may produce spatial, temporal or functional structures [40] An analytical technique for pattern recognition can help to identify organizational principles and control strategies of the nervous system Such a technique for identifying common feature signals among a set of rhythmic movement patterns has been developed [71] An intermediate way is used in animal research to model rhythmic stereotyped movements by calculating certain oscillator configurations [24] The results of this human research makes it likely that the human nervous system is at least partly built up of self-organized populations of interacting nonlinear oscillators Modelling of basic human network functions will be difficult, because basic data on neuron cell properties have not been obtained so far The much lower nerve fibre conduction velocities (highest conduction velocity is ~ 70 (man [96]) instead of 120 m/s) and the much higher transmission frequency (~ 5 kHz [94] instead of 1 kHz) indicate that the neuronal cell properties are at least partly very different For a better understanding and interpretation of human rhythmic neuronal network properties however a comparison is performed here with mathematically derived general features of populations of interacting nonlinear biological oscillators [72]

When a linear oscillatory system is driven by an external periodic input its response contains both frequency components In general, this is also true for nonlinear oscillators Similar response phenomena can be seen in oscillation period and interspike interval distributions of spinal oscillators following spinal cord lesion [104] However, if 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 (page 71 of [72])

Some oscillator features are given here (page 156 of [72]) with the corresponding human data

1 Populations of interacting biological nonlinear oscillators may have more than one stable state of synchronization The corresponding human data are The α_2-oscillators have three or more stable states [90,97] Thus after a disturbance, the sys-

tem may return to a cycle different from the one before: change from 2 to 3 or 4 action potential firing of α_2-oscillators upon an increase of afferent input. It has been argued that a simple oscillator model with another functional mechanism can easily explain the change in the length of the impulse train. In Fig.19A an oscillator generates a rhythm, two interneurons produce the 2 AP impulse train, and the switching on and off of afferent inputs makes the motoneuron firing with 1 AP or two APs. Such a model however, is in contradiction with other measurements on human premotor spinal oscillators, as the motoneuron, e.g., has to be a part of the oscillator itself, by changing from 1 AP firing to two AP firing the oscillation period has to increase, the distributions of the interspike intervals of the impulse train show peaks which make coupling with other oscillators likely [90,96]. In α_2-oscillators, additional firing in between the period from one impulse train to the next one has not been observed so far. A model of human premotor spinal oscillators make only sence if all the known properties of human spinal oscillators are incorporated. For the time being, more properties of human spinal oscillators have to be measured and their coupling possibilities; modeling comes afterwards.

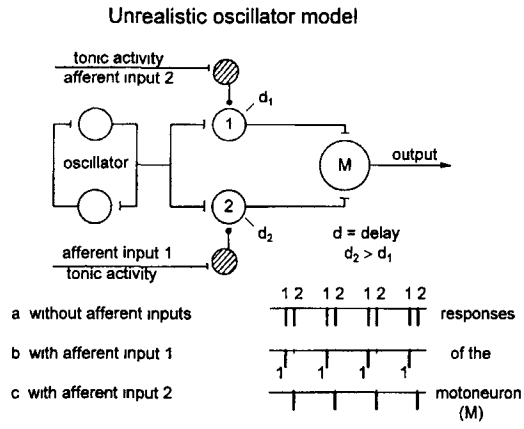

Figure 19A. Oscillator model which can generate with a few neurons a repetitive firing with impulse trains consisting of one or two APs With no afferent input, the motoneuron fires repeatedly with two APs With afferent input 1 or 2 the interneurons 1 or 2 are inhibited, and the motoneuron fires repeatedly only with 1 AP Such a model however, is far from human reality, since the motoneuron is not a part of the oscillator (left part), the two interneurons cannot generate an oscillation period of approx 130 ms, and the change from one to two AP firing is not accompanied by an increase of the oscillation period from appox 100 ms to 130 ms For further objections, see text

2. There is a possibility of multifrequency oscillations. Human data: FR-type premotor oscillators (α_2) can change their oscillation period from 130 to 160 and to 190 ms [90,97]; synchronization of premotor α and γ-oscillators [99] with different degree of synchronization; change of focus of synchronization; change from symmetrical to alternating oscillatory firing (Figs.8,9). If the coupling is weak, one expects that states of stable synchronization may not be reached from arbitrary initial conditions or after a disturbance has shifted the system away from a limit

cycle Premotor α_2 and α_3-oscillators, built up of a few coupled suboscillators (physiologically characterized by different lengths of different overlapping synfire chains [96,99]), change their properties (shorter impulse trains, instability) following spinal cord lesion [90,96], probably by decreasing their coupling strength, more generally, modulation of the coupling strength may be one strategy to change the functioning of neuronal networks, following spinal cord lesion, the modulator of the coupling strength may work outside of the regulation range so that pathologic movement patterns are generated

3 The macroscopic behavior of populations of oscillators depends on the average values of its parameters rather than on their values in individual units This property is in accordance with the principle that the death of a single neuron should not change neuronal network functions (synfire chains remain rather unaffected by single interneuron cell death), α_3-oscillator neuronal networks consisting of many interneurons [96] seemed to be more changed following spinal cord lesion than α_2-neuronal networks, built up of fewer interneurons, which may mean that integrative functions are mainly changed

4 The frequency of oscillations may depend significantly on the coupling strength between oscillators, and therefore the frequency of synchronization in a population of oscillators may be quite different from the frequencies of the individual oscillators With the transient increase of the coupling strength by the simultaneous afferent input to α and γ-oscillators from skin receptors following touch and pinprick stimulation, the oscillators synchronized and transiently increased (and therefore changed) their common frequency [98], from neuronal cell aspect, the transient increase of the coupling strength is achieved through the motoneurons and interneurons, integrated in the premotor and propiospinal oscillators, sharing approximately the same afferent input patterns (coincidence activation)

Most important in the features of systems of coupled nonlinear oscillators is the multiplicity of stable solutions which predicts that after a - possible minor- disturbance one can observe a drastic change in the macroscopic dynamical behavior of the system (page 159 of [72]) If the number of units in a subsystem is very large, such a system can behave as a continuum The α_3-oscillators, which are mathematically a population of coupled oscillators, can change their frequency rather continuously within a certain range [84]

It seems likely that the neuronal network of the spinal cord consists of populations of different kinds of nonlinear biological oscillators which generate integrative (macroscopic) functions by modulating the coupling strength of the interacting oscillators at the cord level or by synchronizing spinal oscillators with supraspinal oscillators For the coupling strength, the modulators are the afferent input patterns from the periphery and the impulse patterns from supraspinal centres The functioning of the spinal cord network could be achieved by the ongoing modulation of the coupling strength and the correcting influence from the function-induced afferent input patterns from the periphery For the self-organization of neuronal networks to oscillators, a certain excitation is necessary, which can come from the periphery

(see Fig 4 of [97]) or from supraspinal centres (Fig 7) For entrainment rules, see below Repeated stereotyped modulation of the coupling strength between spinal oscillators will lead to a change of synaptic strength (re-preformation of neuronal networks) and will change the properties of oscillators and the strength of coupling between them In other words, entrainment among spinal oscillators takes place with the normal functioning of the neuronal network Repeated entrainment of premotor spinal oscillators and probably also propriospinal oscillators, initiated and maintained by supraspinal inputs and improved by the stereotyped rhythmic movement-induced afferent input patterns, will lead to re-preformation of neuronal networks, and is the basis for the oscillator formation training Because of larger and more complex networks, probably α_2 and α_3-networks can be trained better than α_1-networks The contributions to the self-organization of spinal networks comes from the input of receptors (mainly the periphery) and supraspinal centres The proportions of the contributions of supraspinal and peripheral inputs will vary with the function Reflex neuronal network organizations (with special task-oriented network preformations) will mainly be generated by the afferent input from the reflex zone or organ, whereas volitional fine control of nonrhythmic goal-oriented movements will mainly be generated by the input from supraspinal centres Rhythmic, dynamic, stereotyped movements probably need only little tonic or patterned supraspinal drive, which is the reason to train them in incomplete spinal lesions Future studies have to show how much ascending and descending control is necessary

Mathematically derived rules for harmonic, superharmonic and subharmonic entrainment among populations of biological oscillators in relation to probably existing coupling rules of human spinal oscillators

The following equations describe a large class of populations of interacting nonlinear oscillators (pages 153 156 of [Pavlidis])

$$dx_k/dt = f_k(x_k, y_k, z_k),\ k = 1, 2, \ , n$$
$$dy_k/dt = g_k(x_k, y_k, z_k),\ k = 1, 2, \ , n$$
$$z_k = F(\Sigma_{j=1\ n}\, a_{kj}x_j),\ k = 1, 2, \ , n$$

F is a dynamic operator with the property that, if its argument is a periodic function, the same will be true for z_k, and its period will be the same as the period of the argument This condition is satisfied for delay operators, simple nonlinearities with hysteresis, the inverse of linear differential equations, and superpositions of such operators If one considers z_k as an external input, a synchronous solution, i e , one where all the x_k's and y_k's oscillate with the same period T, can be achieved only if z_k entrains the corresponding oscillator to that period

The entrainment of each unit can be harmonic (z_k has itself period T), subharmonic (z_k has a period which is an integer multiple of T, mT), or superharmonic (z_k has a period which is an integei fraction of T, T/m) Because of the assumptions about F the sums $\Sigma a_{kj}x_i$ will have the corresponding periods This imposes the condition for achieving synchronous solutions

Special cases are

1 All the units are in phase Then, if $a_{kj} > 0$, all the sums will oscillate with that period and a synchronous solution can exist if the individual oscillators are entrainable by z_k to a common period This usually means that the mutual coupling is strong enough
2 The units form two groups with a half period phase difference The sums will oscillate with a fundamental period equal to T/2, and a synchronous solution can exist only if z_k can cause subharmonic entrainment of the individual units
3 The previous case can be generalized by assuming that the units form m groups which have phase difference T/m and they are entrained by z_k to m times their period

Each of these possibilities will be called an mth-order synchronization, where m is the number of groups which the oscillators are split into

The units need not actually be in phase but small phase differences are allowed as long as the sums $\Sigma a_{kj}x_j$ have a significant fundamental at the particular period and phase [72]

If spinal neuronal networks, which are excited and organized to populations of different kinds of oscillators, are additionally subjected to a rhythmic afferent input induced by rhythmic movement, the entrainment of the different kinds of spinal oscillators with different oscillation frequencies can be harmonic (entrainment period = T), superharmonic (entrainment period is an integer (m) fraction of T (T/m)), and subharmonic (entrainment period is an integer multiple of T (mT)) with respect to the different oscillation frequencies

Even though the self-organized human spinal neuronal network is more complexly structured than the above mathematically assumed one (e g , different kinds of spinal oscillators (premotor (α_1, α_2, α_3) and propriospinal), special connections such as the monosynaptic stretch reflex or change of functional connectivity by primary afferent depolarization), some mathematically obtained results can be observed in real human networks For considerations concerning the stability of the various states of synchronization, see page 155 of [72]

In recordings from α-motoneurons it was found that premotor oscillators can fire with symmetrical and with alternating oscillation periods [84,96] In Figs 8 and 9, a phase change in the coupling of oscillators on one side, measured by motor unit firing, was correlated to the change of oscillatory firing from alternating to symmetrical on the other side At a first glance, it is not clear whether alternating oscillatory firing is due to the coupling of two half-centre oscillators correlating both sides of the body [38] or whether it is a feature of spinal oscillator coupling, namely that an oscillator can fire with same oscillation periods or with alternating long and short oscillation periods (including changes of the alternation, called here change of focus) A change of the same oscillator (system of coupled sub-oscillators) from alternating to symmetrical firing and its correlation to phase changes on the other side of the body indicate that changes from symmetrical to alternating firing and changes in alternation reflect existing general rules underlying the coupling of oscillators (rhythm coordination) Alternating oscillatory firing could be due to alternating coupling of one oscillator with two others or, according to the above mathematically obtained results, a second order

synchronization of a population of oscillators split into two groups in which the two groups fire oscillatory in phase opposition (180°) (Fig 7 6 1 of [72]) The amplitudes of two oscillators firing with opposite phase at 5 Hz, e g would add up to a 10 Hz firing If the phase difference is slightly different from 180° (mathematically allowed, see above), an alternating firing with long and short oscillation periods would be the result

If the rhythmic movement (jumping, running, etc) has a frequency of 0 8 to 1 Hz and the α_1, α_2 and α_3-oscillators fire with frequencies (endogenous frequency, „Eigen"-frequency) of approximately 10 Hz, 6-8 Hz, and 0 6-1 Hz respectively [96] (if the synaptic transmission would last approx 3 ms, then there could be hundreds of interneurons involved in the oscillatory firing), most oscillators would be entrained subharmonically and the entrainment energy would probably be rather small It seems therefore that not much entrainment (see also [99]) will be achieved It should be remembered however that the skin receptors fire with impulse trains with increasing interspike intervals already upon a single short touch or pin-prick stimulation The first interspike intervals of an impulse train of a single skin afferent fibre can be 10 ms (corresponding to 100 Hz) and less [83,87,96], so that the oscillator may get many entrainment pulses per entrainment cycle Also, many afferents will project on a single oscillator The timing is most likely properly arranged by the human CNS Even α_1-oscillators, innervating FF-type motor units, will probably be entrained harmonically (see also below (mechanism of oscillator formation training)) But primary and secondary muscle spindle afferents, with their natural impulse patterns will also essentially entrain premotor α_1 and α_2-oscillators harmonically (same frequency of firing [91,92,97]) The α_2-oscillators can even include a γ-loop in their oscillatory firing [99] If the movement is dynamic, also the dynamic oscillators (α_1) and the dynamic spindle afferents (primary) are fully included in the entrainment The α_1-oscillators and the primary muscle spindle afferents are fire time-locked [99], and the primary spindle afferents can therefore entrain the premotor α_1-oscillators harmonically The dynamic movement is therefore an essential feature in the rhythmic, stereotyped movement training, as also felt by our patient himself

Most likely, there is a certain frequency range of entrainment around the „Eigen"-frequency, in which the rhythm can be synchronized by the superimposed rhythm of stimulation elicited by the rhythmic movement Outside this range, more irregular or alternating forms of coordination are observed [90], switching over to more stable multiple integer relationships in faster or slower ranges of rhythmic stimulation These rhythm correlations are similar to those found by E v Holst [45] in fish, where the movements of the fins are correlated according to certain rules Another consequence is a resonance-like enhancement of the amplitude of the oscillations when the stimulating rhythm approaches the endogenous frequency Following spinal cord lesion the pathologically enhanced frequency band of the premotor spinal oscillators [90] can therefore most likely be reduced, but this has still to be shown explicitly The impulse patterns of joint receptors and Golgi tendon organs have not been measured so far in this research project Generally, it seems that the spinal oscillators get enough drive (energy) for entrainment by the movement-induced afferent input, if the movement is rhythmic, stereotyped and dynamic

Mathematically, it should be possible that in one kind of oscillator population the individual oscillators can be entrained with a different phase with respect to the cycle of entrainment (page 148 of [72]), if the oscillator population is split into m groups, so that the amplitudes of oscillators of the different groups have a phase difference T/m with respect to each other Then, mth-order synchronization takes place (see above) Such distributed firing of premotor oscillators (see Fig 3 of [95], no firing of functionally nearby motoneurons at the time) seems to be the physiologic case Only, upon touch or pin-prick stimulation, the phases between the APs of the oscillatory firing different premotor oscillators change transiently by a transient shortening of the oscillation periods [98] At least premotor oscillators can partly be entrained at different phases with respect to the oscillation cycle [98] Skin afferents including pain afferents can reset the cycle of spinal oscillators considerably, depending on the composition of the afferent input patterns and whether the skin is stimulated outside or inside of a reflex zone [98] Since for example, T1 skin afferents (most likely innervating Pacinian corpuscles) can be activated by skin traction from a distance of up to 10 cm [87], the skin afferent input patterns can change considerably with slight changes of the movement or changes of the ground on which the patient is moving

