Institute of Physiology
University of Fribourg (Switzerland)

Rehabilitation of stroke and cerebellar patients

THESIS

Submitted to the Faculty of science
of the
University of Fribourg
Switzerland

for the degree
Doctor rerum naturalium

presented by
Shahid Bashir

Pakistan

No.1527

Fribourg University Press, 2006

Accepted by the Faculty of Science of the University of Fribourg, Switzerland, on the proposal of:

Prof. Dr. Dieter Rüegg, University of Fribourg, Switzerland, (Director)

Prof. Dr. Jean-Pierre Montani, University of Fribourg, Switzerland, (President of the jury)
Prof. Dr. Eric Rouiller, University of Fribourg, Switzerland, (Expert)
Prof. Dr. Jean-Pierre Gabriel, University of Fribourg, Switzerland, (Expert)
Prof. Dr. Friedrich Bodem, University of Mainz, Germany, (Expert)

Fribourg,26-06-2006

Prof. Dr. Dieter Rüegg
Director

Prof. Dr.Marco Celio
Dean

I dedicate this work to fingertip of my father (May Almighty GOD place him in paradise. Ameen).

Contents

Summary (English**)** 1
Résumé (French**)**
Chapter 1- General introduction 5
1.1 Plasticity of cerebral cortex 5
1.2 Adaptation in normal subjects 7
1.3 Rehabilitation in patients 8
1.4 Rehabilitation in stroke patients 10
1.5 Spasticity 12
1.5.1 Spasticity of the upper extremities 13
1.5.2 Spasticity of the lower extremities 13
1.5.3 Tremor 14
1.6 Climbing wall training 14
1.7 Objective 15

Chapter 2- Rehabilitation of stroke patients with an arm ergometer

2.1 Introduction 16

2.2 Methods 17
2.2.1 Patients 17
2.2.2 Material and methods 18
2.2.3 Experimental protocol 19
2.2.3.1 Recording on the ergometer 19
2.2.3.2 Clinical Assessment 20
2.2.4 Data Analysis 20
2.2.4.1 cycling torque 20
2.2.4.2 Cycling speed 21
2.2.4.3 EMG 21
2.2.4.4 Spasticity and muscular force 21
2.2.4.5 Range of movement 22

2.3 Results 23
2.3.1 Pedaling 23
2.3.1.1 Minimum pedal torque on the lesion side 23
2.3.1.2 Cycling speed 24
2.3.2 Spasticity 25
2.3.3 Muscular force 26
2.3.4 Range of movement 28

2.4 Discussion 29
2.4.1 Arm ergometer. 29
2.4.2 EMG 29
2.4.3 Patients performance 30
2.4.3.1 Spasticity 30
2.4.3.2 Force 31

2.5 Conclusion 32

Chapter 3- Climbing as a therapy for patients with cerebellar disorder (Part 1)

3.1 Introduction **33**

3.2 Methods **35**
3.2.1 Patients 35
3.2.2 Materials and methods 35
3.2.3 Experimental protocol 38
3.2.4 Climbing training 38
3.2.5 Test 39
3.2.5.1 Climbing tests 39
3.2.5.2 Pointing task 40
3.2.5.3 Reaction time 40
3.2.5.4 Flexion/Extension movements 40
3.2.6 Data Analysis 40
3.2.6.1 Parameters of the pointing task 41
3.2.6.2 Parameters of the RT task 41

3.3 Results **43**
3.3.1 Global results 43
3.3.1.1 Clibing performance 43
3.3.1.2 Simple RT 45
3.3.1.3 Complex RT 47
3.3.1.4 Interaction of fixed factors shown by RT 48
3.3.1.5 End point variability 49
3.3.1.6 Tremor 51
3.3.1.7 Non-analyzable test 55
3.3.2. Results from individual patients 56
3.3.3. Patient A 55
3.3.3.1 Climbing performance 56
3.3.3.2 RT task 57
3.3.3.3 Endpoint variability 58
3.3.3.4 Tremor 60
3.3.4 Patient B 62
3.3.4.1 Climbing performance 62
3.3.4.2 RT task 63
3.3.4.3 Endpoint variability 64
3.3.4.4 Tremor 65
3.3.5 Patient D 67
3.3.5.1 Climbing performance 67
3.3.5.2 RT task 67
3.3.5.3 Endpoint variability 68
3.3.5.4 Tremor 69

3.4 Discussion **71**
3.4.1 Spatial abnormalities 72
3.4.2 Scaling 72
3.4.3 Interaction torques 73
3.4.4 Locomotion and balance 73

4. Climbing as a therapy for patients with cerebellar disorder (Part 2)

4.1 Introduction **75**

4.2. Methods **78**
4.2.1 Subjects 78
4.2.2 Experimental setup and procedure 78
4.2.2.1 Kinematic and kinetic movement parameters 78
4.2.2.2 Fast-accurate pointing movements 80
4.2.2.3 Slow-with vision pointing movements 80
4.2.2.4 Balance and manual dexterity 80
4.2.2.5 Box and block test 80
4.2.2.6 Berg test 80
4.2.2.7 Self-perception of symptoms 80
4.2.3 Climbing training 81
4.2.4 Data analysis 83
4.2.4.1 Kinematic and kinetic movement parameters 84
4.2.4.2 Balance and manual dexterity 85
4.2.4.3 Self-perception of symptoms 85

