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Neuromuscular Skeletal Plasticity (N.A.P.). Moving on from Traditional Physiotherapy Concepts

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SUMMARY

Background. *N.A.P. (Neuromuscular Skeletal Plasticity) an integrative neuro-orthopaedic concept to facilitate motor strategies in daily life. The primary thesis is that treatment of body functions and structural impairments should be integrated within goal-oriented activities. The purpose of this article is to demonstrate that the functional activity itself, determines the structure.*

Material and methods. *A case report of a dentist with brachial plexus lesion after a motor vehicle accident is presented. The necessity for training body functions within relevant tasks is undermined by references which emphasize the importance of training realistic activities to enhance long-term changes in neural representation.*

Results. *The treatment methods presented in this case show significant effects for the patient's ability to participate in his profession within less than a year's time after his motor vehicle accident.*

Conclusions. *Current evidence supports the treatment methods of this concept. The inability to flex his elbow and supinate his forearm placed a considerable doubt to his ability to ever be able to participate in his profession again. Structural reorganization is possible and depends on functional demands which need to be trained task-specifically. Single case reports may serve as the basis for further randomized controlled studies to support the efficacy of the treatment methods within the N.A.P. concept.*

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INTRODUCTION

In this article an integrative neuro-orthopaedic concept to facilitate motor strategies in daily life is presented. The underlying idea of this concept is that treatment of body functions and structural impairments, such as limited joint mobility or stability or muscle weakness is always integrated within the goal-oriented activity of the patient. The basic idea is that the functional activity itself, determines the structure.

Treatment principles which underly the treatment methods and techniques of this concept incorporate knowledge of traditional manual therapy concepts, pertaining to joint mechanics and neurodynamics and neurophysiological knowledge, which has its origin in the traditional neurophysiological concepts. Biomechanical and neuroscientific knowledge underlies a constant flow, as medical-technical development continues.

PLASTICITY MEANS CHANGE, OR "DEVELOPMENT"

Within this concept, biomechanical and neurophysiological basics are put into practice to enhance learning and re-learning of economical and safe motor strategies in daily life and in the working field. Musculoskeletal prerequisites are trained during activities of daily life or work specific tasks, themselves. This means that structural treatment is not done separately as a preparation for functional activities, but rather, that it is integrated within the goal-oriented movement, which is performed actively or mentally envisioned by the client. The therapist's hands control the best possible biomechanical situation in which the movement can occur. In doing so, the neuromuscular coordination which is required for the specific task is facilitated.

TRADITIONAL CONCEPTS

The paradigm of the 80 and early 90's of Manual Therapy was that passive mobilization of joint structures sufficed to restore normal functional activity. Structural treatment, to avoid or to treat limitations in range of motion is fundamental to many Manual Therapy concepts (e.g. Maitland, Kaltenborn-Evjenth, McKenzie). The tests and treatment procedures are mainly passive. The therapist mobilizes the joints with traction and gliding techniques, oscillations and muscle stretching techniques, which are mainly passive. Facilitation concepts (e.g. Bobath, PNF, Vojta) follow the goal to enhance neuromuscular coordination by use of specific stimuli. Application of external stimuli by the therapist is fundamental to both orthopaedic manual therapy and neurophysiological treatment concepts.

As long as voluntary action is not possible, these methods may be very appropriate to avoid contractures and muscle atrophy. The N.A.P. concept is based on the principle that peripheral stimulation leads to central changes, which, in turn, influence peripheral output. The general hypothesis underlying the methods of this concept is that structural treatment (joint mobilizations and muscle strengthening) is more effective for learning if it is done during the

voluntary performance of realistic and meaningful daily life activities.

Clinical observation has shown that therapy at the impairment level doesn't automatically carry over to the activity and participation levels in accordance with the international classification of function (ICF) [1]. This undermines the necessity to search for new treatment methods which may lead to long-term, relevant changes.