Mechanisms of re-preformation of neuronal networks by oscillator formation training

The working hypothesis is that the spinal cord is built up of neuron (mainly interneurons) assemblies, which organize themselves to rhythmically firing units The rhythmicity is generated in reverberating interneuronal circuits Most probably, the activation is maintained by circulating synchronized firing (closed „synfire chains") The stabilisation of the reverberatory activity is positive (re-excitatory) The premotor α_2 and α_3-neuronal networks appear to exist in different activity states (with different oscillation frequencies), which are correlated by the overlap of different synfire chains ($T \approx 70$ ms + 30 ms $\cdot n_{AP}$, T = oscillation period, n_{AP} = number of APs per impulse train) [90,95,96] The rythmically firing units (premotor spinal oscillators (motoneuron included) or pure interneuronal cell assemblies) couple by rhythmicity, according to afferent and supraspinal input To generate macroscopic (integrative) structures, propriospinal oscillators (pure interneuronal cell assemblies) will drive the motoneurons directly in the low activity mode [88,89] or via the premotor spinal oscillators for the high activity mode (dynamic organization) (Fig 20) The amount of excitation or inhibition is less of importance for the self-organization than the natural impulse patterns of afferent and supraspinal inputs, which organize the self-excitatory reverberatory loops The natural impulse patterns may activate different groups of cells („task groups" for self-excitatory reverberatory loops) than does artificial electrical stimulation of axon collaterals („task group" for inhibition (Renshew cell)) Each self-excitatory reverberatory loop consists of a synfire chain which probably overlaps with other synfire chains for rhythmic coupling and the chain of which may consist of a varying number of neurons Subthreshold activated interneurons at the functional (excitatory) fringe of the synfire chain probably contribute to the coupling of different premotor and propiospinal oscillators

Possible connectivity of the spinal oscillators has been derived from naturally induced discharge patterns [84,90,92,95]. Also, the coupling phenomenon of spinal oscillators has been derived from discharge patterns. The interaction between different pattern generators (macroscopic self-organized neuronal network) is produced by the movement-induced afferent inputs and the driving supraspinal input patterns. Short-term synchrony of spinal oscillators was measured with repeated skin stimulations (touch and pin-prick) [98]. The repeated input probably synchronized the spinal oscillators by the shared afferent input and supraspinal input patterns. This concept of the self-organization of preformated neuronal networks is far from those of the classic postural reflexes of the Sherrington school although these descriptions per se are still valid and useful.

The oscillator formation training changes the efficacies of synapses [27,112] (re-preformation of neuronal networks) to allow more physiologic self-organization at three levels of the network organization. Synaptic plasticity will work at the rhythmic unit level (premotor and propriospinal oscillatory firing subnetworks), at the macroscopic network level with functional output for movement already, and at the level of interaction of different spinal pattern generators (Mitbewegung).

Consequences for training movement functions of the spinal cord in incomplete spinal lesion

When muscles, e.g. the soleus, are strongly steadily activated, the premotor spinal oscillators will fire continuously oscillatory to produce ongoing output activity. However, large parts of the neuronal networks such as the pattern generators generated by propriospinal oscillators will be bypassed (Fig.19). Therefore, the training of volitional muscle activation does only little re-preformate neuronal networks for better functioning. Mainly recovered tract fibres, at the spinal cord lesion site, can only be strengthened by the repetitive activation, and of course muscle fibre and motor unit size can be increased by this type of activation. Complex natural movements like running can only little or not at all be improved in this way. In physiotherapy it is believed that muscle power needs to be improved to improve movements. At least partly, this belief does not apply to spinal cord lesions. The main task in incomplete spinal cord lesion is to improve the self-organization of the spinal pattern generator to improve movements.

Rhythm coordination as a basic principle of physiological self-organization and nonuse

The improvement of locomotion by the rhythm training and the measured improvement of rhythmic properties during jumping (Fig.5B) may indicate that premotor and more upstream propriospinal oscillators improved their rhythmicity and their coupling to macroscopic functions such as jumping, running and walking. It may further indicate that rhythmic organization of neuronal subnetworks and their rhythm coordination for integrative functions are really basic principles of physiologic self-organization of neuronal networks.

Actually, the extension of the frequency range of the premotor spinal oscillators follo-

wing spinal cord lesion [90] may be viewed as a sign of nonuse, to get as much activation as possible The extension of the frequency band of spinal oscillators may be understood as an increase of the sensitivity of the oscillators to get more coupling possibilities, with the price being oscillator coupling to pathological organization forms Probably, the offer of rhythmic inputs decreases the frequency band of the oscillatory firing subunits because of the synchronization of the frequency input (entrainment) and increase of activation (decrease of sensitivity) With the improved rhythm of the neuronal subnetworks and the more specific coupling between the subunits, a macroorganization was achieved closer to the physiologic one What was not shown here is that the premotor spinal oscillators really reduced their frequency band (improvement of rhythmicity of oscillators)

Coordination between somatomotor and autonomic functions

During the process of self-organization and re-self-organization by the superimposed rhythm of stimulation when performing a rhythmic movement, one rhythm can lead, entrain, or influence another more or less strongly Since there is no basic difference between the mechanism of coordination between different motor rhythms, different vegetative rhythms, and between vegetative and somatomotor rhythms [53], it should be possible to improve vegetative and vegetative-somatomotor functions by a rhythm training

It seemed in our patient (with an incomplete spinal cord lesion) that also continence functions improved slightly (increase of urine storage volume of the bladder and reduction of urge to void when performing the rhythm trainings) with the improvement of locomotion Unsolved has remained the problem, how the detrusor (parasympathetic)-sphincter (somatic) dyssynergia [93-95] and spastic bladder (hyperactivity of the bladder = nearly no storage volume) of paraplegics (with a complete spinal lesion) can be improved by a rhythm training Our patient became euphoric, when he started to sweat (sympathetic) for the first time again after the accident (more than one year), during running

Direct and indirect interlacing (via projections) of somatic and autonomic neuronal networks will take place at the level of the spinal cord, the brainstem and higher centres It has been shown in dogs that reticular neurons of the lower brainstem constitute a common system for basic regulation and integration of visceral and somatomotor systems and vigilance [54,55] Bulbospinal projections follow the principles of divergence, reaching motoneurons, preganglionic neurons of the autonomic nervous system and dorsal horn neurons [48, 126] The „common brainstem system" (CBS) neurons always receive afferents as well from tho se systems to which their efferents are directed, the CBS is a system with manifold feedback loops Discharges of CBS neurons exhibit rhythms of different time ranges The same rhythms can be found in the functional systems influenced by the CBS, e g , in efferent sympathetic and parasympathetic nerves, in motoneurons as well as in the neuronal activity of higher brain structures, e g , the amygdala complex [55] Cardiac rhythmical discharge patterns in neurons of the nucleus tractus solitarii, the first relay station of baroreceptor afferents, are modulated by their activity level Cardiac rhythmical discharge patterns are tran-

sferred to their connecting neurons, e.g., those in the CBS or in the amygdala complex. Therefore, cardiac rhythmical discharge patterns are found in the neuronal activities of these systems (for references, see [55]).

In human volunteers, cardiovascular-respiratory phase coordination and coordination of limb movements and respiration has been observed [77]. The mean oxygen uptake during walking on a treadmill showed a minimum if spontaneous breathing was allowed but not if the breathing rhythm (inspiration) was coupled with different phases to the walking cycle (heel strike). With respect to energy expenditure, an optimal matching was already realized under spontaneous conditions, which was reestablished when voluntary breathing was put into identical phase reference [77]. Our patient suffered a traumatic pneumothorax in the accident. During the exercise of swimming, the patient had problems with the breathing (rhythm) at the beginning of the training. After 6 weeks of rhythm training, the patient did not any more complain about breathing problems while swimming.

By local mechanical destruction or cooling at a defined site in the brainstem of dogs, it was possible to impair the partial mechanism which normally terminates inspiration [52]. This interference resulted in extreme prolongation and irregularity of the inspiratory phase with a decrease in respiratory frequency. The most interesting result, however, was the spontaneous restoration of the normal respiratory rhythm in the course of some hours, without any change in the external conditions or the afferent information. This suggests that the special function of respiratory rhythmogenesis is not necessarily bound to a certain anatomical substrate.

In patients with a very high spinal cord lesion including parts of the breathing centre of the brainstem or patients with tick-induced spring-summer-meningo-encephalitis (RSS), with a partial loss of the breathing function, it seems possible to improve the breathing function by a rhythm training.

Possible neuronal network organization of the human nervous system

The features of the peripheral organization of the motor system are immensely complicated. This may be a reason for the complexity of the spinal and central neuronal networks which have to deal with the periphery. A particular aspect of this complexity is the polymodal or „multisensory" convergence of many input systems on the interneurons of the neuronal networks.

In considering spinal cord functions, the complexity of parallel neuronal networks cannot be reduced to a chain of some serially connected individual neurons [117]. The reflex concept misleads us to believe that „reflexes" are conceptually equivalent to the entire neuronal assembly. Rather, the multidimensionality of parallel organization of neuronal networks together with their intricate signal processing capabilities must be taken into account. In the view of this, spatio-temporal patterns of cell assemblies are important, in conjunction with plastic synaptic processes, which in turn depend upon neuronal activity patterns induced by movements or other natural stimulation. Spinal circuits should be capable of pattern

recognition (especially of rhythmic ones) because the polymodal input to many neuronal systems in the spinal cord is fractionated, thus providing for individualized receptive properties of the neurons These may then participate in various combinations in cell assemblies varying with the input pattern and the task These spinal networks, including reflex organizations, perform some functions such as spatial transformation and predictions, which are also executed by supraspinal structures, particularly the cerebellum [117] There is a broad spectrum of physiological rhythms in many different systems extending over a large range of frequencies The medium ultradian range is characterized by a relatively great variability of frequency, intense mutual interactions and interference with the homeostatic regulatory circuits and behavioral influences In spite of the resulting multiform phenomenology, certain basic rules of „relative" sliding coordination [45] can be identified between the subunits of one system, and between the systems themselves They are revealed through certain kinds of mutual entrainment, the occurrence of multiple integer frequency relations, instability of phases and amplitudes during transitory rhythm-related cell excitability, and through variable periods of synchronization and desynchronization The fact that the same general kind of rhythm coordination is found, irrespective of the particular system and frequency range, justifies the hope for a successful analysis and understanding of rhythmicity as a basic principle of physiological self-organization [53]

With the discovery of premotor spinal oscillators, a first step into the human CNS neuronal network was done These premotor networks, which for high excitation are the output channels of upstream networks, are self-organized of preformated neuronal networks (most likely self-excitatory) by the adequate natural afferent or supraspinal input patterns The anatomical network alone does not specify the behavior that will result from its activation, rather, it somehow represents a library of possible interactions from which different functional states are built

With the oscillator formation training, the preformation of the premotor spinal oscillators (premotor neuronal network) and further upstream rhythmic systems (propriospinal oscillators) was changed by changing the efficacy of synapses (plasticity [27,112]) by some reinforcement training [10]

The important question is now, what are the capabilities of the spinal cord, and what neuronal network organizations of the cord need rather strong supraspinal drive The multiplicity of interconnections enables the spinal neuronal network to generate many different macroscopic activity patterns (movements) and to generate short- and long-term memory However, what are the movements for which mainly the movement-related afferent inputs are sufficient, and for what movements there also are strong supraspinal impulse patterns necessary for the spinal network organization and reorganization? In our patient the stereotyped rhythmic dynamic movements were mainly self-organized by the phasic movement-related afferent input and mainly located in the lumbosacral spinal cord More supraspinal control was necessary for getting into the stereotyped rhythms and for a change of the stereotyped rhythms, because the patient felt difficulties in changing stereotyped rhythms

A person can walk with a variety of gaits, quickly or slowly, and forwards and backwards

While each variation could, in theory, be produced by a different neuronal program, it is simpler to assume that a single neuronal network is continuously changing with the movement-related and supraspinal input patterns, to produce all the variants on a common theme, even though a few principle programs, manifested by certain preformations, may exist Preferential movements are probably those, which are as economical as possible in terms of energy expenditure, and which can use oscillatory firing networks (rhythmicity) as directly as possible

Cause and development of spasticity

Spasticity is a common but not inevitable consequence of lesions of the cortico-fugal pathways including the pyramidal tract, at any level, whether the cortex, the internal capsule, the brainstem or the spinal cord

Spinal spasticity has a slow time course of development following the initial insult, except in cases of high brainstem lesions in which there is an immediate increase in tone This slow time course suggests that plastic changes in synaptic connections may contribute to the development of spasticity [21] One response to denervation may be formation of new synaptic connections through axonal sprouting Since this sprouting has the same time course of development as that of hyperreflexia it may be the new, functional synaptic connections that actually mediate the hyperreflexia Another response is an increase in, and abnormal sensitivity of pre- or post-synaptic elements to the remaining afferent input (increased chemical sensitivity, loss of pre-synaptic inhibition) A third possibility is that previously inactive synapses may become active Of particular interest is the evidence that the process of reorganisation of remaining circuitry as well as sprouting within the CNS may be directly influenced, either positively or negatively [41,58,61]

Conventional explanation for spasticity on the basis of the „reflex concept"

Spasticity has been defined as a motor disorder characterized by a velocity-dependent increase in tonic stretch reflex („muscle tone") with exaggerated tendon jerks resulting in hyperexcitability of the stretch reflex as one component of the upper motor neuron syndrome [16,46] Loss of dexterity, and fatiguability are recognized to be more disabling to the patient than the changes to muscle tone [19,56]

In the clinical sense spasticity is a manifestation of both disordered motor control and adaptive changes in soft tissue Abnormal „spastic" patterns are reported by clinicians, and are often attributed to the release of abnormal reflex activity only [16,64] Connective tissue in muscle also undergoes remodelling as a result of immobility, and probably contributes to the increased stiffness found in shortened muscle The soft tissue adaptations provide, therefore, a mechanical cause for the increased resistance to passive movement

Normal resistance to passive movement is determined by several distinct components physical inertia of the extremity, mechanical-elastic factors, particularly compliance of muscle, but also of tendon and connective tissue, and reflex muscle contraction (stretch re-

flex) [50] Since inertia of a limb does not change in the „upper motor neuron syndrome", the resistance to passive movement found in clinical examination must represent changes in the musculo-tendinous unit, i e contracture and/or changes within the segmental reflex arc [50] Patients following a spinal cord lesion complain of muscle stiffness which hinders movement

Spasticity in the neuronal network concept and inhibition of spasticity

Spasticity has only partly been measured on the basis of the self-organization of neuronal networks (spastic urinary bladder [93-95]) The occurrence of spasticity in our patient, namely the velocity or accelleration-dependent increase in muscle stiffness which obstructed the flexion of the left knee during too fast running, was not recorded electromyographically, since it did not occur during the examination It can be seen from Figs 13,14,17,18 that the rectus femoris and vastus lateralis muscles were almost continuously active and hindered knee flexion Probably at higher running speed or a quick change of speed, these muscles became permanently fully active and blocked knee flexion completely