4.3. Results and discussion **86**
4.3.1 Patient 1 90
4.3.1.1 Kinematic and kinetic movement parameters 90
4.3.1.2 Balance and manual dexterity 90
4.3.1.3 Self-perception of symptoms 91
4.3.1.4 Discussion 91
4.3.2 Patient 2 96
4.3.2.1 Kinematic and kinetic movement parameters 96
4.3.2.2 Balance and manual dexterity 97
4.3.2.3 Self-perception of symptoms 97
4.3.2.4 Discussion 97
4.3.3 Patient 3 101
4.3.3.1 Kinematic and kinetic movement parameters 101
4.3.3.2 Balance and manual dexterity 101
4.3.3.3 Self-perception of symptoms 101
4.3.3.4 Discussion 102
4.3.4 Patient 4 106
4.3.1.1 Kinematic and kinetic movement parameters 106
4.3.1.2 Balance and manual dexterity 106
4.3.1.3 Self-perception of symptoms 106
4.3.1.4 Discussion 107

4.4. Conclusion **111**

5. General discussion **114**
6. References **119**
Acknowledgments **130**
7. C.V **131**

Summary

The purpose of this thesis was to investigate whether (1) the motor performance of stroke patients can be improved by training on a hand ergometer and (2) the motor performance of cerebellar patients by training on a climbing wall. The thesis consists of 3 experimental parts. The first part concerns the rehabilitation of chronic stroke patients on a hand ergometer and the development of an index in order to quantify the spasticity of a given muscle. The second part is a pilot study on cerebellar patients who performed training on a climbing wall. The third part is the main study on cerebellar patients in which the results from the pilot study had been considered in the design of the test experiments.

The aims of the first part were (1) to test whether training on an arm ergometer of stroke patients decreases spasticity, increases muscle force and movement range, and (2) to develop a technique to quantify individual muscle spasticity. Nine patients with a stabilized hemisyndrome underwent a 3-week training on an arm ergometer during 5 days/week. Patient testing was performed one week before training, at training onset, at the end of training and 2 weeks after training. Spasticity was quantified by (1) the Ashworth scale, (2) the maximum active extension of the biceps, and (3) the minimum torque on the lesioned side during arm cycling. Muscle force was evaluated by the Rivermead Motorik Assessment, the Motricity Index and the cycling force, and the range of active movement was quantified by the sum of the angles at a maximum shoulder flexion, shoulder abduction, elbow flexion and elbow extension. By the training, spasticity decreased, muscle force and range of movement increased significantly. The spasticity index - the relation between the muscle activity modulation on the normal and lesioned side - was shown to be a useful tool in quantifying individual muscle spasticity. It was concluded that cycling on an arm ergometer is a useful tool for rehabilitation.

The objective of the second pilot study was to evaluate whether the training on a climbing wall of patients with a cerebellar lesion improves their motor performance. Five patients participated in the training, which lasted 45 min a day, during 5 days a week and over a period of 3 weeks. Each patient was tested for the climbing performance, reaction time (RT), pointing movement and flexion/extension movements of the upper limbs during test sessions which were performed (1) at T0, the first day of the pre-training phase, (2) at T1, 3 weeks later, at the end of the pre-training phase, (3) at T2, 3 weeks after T1, at the end of training period and (4) at T3, 3 weeks after T2. The results showed that the training improved the performance of the patients in some of the tests. It turned out, however, that part of the tests were not optimally adapted to test the performance of the patients and were eliminated for

the main study. Mainly the tests on the climbing wall could hardly be quantified due to the different performance of the patients. Furthermore the pointing tasks were adapted with the aim to test specifically cerebellar deficiencies.

The aim of the third investigation was, similar as in the second study, to evaluate the effect of a 6-week climbing training on motor control of 4 patients with cerebellar damage. Test sessions, which were taken before, during and after the training included 3-dimensional analysis of arm and leg movements during pointing tasks, clinical balance tests, motor skill tests and self-perception of symptoms. The results of this investigation showed a positive effect of the climbing training on the coordination of the upper and lower limb during pointing moments and on balance of patients with cerebellar damage.

In conclusion the training of stroke patients on a hand ergometer and of cerebellar patients on a climbing wall has a positive effect on their motor performance. It should therefore be envisaged to replace some physiotherapy treatment by cycling on a hand ergometer in stroke patients and by climbing on a climbing wall in cerebellar patients

Résumé

Le but de cette thèse est celui d'analyser, d'une part, comment la performance motrice des patients avec des attaques cérébrales peut être amélioré à travers un entrainement avec un ergomètre à bras et, d'autre part, et la performance des patients cérébelleux qui s'entrainent avec l'escalade. La thèse consiste dans trois parties expérimentales. La première partie concerne la réhabilitation des patients avec des attaques cérébrales parmi un ergomètre à bras et le développement d'un index qui puisse quantifier le degré se spasticité d'un muscle donné. La deuxième partie est un avant-projet sur les patients cérébelleux qui pratiquaient l'escalade. La troisième partie concerne l'étude principale sur les patients cérébelleux, qui se base sur les résultats obtenus dans l'avant-projet.