PLASTICITY

The basis for the treatment methods is the idea of "Plasticity," which may be defined as the ability to adapt to functional demands. When tasks vary or environmental conditions change, then variability in patterns of interconnections within the sensory and motor system, as well as changes in the effectiveness of neural connections are required for learning [2].

NEURAL PLASTICITY: CHANGES IN THE PERIPHERY LEAD TO CENTRAL CHANGES

Many collateral connections within the brain allow variability according to behavioral needs [3]. Depending on use, receptors show plasticity, which leads to stronger or weaker synaptic transmission. If certain body parts aren't used due to weakness, chronic pain or even because of fear, changes in representation fields within the cortex can be determined [4,5,6,7,8].

WHAT YOU DON'T USE, YOU LOSE!

Merz nich [9] showed in his studies with monkeys that depending on use, changes in representation occur. Body parts which aren't used lose representation fields, which are taken over by those, which are used more.

Ramachandran [10] discovered that following amputation subjects actually "felt" their lost hand in their face and shoulder area. The loss of afferent information can cause unpleasant sensations, such as phantom pain. He had the idea to give the patient the representation of his lost hand back by using a mirror for visual input.

The recent discovery of so-called "mirror neurons" (see below) offers a possible explanation for the importance of visualizing realistic movements that can not be performed actively. It is presumed that these neurons are the basis for recognition of movement [11]. Experiencing the activity with the therapist's manual guidance can help the patient to "get the picture" or gain knowledge about the movement characteristics of the movement.

MOVEMENT ALONE, WITHOUT A CONTEXT DOESN'T HAVE THE SAME MEANING FOR THE BRAIN

Current evidence supports the underlying hypotheses of the N.A.P. concept, that the functional relevance of joint mobilization, demands placed upon the skeletal system

and neuromuscular activation patterns depend on treatment of these structures within realistic activities in order to achieve long-term changes in synaptic connectivity and neural representation [12,13,14].

If goal-oriented actions are observed the same neurons are activated in the observer as in the one performing the actual activity. If the same movements without a context are performed, then the same neurons will not be activated in the observer [15].

VOLUNTARY ACTION ENTAILS MORE THAN JUST MUSCLE CONTRACTION

Different neuron populations are activated when a movement is performed without a context than when it is performed within a context. Activation of the motor cortex alone, leads to a caricature of a movement as opposed to an activity within an environmental context (fig. 1a, 1b, 1c). Body representations within the cortex are also not limited to just representing a specific part of the body, but show functional connections [16].

CLINICAL EXAMPLE

A 16 year old patient E. L. experienced spontaneous pain in her left wrist and was diagnosed by her medical doctor with acute tendinitis. Immobilization in a cast was prescribed. After 5 days she complained about excruciating pain and the cast was removed. Her entire arm was extremely painful and absolutely no voluntary action of her wrist and finger extensors was possible, although nerve conduction tests proved normal. After 2 months she was able to achieve a voluntary contraction of these muscles, although her activation pattern was quite unnormal, since only mass movements were possible. The clinical picture of spastic dystonia prevailed (fig. 1a). On the same day she was asked to bounce a gym ball and to return overhead

volleys with a volley ball (fig. 1b). These movements were totally normal in the videodocumentation as were her selective finger movements when playing a flute (fig. 1c).

MIRROR NEURONS

Mirror neurons are located in premotor areas that organize the coordination (timing) of muscle synergies required for the desired action. These areas are also responsible for selecting relevant information needed to complete the motor task. This information is mainly visual and is called "feed-forward", because it is "fed" into the central nervous system before the actual motion occurs. These areas project into the Motor Cortex, which actually fulfills the function of an interneuron, since it integrates sensory information and organizes parameters such as speed, direction and the type of muscle fibers which are required for the action.