The premotor spinal oscillators as basic functional neuronal units of the spinal cord change their properties following spinal cord lesion [90,96] It is therefore likely that also the more upstream propriospinal oscillators change their properties, since they are organized by the same neuronal elements (interneurons) apart from the motoneurons Probably, the spinal pattern generators organized by the changing coupling of these propiospinal oscillators, almost oscillators and possibly not rhythmically firing subnetworks, change to pathologic pattern organization for leg muscle activation Whereas the pathologic motor programs for locomotion are mainly generated by somatic networks, the dysfunction of the urinary bladder is generated by somatic, parasympathetic and sympathetic networks (detrusor-sphincteric dyssynergia and „spastic bladder" (hyperreflexia) [93 95])

Following spinal cord lesion, we have to expect a change in preformation and function of spinal neuronal networks because of nonuse and missing supraspinal control, which includes FF, FR , S and γ-type subnetworks of the somatic nervous system and the parasympathetic and the sympathetic nervous system divisions (and the vegetative plexus), and interactions between them Due to the lesion, we have further to expect an unbalanced supraspinal control Tissue changes and infections may strongly change the afferent input patterns to spinal and supraspinal neuronal networks [95] Pathologic functioning in, and among the different nervous system divisions and subdivisions has to be expected They may include, among others, permanent hyper-activation of S-type motoneurons (antigravity muscle fibres) to stabilize the body and joints, general tonus increase (increased firing of motoneurons in the occasional firing mode), dysregulation of the γ-loop which may result in overactivation of primary (SP1) and secondary (SP2) muscle spindle afferents and overactivation of FF and FR-type motoneurons (which, in turn, will result in hyperexcitability of stretch reflexes), spastic bladder (hyperactivity of the detrusor by preganglionic parasympathetic fibres), and spastic external sphincters, hyperactivity of sympathetic fibres may result in transient

hyperactivation of smooth muscles and will lead to transient events of hypertension The possibilities of disorders are probably as many as there are nervous system functions located below the spinal cord lesion level

In this CNS concept, „inhibition of spasticity" means induction of rather physiologic neuronal network organizations and functions and attempt to avoid as much as possible pathologic network organization and functioning Spastic and rather physiologic functions cannot coexist in the same subnetwork, because at a given moment a network can only have one network organization However, one subnetwork may show physiologic organization whereas another one may be pathologic in its organization Since probably synfire chains are involved in the network organization [96], characterized by coincidence firing, and since they can cross one another [1], some kind of overlapping of physiologic and pathophysiologic functioning may be possible Therefore some competition between physiologic and pathophysiologic functioning is possible if both originate in different subnetworks

Possible mechanism for „Mitbewegungen" (co-movement) on the basis of spinal pattern generators

The term „Mitbewegung" denotes a situation when one leg makes the other one to improve moving through an increased simultaneous afferent input

It was observed in our and another patient that during breast-swimming the poorly movable leg could only be made to flex and then to stretch again if the patient closed his legs before flexing them so that they touched each other Similarly, when jumping on a springboard (oscillator formation training), also the left heel was lifted, which was not the case while running We shall try now to give an explanation for the phenomenon of „Mitbewegungen" (mutual influences mediated by short and long propriospinal pathways)

In similarity to locomotion in tetrapods [34], in man each leg is probably controlled by a separate self-organized neuronal network, termed here spinal pattern generator, mainly located in the spinal cord Probably, such network organization is generated by cell assemblies of single neurons (called here propriospinal oscillators, in similarity to premotor oscillators [90,96], by closed reverberatory self excitatory synfire chains [1]), which group and regroup for varying tasks by dynamically changing the effectiveness of their connections The net work organizations and reorganizations are achieved through various forms of correlated discharge patterns of polymodal inputs of afferent and supraspinal origin For systems of coupled oscillators as models of central pattern generators, see [23,35,76] The pattern gene rators determine the main characteristics of rhythmic leg movement, i e , the cycle duration, phases of activity of various muscles in a cycle, etc

How many spinal pattern generators do then exist in man to allow the different movements? There are probably two border positions in neuronal network organization for rhythmic stereotyped movements First, it could be that one spinal pattern generator, with a large variability, is able to generate all rhythmic movements, or second, each slightly different rhythmic movement is generated by a different spinal pattern generator At least the second

case, namely that each different movement is generated by a different spinal pattern generator, especially if they are somehow fixed-wired, is unlikely, since then an enormous number of different spinal pattern generators would have to exist Probably, a few basic preformated network organizations with quite a variability exist in human, which are activated (self-organized), maintained, supported and modulated by the input patterns of supraspinal centres, and by the movement-induced afferent input from the periphery Whether human network organization for locomotion can be induced by movement-induced afferent or supraspinal input alone is not clear Some kind of both drives seems to be necessary

In animals, afferent signals from receptors located in the moving limb are unnecessary for producing the rhythmic activity in the control system, since movements can be observed in animals with the limbs deafferentated or blocked with curare or other myorelaxants (fictive locomotion) [34,66] The central pattern generator is sometimes defined as the spinal pattern generator deprived of sensory feedback [34] Whether man can perform fictive locomotion is not clear either Some sensory feedback to supraspinal centres seems necessary for the different movements Certain afferent inputs are more important than others For example, the input from the skin receptors in the foot sole seems to be of crucial importance, primary automatic stepping in newborn infants can be induced by stimulation of the foot sole (see below)

In animals, the spinal pattern generator is divided into the rhythm generator and the output mechanism [34,38] Such a division was possible because a portion of the spinal neurons (in particular the motoneurons) influence neither the cycle duration nor the duration of the flexor and the extensor parts of the cycle, although they exhibit rhythmic discharge modulation during locomotion In man, the division into rhythm generating network and output mechanism is also possible for high activations The premotor spinal oscillators (motoneu rons plus reverberating synfire chains of interneurons) are a part of the output mechanism They also fire oscillatory when there are no stereotyped rhythmic movements activated, such as during sustained volitional contraction of a muscle (Figs 7-10,19) or when muscles (striated sphincters, pelvic floor) are activated for continence functions [95]

A spinal pattern generator controlling an individual leg is independent since it can operate separately from other limb pattern generators However, during locomotion and swim ming (and other movements), this autonomy is restricted, because stepping and swimming movements of the individual limbs must be mutually synchronized and properly phased This coordination is achieved through an interaction between the spinal pattern generators Each generator sends signals concerning its current state to other generators These signals come both from intraspinal mechanisms and from the sensory receptors of the moving limbs

Each spinal pattern generator has inputs for its „switching-on" and for the control of its level of activity During locomotion, the spinal generators for the two legs, and maybe the two arms, are switched on simultaneously Most likely, both types of the control mechanisms, the descending input and the afferent input, sum on some of the same key elements constituting the central pattern generator or sum on the same network structures Thus, if

descending inputs or afferent inputs are removed, some adaptation of the pattern generator can still be achieved by the remaining system because the different control systems are additive (in similarity to [34]).

When our patient tried to swim, the command signal activating the pattern generators seemed sufficiently strong on the right side (the leg moved voluntarily) while being insufficient on the left side (the left leg could only little be moved voluntarily). When closing the legs, also the left leg flexed and performed the swimming cycle movement. Two explanations are at hand. First, at the pattern generator for the left leg, the missing command signal

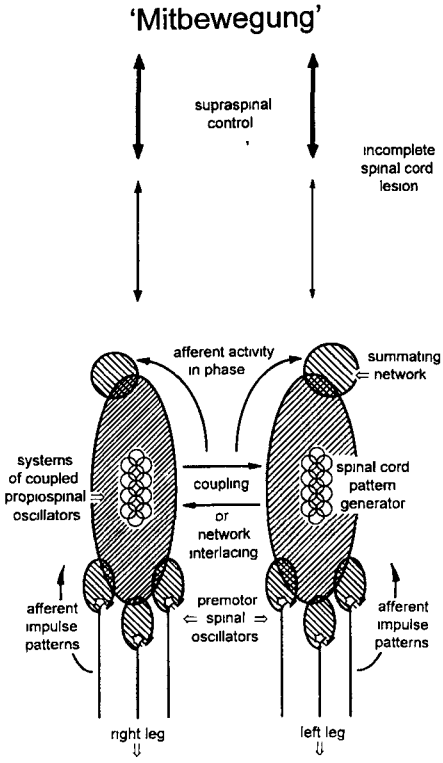

Figure 20. Possible neuronal network states upon „Mitbewegungen" (co-movements) Schematic drawing of possible subnetworks and impulse pattern pathways to explain during breast-swimming that the right leg made the left leg move when closing the legs before flexion („Mitbewegung") Oscillatory firing networks are split here into the premotor „output" mechanism for high activation and the propriospinal oscillators It remains unknown how the propriospinal oscillator networks couple to spinal pattern generators The strength of supraspinal control is indicated by the thickness of the arrows

(because of the unbalanced incomplete spinal cord lesion) was substituted by additional afferent input from the left leg, when closing the legs. Second, because of the simultaneous skin afferent input (i.e. synchronized and properly phased) to the left and right spinal pattern generators, the coupling between both spinal pattern generators became enhanced, so that both legs moved in coordination. The reduced command signal on the left side was compensated for by a stronger coordinated action of both spinal pattern generators (Fig.20).

The spinal oscillators, which both pattern generators are built of, will have increased their coupling strength upon synchronized afferent input. Following touch and pin-prick sti-

mulation premotor spinal oscillators synchronized transiently after a delay of approximately 10 to 100 ms (for touch and pin-prick respectively (Fig 4 of [98]) for up to a few hundreds of milliseconds (Fig 3 of [98]) Probably, the transient coupling increase of spinal oscillators due to skin afferent input will therefore last for only a few hundred milliseconds Even though the shared input from muscle spindle and other afferents may last a bit longer, only a repeated increase in the coupling will have ongoing effect with respect to „Mitbewegung" (co-movement) During breast-swimming and during jumping on a springboard, there was synchronization once per movement cycle Not as exactly timed simultaneous afferent input to both legs will probably also have some beneficial effect

At the spinal neuron level, the interaction (by similar action) or coupling of motoneurons and interneurons on both sides of the lumbosacral spinal cord is strongly increased by obtaining similar afferent input patterns from the ipsilateral side and by partly sharing the afferent input from the contralateral side Due to the coincidence input from the ipsi- and contralateral side, the neurons on both sides of the cord share very similar inputs, and therefore respond very similarly and are coupled with the same or the opposite phase, since spinal oscillators have two coupling phases per cycle per somatic nervous system [95,99] Crucial for the induction of „Mitbewegung" seems to be the exactly timed afferent input from both legs

The improved action of the left-sided pattern generator by substituted afferent input or stronger mutual interaction between the left and the right-sided pattern generators or both, for the missing tonic command signal not only occurs in spinal cord lesion The closing of legs in normal individuals while swimming also seems to facilitate the flexion of both legs

„Mitbewegungen" and the „reafference principle" (anticipatory postural adjustments)

A slightly different understanding of the improved movement of one leg induced by the other one comes from the „reafference principle"

Since long Gray [36] and his colleagues have been claiming that locomotor movements entirely depend on sensory signals, whereas von Holst [44,47] has advocated the opposite view, namely that central mechanisms were all that matters These claims were based on experiments in which dorsal root transsection was performed Grillner [38] and Székely [127] observed in the isolated dogfish and urodela spinal cord that a coordinated pattern could be produced if the cord was left intact in its entirety Moreover, the pattern-generating capacity was distributed along the cord so that if the cord was cut into several pieces, each piece could be made to generate coordinated activity, even when only a few segments were left intact That the pattern-generating capacity is distributed along the cord, was demonstrated in older times to medical students on frog preparations When the head of a frog (Rana temporaria) was cut off, the frog still jumped away upon touching, when the spinal shock had worn off after a few minutes (this property holds for days) When only the part of the animal was taken, which was connected to the forelimbs, upon touching the remaining skin after the spinal shock phase, the forelimbs moved with the part of the animal (and the spinal cord piece) We can therefore expect that also in man the pattern-generating capacity is distributed along

the spinal cord The capacity for locomotion will be located in the lumbosacral enlargement and that for arm movements in the cervical cord enlargement It is the working hypothesis of this research project that the pattern-generating capacity for locomotion and movements is given by the preformated neuronal networks mainly located in the lumbosacral and cervical cord enlargements, for locomotion this is supported by the primary automatic stepping of infants after birth (see below) The difference only concerns the functional independence Supraspinal drive and movement-induced afferent input from the periphery is necessary for self-organization But the phylogenetically old rhythmic, stereotyped, dynamic movements seem to need only little supraspinal drive, and right-left unbalanced supraspinal drive (a big problem in incomplete spinal lesion) can partly be compensated for by an increased coupling of pattern-generating networks of the left and right side, called „Mitbewegung"

In 1950 von Holst and Mittelstaedt published their now famous and widely discussed „reafference principle" [46,63] An organism usually responds differently to sensory messages that originate from changes in its environment and to those which originate from movements caused by the organism itself The messages coming exclusively from the environment were called „exafference", those resulting from movements of the organism were termed „reafference" The problem then is the mechanism by which the organism can distinguish between these two „afferences" The general reafference principle can be described as follows A command k initiates a motor act by means of the motor system (M) The resulting movement changes the spatial relation (y) between the subject and its environment The same can occur as a consequence of external disturbances (z) Both superimpose and generate the actual spatial situation (x = z-y) of the individual The variable x is transformed by the sensory system (S) into „total afference", which is thus a mixture of reafference and exafference Total afference and command are now compared at a level labelled Z_1 The result of this comparison generates a „message" that is sent to a higher CNS level (labelled Z1) for further evaluation, be it for recognition (in perception) or for a compensatory response (which may be unconscious) The general principle is thus that the comparison functions in such a way that the message only reflects external disturbance inputs (z), and not the endogenous activity resulting from the command (k) Any compensatory response would then only counteract exogenous influences

Now, there are two specific hypotheses the „copy hypothesis" and the „regulating hypothesis" According to the „copy hypothesis", the command (k) controls, in addition to the movement, an „efference copy", which is compared to the total afference If all the interactions are calibrated appropriately, the message (m) will only depend on the disturbances (z) and not on the command (k) With the second hypothesis („regulating hypothesis"), the total afference is compared directly with the command (k) itself This results in a simple feedback loop

According to Mittelstaedt [63] the above two hypotheses both comply with the reafference principle, but they are not functionally equivalent The feedback circuit yields a compensatory response but no „message" to higher centres The „efference copy" yields such a message but no compensatory response (only a higher centre could generate such a response

based on the message) Thus, the two hypotheses are not alternatives, but are rather complementary to each other. For further details, see [117] Both regulation hypotheses seem to work simultaneously in a patient with incomplete cervical spinal cord lesion, during running

When our patient got into the rhythm of running, he could run, even though asymmetrically If he could not get into the rhythm, the running was more pronouncedly asymmetric The command signal of the patient himself (the will to run) was supported visually (the physician (author G S) was running besides the patient), vocally (the patient was pushed by calling repeatedly flex-flex-flex. (the left leg)) and by audible noise (shaking of keys in the trainer's pocket) The pattern generator for the leg was supported by increasing the correlation between both pattern generators for the legs (see above) and by increasing the command signal, especially to the left leg Small changes of the ground (grass) were managed easily by the patient Thus, small modulations during running (adaptation to the ground) were mainly regulated on the spinal level, well below the cervical lesion area (regulation hypothesis) More pronounced changes of the ground (incline) could not easily be managed by the patient He was afraid that he may not be able to adapt his running to the change in gradient The supraspinal correction of the command to run downhill was difficult for him because of the incomplete lesion Probably, more significant changes of the running pattern could not be managed by the spinal cord, and the getting through of the command (k) and the message (subtraction of the efference copy and the „total afference") were hindered or disturbed by the spinal lesion Also, the patient would have to get into a good rhythm again, i e the right-left correlation had to be increased again to improve the movements of the left leg Therefore, rhythmic, strereotyped, dynamic movements were easy to perform by the patient (as the patient stated himself), because they were mainly generated at the spinal levels with little tonic supraspinal drive (command) More significant changes of the spinal pattern generator (self-organization of another spinal pattern generator due to command impulse patterns from supraspinal centres (see above)), generating the stereotyped dynamic rhythmic movements, are induced (via the command signal) and may be preregulated (via the „total afference") by supraspinal levels