L'objectif de la première partie est double : premièrement il s'agit d'analyser si l'entrainement avec un ergomètre à bras, sur les patients avec des attaques cérébrales, réduit la spasticité, s'il augmente la puissance du muscle et s'il augmente l'étendue du mouvement du muscle ; deuxièmes il s'agit de développer une technique qui nous permet de quantifier la spasticité individuelle d'un muscle. Neuf patients avec niveau stable de hémisyndrome cérébelleux ont été soumis à un entraiment avec l'ergomètre de trois semaines pendants cinq jours/semaines. Le test sur les patients a été conduit quatre fois : une semaine avant l'entrainement, pendant l'entrainement, à la fin de celui-ci, et deux semaines après l'entrainement. La spasticité a été quantifiée à travers trois moyens : l'échelle d'Ashworth, l'extension maximale du biceps, et la torque minimale sur la partie lésinée pendant la rotation du bras. La puissance du muscle est évalué grâce au « Rivermead Motorik Assessment », au « Motrocity Index » et la puissance de la rotation; en outre, l'étendue du mouvement actif a été mesuré par la somme des inclinations maximales crées par une flexion de l'épaule, par une abduction de l'épaule, par une flexion de la coude, et par une extension de la coude. Pendant l'entrainement on a pu constater une réduction de la spasticité ainsi qu'une augmentation remarquable de la puissance du muscle et de l'étendue du mouvement. L'index de spasticité- à savoir, la relation entre la modulation de l'activité musculaire sur la partie normale et sur la partie lésinée - a montré de pouvoir être un important outil dans la quantification de la spasticité musculaire. On a pu conclure que la rotation avec un ergomètre à bras est un outil important pour la réhabilitation.

L'objectif de l'avant-projet était celui d'évaluer l'amélioration de la performance motrice des patients cérébelleux suite à un entrainement en escalade sur mur artificiel. Cinq patients ont participé à un entrainement de 45 minutes par jour, pour cinq jours la semaine et sur une période de trois semaines. Chaque patient a été testé sur les suivants critères : la performance en escalade, le temps de réaction, le mouvement, et la flexion/extension de la partie supérieure du

membre. Les sessions du test ont été conduites à T0, le premier jour dans la phase avant l'entrainement, à T 1, trois semaines plus tard à la fin de cette phase, à T2, trois semaines après T1, à la fin de l'entrainement et à T3, trois semaines après T2. Les résultats ont montré que l'entrainement a amélioré la performance des patients dans quelques tests. On s'est aperçu, pourtant, que une partie des tests n'étaient pas adaptes à tester la performance des patients et ont donc été supprimé pour l'étude principale. Les tests d'escalade sur mur artificiel peuvent difficilement être interprétés à cause des différents niveaux de performance des patients. En outre les taches ont été adaptées avec le but de tester les déficiences cérébelleux.

L'objectif de la troisième partie est similaire à celui de l'avant-projet de la deuxième partie : évaluer les effets d'un entrainement d 'escalade de six semaines sur la performance motrice de quatre patients avec des lésions cérébrales. Les sessions de test, qui ont été conduites avant, pendant et après l'entrainement, incluaient des analyses à 3-D du mouvement du bras et jambe ; ces analyses ont été effectuées sur la base des taches ciblées, des tests d'équilibre, de test sur l'habilité motrice et de l'auto-perception de symptômes. Le résultat de l'analyse montra un effet positif de l'entrainement en escalade sur la coordination de la partie supérieur et inférieur du membre.

En conclusion, les deux types d'entrainement sur les deux types des patients, cités plus haut, ont montré un effet positif sur leur performance motrice. En outre, c'est envisageable de remplacer une partie des traitements de physiothérapie, d'une part, avec des exercices de rotation avec un ergomètre à bras chez les patients avec des attaques cérébrales et, d'autre part, avec l'escalade sur mur artificiel chez les patients cérébelleux.

Rehabilitation of stroke and cerebellar patients

1. General Introduction

Rehabilitation measurements essentially focus on clinical observations. To date, these have not been able to differentiate with certitude the spontaneous recovery by different mechanisms of adaptation from the effects of regular rehabilitation exercise. A major problem is that patients are unique and it is nearly impossible to have a homogenous population of patients for controlled studies. Mechanisms of rehabilitation and motor adaptation can thus much easier be studied in animal models than in patients.

1.1. Plasticity of the cerebral cortex

Plasticity, which is generally referred to a biologic system altering its structure or function to accommodate to external conditions or stimuli (Wilson et al. 1975), is not limited to patients but can also occur in normal subjects and animals. Plasticity of the cerebral cortex can be investigated during development when intrinsic factors such as genes or molecular gradients and extrinsic factors such as sensory experience shape the final structure and function of the cortex. The ability of the brain to adapt to changes in its environment provides vital insight into how the brain develops, functions and recovers from damage. Environmental influences can change the electrical activity and shape the connectivity and function of the cortex. Experiments dating back at least four decades have explored this issue and considerable progress has been made in describing the phenomena and mechanisms of plasticity in the cortex (Stein et al. 1988). Cortical development is divided into two stages, an initial phase where connections are formed, and a secondary phase where existing connections are refined. Both intrinsic and extrinsic factors impact on these two phases and consequently the structure and function of the cortex. Understanding how genes, molecules, and experience contribute to the different phases of cortical development and how they influence the formation of cortical areas, maps and connections is critical to understanding developmental plasticity. Molecular gradients within an area may play a role in the establishment of cortical maps, such as the retinotopic map. Interestingly, some gradients are abruptly down-regulated at a time when maps are refined, suggesting a dynamic interaction between intrinsic and extrinsic factors during cortical map development (Stein et al. 1988). Factors extrinsic to the cortex, such as the amount and pattern of electrical activity in input pathways, also contribute to cortical development.