MUSCLAR PLASTICITY

According to functional demands, muscle mass, in general, increases or decreases. Although strength training induces muscle hypertrophy, it cannot be automatically concluded that this trained muscle is able to perform different activities skillfully. Each activity requires a specific recruitment order within the muscle itself (intramuscular coordination) and a specific timing among the muscles within the synergy performing the action (intermuscular coordination). Also the frequency of muscle fiber recruitment is determined by the task itself. Muscle strengthening therefore requires training in variable conditions in order to attain the coordination as needed for different tasks.

Certain pathologies cause changes in the type of muscle fibers. It has been found that in spasticity, for example, phasic (fast-twitch) fibers change into tonic (slow twitch) fibers [17]. This is also the case during increase of age, where a gradual change from phasic fibers into tonic fibers occurs.



Fig. 1a



Fig. 1b



Fig. 1c

Fig. 1a. Clinical picture of spastic dystonia, 1b. Bouncing a gym ball, 1c. Selective finger movements when playing a flute

STRUCTURAL ADAPTABILITY

Muscles must be capable to change their length according to the demands of the activity and the environment. Postural adjustments require eccentric control of extensor synergies. For this structural elasticity is required.

If immobilisation is necessary for wound healing, stiffness may occur. Muscle stiffness is defined by the force required to change the length of a resting muscle [18].

Changes in tendon and connective tissues such as water loss and collagen deposition are presumed to cause stiffness [19].

Muscle stiffness may also be the result of protective strategies. One just has to imagine walking on ice. A very efficient strategy to gain motor control in this situation is co-contraction. Momentary stiffness is not only required to gain stability but also a very natural consequence to fear of falling. If co-contraction persists then structural stiffness results.

ARTHRO-OSSAR (SKELETAL) PLASTICITY

Since muscle activation is required to move and stabilize joints, changes in muscle activation patterns will cause changes in the skeletal system. For example, if the hip extensor synergy is not strong enough to stabilize the ileum on the femur head, then the ileum will tilt forward and the load to the femur head will change. Osteophytes are produced as a protective mechanism. If pressure to bone mass is decreased, then adaption also occurs. Astronauts loose bone mass after a period of time in space, because their bones are not exposed to gravitational demands. Functional demands determine the structure. Even throughout evolution one can observe this principle. Throughout time the form of our skull has changed, according to functional demands. The area where speech is organized (Broca Center) grew larger when homo sapiens began to speak. This area also controls finger, tongue and face muscles as well as the hearing of sounds, all of which are attributes involved in communication.

TASK SPECIFIC ORGANIZATION OF POSTURAL CONTROL AND RECIPROCAL INNERVATION

Postural control may be defined as the ability to maintain the center of body mass over the base of support, under both static and dynamic conditions. It includes organizing multiple sensory strategies for orientation. An important feature of postural synergies, which distinguishes them from abnormal synergies, is their ability to be modified.

Sherrington regarded reciprocal inhibition as a general method for coordinating priorities, which enables the unique character of goal-oriented behaviour [20]. As discussed above, executing a voluntary movement requires a specific recruitment order of the agonists (intermuscular coordination) and of the muscle fiber types within the muscles (intramuscular coordination), as well as a specific frequency of recruitment [21]. Depending on the task, the

antagonist may have to relax or may have to maintain co-activity (co-contraction). Different environmental conditions also require variable reciprocal innervation. Gravity conditions, for example, determine if the antagonists have to control the movement eccentrically.

FEEDFORWARD AND FEEDBACK

At the beginning of voluntary goal-oriented movements information is "fed" into the central nervous system which can be used to plan and initiate the movement. Towards the end of the movement, feedback-mechanisms become more important, so that corrections can be made, if necessary [22]. Different tasks require and use different information. Quick movements rely more on feed-forward mechanisms. There is no time for feedback to play a role. Sensory feedback is necessary, however, to create the brain's model of the movement in the first place and this process contributes to the acquisition of new motor skills [23]. Feedback is also needed for making corrections, especially if unpredictable changes occur during the execution of a movement.