Sensory feed-back The proprioceptive feedback from joints and muscle spindles, carrying information on internal (y) and external (z) variables, are important The patient himself wanted dynamic movements to get a better stability, which cannot be explained by an increased kinetic energy for better stability (balance) only Patients complain when, e g they loose the perception of joint feeling in one knee A partial substitution of hip joint perception for knee joint perception, with respect to upright staying or moving, took a few weeks

However, the sensory feed-back from the skin to higher centres for perception are also very important The spinal cord below the lesion gets all afferent information anyway It will be extremely difficult for a patient to run when he has no feeling in the soles of his feet An increased perceptional input from the skin receptors in the soles of the feet to supraspinal centres will improve walking and running The patients know that they can walk better in the sand of a beech than on a flat ground The deformation of the sand gives a suitable afferent

input for improved walking or running Probably, the T4 skin afferents (maybe similar to SAII afferents in animals), sensing touch movement alongside the skin, are strongly contributing to the improved afferent input to enable running or walking

It is therefore not only important what afferent input the spinal cord gets for the functional organization, but also the afferent input to supraspinal levels for perception is of high importance for walking and running Therefore the „reafferent" input or the message m (evaluation between efference copy and total afference) to and from supraspinal levels for the poorly volitionally innervated (afferent and efferent) left leg were very important for improving the movements of the left leg during running This means improvement (modulation) of the command k in a way that the left and the right-sided spinal pattern generators interact more strongly, so that the movements of the left leg improved upon running

On the other hand, the synchronized (properly phased) movement-induced afferent input from both legs to the spinal cord is of similar importance When the patient performed breast-swimming, the left leg could only be made moving (flexing) if the patient closed the legs before flexion (see above) The left and right spinal pattern generators got additional exactly timed afferent input from the skin, which probably increased the interaction between both spinal patterns generators, and the left-sided pattern generator improved its function and the movements of the left leg improved (became co-moved („mitbewegt")) The patient himself did not feel very much of this additional afferent input The major effect towards the improved movement of the left leg therefore probably came mainly from spinal levels

Similar regulatory mechanisms as in individuals with incomplete spinal lesions also occur in „half drunk" individuals If such a person runs in the dark along a flat road, he somehow feels that the running is produced in the spinal cord (the legs seem to move by themselves), and this works nicely even with some alcohol No problem arises with the stereotyped running As soon as one foot steps on an unexpected stone, lying on the road, big problems arise for the CNS The „half drunk" man has to change the movement, to adapt to the strongly changed ground, and this is what supraspinal centres are needed for Because of the alcohol however, the supraspinal centres are not working appropriately and cannot quickly enough reorganize the spinal pattern generators for other rhythmic or non-rhythmic movements The man may fall and/or overstretch his ankle ligaments A sober person is mostly quick enough to send changed command signals for forefoot adjustment according to the strongly changed „exafference" input

Even a normal individual may face problems if the command impulse patterns are in contradiction to the surrounding, which means that the afferent input is very different from „reafference" This can happen when a normal person walks downstairs on a known staircase in the dark (nearly no visual afferent input) and miscounts the number of steps The person expects another step which is not there The CNS obtains an afferent input which is very different from „reafference", i e „exafference" is very large Often, the nervous system can not cope quickly enough with such a situation, and the person may fall In this connection, the visual input is also of importance since it helps to quickly correct the command The visual afferent input reaches the supraspinal CNS more directly, since the eyes are a part of the

brain The importance of the visual afferent input was pointed out before, when suggesting bio-feedback supported training

Anticipatory postural adjustment Another formulation of the „reafference" principle is the anticipatory postural adjustment Unlike the postural reactions in response to posture or balance disturbances, the anticipatory postural adjustments precede the disturbance and therefore minimize the effects of the forthcoming disturbance in a feedforward manner [59]

Postural control

The postural control system in man has two main functions first to build up posture against gravity and ensure that balance is maintained, and second, to fix the orientation and position of the segments that serve as a reference frame for perception and action with respect to the external world This dual function of postural control is based on four components reference values, such as orientation of body segments and position of the centre of gravity (an internal representation of the body or postural body scheme), multisensory inputs regulating orientation and stabilization of body segments, and flexible postural responses or anticipations for balance recovery after disturbance, or postural stabilization during voluntary movement [59] There is indication that a single control fixes the ratios between angular changes in the hip, knee and ankle joints, and synchronizes their changes over time The CNS is unable to control individual muscles separately, and it only controls a small number of degrees of freedom by activating functional synergies, involving a set of muscles regulated as a whole Higher level of organization may be involved in the postural reactions to stance disturbance Hip strategy (torques and movement at the hip joint, cat), ankle strategy (torques and movements at the ankle joint, man), and stepping are different ways of restoring balance, depending on the intensity of the balance disturbance and the constraints The strategy level is also flexible and adaptable to task constraints For example, the hip and ankle strategies are not „all or none" reactions but rather form a continuum under progressively changing external constraints [59]

When our patient jumped on a springboard, the left musculus soleus showed no push off at all when the left foot should move from forward to backward (Fig 11) It was suggested therefore in the Results that the patient used his hip flexors for forward movement of the left leg Since in the right leg the change from stance to swing was initiated by the ankle (as normally) and in the left leg probably by the hip, the patient had changed from ankle to hip swing initiation in the left leg The muscle activation reasoning is one possibility for the swing initiation changes A second explanation could be the changed afferent input to supraspinal centres The patient had problems walking because he could not feel his left ankle joint any more So, for the ankle joint feeling in a few weeks' time he substituted the hip joint feeling to get control when walking With no afferent feedback he reported that his will to voluntarily make a walking step was blocked This may be an indication that there is no fictive locomotion in man The possible changing from ankle to hip swing initiation in the left leg of the patient could be due to the missing muscle activation of certain muscles (soleus

and other muscles) or due to the substitution of the ankle joint afferent input by the hip joint afferent input for swing initiation or both

Reinforcement learning and oscillator formation training

In reinforcement learning [10], a neuronal system generating a movement pattern to achieve a specific goal would learn by strengthening the synaptic transmission in the network, when the attempt has been successful or at least more successful than previous attempts This requires a „critic", who evaluates the overall result of each attempt and rewards success Reinforcement learning emphasizes learning feedback that evaluates the learner's performance without providing standards of correctness in the form of behavioral targets Instead of trying to match a standard of correctness, reinforcement learning tries to maximize the goodness of behavior as indicated by evaluation feedback Whereas supervised learning is instructional, reinforcement learning is selectional [10]

Oscillator formation training tries to strengthen and weaken synaptic transmissions in self-organizing neuronal networks according to adequate afferent and supraspinal inputs in the way that oscillatory firing systems fire more rhythmically again and that rhythmic, stereotyped, dynamic natural movements, such as running or jumping on a springboard, be improved and approach those of normal individuals The relearning of physiologic self-organization of spinal and supraspinal CNS networks with respect to physiologic movements of lesioned CNS is instructional The instructions are given by an improved adequate movement-related afferent input to the self-organizing network of the spinal cord and supraspinal centres The movements are trained by instructions from the patient (voluntary corrections of the movement), from the springboard (rhythmic constants of the equipment) and from the trainer The trainer gives visual and auditory feedback to the patient from his physiologic movements The patient should copy the movements of the trainer The trainer adapts to the possible movements of the patient (speed, rhythm), but guides physiologic movement The inertia of the moving limbs helps to generate more physiologic natural impulse patterns for the self-organization of the networks

If the patient's movements are not improving into the direction of physiologic movements, then the neuronal networks will learn via the efficacies of synapses to organize pathologic patterns The relearning from pathologic to more physiologic movements will be difficult and time consuming Normal individuals performing sports such as running or swimming also have difficult time to relearn rhythmic movements

The oscillator formation training provides standards of correctness in the form of stereotyped movements to be learned Those synaptic transmissions in the network have to be strengthened or weakened which leads to a better rhythmicity of the rhythmic subunits and the best macroscopic pattern

Supraspinal control

Our patient initiated running voluntarily The dynamic, stereotyped, rhythmic movements, generated by spinal pattern generators, were organized by the movement-related afferent input and supraspinal input These spinal movement patterns were turned on, maintained and partly controlled by the brainstem and higher centres Nothing is known about how the human brainstem initiates and modulates the movement patterns of the spinal cord The up- and downstream impulse patterns are not known However, if rhythmicity is a basic principle of self-organization at different levels of organization (see above), then synchronization in its various forms in the neuronal networks of the brainstem and the spinal cord will essentially contribute to the tonic and patterned brainstem drive

Reticulospinal neurons are modulated during fictive modulation in the lamprey brainstem-spinal cord preparation [38] When the fictive locomotor activity is powerful, the reticulospinal neurons are often spiking, whereas at low level locomotor activity, the phasic oscillations are usually subthreshold Many of these reticulospinal neurons monosynaptically excite both motoneurons and excitatory and inhibitory premotor interneurons in the spinal cord [38,79]

In tetrapods, signals from the spinal generator of a hindlimb reach the cerebellum via the dorsal and ventral spinocerebellar tracts (DSCT and VSCT) and the spinoreticulocerebellar pathway (SRCP) The DSCT transmits detailed information about the operation of the peripheral motor apparatus such as the phase and strength of contraction of single muscles, the joint angles, the time at which the limb touches the ground, etc [4] The rhythmical activity of DSCT neurons is determined by afferent signals from the peripheral motor apparatus rather than from central structures, and during locomotion in cats with deafferentated hindlimbs, as well as during fictitious scratching, any rhythmical modulation in DSCT neurons is absent In contrast, information conveyed by the VSCT and SRCP is of central origin The VSCT conveys information about the activity of central spinal mechanisms but not about peripheral events [57], because the activity of VSCT neurons was rhythmically modulated during locomotion after deafferentation of the hindlimbs [5] The intraspinal processes are the main source of rhythmic activity of these neurons The same result has been obtained for neurons of the SRCP [6] Thus, the VSCT and SRCP transmit signals to the cerebellum about the activity of intraspinal mechanisms These signals monitor mainly the activity of the rhythm generator rather than that of the output spinal mechanism This has been demonstrated by experiments with cooling and lesions of the spinal cord [9]

Thus, two kinds of messages come from the spinal cord to the cerebellum those concerning the operation of the rhythm generator (through the VSCT and SRCP) and those concerning the current state of the peripheral motor apparatus (through the DSCT) It is on the basis of these signals that the activity of the cerebellum and other brain centres related with it is organized While studying rhythmic signals coming from the brainstem to the spinal cord through the reticulo-, vestibulo-, and rubro-spinal tracts, it was demonstrated that they are produced on the basis of a „generalized picture" of operation of the spinal generator(s)

which is conveyed to the cerebellum through the VSCT and SRCP [6-9,68,69] In this connection, a hypothesis has been advanced that while interacting with one another, each motor center considers the essential data only concerning the state of the other centres The „essentiality" of data depends on the concrete motor and behavioral task [8,9] This essential data coupling lies somehow in the line of coupling by rhythmicity of neuronal networks.

Putative descending systems for activation of spinal pattern generators

In animals, locomotor regions of the brainstem are the subthalamic and mesencephalic locomotor regions and the pontomedullary locomotor strip [34] The locomotor column is a polysynaptic pathway

The three descending systems are the polysynaptic pathway of the bulbospinal pathway, the reticulospinal tract, originating in the reticular formation of the lower brainstem and pathing through the ventrolateral funiculus, and the monoaminergic descending system

Gelfand et al. [34] believe that the effects of the three descending systems supply one another Possibly, each of them is addressed to its own targets in the spinal cord and supplies locomotion with a certain „color" by changing, for example, the tonic component of stepping, or influencing different types of neurons in the stepping generator, or affecting those inhibitory neurons which tonically repress activity of the generator In particular, the reticulospinal tract, by projecting monosynaptically to certain flexor motoneurons [101], could enhance their excitability without interfering with the rhythm generator The vestibulospinal tract could play a similar role in relation to extensor motoneurons [68,69] There are parts of the brainstem (the rostroventral portion of the midbrain, as well as dorsal and ventral midsagittal areas of the pons) which do not elicit locomotion themselves but influence, essentially, the possibility of its elicitation [65,102] The command tonic signal, activating the spinal generator of cyclic movements, is a flow of impulses in a great number of descending fibres, and the effect of this flow depends, for example, on the degree of synchronization between neurons, projecting to the common targets Certain nervous mechanisms can be explained provided that a large number of neurons involved are considered One example is „the distributed rhythm generator" the definition means that the generator consits of many neurons, and this is its essential feature Another example is a group of spinal neurons which are recruited in a proper order during the cycle (Fig 6 of Ref [34]) A third example is a polysynaptic system of propagation of activity from the locomotor region of the brainstem to spinal stepping generators [34]

These animal data are of some help to the understanding of the improvement of the supraspinal control in our tetraparetic patient During 6 weeks of training, also the voluntary power of muscles increased, which may not only be attributed to a recovery of tract fibres If different descending systems can supply one another then training-induced reorganization of the brainstem neuronal networks could have given rise to a more balanced (unbalanced due to the lesion) and therefore more effective supraspinal drive Further, the patient had problems in flexing his left leg During running exercise, the trainer vocally stimulated the pati-

ent in phase with the stepping cycle to flex the leg (see above) The patient had the impression that it helped a bit to flex better the left leg and to get better into the rhythm of running When a good running rhythm was reached, the patient felt the support by the spinal pattern generators („it went better by itself") It is of value to know the descending system, including that part which indirectly elicits locomotion, to optimize the remaining supraspinal drive, best by biological means, including a transient pharmacological intervention

Similarity between oscillator formation training and the Bobath therapy of hemiplegia

In incomplete cervical spinal cord lesion, there is a deterioration in the organization (functioning) of spinal neuronal networks (as measured by the premotor spinal oscillators [90,96]) due to nonuse, but there is nearly no neuron soma cell death Supraspinal centres are mainly unaffected because there is no lesion The grey and white matter of the cervical cord are lesioned, so that the arms lose power (and coordination) and the supraspinal drive of lumbosacral networks is strongly reduced and unbalanced, and also the afferent input to supraspinal centres is strongly reduced The oscillator formation training tries to re-preformate the lumbosacral neuronal networks by a natural rhythm training with a synchronization of the pattern generators for each jumping cycle of the right and left leg, to induce re-preformation by movement-induced afferent input, and to improve the activation of the left-sided pattern generator by inducing „Mitbewegungen" The lumbosacral neuronal network is forced to useful organization by the afferent input On the other hand, the physiological functioning supraspinal neuronal networks can send physiologic natural impulse pattern to the movement pattern generators of the lumbosacral spinal cord for movement However, because of the unbalanced lesion of the ascending and descending tract fibres, supraspinal centres get false sensory information (but normal pattern in the remaining fibres) from the periphery and probably send pathologic impulse patterns to the periphery These impulse patterns altered by the reduced and unbalanced sensory information reach the lumbosacral network, again strongly reduced and unbalanced because of the lesion of the descending fibres The descending control includes that of the afferents performed by primary afferent depolarization (PAD) [67] Therefore, supraspinal centres have to be forced to relearn their task by plasticity With the information they get from ascending fibres they have to supply the lumbosacral cord with a message that the most possible physiologic movements are generated To give a simple strong drive to supraspinal centres, rhythmic stereotyped dynamic movements have to be performed which need only little drive from supraspinal centres The input from the eyes concerning the state of movement will additionally supply very important input for supraspinal adaptation, especially because the eyes are a part of the brain, and their input to the supraspinal centres is not altered by the lesion of the spinal cord Unnatural movements, such as walking on a treadmill, may not be as advantageous for readaptation of supraspinal centres, since unnatural afferent input is fed to supraspinal centres (see below)