During the past two decades, experimental studies in animals and neurophysiological and neuroimaging studies in humans have demonstrated that the adult brain maintains the ability to reorganize throughout life. Cortical reorganization or plasticity as defined by Donoghue is "any enduring changes in the cortical properties either morphological or functional" (Garraway et al. 1983) and it is of major interest as it may play an important role in learning and functional recovery after injury to the nervous system. The availability of noninvasive neuroimaging and electrophysiological techniques allows us to study reorganization in the intact human brain. Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) are used for studying the reorganization of functional representations in relation to motor learning and recovery from human brain diseases. Transcortical magnetic stimulation (TMS) provides additional information on processes involved in cerebral reorganization as it can measure changes of the human corticospinal motor output system in different circumstances such as use or injury of the brain. More recently, paired-pulse TMS has provided means to study the differential regulation of intracortical inhibitory and excitatory networks involved in reorganization of the brain (Bütefisch et al. 2000). Furthermore, by combining TMS with drugs that either block or enhance TMS-evoked responses, neurotransmitter system mediating the observed effects can be identified (Bütefisch et al. 2000; Stefan et al. 2002). In addition, "artificial reversible brain lesions" can be introduced with repetitive TMS, which allows the investigators to probe the specific role of a cortical area for a given behavioral task (Bütefisch et al. 2000). An important concept of reorganization in the motor cortex is that of a distributed neuronal network in which multiple overlapping motor representations are functionally connected through an extensive horizontal network. By changing the strength of horizontal connections between motor neurons, functionally different neuronal assemblies can form, thereby providing a substrate to construct dynamic motor output zones (Stein et at. 1988). Modulation of inhibition and synaptic efficacy are mechanisms involved. Recent evidence from animal experiments indicates that these functional changes are accompanied by anatomical changes (Donoghue et al. 1996). Because plasticity of the brain plays a major role in the recovery of function after stroke, the knowledge of the principles of plasticity may help to design strategies to enhance plasticity when it is beneficial, such as after brain infarction (Langhammer and Stanghelle 2000).

Numerous studies have described plastic changes in the cortical motor areas after a stroke. These include decreases in motor output areas (Traversa et al. 1997), increases in motor thresholds (Byrnes et al. 1999), and changes in regional blood flow demonstrated by PET

(Dettmers et al. 1997; Nelles et al. 1999) and fMRI (Cramer et al. 1997). When patients underwent a training program of neuro rehabilitation they showed, simultaneously with improved motor functions, an increase in the number of cortical sites from where motor evoked potentials (MEP) of the paretic hand could be elicited (Traversa et al. 1997; Wittenberg et al. 2003), indicating that the cortical representation of the target muscle (muscle map) enlarged compared to the pretraining mapping. The shift of the muscle map or the increased number of abnormal location of cortical stimulation sites indicate that cortical motor output zone has expanded into the adjacent spared cortex, involving cortical areas previously not dedicated to this muscle. Similarly, recent studies in adult monkeys have demonstrated that behavioral experience has a clear impact on the cortical motor representation following injury to the motor cortex. The effect of training of the affected limb on the reorganization following small lesions to the hand area of the primary motor cortex was studied. In monkeys not receiving postinfarct behavioral training, the remaining, undamaged hand representation decreased in size (Nudo et al. 2001). In contrast, monkeys that received post injury behavioral training showed retention of the undamaged hand representation. In some cases, the hand territory expanded to the elbow and shoulder representation (Nudo et al. 2001).

Basic neurophysiological research suggests that repetitive motor activity forms the basis of motor learning and recovery. (Asanuma et al. 1997) provided electrophysiological and anatomical evidence that the activation of pathways to the sensorimotor cortex can provoke long-term potentiation (LTP) phenomena and structural transformations of synapses. Further experimental evidence comes from studies involving TMS in humans. Short-term repetitive execution of simple movements of the thumb was shown to induce representational changes within the cortical motor map (Classen et al. 1998).

1.2. Adaptation in normal subjects

Repeated physical practice improves motor performance and elicits over time long-term neuromuscular adaptations (Herman et al. 1986). The increase in muscle strength during the first 2 weeks of strength training is primarily neural, whereas muscle hypertrophy is produced by resistance training for as much as 4 months (Hakkinen et al. 2000; Staron et al. 1994). Over time, repeated hypertrophic conditions also yield lasting changes in the number of contractile proteins within the exercised muscles, in ratios of the muscle fiber types (Staron et al. 1994), and in muscle strength. Lasting neural adaptations also occur during resistance exercise regimens and are sometimes more pivotal to adaptation than muscular

factors such as hypertrophy (Hakkinen et al. 2000). Examples include changed electromyography-to-force ratios (Liepert et al. 1998) and increased neuromuscular junction size (Deschenes et al. 1993). Long-term changes in the topography of cortical maps are also thought to accompany repeated physical practice, although the time course of these changes in concert with physical practice is still unknown. For example, specific areas in the primary motor cortex of healthy participants engaging in daily practice of motor tasks are enlarged (Karni et al 1995). Even simple thumb movements repeated over a short period of time induce lasting cortical representational changes and an enlargement of these representations as learning occurs (Classen et al 1998).