Fast goal-oriented voluntary actions require a so-called "tri-phasic activation pattern" [24,25]. First the agonists fire to accelerate the movement. Shortly before arriving the goal the antagonists contract to decelerate after which the antagonists fire a second time to stabilize the end position. During the acceleration phase, the antagonists need to be reciprocally inhibited. They receive this information via interneuron connections. One can say that when an agonist contracts, the antagonist must "know" what to do. When catching a ball, for example, not only the biceps must react to the stretch stimulus caused by the weight of the ball, but the triceps must also contract for stability. This co-contraction is organized even before the ball actually reaches the hand, in anticipation that something instable is going to happen [25]. This depends primarily on visual information (feedforward). The impact of the ball provides proprioceptive information so that the biceps can react (feedback). Anticipation of the destabilisation, causes the triceps to contract as well. An apple of the same weight held in the hand, which someone wants to bite into, won't cause the triceps to co-contrast. For this task it needs to be inhibited.

PROTECTIVE MECHANISMS

The underlying hypothesis for the treatment methods within the N.A.P. concept is that during a goal-oriented voluntary movement, when antagonists should normally relax, they may instead co-activate, in order to avoid movements which have been painful or still are. In this way, the need for protection could be fulfilled. If protection of a body part is necessary for healing to occur, then the muscles will try to "freeze" the painful and injured body parts.

Scientific evidence has shown that protective strategies are triggered by the amygdala of the limbic system and that these are organized subconsciously [26]. The fact that muscles need to alter their activity according to changing demands and that reciprocal innervation is organized variably, as illustrated above, supports this treatment hypothesis.

The amygdala, a structure of the limbic system, is directly connected to the sympathetic nervous system, which in turn triggers bio-chemical changes. The aim of this mechanism is to keep painful body parts from moving so that healing may occur.

If harmful stimuli continue, hypersensitivity within the entire nervous system may result [27]. Serotonine is an important transmitter for long-term memory, which explains why all these changes may be "learned" [26,28]. These protective mechanisms entail physiological changes which are necessary in the acute phase of wound healing. To prevent these changes from become chronic, it is very important to make positive movement experiences with the injured body part as soon as possible!

INHIBITION AND HABITUATION

Habituation may be seen as the behavioral reaction to repeated stimuli, which are uncomfortable, but cause no harm. It entails progressive decrease in response to repetition of a stimulus. The process of habituation is not conscious. Without it one wouldn't be able to shift attention when background information seems more important, although the same stimuli continue. As soon as these seem unimportant one can focus one's attention to the seemingly more important matter. For this, neural adaptation is necessary.

HABITUATION DEPENDS ON INHIBITION

Inhibitory neurons trigger a stable, predictable and coordinated reaction to a specific stimulus, by inhibiting all competing reflexes, except one. A single motoneuron adds up all facilitators and inhibitors impulses which it receives from other neurons. On the basis of this calculation an appropriate action occurs [20].

SUBCORTICAL ACTIVITY RELATED WITH MOTOR AND CORTICAL CONTROL

Voluntary goal-oriented actions are organized both cortically and subcortically [29]. It was long believed that sensory input is necessary before a movement can be initiated. Experiments have shown that movement initiation requires cognitive information pertaining to the environment, such as visual and auditory input. Tactile sensory information is used for feedback, to control if the desired action plan has occurred and if corrections may be required [22]. The result of this evidence is that tactile information can be used to gain coordination of skillfull movements during the execution of a specific task. Perception requires searching the appropriate information which is relevant for the task and the most beneficial strategies to accomplish the goal. Feeling alone does not enable the brain to organize movements. The feeling of what is happening is what counts. This is not dependant on consciousness.

Distal body parts are organized primarily consciously (cortically) and require visual information from the environment.

Proximal body parts are organized primarily subconsciously (subcortically) and require proprioceptive information.