Now, the question arises how few fibres are needed to enable stereotyped movements Kimura et al [51] argue with respect to the self-organization of walking patterns of insects

that the aims of the locomotion of animals are direction and velocity In order to achieve these aims, the animals must adapt their locomotion to unpredictable changes in the external world, which requires rapid and flexible information processing If the brain were responsible for integrating all input from sensory organs and for producing all behavioral information, it would take much more time and a much greater capacity for information processing However, information generated in the brain may not have one-to one correspondence with each effector organ because the number of neurons descending from the brain is far less than the number of effector organs This indicates that the lower center, the central pattern generator, self-organizes the information to move the effector organs using this limited information from the brain Generally, in order to self-organize some order in the system, it is necessary to have some constraints on the system This suggests that the information on the locomotion generated in the brain might act as a constraint on the central pattern generator [51] The dynamic properties of muscle contraction may be of great importance in helping to self-organize the walking pattern, because it is advantageous for animals and humans to walk efficiently Muscles contract with a distinct relationship between the shortening velocity (V) and the force generation (P), called the P-V relation [43] Kimura et al proposed „the least dissatisfaction for the greatest number of elements" rule A rule of this type seems to be necessary for biological systems to self-organize a spatio-temporal pattern to achieve some purpose To walk efficiently, afferent input to different levels is necessary

For rhythmical stereotyped dynamical movements we expect least tonic drive from supraspinal centres for movement activation In the competition for pattern self-organization in the lumbosacral cord, between movement-induced sensory input and internal patterns generation by descending control we pushed the equilibrium to the sensory input side and forced the supraspinal centres to re-adapt

Stereotyped movements can only be recruited from the spinal cord if the patient is brought into rhythmic and stereotyped movements (movement initiation problem) Therefore, it must be tried to make the poorly movable leg to move better by training and „Mitbewegungen" rather than to worsen the situation by nonuse or to put too much emphasis on the use of the better side If the spine stabilization allows limited training, it has to be started, to prevent re-preformation of neuronal networks for nonuse

In the treatment of hemiplegia according to Bobath [16] the treatment also has to be started as early as possible, and also the ill side has to be included in the training program rather than letting its functional potentials drift away An overcompensation of the healthy side has to be avoided as much as possible The ill side has to be prepared for future usage The problem does not reside in the lack of muscle power on the ill side, but in bringing the voluntary neuronal activation to the muscles for senseful natural movements Natural movements have to be tried and abnormal patterns to be reduced and spasticity of the muscles avoided as much as possible [16]

In hemiplegia, supraspinal centres on one side are damaged and the descending fibres are falsely or not at all activated, and the healthy side has to take over for repair and function In incomplete cervical spinal lesions, the lower cord is undamaged (it only shows functi-

onal drifting away because of nonuse) and the cord gets the physiologic input from the periphery (legs), the supraspinal centres are undamaged and get physiologic input from the eyes and ears By different rhythm training programs, the remaining few unbalanced ascending and descending tract fibres have to be „reconnected", which takes place by re-preformation of neuronal networks of the lower cord and of supraspinal centres More plasticity for re-preformation can be expected in supraspinal centres In the human CNS, there is an enormous capacity to establish connections from supraspinal centres to the cord for spinal control and for separation of movements and muscle activations (contergan-babies (nearly no arms) can practically learn to do everything with their feet, what normal individuals do with their hands (women can cook with the feet!)) A very small number of these tract fibres are used for the simple „primitive" stereotyped movements, which are of vital importance for the patient

In hemiplegia, the cord and one side of the brain are undamaged, but there are plenty of pathways, which connect both sides of the brain In the process of training, it may be worthwhile to relearn rhythmic stereotyperd dynamic movements first, because only little tonic drive is needed In the reorganization of the damaged brain side by the healthy side, the functionally easy end of brain functions can be taken first, namely those where there is only little drive necessary because the functions are mainly located in the spinal cord

The human CNS can only be changed on the long term Re-preformation will take weeks up to months, and since there is indication for recovery of descending control after even a few years, the oscillator formation training may make sense even long after the injury

Normal gait versus walking on a treadmill

Frequently, walking on a treadmill is used in the treatment of incomplete spinal cord lesions Improvements in locomotion are reported [26,116] Some differences between normal gait and treadmill walking are given here [118] Changes in visual inputs (see above) and activation of muscle spindles are not tackled

When walking on a level ground (normal walking), the body pivots, like an inverse pendulum, over the foot which acts as a fulcrum In contrast, during treadmill walking the foot is passively moved backward under the trunk The supporting leg moves like a pendulum accelerated backward by the treadmill belt

During stance phase in normal walking, the motor pattern of the stance leg is different from that observed on a treadmill Some subjects with „upper motor neuron lesion" or balance deficits are able to walk on a level ground but are unable to walk on a treadmill even at the same or slower speed

In stance, the braking activity (power absorption) of tibialis anterior and extensor digitorum longus muscles is increased by the treadmill As the knee tends to flex more from initial contact to mid stance the power generation by the quadriceps muscle is greater and lasts longer After the foot has passed behind the trunk, it continues to travel backwards until the knee reaches full extension Excentric activity of the hip flexors controls hip extension in

pre-swing Initiation of the swing phase depends on concentric activity of the hip flexors Thereafter in swing, there are no major differences when compared to normal gait During normal gait forward progression is dependent on the power generated by the calf muscles in mid and terminal stance Although even the speed is the same, the differences in muscle activities (timing, on-off periods, or time of peak activity) cquld be considered as minor, the motor program is not the same for the two types of movement The main differences occur for movements in the sagittal plane There are no major differences in muscle moment and power in the hip abductors between normal and treadmill walking

Pathologic activation of two-joint muscles

The essential limitation of our patient for further progress was that he only could flex little the left knee The rectus femoris muscle was activated permanently with phasic activity intermingled (Fig 13) This pathologic activation of the rectus femoris muscle was probably strongly exaggerated upon running for longer distances, and terminated running and other locomotions

In an earlier paper, this nearly permanent activation of the two-joint rectus femoris muscle was related to a false coupling of spinal oscillators [96] Physiologic self-organized premotor spinal oscillators seem to have two coupling phases during an oscillation cycle per somatic nervous system, and they get afferent and supraspinal drive through one of these phase input channels during locomotion With the deterioration of oscillator functions following spinal cord lesion, most of the premotor spinal oscillators driving the rectus femoris muscle motor units probably obtained coupling drive from other oscillators during both coupling phases, because of the partial loss of the coordinating system and the stabilizing sensory feedback, so that the rectus femoris muscle was nearly permanently activated and the knee could not be flexed any more The nearly permanent activation of the rectus femoris muscle could mainly be generated by a false organization of the spinal motor program or by a false drive of the descending activation and control system It will be shown now that the main cause for the permanent activation of the rectus femoris probably was a pathologic drive of, or synchronization with, the descending control and activation system

In newborns, primary stepping is elicited by stimulating the soles of their feet Probably, the neuronal networks which organize this automatic motor program for stepping are mainly located in the spinal cord, in similarity to the micturition reflex in infants [25]

Infants who suffered cerebral palsy, e g one month after the birth, will show physiologic primary automatic stepping at birth The voluntary stepping normally occurring 11 month after the birth, will be delayed and pathologic The interesting question is, whether or not automatic primary stepping becomes pathologic at cerebral or spinal lesion occurring after one month? It was questioned earlier [95], whether automatic micturition becomes pathological, when the infant suffers a spinal lesion one year after the birth (voluntary micturition occurs normally 2 years after the birth) If automatic stepping or micturition became pathologic, then automatic micturition or stepping would already have some supraspinal control

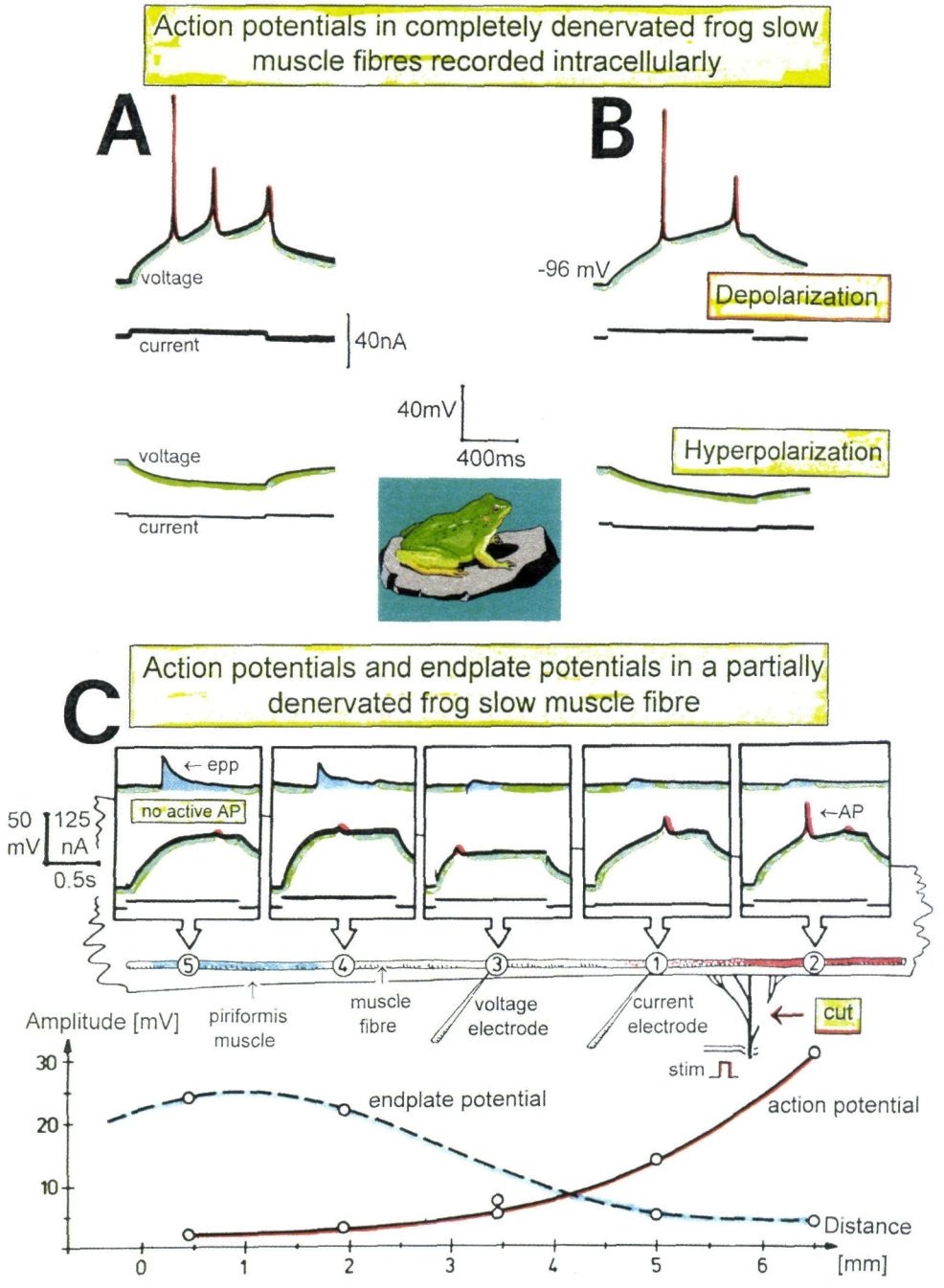
Action potentials in completely denervated frog slow muscle fibres recorded intracellularly
A
B
voltage
current
40nA
-96 mV
Depolarization
40mV
400ms
voltage
current
Hyperpolarization
C
Action potentials and endplate potentials in a partially denervated frog slow muscle fibre
← epp
no active AP
←AP
50 mV
125 nA
0.5s
5
4
3
1
2
piriformis muscle
muscle fibre
voltage electrode
current electrode
cut
stim
Amplitude [mV]
30
20
10
endplate potential
action potential
Distance
0
1
2
3
4
5
6
[mm]

Figure 21. Simultaneous occurrence of action potentials (APs) and endplate potentials in slow muscle fibres of the frog Rana temporaria Slow muscle fibres of frogs normally do not generate APs to depolarize the muscle fibre to increase Ca^{2+} concentration for contraction, the slow muscle fibres are depolarized by the endplate potentials of several distributed endplates connected to one or two thin motor axons When impaling a voltage and a current microelectrode into the slow muscle fibre (C) and applying constant current, the membrane resting potential can be hold at -90 or -100 mV Upon applying an additional current pulse for 100 ms, the muscle fibre can be transiently depolarized or hyperpolarized When hyperpolarizing the muscle fibre, the slow membrane potential deflection indicates high membrane resistance (≈10 MΩ) typical for slow muscle fibres Twitch muscle fibres (not shown here) show a faster time course and have a lower membrane resistance (≈1 MΩ) When depolarizing a normal slow muscle fibre by a depolarizing current pulse, no AP is generated (similarly to voltage electrode impaling site 5 in C) When depolarizing a denervated slow muscle fibre (cut nerve supply to the muscle), after 10 to 15 days the frog (held at ≈ 18°C) slow muscle fibres generating APs similarly as in A and B Upon partial denervation of a slow muscle fibre (C), which is innervated by two motor axons one of which is cut, the innervated muscle fibre part responds with a motor endplate potential (and no AP), and the denervated muscle fibre part with an AP (and no endplate potential) The AP and the endplate potential will spread electrotonically (passively) to other parts of the muscle fibre (lower part of C) It seems therefore that the different parts of the muscle fibre are genetically differently controlled by the different muscle fibre nuclei

A,B. APs generated in denervated slow muscle fibres of frog piriformis muscles upon depolarization by transient current pulses of 100 ms duration The slow time course of the voltage upon hyperpolarizing the fibre shows that the microelectrodes were impaled into slow muscle fibres With increasing depolarizing current pulses (and fully developed AP mechanism) first one AP is mostly generated (C, impaling site 2), then 2 APs (B), and then 3 APs (A) (in this case only shown for 3 different fibres) Note with respect to the relative length of the interspike intervals that the 2 AP impulse train in B and the 3 AP impulse train in A bear similarity to the impulse trains recorded from oscillatory firing human (2-motoneuron axons

C. Recording of APs and endplate potentials along a partially denervated slow muscle fibre by keeping the current microelectrode at site 1 (close to the nerve entrance to the piriformis muscle) and impaling the voltage electrode successively along the muscle fibre from site 1 to site 5 At each site of the voltage electrode impalement, the muscle fibre is directly stimulated by the current pulse from the current electrode (the reference bath electrode is not shown, muscle in frog Ringer solution) to elicite an AP, and indirectly stimulated, by applying to the nerve supplying the muscle a voltage pulse of 0 5 ms duration and 1 to 10 V in amplitude, to elicite an endplate potential The results of both stimulations are shown in the pictures related to the sites of successive impalements of the voltage electrode