If an individual begins a running exercise regimen and has never run before, initial changes in endurance will be dramatic. However, after training for 6 to 8 weeks, the gains will be small in comparison. Eventually, if the regimen is not varied, either by modifying the exercise regimen and/or by continually overloading the muscles, a performance plateau will occur. Such plateaus are common in all areas of neuromuscular performance and are typified by stabilization of maximal motor performance at some peak level in response to a stable training stimulus. This general adaptation syndrome is characterized by 3 phases (Garhammer et al 1979). First is the alarm phase, in which a new stress (i.e., resistance training) may cause excessive soreness, fatigue, and perhaps even a temporary drop in performance. Second is the resistance phase, in which the body adapts to the stimulus and returns to a normal, albeit enhanced functional level. During this phase, the hormonal milieu responds to increases in neuromuscular stimulation by increasing anabolism to support biochemical, structural, and mechanical changes in muscle physiology. And third is the exhaustion phase, in which continued training at similar sets and repetitions with increased intensity will eventually lead to a plateau and subsequent decline in function, as the hormonal milieu shifts to one favoring catabolism in response to an increase in stress hormones relative to the available anabolic mediators.

1.3. Rehabilitation in patients

In recent years, understanding of motor learning, neuroplasticity and functional recovery after the occurrence of brain lesion has grown significantly. Repeated motor practice and motor activity in a real world environment have been identified in several prospective studies as favorable for motor recovery in stroke patients (Langhammer and Stanghelle 2000). Although a considerable number of physiotherapeutic "schools" has been established, a conclusive proof of their benefit and a physiological model of their effect on neuronal

structures and processes are still missing. Correspondingly, interventions and methods of physical exercise therapy in motor rehabilitation vary considerably depending on the physiotherapist's preferred therapeutic approach and on the patient's physical and motivational state. However, evidence-based strategies for motor rehabilitation are more and more available. Unfortunately, the benefit of therapeutic strategies aiming at improving motor function in stroke patients has only been demonstrated on a general level, i.e. without specification of the influence of a single well-defined intervention (Hummelsheim and Eickhof 1999).

Briefly, we know that occupational therapy and physiotherapy improve motor function although the operative components within the entire rehabilitation process are not yet identified. Furthermore, little is known about the neurophysiological mechanisms.

As examples, the physiotherapeutic method according to (Bobath et al. 1990) involves the reduction of an enhanced muscle tone (spasticity) before voluntary motor activities are facilitated. However, Langhammer and Stanghelle (2000) pointed out that a task-specific "motor relearning program" is more effective with respect to motor recovery and to the level of independence in the activities of daily living as compared with the Bobath approach.

Task-specific, repeated practice regimens can induce lasting cortical reorganizations (Classen et al. 1998) that appear to precede motor improvement. The patients become gradually neuro-physiologically accustomed to exercise regimens to which they have been exposed repeatedly. Like an athlete who executes the same training regimen until adaptation has occurred, we assume that many stroke patients experiencing plateaus may actually be adapting to their therapeutic motor exercise regimens. It is usually argued that such recovery "plateaus" reflect diminished capacity for additional motor improvement, warranting discharge.

How cortical and subcortical structures react to such a condition has been the subject of several investigations with various, partly divergent findings. On one hand, EEG in SCI patients has shown reorganization related to the recovery of limb functions with a posterior shift of cortical activation towards the primary somatosensory area (Karni et al. 1995). On the other hand, TMS in paraplegics disclosed an enlargement of the cortical representations of non-affected muscles in the primary motor cortex, together with an increased excitability (Cao et al. 1998). In addition, PET in paraplegic and quadriplegic patients revealed extensive changes in cortical and subcortical activation during specific motor performances of the upper limbs (Curt et al. 2002).

1.4. Rehabilitation in stroke patients

A stroke occurs when a blood vessel that brings oxygen and nutrients to the brain bursts (hemorrhagic stroke) or is clogged by a blood clot or some other mass (ischemic stroke). Because of this rupture or blockage, part of the brain doesn't get the blood and oxygen it needs. Deprived of oxygen, nerve cells in the affected area of the brain can't work and die within minutes and the part of the body they control can't work either.

Stroke can affect people in different ways. It depends on the type of stroke, the area of the brain affected and the extent of the brain injury. Brain injury from a stroke can affect the senses, motor activity, speech and the ability to understand speech. It can also affect behavioral and thought patterns, memory and emotions. Paralysis or weakness on one side of the body is common.

Most of these problems can improve over time. In some patients they will go away completely. Stroke often causes people to lose mobility and/or feeling in an arm and/or leg. If this affects the left side of the body (caused by a stroke on the right side of the brain), stroke survivors may also forget or ignore their weaker side. As a result, they may ignore items on their affected side and not think that their left arm or leg belongs to them (neglect). They also may dress only one side of their bodies and think they're fully dressed. Bumping into furniture or door jambs is also common. A stroke can also affect seeing, touching, moving and thinking, so a person's perception of everyday objects may be changed. Stroke survivors may not be able to recognize and understand familiar objects the way they did before. When vision is affected, objects may look closer or farther away than they really are. This causes survivors to have spills at the table or collisions or falls when they walk. With injury in areas where the short-term and long-term memories are located, it may be hard for patients to plan and carry out even simple activities. Stroke survivors may not know how to start a task, confuse the sequence of logical steps in tasks, or forget how to do tasks they've done many times before.

By studying stroke patients it has been possible to explore the contributions of various brain regions to normal cerebral operations and the adaptation of remaining tissue to selective neuronal loss (Bhakta et al. 2000). In addition, the understanding of mechanisms underlying observed recovery of function has led to improvements in the methods and timing of interventions with stroke patients (Dombovy and Bach-rita 1988).