Within the N.A.P. concept, goals are directed by use of visual and verbal information. The therapist's hands are used as a tool to establish the biomechanical situation which the muscles are not able to coordinate automatically. In doing so, the brain is able to organize the appropriate muscle synergies which may be recruited automatically as motor learning progresses.

THERAPY GOALS AND METHODS

Therapy goals within the N.A.P. concept are:

- Increase elasticity to prevent or treat stiffness
- Prevent pain awareness and fear
- Facilitate cortical representation and postural control
- Facilitate task specific daily life and professional activities

Methods include:

- Eccentric activity of stiff muscles
- Cognitive pain and fear management
 - habituation training
 - aerobic training
- Specific use of input systems
- Facilitation of appropriate strategies (trial and error) using appropriate feedback.

CASE REPORT

A 36 year old dentist suffered a plexus brachiales paresis after a motor vehicle accident. Especially the loss of mobility as well as activation in elbowflexion and supination were detrimental for being able to resume his professional carer. He also had limited range of motion in the shoulder. The feeling in his fingers and mobility was intact.

HYPOTHESES

1. Scar tissue in the surroundings of the musculocutaneous nerve has a negative effect on synaptic efficacy and leads to weakness in the biceps muscle.
2. Structural treatment must be performed within meaningful tasks.
3. The patient will only be able to learn to use his hand and arm by practicing within relevant contexts.

ASSESSMENT AT ACTIVITY LEVEL

3 months after his accident he is not able to touch his mouth with his hand. He is able to reach his nose in side-lying. The biceps shows slight activation which is palpable. In supine he is able to flex his elbow to 80° with no supination (Figure 2).

7 months after his accident he is able to lift a glass to his mouth two times in sitting position (Fig.3).

8 months after his accident the same activity is possible 10 times, but still with pronation and no supination. He is also able to reach his mouth in supine (Fig. 4).

THERAPY

To increase the mobility of elbow flexion the therapist has him pull against her manual resistance of her distal