In the partially denervated slow muscle fibre (C), the endplate potential did not elicit any AP generated in the other denervated part of the muscle fibre But often, the endplate potential evoked in the still innervated muscle fibre part (here left side) is still high enough in the denervated muscle fibre part (here right side) to elicit an AP there, which is then actively conducted in the denervated area of the muscle fibre, and spreads electrotonically (passively) into the innervated muscle fibre part - This animal example shows how delicately membrane properties can change on the cellular level with functional consequences, which cannot be understood with molecular, genetical or pharmacological methods alone Avoiding regeneration, it seems possible to increase by training the size of one or two left synapses [120] in the innervated area of the muscle fibre, so that the endplate potentials can generally reach the threshold for AP generation in the denervated muscle fibre segment It is conceivable that similar mechanisms are working in the human CNS, e g with respect to the integrated functions of dendrites (apart for electrotonic potential spread), cell soma (summing point) and axon hillock (AP generation for active conduction along the axon), when changing neuronal network properties by re-preformation of the neuronal network structures due to changes in efficacy and properties of synapses and changes of the excitability of membranes

Since most likely, the descending and the ascending tracts of the injured spinal cord in our patient had a pathologic composition, it was the descending driving and control system that induced the pathologic activation pattern of the rectus femoris muscle

This reasoning is supported by the functional outcome following hemiplegia in adults Following hemiplegia, the spinal neuronal networks and the descending and the ascending tract fibres are mainly undamaged The pathologic organization of the spinal networks to generate pathologic motor programs, e g , false activation of two-joint muscles are mainly caused by a pathologic drive through the descending tract fibres

In incomplete higher spinal cord lesions (sub C5 to sub TH6 [96]), the spinal networks deteriorate and are functioning pathologically One measure for pathologic self-organization are the spinal oscillators (subunits of the system for high activity self-organization) which deteriorated in their functioning Supraspinal centres are not lesioned However, because of the unbalanced lesion of the descending and the ascending tract fibres, additional supraspinal centres will pathologically activate spinal centres

In incomplete spinal lesion, it seems therefore that the drifting of spinal cord functions is caused by the deterioration of spinal networks, whereas the completely false activation of two-joint muscles is induced by physiologic and pathologic functioning of supraspinal centres due to the unbalanced lesion of the ascending and the descending tract fibres

Since most network plasticity can be expected in supraspinal centres it should be possible to retrain supraspinal centres to improve spinal cord functions in general, and cord drive for the activation of two-joint muscles in particular Movements are most beneficial which are mainly generated in the networks of the cord, namely rhythmic dynamic stereotyped movements such as running or jumping, because little descending control is necessary Since the movement-induced afferent input stabilizes or partly induces the movement, strong physiologic movement-induced afferent input (dynamic movement) will be beneficial

Similarity between ontogenesis and lesion-induced reinnervation in frog muscles

In the frog Rana temporaria it has been shown that following denervation (cutting of muscle nerves), the lesion-induced reinnervation of the piriformis muscle [62,80] is very similar to the innervation of the piriformis muscle [81] during ontogenesis

During the metamorphosis from the tadpole to the frog, thin and thickly myelinated motor axons innervate slow and twitch muscle fibres respectively But since the thick motor fibres grow faster than the thin ones, they innervate their own twitch muscle fibre type, but also transiently the slow muscle fibres, which in the adult animal are innervated by the thin motor axons The slow muscle fibres, controlled by the wrong fast axons, show functional similarity to the twitch muscle fibres With the reaching of the muscle by the slowly growing thin motor axons, the slow muscle fibres become now selectively innervated by their own slowly conducting thin axons, and change their functional properties to those of slow muscle fibres, namely fatigue resistancy and no excitability of the muscle fibre membrane (no AP generating mechanism) Since the functional control of the slow muscle fibres only concerns

the excitability of the membrane and the speed and fatiguability of contraction, the slow muscle fibres can always be distinguished from the twitch fibres by their passive membrane properties (see lower traces of Fig 21A,B for the slow time course of the membrane potential of the slow muscle fibres following a hyperpolarizing current pulse) and their structural properties in electron microscopy pictures

Similarly, following denervation in adult frogs, the thick motor fibres grow faster than the thin axons, and they reinnervate both twitch and slow muscle fibres, and turn the slow muscle fibres functionally into twitch muscle fibres With the arrival of the slowly conducting slowly regenerating thin axons which selectively innervate the slow muscle fibres, the slow muscle fibres become slowlier and fatigue resistant again, and the muscle fibre membrane loses its AP generating mechanism

Control of partially denervated frog slow muscle fibres as one possible model for lesion-induced synaptic plasticity in the CNS

A slow muscle fibre, innervated by two thin motor axons, one of which is cut, can therefore comprise a segment which responds with endplate potentials to nerve stimulation and no AP generating mechanism (left side of Fig 21C, small APs occur because of electrotonic spread) and another segment which responds with an AP to direct stimulation (current application) and no endplate potential upon nerve stimulation (right side of Fig 21C, small endplate potentials are due to electrotonic spread) The incorporation of the AP generating mechanism starts around the denervated slow muscle fibre endplate(s)

This animal model, even though phylogenetically distant from man, is of importance for several reasons First, it clearly shows a close similarity between the innervation of muscles during ontogenesis and during their lesion-induced reinnervation following denervation Second, it shows that maturation of muscle fibre functions depends also on the growing speed of the different kinds of motor axons Thirdly, muscle fibres are functionally controlled by their innervating extrafusal motor axon type Fourth, under certain conditions, motoneurons can control parts of muscle fibres Fifth, similar control or regulatory mechanisms may work in interactions between neurons in the CNS with respect to the integrated functions of synapses on dendrites, cell soma and axon hillock, when neuronal networks are re-preformated in a rhythm training, namely by the size of endplate potentials [120] generated in dendrites (size of synapse), the distance for the electrotonic spread (length of a dendrite) to the summing point (soma), and the membrane excitability (axon hillock) Synapses may even migrate [120] in direction of the soma for higher efficacy or partly change the transmitter substance For other details, see legend to Fig 21

If there is similarity in the peripheral nervous system between ontogenesis and lesion-induced reinnervation (adaptation), there also may be similarities between the development of infants and lesion-induced adaptation of the CNS in adult man It seems therefore worthwhile to compare the development of infants with the lesion-induced adaptation of the nervous system in patients with an incomplete spinal cord lesion (see below)

Further, the functional control of muscle fibres by the type of the innervating motor axon is of importance when, in high spinal cord lesion, the phrenic nerves are electrically stimulated for breathing, since the trophic substance and the impulse patterns of motor axons control muscle fibre functions The pattern of electrical stimulation will most likely influence the functional properties of the muscle fibres of the diaphragm

The theoretical model of neural maturation and the system theory of infant motor development

There are two theories of infant motor development the model of neural maturation and the system approach [73]

Four assumptions chatacterize the model of neural maturation

1 Movement progresses from primitive, mass movement reflex patterns to voluntary, controlled movement
2 Motor development progresses in cephalo-caudal direction
3 Movement is first controlled proximally and then distally
4 The sequence of motor development is consistent among infants, and the rate of motor development is consistent for each infant

Within the model of neural maturation, the neonate"s movement patterns are interpreted as being initially dominated by reflexes such as the plantar and palmar grasp, the asymmetrical tonic neck reflex, primary stepping, the tonic labyrinthine reflex, the Moro reflex, and rooting These movements operate in a stimulus-response fashion, with the appropriate stimulus eliciting a predictable, stereotyped response [31]

Primitive reflexes are assumed to represent the dominance of lower levels of the CNS - the subcortical nuclei located in the brainstem Similarly, the integration of these early reflexes is perceived so as to indicate maturation of the CNS and inhibition of the lower centers by the higher, functioning cerebral cortex Motor skills have been hypothesized to emerge in cephalocaudal direction, motor control has been described as proceeding in proximal-distal direction The theory of neural maturation of motor development is based on an intrinsically driven, maturational model controlled by the cerebral cortex It provides the rationale for many of the therapeutic strategies used extensively by pediatric therapists

Within the framework of the theory of neural maturation of motor development, reflexes are described as stereotyped responses to external stimuli, and their integration indicates inhibition of lower brainstem centers by the cerebral cortex Touwen [110] preferred the term reaction over reflex, and queried the stimulus-response definition He argued that the brain is capable of spontaneously generating its own activity, therefore, reactions may not be stimuli-dependent He also questioned the description of reflexes as being stereotyped, and suggested that a normal neonate can respond to the same stimulus with a variety of motor responses He concluded that the early reflexes of newborns cannot be compared with the reflexes present in neurologically damaged infants and adults or with the reflexes present in decerebrated animals The responses of healthy newborns were characterized by variability

rather than stereotyped responses This concept of normal variability of primitive reflexes is contrary to that put forward by the model of neural maturation Zelazo [119] demonstrated that primary stepping movements (primary stepping lasts from birth (or before) till 1 5 to 6 months after birth (contradictory reports), voluntary stepping starts approximately 11 months post partum) can be maintained with continued pratice Infants whose parents supported their bodies and stimulated stepping for 8 minutes daily retained the movement longer than did a comparable group of infants who received either passive exercise or no exercise at all The results of the above author suggest that primary stepping can be retained with practice, and its disappearance is not totally dependent upon cortical maturation Based on these infants demonstrating stepping skills before adequate trunk control had developed, Zelazo also questioned the validity of the assumption of motor developing in cephalocaudal direction He proposed that the cephalocaudal assumption may be based on cultural biases of motor development Thelen and Fisher [107] questioned the accepted explanation that primary stepping disappears because of the inhibition of the lower centers in the CNS Rather, they attributed the disappearance of primary stepping to biomechanical factors

Critical limitation exists in adopting the neuromaturational theory of motor development as the foundation for therapeutic treatment principles Within the model of neural maturation, all changes in motor bahavior are viewed as intrinsically driven, the environment has minimum impact on evolving motor skills The rate, quality, and sequence of motor skills are genetically predetermined Since treatment represents a form of environmental manipulation, it cannot be assumed from the model of neural maturation that treatment is capable of either changing a motor behavior or having an impact on the CNS It is contrary to the model of neural maturation to surmise that damage to the cerebral cortex can be modified by external factors Yet, this is precisely what therapy advocates, motor output can be influenced by more normal sensory and motor cue input In fact, intervention is the antithesis of the hierarchical, cerebral cortex-dominated framework associated with the model of neural maturation

The system theory encompasses all areas of development and has been derived from developmental psychology Researchers involved in the natural sciences observed that when elements of a system work together, certain behaviors or properties emerge that cannot be predicted from the elements separately A new behavior is constructed, which is dependent on the input of all the contributors in the system This behavior may have characteristics that could not have been determined by evaluating the contributing behaviors individually [108] Bernstein [12] observed that joints and muscles never work in isolation but rather in coordinated patterns Muscle synergies are a familiar concept for clinicians using the exercise technique of „proprioceptive neuromuscular facilitation" (PNF), in which muscles are strengthened and recruited in functional patterns rather than individually Bernstein postulated that the brain controls muscle groups rather than individual units He further suggested that the muscle synergy itself is able to autonomously modify a movement independent of, or at least not totally controlled by, higher centres of the CNS That is, a group of muscles, bones, and tendons can modulate a motor behavior without receiving instructions from the cerebral cor-

tex This concept is in contrast to the hierarchical, intrinsic structure of the model of neural maturation

The theory of neural maturation concerning development evolved from a prescriptive, structural framework in which instructions controlling movement exist before the motor behavior emerges The instructions are encoded in the CNS, and the higher centers control movement by a „feedback" system, all modifications to a movement must originate from the cerebral cortex - the command centre In contrast, the system approach is developed from a functional rather than a structural framework Within this framework, the behavior itself can affect and modify the resulting behavior in contrast to all the commands being issued by the cerebral cortex This model exemplifies a „feedforward system" that is self-correcting en route rather than hardwired from the cerebral cortex It also implies that all factors contributing to the motor behavior are important and exert an influence on the outcome Both of these assumptions are implicit in the dynamic motor theory arising from the systems structure [108]

The dynamic motor theory also recognizes the maturational level of the CNS as an important component for the success of the task, but it is not the only factor Other variables influencing the final motor behavior include the emotional state of the infant, the degree of motivation, cognitive awareness, the infant's posture while attempting to reach, muscle strength, and mechanical leverages (in similarity to the final motor behavior in incomplete spinal lesion)

As shown in the animal model above, motor control in proximal - distal direction can be explained at least partly by the growing of nerve fibres Proximal muscles are reached and innervated before distal muscles Different growing speeds of nerve fibres may even give rise to transient functional changes Such arguments may also hold for the growing of spinal tract fibres

Similarity between the system theory of infant motor development and the self organization of the adult human CNS

The self-organization of neuronal networks of the adult human CNS is similar to the system theory of infant motor development, namely that the CNS is not hardwired and that the motor behaviors are not intrinsically driven by the CNS in a feedback manner Similar is further that, in addition to the vertical pathways terminating in the cerebral cortex, there must be horizontal motor control mechanisms

But whereas the system theory is derived from developmental psychology, the principles of self-organization are derived from human simultaneous natural impulse patterns of afferents and efferents, which means from measurements with basic methods of natural sciences The organization to premotor spinal oscillators and the coupling of oscillators for generating integrative motor functions can even partly be measured non-invasively by electromyography with surface electrodes

Similarity between automatic micturition and automatic stepping in infants and spinal cord-lesioned patients

Micturition in infants is automatic (Fig 4 of [25]) till to approximately 2 years Then, supraspinal centers take over Following spinal cord lesion, the automatic micturition is not re-established again The detrusor (parasympathetic nervous system) and the striated external sphincter (somatic nervous system) do not cooperate in a coordinated way Detrusor-sphincter dyssynergia occurs [25,94] Similarly, infants step automatically till 1 5 to 6 months post partum (neuropediatricians differ in their opinions) Then, supraspinal centres take over, and volitional stepping occurs 11 months post partum Following complete spinal cord lesion, the automatic running, when stimulating the sole of the foot, is not re-established

It seems therefore that with the establishment of the supraspinal control the spinal neuronal networks, generating automatic micturition and automatic stepping, have changed Probably, the neuronal networks became more complex and in this way also more instable with the ongoing ontogenesis, in similarity with the ongoing phylogenesis The price for the increased complexity of functioning seems to be instability when the supraspinal control and stabilization is removed due to spinal cord lesion

Since no detrusor-sphincter dyssynergia could be found in a brain-dead individual [95], further human measurements are needed to clarify automatic and voluntary micturition In the system theory of infant development above the explanation of automatic functions by reflexes was questioned

The training of rhythmic, stereotyped dynamic movements can be expected to be most beneficial since firstly, those movements use the same principles as does network organization (namely rhythmicity), secondly, they recruit ontogenetically predetermined network functions of the spinal cord (former automatic stepping organization in infants according to the afferent input from the soles of the feet), and since thirdly, those rhythmic, dynamic stereotyped movements will induce most strongly movement-related afferent input which stabilizes and partly organizes spinal cord movement network organizations as was shown by the induction of co movement By changing, for example, synaptic strength, long-term training will imprint these most fundametal movement functions more strongly

Gravity has an impact on an infant's development from the moment of birth, and all movement during the first year of life involves gaining greater control against gravity Increasing postural control permits an infant to overcome the forces of gravity, thus lack of postural control can be viewed as a limiting factor preventing the appearance of more mature motor skills The „liberated movement activities" of Amiel-Tison and Grenier [2] support this view Using this technique, the infant's lack of head control is compensated for by manual support of the head Under the influence of this artificial postural control, more mature skills emerge From these results it can be argued that these motor capabilities are present at birth, but because of gravitational force they do not emerge until postural control has matured to counteract the influence of gravity Gravity probably has a similar impact on the adap-

tation of the nervous system of spine-lesioned patient with respect to the vertical position from the moment of the lesion. The patient's lack of head and body control has to be compensated for by manual or other support. In particular, in incomplete spinal lesions the recovery of leg movement starts with the toes and the feet, often before trunk control.