Although the timing and extent of motor recovery vary for individual patients, several studies indicate that most functions either re-emerge in a short period of time or remain permanently

lost. In a study in New Zealand, 598 of 680 patients (88%) exhibited motor impairment at the onset of stroke. After 1 month, much improvement had occurred and after 6 months, three quarters of the survivors recovered substantially or completely. Recovery usually occurs by 8–12 weeks and sometimes 6 to 12 months after the stroke (Smith et al. 2000).

In relation to the timing of the therapy for stroke patients, it has to start as early as possible after the brain lesion (Ernst et al. 1990). It is a common clinical believe that stroke patients past a certain time window are unlikely to benefit from motor rehabilitation (Jorgensen et al. 1995), although it has been convincingly demonstrated that motor rehabilitation of stroke patients remains efficacious even in the "chronic" stage, i.e. several months or years after the acute stroke (Kunkel et al. 1999; Page et al. 2002; Smith et al. 2000; Whitall et al. 2000). Even so managed-care providers often restrict the number of rehabilitation sessions, and motor therapy is usually only reimbursed when provided to the most acute stroke patients. When entering the chronic stage, their clinicians tell them that additional motor improvement was not to be expected, and motor therapy is discontinued.

In order to study the efficacy of a treatment, factors that predict recovery have to be identified. Improvement seems to be more likely when initial deficits are limited and rate and extent of recovery are often greater when early impairment resolves quickly (Duncan et al. 1994). Gender and age, on the other hand, do not appear to reliably predict recovery (Nakamura et al. 1992). Although information about initial severity and early course might enhance prognostic accuracy, it is still difficult to determine outcomes for particular patients (Duncan et al. 1994).

In principle the use of the affected limb improves function and maintenance of the cortical representation of the affected limb. For example, repetitive finger and wrist movements improved the kinematics of the trained movement and overall hand function. This effect was specific for the repetitive training as it was not seen with training a variety of complex movements (Bütefisch et al. 2000). Another example is the constraint-induced therapy that encourages using the affected limb by constraining the non-affected limb (Tate and Damiano 2002) and has been shown to improve motor function of stroke patients (Wittenberg et al. 2003).

The relationship between improvement of motor function and movement-related brain activation in fMRI is still unclear as some studies show an association between improvement in motor function and increased activation of the motor area ipsilateral to the lesion (Johansen-Berg et al. 2002) when moving the affected limb whereas others show a negative

correlation between the amount of motor-related brain activation and improvement of function after therapy (Wittenberg et al. 2003).

As exposed above, many studies demonstrated plastic changes in cortical representations. However, these studies did not differentiate between a spontaneous recovery and plasticity induced by physiotherapeutic interventions. A decade ago the therapeutic value of stroke rehabilitation was still controversial (Dobkin et al. 1989). However, in recent years several studies have demonstrated the clinical efficacy of physiotherapy in stroke rehabilitation (Weder and Seitz 1994). The effects are more pronounced with high treatment intensity (Bütefisch et al 2000; Kwakkel et al. 1999) and with an early onset of the training after the stroke (Bhakta et. al. 2000).

1.5. Spasticity

Spasticity is a disorder of the sensorimotor system characterized by a velocity-dependent increase in muscle tone with exaggerated tendon jerks, resulting from hyper excitability of the stretch reflex (Reddihough et al. 2002).

The pathophysiological basis of spasticity is incompletely understood. Unlike healthy subjects, in whom rapid muscle stretch does not elicit reflex muscle activity beyond the normal short-latency tendon reflex, patients with spasticity experience prolonged muscle contraction when spastic muscles are stretched. After an acute injury, the ease with which muscle activity is evoked by stretch increases in the first month of spasticity; then the threshold remains stable until declining after a year. The changes in muscle tone probably result from (1) loss of descending tonic or phasic excitatory and inhibitory inputs from reticulospinal and other descending pathways to the spinal motor apparatus, (2) alterations in the segmental balance of excitatory and inhibitory control, (3) denervation supersensitivity and (4) neuronal sprouting. The excitability of motoneurons is increased, as is suggested by enhanced H-M ratios and F-wave amplitudes. Judged by recordings from Ia spindle afferents, muscle spindle sensitivity is not increased in human spasticity. Once spasticity is established, the chronically shortened muscle may develop physical changes such as shortening and contracture that further contribute to muscle stiffness (Dietz et al. 2000).

Spasticity is associated with some very common neurological disorders—multiple sclerosis, stroke, cerebral palsy, spinal cord and brain injuries, and neurodegenerative diseases affecting the upper motor neuron and pyramidal and extra pyramidal pathways. Spasticity is one of the main causes of disability among post-stroke patients because of functional limitations during daily living activities. Furthermore, it is a major risk for secondary

articular damage: contractures, pain and vitiated postures. Spasticity can be relieved by means of systemic and local drug treatments; in particular botulinum toxin has been much used to manage spasticity in several anatomical areas in a variety of conditions such as multiple sclerosis (Schapiro et al. 2001), cerebral palsy (Flett et al. 2003 and Yang et al. 2003), and traumatic brain injury (Smith et al. 2000). Botulinum toxin plays a role in the management of upper and lower limb spasticity also in hemiparetic patients after stroke in reducing disability and reducing pain (Bhakta et al. 2000; Brashear et al. 2002). It presents several advantages: (1) the absence of side effects and optimum tolerance by patients, (2) the lack of sensory effects, and (3) the ability to target specific muscle groups, so allowing harmful spasticity to be reduced in one area while preserving useful spasticity in another.