Fig. 2



Fig. 3



Fig. 4

Fig. 2. Slight activation of biceps

Fig. 3. Ability to lift a glass

Fig. 4. Activity possible 10 times, but still with pronation and no supination



Fig. 5. The increase of the mobility of elbow flexion

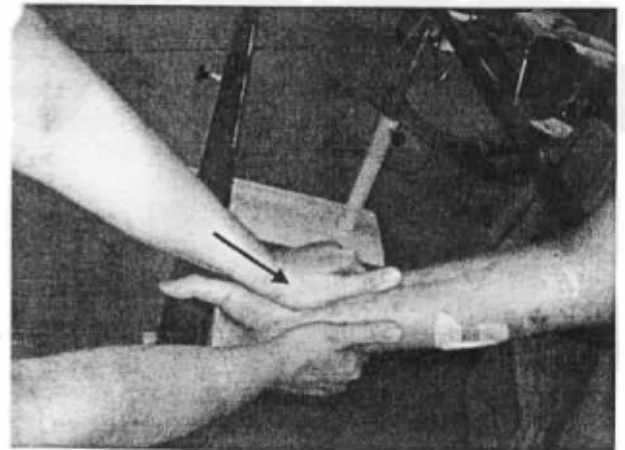


Fig. 6 The mobilization of the distal radio-ulnar joint



Fig. 7. Mobilization of the proximal radio-ulnar joint



Fig. 8. Inability to supinate his forearm – 8 months after his accident

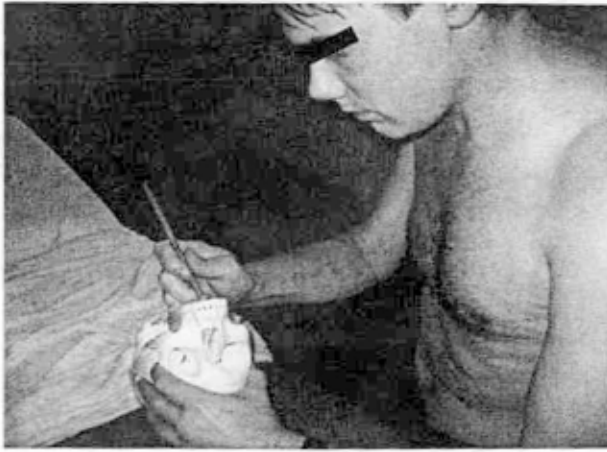


Fig. 9. Ability to perform supination – 9 months after his accident



Fig. 10. Task with dental instrument



Fig. 11



Fig. 12

Fig. 11, 12. Ability to perform quick, skillful supination movements

hand during which she mobilizes the olecranon to increase elbow flexion with her proximal hand (Figure 5).

To increase mobility in supination the therapist mobilizes the distal radio-ulnar joint by application of pressure to the distal radius dorsally while the patient tries to grasp the holm (Figure 6).

The proximal radio-ulnar joint is also mobilized during the same activity by applying pressure to the radius head in a ventral direction (Figure 7).

8 months after his accident he is still not able to supinate his forearm in elbow flexion (Figure 8).

9 months after his accident he is able to perform supination with elbow flexion while trying to simulate his professional activity (Figure 9).

The therapist assists his supination activity and stabilizes his shoulder while he performs the actual task with his dental instrument on a real person (Fig. 10)

11 months after his accident the patient is able to perform quick, skillful supination movements during elbow flexion and retained full strength of his biceps muscle (Fig. 11 + 12).

He returned to work to treated his own patients successfully!

CONCLUSION

These amazing results are not only due to specific treatment methods but also thanks to his personal motivation, despite the negative attitude of his medical doctors and some of his therapists. The central goal in rehabilitation is to prepare the patient for his "normal" life and to encourage his social interaction [30]. Especially at the participation level, the therapist may be able to find hidden potentials and key factors for motivation which can enhance the rehabilitation process. The central thesis of the N.A.P. concept is to incorporate structural requirements within meaningful activities and during participation. Single case reports are the beginning and can serve to document individual positive results. They can lead the way to future randomised controlled trials to support the treatment approaches within the N.A.P. concept.