In similarity to infants' development, all subsystems contribute to the enhancement or delay of motor behavior. Palmer et al. [70] found that infants with cerebral palsy participating in a stimulation program achieved higher scores than a comparable group of infants receiving physical therapy only.

Pedriatic therapists have long claimed that no two children with a diagnosis of cerebral palsy are alike; the system approach suggests that no two treatment approaches should be alike. If treatment strategies become more personalized and adjusted to the needs of individual infants, it will become more difficult to evaluate the effectiveness of any one treatment program. This is exactly what also holds for the treatment in incomplete spinal lesions. Since no two spinal lesions are alike, treatment strategies have to be personalized, and it becomes difficult to evaluate the effectiveness of any one treatment program.

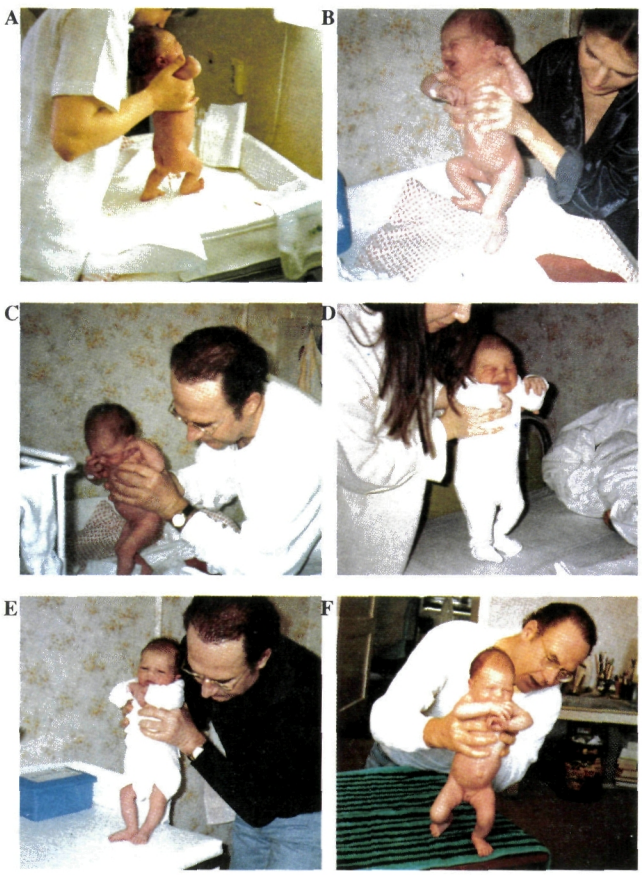

Figure 22. A. Primary automatic stepping in a 5 days old infant with a slight backward posture; the heel touches the ground first.

B. The mother holding her baby; the left leg lifts up for forward movement; the ankle, knee and hip joints are strongly flexed; infant 5 days old.

C. The newborn infant (5 days old) is supported in a forward posture (by the author G.S.); it seems as if the forefoot is touching the ground first.

D. Same newborn (2 days old) with clothes on; no primary stepping can be induced.

E. With bare legs, rudimentary primary stepping can only be induced (infant 3 days old).

F. Primary automatic stepping in an 8 days old infant at home, supported by the researcher.

Primary stepping as the precursor for later walking and running

In a 5 days old naked infant, primary automatic stepping was induced (a larger group of newborns, see Results), whith the soles of the feet touching the ground and the body manually supported (Fig.22A,B,F). When the trunk was slightly backward, the heal touched first the ground (Fig.22A). With roling over to the forefoot, the other leg was lifted (Fig.22B). The movement of one leg was therefore determined by the moving status of the other one. If the infant's body was slightly inclined forward (Fig.22C), the primary stepping seemed to be slightly different. Sometimes, the forefoot touched the ground first. Further analyses are necessary to see whether there are really two kinds of primary stepping. If there are two kinds of primary stepping or a whole spectrum of stepping modifications, then there would be similarities to the two different kinds of walking or different kinds of locomotions in adults. If adults walk with the trunk backward, then during walking the heal strikes first the ground. But with the trunk in a forward position, the adult will first touch the ground with the forefoot. If there really are two kinds of primary stepping, then they would be the precursors of the two later kinds of walking.

On the other hand, during primary stepping the ankle, knee and hip joints were flexed by 90° or more. In comparison to the walking and running of the patient with the incomplete spinal cord lesion (Fig.2), the strong flexion of the ankle, knee and the hip joints are more similar to running than to walking (especially compare Fig.2G with Fig.2H). It could therefore also be that there is only one kind of primary stepping in infants which is the precursor of the different kinds of walking and running generated mainly in the spinal cord. It would be interesting to follow up the different kinds of bipedal locomotion from the primary automatic stepping of newborns to the volitional stepping of infants via the locomotion of children to the different kinds of bipedal movements in adults.

The adequate afferent input patterns are essential for inducing primary stepping

With clothes on, it was not possible to induce primary stepping in the two-day-old infant (Fig.22D). With only the feet bared, it was only very little possible to induce primary stepping (Fig.22,E), regardless whether the infant was manually supported by his/her mother or the research worker (G.S.). In the Result section it was shown that all 7 healthy naked infants performed primary stepping, whereas only 2 out of 9 walked when barefoot. The induction of the primary stepping therefore depended on the clothing but not on the person who supported the newborn infant. The touch support with the hands seemed to give additional afferent input to facilitate locomotion. The infant therefore strongly differentiated between the afferent input induced by the clothes and the manual hand support and the hand grip with the naked hand. The optimal posture of the infant seemed to be only of secondary importance. The afferent input from the skin probably included the input patterns of the different myelinated and unmyelinated afferents for that crucial differentiation. Our incomplete

spinal cord lesioned patient also liberated the different kinds of locomotion better, when he felt the closeness of, and the safety provided by the trainer

Similarity between primary stepping of infants and Mitbewegung (co-movement) in an incompletely spinal cord lesioned patient

Thelen [122] described the patterned leg movements in newborns and young infants as a result of anatomical and neural structures that link the segments of one leg in a tight, co-active synergy At the initiation of a leg flexion, both flexors and extensors contract The extension phase of the movement is passive, produced by gravity and the inertial and elastic properties of the limb This early pattern is not similar to walking either in the phasing of the joints, in the pattern of muscle contraction or in the interplay of passive and active torques that produce movements Coordination between the two legs is dynamic rather than obligatory or rigid This means that the movement of one leg is determined by the moving status of the other one, and that the neural connections between them transmit this information The stability of the coupling between the legs changes during the development

Our observation on primary stepping is similar to some differences in the coupling between the right and the left leg Especially when the newborn infants were wearing clothes but had bare feet, when the primary stepping was partly inhibited, the touch of the ground by one leg initiated the lift off of the other leg (Fig 22B) and its forward movement When the forward moving leg did not terminate in the touch of the ground, the stepping stopped When the forward moving leg just succeeded to touch the ground, then the first leg lifted up and moved forward The touch of the ground by one leg seemed to represent the stimulus for a further half step cycle, and so on When the infants were wearing no clothes, and the stepping was not (partly) inhibited, they got into a stepping rhythm, and the initiation of the half step cycle could not be seen so well any more

Similar rhythmicity in running was observed in the patient with an incomplete spinal cord lesion When the patient got into a good running rhythm, then the running improved further With an improved rhythmicity and dynamicity in this stereotyped infant stepping movement, and probably with the remembrance of the former stepping cycle (see above for spinal cord memory), the self-organization of the spinal neuronal networks probably improved in organizing (with the movement-induced afferent input) the primary stepping pattern

The interesting point is here the slightly inhibited stepping The touch of the ground by one leg seems to drive the next half stepping cycle This movement induction is similar to the Mitbewegung (co movement) of the poorly volitionally innervated leg by the better innervated leg best observable during chest-swimming in the partially spinal cord lesioned patient When the legs were not closed after the extension before flexion, then the poorly innervated leg made nearly no movement at all But when the patient closed the legs, so that the pattern generating network of both legs got additional simultaneous skin afferent input, then the poor leg also flexed and moved (this can be clearly seen on the videofilm) But the additional drive of the poorly volitionally innervated leg by the simultaneous afferent input

lasted only for a part of the swimming cycle or at best for one swimming cycle When after the next stretching (pushing), the legs were not closed again, then the poorly innervated leg did not further co-move

During the chest-swimming, the co-movement was induced by the additional simultaneous input from the skin of the legs which coupled the pattern generating neuronal networks of the left and right leg (macroscopic standpoint) or which enhanced the coupling of the propriospinal or premotor oscillators of both legs (Fig 20) (oscillator level of interpretation) or which increased the shared simultaneous afferent input of the interneurons and motoneurons, driving by self-organization the right or left leg for better coordination (cellular interpretation level)

For the initiation of the lift off (Fig 22B) and the forward movement of the infant's leg, mainly the afferent input from the other leg alone was sufficient (apart from some proprioceptive afferent input) It seems therefore that the coupling between right and left was stronglier in the primary stepping of the infant than during the swimming cycle of the incompletely spinal cord lesioned patient This would mean that with the maturing of the neuronal networks for stepping (including the splitting into several kinds of bipedal locomotion), the variability in bipedal locomotion increases, but also the instability increases, and therefore the need for stabilizing supraspinal control This is what Cohen [23] proposed with respect to the central pattern generator control of the limbs in animals during evolution, which may also hold for the ontogenetic development, namely the need for intrinsic control and the general lability of the coordinating system with ongoing ontogenesis This instability of the CNS organization following complete spinal cord lesion would previously be (with respect to the occurring incontinence) the life limiting factor in paraplegics [94,95]

Direct comparison between primary stepping of infants and rhythmic movements in a patient with an incomplete spinal cord lesion

In the few days old infants, automatic stepping was induced when the soles of their feet touched the ground and when the body was manually supported The stepping frequency was approximately 0 2 Hz The incompletely spinal cord lesioned patient induced walking running or jumping on the springboard volitionally The locomotor frequencies were higher, namely 0 8 Hz for walking, 1 5 Hz for running, and 0 9 Hz for jumping Further, the infants lifted the foot quickly, but the forward movement of the leg was comparably slow The spinal cord lesioned patient moved more like a normal adult, namely a quick lift off and a quick forward movement It may therefore be that the primary automatic stepping is very slow and the quick lift off of a leg before the forward movement was an avoidance reaction which activated the spinal pattern generator for primary automatic stepping Interesting is the report that a patient with an incomplete spinal cord lesion was able to run but not walk This observation supports the view that different kinds of locomotor patterns should be tried in old and young patients with lesioned CNS, and one should not argue that there is no need to try running as long as the walking pattern is not fully established Since „nonuse" of integrative

neuronal network functions seems not to be beneficial for the maintenance and the re-development of motor skills in spinal cord lesioned patients, locomotor patterns in infants and spinal cord lesioned patients should be trained before adequate trunk control is established or re-established

Difficult to understand is, why the primary automatic stepping is so slow, apart from the quick lift off The avoidance reaction when tickling the soles of the feet is quick It may therefore be that the neuronal network in the infant spinal cord (neuronal substrate for the generation of primary stepping) is immature It is unlikely that also in adult man the not supraspinally driven spinal pattern generators are so slow when activated by the movement-induced afferent input (if possible)

A young infant can loose its primary automatic stepping locomotion for a longer period of time following encephalitis. If further the induction of primary stepping depends on the condition of the infant, i e on the emotional state of the infant, the degree of motivation, cognitive awareness, the infant's supported posture and mechanical leverages, then it may be that the primary automatic stepping is not completely automatic Maybe, some tonic drive is already available from supraspinal centres If this is the case, then it becomes very important to compare the mainly spinal locomotion in infants with the mainly spinal locomotion in patients with high incomplete but severe spinal lesion, to find out the capabilities of the spinal cord and the possibilities for re-preformation of spinal networks and functional changes.

If the most important basic stereotyped rhythmic movements like walking or running are generated in the networks of the spinal cord, then there are more possibilities in the treatment of high spinal cord lesions and supraspinal lesions (hemiplegia, cerebral palsy), because the basic neuronal networks for locomotion are not damaged Via natural rhythmic stereotyped physiologic movements, Mitbewegungen (co-movement to improve locomotion of the poorly activable side) and movement-induced afferent input, the lesioned CNS of infants and adults has to be forced to reorganize its networks in such a way that physiologic movements of the legs and physiologic posture of the trunk emerge

Since afferent input stabilizes neuronal network organization, it should be tried to enhance the afferent input during primary stepping, e g by using deformable ground, to increase the afferent input in the stance phase, to see whether the primary stepping frequency can be increased Judging upon the slow speed of the forward movement, the swing phase is actually too slow for a swing In incompletely spinal cord lesioned patients, the locomotion can be improved by increasing the movement-induced afferent input (see above)

Oscillator properties in developing infants

With 0 2 Hz the stepping frequency was in the frequency range of spinal α_3-oscillators of adult humans The rhythms of α_3-oscillators could therefore contribute to the initiation and termination of the primary stepping cycle in newborn infants

First however, it has to be measured in infants how are the oscillator frequencies and

the firing patterns of premotor α_1, α_2 and α_3-oscillators It has to be seen how different their properties are with respect to adults The human classification scheme for the peripheral nerve fibre groups [96] will anyway be different, since in infants the conduction velocities of nerve fibres are lower and the growing and maturing nerve fibres are thinner Anyhow, the measuring of the premotor spinal oscillators from the firing of motor units of developing infants by EMG with surface electrodes may give details concerning the maturing of neuronal network organization

Vojta physiotherapy and oscillator formation training

The neuropediatrician V Vojta discovered in an empirical way the movement complexes of „reflex locomotion" [124] Global and automatic locomotion is provoked in infants by external stimuli This locomotion shows close similarities in coordination and differentiation of muscle function (more muscle chains become able to coordinate in various forms of contraction) with regard to the automatic control of posture and the uprighting mechanisms against gravity[125]

It is possible to provoke reflex locomotion with its different complexes of coordination, the so-called „reflex creeping" and „reflex turning" in newborns and adults These coordination complexes are inborn, already present at birth, and inducible from the delivery onwards The eliciting of these patterns of reflex locomotion only functions when 1) the patient lies in a certain position, 2) the stimuli are given on clearly defined body points (so-called „zones"), 3) these stimuli must have been experienced by the infant prenatally There are appro ximately 20 different positions, which are mainly variations of the three original positions, which are prone, side-lying and supine During the reflex locomotion the body always moves from a certain starting point into an end position This dynamic way means passing of many movement sequences, which in turn could be starting positions again

There are 9 zones where stimulation can be applied to provoke the pattern of reflex locomotion The stimulation of the points shows mainly an effect on the proprioceptors and the periost Pressure given is always three-dimesional and varies in intensity from patient to patient Each stimulus applied to the appropriate zone can be combined with other zones, so there are more than 10,000 combinations to elicit the whole complex of reflex locomotion [125] An important point in this physiotherapy of e g infantile cerebral palsy seems to be that „functional reversal" can be generated in all muscle chains Functional reversal of muscle chains means the ability to change the direction of the effect of muscle action, it means the replacement of a mobile point with a fix point in the muscle chains