1.5.1 Spasticity of the upper extremities

Muscles that often contribute to spastic adduction/internal rotation dysfunction of the shoulder include latissimus dorsi, teres major, clavicular and sternal heads of pectoralis major, and subscapularis. In the flexed elbow, the brachioradialis is spastic more often than the biceps and brachialis. In the spastic flexed wrist, carpal tunnel symptoms may develop. Flexion with radial deviation implicates flexor carpi radialis (Bhakta et al. 2000).

In the clenched fist, if the proximal interphalangeal (PIP) joints flex while the distal interphalangeal joints remain extended, spasticity of the flexor digitorum superficialis (FDS) rather than the flexor digitorum profundus (FDP) may be suspected. A combined metacarpophalangeal flexion and PIP extension also may occur. A patient may be spastic in only one or two muscle slips of either FDP or FDS. Neurolysis with botulinum toxin is beneficial for spasticity of the intrinsic hand muscles because of their size and accessibility (Bhakta et al. 2000).

1.5.2 Spasticity of the lower extremities

Spastic deformities of the lower limbs affect ambulation, bed positioning, sitting, chair level activities, transfers, and standing up. Equinovarus is the most common pathological posture seen in the lower extremity. Equinovarus is a key deformity that can prevent even limited functional ambulation or unassisted transfers. Overactivity of the hamstrings may indicate that knee stiffness is a defense against knee flexion collapse.

Diagnostic motor point block may reveal whether weakening strategies are indicated for reducing knee stiffness. In the flexed knee, overactivity in the hamstrings is more often medial than lateral. (Bhakta et al. 2000).

1.5.3 Tremor

The most frequently seen tremor in MS is largely a function of cerebellar involvement. Patients with lesions in the cerebellum will most likely have balance problems as well. Tremor, however, presents its own set of problems. Tremor in the hands, if severe, may interfere with a person's ability to propel a manual wheelchair, drive a power chair or use an ambulatory aid. If body tremor is present, it interferes with ambulation and movement of any type. Tremor may interfere with transfers, bed mobility, balance and safety. Tremor, if severe, is fatiguing. Tremor also interferes with driving an automobile.

1.6. Climbing wall training

We chose climbing on a wall as a rehabilitation paradigm because it is a complex task for the motor system which probably demands the integratory function of the whole cerebellum and all the sensory systems. Cerebellum helps provide smooth coordinated body movement. It requires precise pointing movements of the feet and the hands to the grips, planning in advance of some movements in order to avoid impossible body positions within the climbing wall, and for more advanced climbers optimal body positions in order to put the largest possible weight on the feet and the least possible force on the hands and an important force in relation to the body weight (mainly in fingers). Climbing has other features making it interesting for patients. The climber has a well-defined task to fulfill to reach the top of the wall without external help. Mobility is a primary area of concern for healthcare professionals treating people with multiple sclerosis (MS). Mobility limitation is often the result of several impairments that are common in MS and can affect a person's vocational and recreational activities, one's self-esteem and quality of life. Many impairments and deficits can influence the mobility of a person with MS. Some of the factors that may affect one's mobility include spasticity, weakness, balance and coordination impairment, sensory and visual disturbances, fatigue, cognitive deficits, and emotional problems such as depression. Many times mobility limitation is due to multiple factors requiring a multi-disciplinary treatment approach. Mobility can be separated into balance impairments.

Balance impairments are common in people with MS and can adversely affect overall mobility. Generally, balance includes the interaction between visual, proprioceptive (muscle, joint and skin) and vestibular (head position and movement) systems. Balance can also be affected by spasticity, weakness, cognitive deficits and emotional distress.

1.7. Main Objective

- We wanted (1) to quantify spasticity, muscle force and the range of active movements of stroke patients trained on an arm-ergometer by means of the arm force, the surface EMG of the biceps and triceps and several clinical tests, and (2) to test whether the training changes them significantly.
- We wanted to investigate the effects of climbing on (1) a reduction of the dismetria, (2) a reduction of the tremor, (3) an improved ability to maintain a constant force, (4) a reduction of the clumsy, impaired ability to perform the rapid alternation movements, (5) a decrease reaction time (RT), and (6) an improved performance on the climbing wall for the cerebellar patients.