REFERENCES

1. Fheodoroff K, Wissel J, Entner T, Freimuller M. Measuring outcome in spasticity rehabilitation. *Wien Klin Wochenschr* 2001; 113: Suppl 4: 11-14.
2. Kandel ER, Schwartz JH, Jessell TM. *Principles of Neural Science* 4th ed. New York, St. Louis, San Francisco: McGraw-Hill; 2000.
3. Edelman GM. *Neuronal Darwinism: The Theory of Neuronal Group Selection*. New York: Basic Books; 1987.
4. Förderreuther S. Klinische, elektrophysiologische und bildgebende Befunde bei Patienten mit komplexem regionalen Schmerzsyndrom (CRPS). *Klinische Neurophysiologie* 2004; 4: 235-240.
5. Pasqual-Leone A, Torres F. Plasticity of the sensorimotor cortex representation of the reading finger in Braille readers. *Brain* 1993; 116: 39-52.
6. Zanette G, Tinazzi M, Bonato C, di Summa A, Manganotti P, Polo A, Fiaschi A. Reversible changes of motor cortical outputs following immobilization of the upper limb. *Electroencephalogr Clin Neurophysiol*. 1997 Aug; 105 (4): 269-79.
7. Flor H, Elbert T, Knecht S, Wienbruch C, Pantev C, Birbaumer N, Larbig W, Taub E. Phantom-limb pain as a perceptual correlate of cortical reorganization following arm amputation. *Nature*. 1995, Jun 8; 375 (6531): 482-4.
8. Maihöfner C, Handwerker HO, Neundörfer B, Birklein F. Patterns of cortical reorganization in complex regional pain syndrome. *Neurology*. 2008, Dec 23; 61 (12): 1707-15.
9. Merzenich MM, Nelson RJ, Stryker MP, Shoppmann A, Zook JM. Somatosensory cortical map changes following digital amputation in adult monkey. *Journal comp. Neurologys* 1984; 224: 591-605.
10. Ramachandran VS. Behavioral and magnetoencephalographic correlates of plasticity in the adult human brain 1993; *Proc Natl Acad Sci. USA.*; 90: 10413-10420.
11. Umiltà MA, Kohler E, Gallese V, Fogassi L, Fadiga L, Keysers C, Rizzolatti G. I know what you are doing. A neurophysiological study. *Neuron* 2001; Juli 19; 31 (1): pp. 155-65.
12. Duchateau J, Semmler JG, Enoka RM. Training adaptations in the behavior of human motor units. *J Appl Physiol* 2006; 101: 1776-1775.
13. Zehr EP. Training-induced adaptive plasticity in human somatosensory reflex pathways. *J Appl Physiol* 2006; 101: 1783-1794.
14. Adkins DL, Boychuk J, Remple M, Kleim JA. Motor training induces experience-specific patterns of plasticity across motor cortex and spinal cord. *J Appl Physiol* 2006; 101: 1776-1782.
15. Iacoboni M, Molnar-Szakacs I, Gallese V, Buccino G, Mazziotta JC, Rizzolatti G. Grasping the intentions of others with one's own mirror neuronsystem. 2005; *Plos Biol.*, March 3 (3): e79.
16. Graziano et al. In: Riehle A, Vaadia E, eds. *Motor Cortex in Voluntary Movements*, 171, CRC Press, Boca Raton, 2002.
17. Hufschmidt A, Mauritz K-H. Chronic transformation of muscle in spasticity: peripheral contribution to increased tone. *Journal of Neurology, Neurosurgery, and Psychiatry* 1985; 48: 676-685.
18. Dietz V, Berger W. Normal and impaired regulation of muscle stiffness in gait: a new hypothesis about muscle hypertonia. *Experimental Neurology* 1983; 79: 680-687.
19. Van den Berg F. *Angewandte Physiologie für Physiotherapeuten*, Bd. 1.-3. Thieme, Stuttgart; 2000.
20. Kandel ER (2006). *Auf der Suche nach dem Gedächtnis*. Siedler, München.
21. Schmidtbleicher D, Gollhofer A. Specific methods of strength training also in rehabilitation. *Sportverletz Sportschaden* 1991; Sep, 5 (3): 135-41.
22. Mulder T. *Das adaptive Gehirn*. Thieme, Stuttgart: pp. 54-57; 2006.
23. Rosenbaum DA. *Human Motor Control*. San Diego, CA: Academic Press; 1991.
24. Beradelli AM, Hallett JC, Rothwell R, Agostino M, Manfredi PD, Thompson CD, Marsden CD. Single-joint rapid arm movements in normal subjects and in patients with motor disorders. *Brain* 1996; 119: 661-664.
25. Ghez C, Thach WT. The Cerebellum. In: Kandel E, Schwarz JH, Jessell TM, eds. *Principles of Neural Science*. New York: McGraw Hill; 2000.
26. Le Doux J. Das Gedächtnis für Angst. In: *Spektrum der Wissenschaft Dossier. Stress, Neurobiologie der Angst* 1999; 3: 16-23.
27. Butler D. *The sensitive nervous system*. Adelaide: Noigroup Press; 2000.
28. Squire LR, Kandel ER. *Gedächtnis. Die Natur des Erinnerns*. Heidelberg: Spektrum; 1999.
29. Ghez C, Krakauer J. The Organisation of Movement. In: Kandel E, Schwarz JH, Jessell TM, eds. *Principles of Neural Science*; 656, 668. McGraw Hill, New York; 2000.
30. Fries W, Lössl H, Wagenhäuser S. *Teilhabe!* Thieme, Stuttgart; 2007.