A direct comparison to the oscillator formation training is only partly possible, since the oscillator formation training has a scientific basis (re-preformation of the spinal oscillators which may be generated by closed reverberatory self-excitatory synfire chains and which organize themselves to integrative functions by changing their relative coupling), and the Vojta physiotherapy (training functional complexes of the so-called reflex creeping and reflex turning) has no scientific basis, even though a somehow theoretical justification has been tried [122]

There are similarities between the Vojta therapy and the bipedal rhythm training (oscillator formation training) The tetrapedal (reflex creeping) and the bipedal locomotion (primary automatic stepping) can be elicited from birth on and they are therefore both genetically predetermined Primary stepping is more prominent at birth than creeping (see below) The bipedal primary stepping in infants is a precursor of later walking and/or running, and is different from walking, running and jumping in adults The tetrapedal creeping seems to partly fade away in adults, since young children seem to be better in tetrapedal locomotion, including creeping, and enjoy it also more than adults do How similar the reflex creeping in newborn infants and adults are has to be shown The disadvantage of the manually supported primary stepping is that the shoulder girdle and the trunk are only little trained The disadvantage of the reflex creeping and the reflex turning is that no continuous locomotion is trained, which is of high importance, since no rhythmic locomotion is generated, which would fit the organization principle of the human CNS, namely rhythmicity, and which is phylogenetically very old

During reflex creeping, induced by the therapist by stimulating the trigger zones, the body moves from a certain starting point into an end position, which in turn could be or actually is the starting position for another creep cycle part This partial creep cycle stimulation is similar to the partially inhibited primary stepping (infant only partly clothed) When touching the ground with the sole of one foot (best the heel), the other leg lifts up and moves forward and performs in this way a half step cycle When supporting the infant in the way that the other foot strikes the ground, a successive half step cycle will be induced, and so on But in the case of no inhibited primary stepping, i e when the infant is naked and is optimally manually supported, the primary stepping of half cycles becomes connected and the stepping becomes continuous and rhythmic with a frequency of up to 0 3 - 0 4 Hz As already pointed out above (Results), this rhythmically becoming primary automatic stepping shows similarity to the change from transiently oscillatory to continuously oscillatory firing of premotor human spinal oscillators It is the rhythmicity which gives the primary automatic stepping priority over reflex creeping It is difficult to see why in infants with CNS lesions the primary stepping is not trained or not tried to induce Neuropediatricians, supporting the Vojta therapy could probably argue that primary stepping fades away 6 weeks after the birth and is therefore not of much help for the treatment in the first year of life of the infant But firstly, it has been reported that the primary stepping lasts up to 6 months post partum [73], and secondly, it has been reported that if one trains primary automatic stepping in infants 8 min every day then the primary stepping fades away later than after 6 months [119], and may even go over into the volitional phase of stepping

The statement that coordinated locomotion without adequate body control and erection mechanisms is not possible in human locomotion development [125] has no given scientific basis As demonstrated in Fig 22, newborn babies can perform a somehow coordinated locomotion The coordination of the primary stepping locomotion even seems to improve with successive stepping cycles or stepping trials, since the spinal cord seems to have a memory for storing former movement patterns (see above, memory of the spinal cord) Anyhow, the

CNS in infants can be trained before adequate body control establishes, already W R Hess argued long ago that one should not think too mechanically (in this respect first trunk control and then limb movement) with respect to the functioning of the CNS

It has been stated that the Vojta physiotherapy is suitable for all patients with neuromuscular disorders and not just for cerebral palsy infants, as is often wrongly assumed [125] But how useful the Vojta therapy is for adult patients with neuromuscular disorders is still debatable First, the creeping of infants, especially young ones, is an important movement But in the adult the creeping is of much less importance Bipedal locomotion is most prominent then, and is also neccessary for the everyday life Second, with respect to spinal cord lesioned adults, it is most important to re-train those movements which the spinal cord lesioned patient performed before the spinal cord lesion, since the spinal cord and the supraspinal centres seem to remember those movements best (long-term memory), and it should be most easy to re establish those movements Our patient with the partial lesion of the cervical spinal cord could at the beginning hardly hold the racket to play tennis, but the CNS seemed to „remember" that old movement, since the patient was able to hit the ball

Another debatable point in the Vojta physiotherapy of spinal cord lesioned patients is the generating of the trigger zones for reflex creeping and reflex turning With the spinal cord lesion, the sensory processing is changing (for example, certain areas of the skin become hypersensitive), and the spinal cord neuronal networks often organize themselves in a pathological way and movement disorders occur (spasticity) As is well known, the skin two-point discrimination depends on the usage of that skin part With strong training it is possible to strongly reduce the two-point discrimination of the skin, since there are already approximately 8 receptors of myelinated skin afferents between the two points of the two-point discrimination in the rather untrained case (see Methods, and [96]) Further, it is possible to train the activation of single motor units It seems therefore possible that with the training of the trigger zones (for one or two weeks) pathological movements of the body of the spinal cord lesioned patient are initiated and trained (especially since there is also reflex generalization following spinal cord lesion) rather than functional components of the reflex creeping according to Vojta, which are supposed to be components of physiologic movements This would mean that the Vojta therapy is actually no Vojta therapy any more

One could generally argue, why the adult situation should be compared with the developing nervous system In the frog model it was already shown that just the different speed of growth of two kinds of axons during the development changed the contraction speed of the innervated muscle and changed the excitability of muscle fibres In earlier stages of the frog metamorphosis, also the piriformis muscle in that animal model is not mature enough to enable comparison between the development and the lesion-induced reorganization of the nervous system Generally, there is an enormous amount of possibilities what could be different between young infants and adults Still, it seems that the young infants are closer to adult humans than animals (judging upon the outside shape), so that an ontogenic comparison seems whorthwile But more often adult human locomotion is compared to animal locomotion (phylogenetic comparison) This could simply have an organization reason Since

most physiologists are animal physiologists, more data are available from animals than from humans

In the oscillator formation training, or more generally, the dynamic rhythm training, bipedal locomotion is trained which is typical for man, which is genetically predetermined by a neuronal network preformation (observable just after the birth), and which is old-learned movements and therefore also strongly encoded in the neuronal network preformations at the spinal cord level The rhythmicity fits the organization of the human CNS, namely the rhythm coupling Since it was measured that spinal oscillators (as a basic functional neuronal unit to allow, via rhythm couplings, the self-organization of integrated functions) deteriorate by „nonuse" and missing descending control, the networks of the spinal cord have to be trained to re-preformate the spinal oscillator networks (closed reverberatory self-excitatory synfire chains), to improve spinal locomotion and to reorganize supraspinal centres in such a way that natural physiological movements are generated by the spinal cord, initiated and maintained by the remaining tract fibres The rhythmic, dynamic, stereotyped movements are of special importance, since they need the least descending drive Dynamic movements are preferential since a higher afferent input better organizes the oscillators, and in turn the pattern generators, for locomotion

Of course, only those movements can be trained which can be trained according to the CNS lesion Artificial support to the trunk, weight reduction and induced „Mitbewegungen" (co-movement) will widen strongly the possibilities of movement training The rhythm training has to be adapted to the possibilities of the patient, but it has to include bipedal locomotion, since it is so important that it already is genetically predetermined in the neuronal network of the cord, as is demonstrated by the primary stepping in newborn infants (Fig 22), the patients used this movement extensively before the accident

The liberation or facilitation of certain movements or „reflexes" as trained by Vojta in infants are alone not sufficient for spinal cord lesioned patients, because the networks of the spinal oscillators are not or only little re-preformated for better functioning Upright bipedal locomotion typical for humans has to be trained at least additionally Frankly speeking, movements have to be trained with the spinal cord lesioned patients, which they easily could have performed before the spinal cord lesion Sport activities will motivate the patient for further exercise and training of cardiovascular-respiratory functions

Most movement training is beneficial for regaining motor control or to improve the regulatory processes of the body But since a newborn can better walk (primary stepping) than creep, priority has to be given in the adult to bipedal locomotion It seems that the training of trunk and shoulder girdle movements has been overemphasized in the treatment of adults with spinal cord lesions

Takeover of functions by the spinal cord after CNS lesions

Juliane showed an outward rotation of the right foot just after the birth (Fig 23A) Maybe, the foot was positioned wrongly in the uterus Upon stepping, the foot showed only

Figure 23. A. The 3 days old infant shows an outward rotation of the right foot.

B. The same infant (5 days old) shows no outward rotation during primary automatic stepping. Note that the stepping is automatic, since the infant tries to step through borders and walls.

a slight or no outward rotation (Fig.22F). But when the newborn girl came into a good stepping rhythm, the right foot was no more outwardly rotated (Figs.22A,23B). The diminution of the outward rotation indicates that the stepping automatism, located in the spinal cord, was physiologic, and when this stepping automatism was fully activated, the stepping was physiologic for this stage of development. It seems therefore that the stepping automatism can be used for treatment.

When the patient with an incomplete spinal cord lesion walked, the left foot showed a transient outward rotation during the swing phase. After good rhythmic running or jumping and with no exhaustion, the patient could walk with no or only little transient outward rotation. But after some time, when the patient walked with no concentration, the unphysiologic outward rotation re-appeared. The neuronal networks of the spinal cord seemed therefore to be able to organize with successive rhythmic movement cycles a rather physiologic movement pattern, which faded away again after some time; probably, this means that the spinal cord lost the memory of this state of physiologic movement pattern organization with not so much rhythmic stereotyped movements initiated and partly sustained by supraspinal centres.

It seems therefore that the immature spinal cord network in the newborn child was able to produce, for this stage of development, a physiologic automatic stepping pattern, and the not lesioned lower spinal cord of the patient with the incomplete lesion sub C5 was also able to generate rather physiologic bipedal locomotion. The not lesioned parts of human spinal cord networks seem to have therefore the capacity to self-organize such network states that

physiologic dynamic stereotyped rhythmic movements are generated if there are no pathologic lesion-induced afferent inputs from the periphery (or pathologic inputs from supraspinal centres)

Reduction of the central body temperature is one sign of the coming up of the brain death In formerly very healthy young patients, it can happen that the temperature rises again, after the manifestation of the brain death, but not because of the recovery of the supraspinal centres, the isolated spinal cord seems to be able to take over the temperature regulation (maybe, on a simpler level) It seems therefore possible that after CNS lesions, the human spinal cord can rather independently generate essential life important integrative functions or can even take over functions from supraspinal centres, which would mean that the CNS functions were repaired on a slightly lower phylogenetic level

Re-preformation and re-preformatting of neuronal networks

From the animal research aspect the treatment of spinal cord lesions is approached by trying to improve regeneration in the CNS In human research it is tried to maximally use the remaining capacity of neuronal network functions of the CNS and their connections In our spinal cord lesioned patient functions still recovered some time after the injury, even as late as after 3 years There are reports of CNS functions recovering even after 10 years Such recovery times are far too long to suggest regeneration or recovery of tract fibres If we assume that some tract fibres regenerate with a speed of 1mm / day, then 30 cm = 300 mm will be covered in 300 days We can expect then the regaining of functions (including synapse formation) from a recovery of tract fibres within a year's time But recovery times from 3 to 10 years seem not be attributable to a recovery of tract fibres A reorganization in the neuronal networks of the grey spinal cord matter seems more likely It seems very important to find out how and where neuronal networks change their structure for an improved self-organization

Starting from the frog model as mentioned above (Fig 21), it was suggested that the size and place of synapses on dendrites with respect to the cell soma (summing point for electrotonic spread for cell depolarization from the numerous dendrites) and the excitability of the membrane at the axon hillock, where the action potential is generated and is conducted along the axon, is a model for network plasticity Such a possible mechanism would change the efficacies and properties of synapses and the integration of the numerous postsynaptic potentials from the different dendrites and the excitability of that neuron, and would somehow be a building stone of a preformatting of neuronal networks The long recovery times of several years suggests that there is also some growing of nerve fibres in the neuronal networks with a formation of new synapses This change would fall more into the category of re preformation The lesion- and training-induced network plasticity of the CNS probably includes formation and formatting of neuronal networks

Concluding remarks

In our clinic, 80% patients with a recent spinal cord injury present with incomplete lesions, due to an improved treatment of acute spinal cord injury, including methylprednisolone [17] application Drugs for treatment of patients will be needed able to repair the blood-spinal cord barrier and to improve the spinal cord function following compression trauma to the spinal cord, ischemic brain damage, stretch-induced injury, and edema The completeness of a lesion has to be quantified simultaneously in the future by magnetic resonance imaging (MRI) and evoked potentials Hopefully, activated subnetworks can be localized in the future by functional magnetic resonance imaging (fMRI) [18]

We have tried to show in this paper that there are essential new therapy possibilities (such as running) for patients with incomplete spinal lesions, so far, this has generally not been considered possible With our theory of human neurophysiology based on new measurements in man, claiming that the spinal cord and supraspinal networks are not fixed wired by chains of neurons, but that the preformated neuronal networks are self-organized by impulse patterns from the periphery and higher centres to generate integrative functions and can be changed by re-preformating of the networks, new treatment possibilities have opened up Activity-induced changes of synaptic transmission are a well known phenomenon in animal physiology [128] For G M Edelman the human CNS is a dynamical system [28] In robotics, self-learning computers are under development

With respect to the treatment of spasticity, it should be remembered that spasmolytics, such as Baclofen may change or suppress the functional organization of CNS networks and are not helpful in the re-preformating neuronal networks, even though they have to be used to a certain extent in patients with severe spasticity

In future oscillator formation trainings, the bio feedback has to be improved still, to better assist with reorganization of especially supraspinal centres If the patient can watch his phasic EMG activity (pathologic) of certain muscles in comparison to those of the healthy normal trainer (physiologic), while jumping on a springboard, he probably can better reorganize supraspinal centres via bio-feedback Sperry transposed the nerve supply of flexor and extensor muscles in the rat and in the monkey [104,105] the monkey relearned the task, the rat did not Monkeys also differ from dogs and rats in the physiotherapy they need In Sperry's experiment on monkeys, their learning to flex or extend the elbow in one situation did not necessarily become generalized to other performances This indicates that the neuronal readjustment was not localized solely in the spinal centres but also involved reoganization at the supraspinal level [111] Surprisingly, few trials were required for poliomyelitis patients to use transposed tendons successfully The visualisation of the task seemed to be a prime aid to the patients [115] Relearning of movements probably depends on the kind and the location of the lesion

The efficacy of synapses can only be changed (re preformation of networks) to produce network plasticity [112] by an active training of natural movements, preferably a rhythmic one Passive movements of limbs increase the mobility of joints but do not improve network

functions. Voluntary contraction of muscle groups increases the muscle power but does not improve the motor program for locomotion. Our patient could quite nicely voluntarily activate the soleus muscle, but during locomotion the soleus muscle was not sufficiently activated, and became activated at the wrong time of the motor cycle The main problem for the time being is to improve the functional organization of the spinal pattern generators, so that the patients get more mobility for an achieved muscle power (muscle state (Fig.1)) and to reduce spasticity (pathologic network organization) Therefore, physiotherapy designed for the orthopedics is only partly suitable for the treatment of patients with an incomplete spinal cord lesion.

Since patients with incomplete spinal cord lesions can voluntarily activate muscles or motor programs and have spasticity at the same time, these patients are of great interest to human neurophysiologic research. The most important question is how many ascending and descending fibres allow a rather normal life including the performance of a profession. In monkeys, approximately 5% of fibres have to be preserved [29]. If also man needs just a few percent, then there may be some surgical (nerve anastomosis [85-87]), pharmacological or genetic interventions possible to reconstruct those few percents of fibres in complete spinal lesions.

Acknowledgement. *This work was supported by the Swiss Paraplegic Foundation.*

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A video-tape of the oscillator formation training is available.