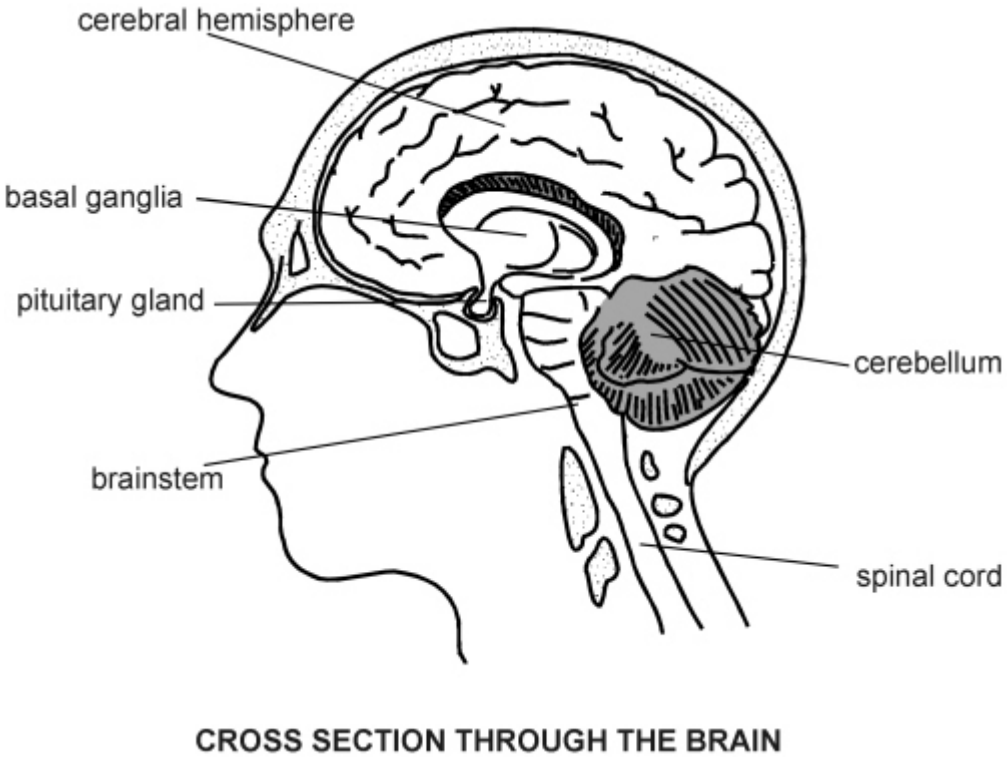

Fig. 1.1: The cross section of the human brain

2. Rehabilitation of stroke patients with an arm ergometer

2.1. Introduction

Patients recovering from a stroke usually receive physiotherapy with the aim to improve the outcome of functional rehabilitation. Often conventional physiotherapeutic exercise programs are applied for which neurophysiological background is not well understood due to missing basic research in this field. In some programs, the difference between the functional outcomes cannot be detected (Dickstein et. al. 1986; Basmajian et al. 1987; Wagenaar et al. 1990). Recently, a new approach based on simple repetitive movements which form the basis of motor learning has been shown to accelerate recovery of hand function after a stroke (Bütefisch et al. 1995). However, the repetitive training of complex movements did not further enhance recovery compared to functionally based physiotherapy (Woldag et al. 2003). The present investigation is based on this approach and was realized by arm cycling.

The main purpose of rehabilitation is to improve motor function and the use of the affected limb in daily life. Recovery itself can be attributed to several factors. One important aspect is to reduce spasticity, which often arises some months after a stroke in anti-gravity muscles. The antispastic effect of exercises on a motorized ergometer, which move the legs similarly as during cycling, was documented by the F-wave, reflecting changes of motor neuron excitability during rhythmic movements (Rösche et al. 1997). Clinical follow-up by the Asworth Scale assessment confirmed these results (Durner et al. 2001). The assessment of spasticity is, however, controversial (Kakebekke et al. 2002). Even if spasticity is tested using its definition, i.e. a velocity-dependent response to passive stretching, results have been ambiguous with significant differences obtained in a supine and sitting position (Kakebeeke et al. 2002). In the present context, the main purpose is to evaluate whether a rehabilitation program can lessen the degree of spasticity. We are thus not so much interested in absolute values of spasticity but in values that change significantly by the training and are related to a reduced spasticity. Correspondingly we accounted for several factors related to spasticity, the Ashworth scale, the range of active movements, the breaking force of the biceps during cycling, and a relational value based on the surface EMG.

Another factor contributing to recovery is muscle force. The muscle force, not just related to the trained movement, was quantified by several factors, in a similar way as spasticity: (1) the cycling force of the arms (the trained movement), (2) the Rivermead Motor assessment (RMA) and (3) the Motricity Index (MI).

The aims of our investigation were (1) to quantify spasticity, muscle force and the range of active movements of stroke patients trained on an arm-ergometer by means of the arm force, the surface EMG of the biceps and triceps and several clinical tests, and (2) to test whether the training changes them significantly. A preliminary account of some of the results has already been presented (Diserens et al. 2004).

2.2. Methods

2.2.1. Patients

One female and 8 male patients with a mean age of 66.3 years (range from 51 to 84; Tab. 2.1) participated in this study. Each of them had given his written informed consent. All patients had a stable hemiparalysis due to an ischemic lesion that occurred in the 22.7 months before inclusion in the study. As revealed by computerized tomography, no patient had more than one cerebral lesion. Inclusion criteria were (1) to be able to participate for at least 30 min. of exercise using a hand ergometer, (2) to have no problems of comprehension, and (3) to be able to give their informed consent. Patients with aphasia, shoulder pain or serious neuropsychological deficits were excluded.

Tab. 2.1: Patient data and clinical signs; F: female; M: male;

Subject	Gender/age	Diagnosis	Duration of disease(years)	Part of the brain affected
A	M/84	Ischemic supra capsular	3	Right
B	M/62	Ischemic capsular	1	Left
C	M/71	Hemorrhagic sylvian	2	Right
D	M/67	Ischemic center semi oval	4	Right
E	F/85	Ischaemic sylvian and cerebral front	3	Left
F	M/52	Ischaemic sylvian	2	Right
G	M/52	Ischaemic sylvian	2	Left
H	M/70	Paramedian Pontiac	1	Left
I	M/54	Sylvian originally Cardioembolic	2	Right

2.2.2. Material and Methods

Training was conducted on a commercial motorized arm-ergometer (Motomed viva Reck; Fig. 2.2.A), which facilitated the training by allowing sophisticated manipulations. Physiotherapists usually have to perform such manipulations to bring patients in a condition to allow optimal training. A second scientific ergometer, developed by the Fachhochschule für Technik und Architektur, Freiburg (Fig. 2.1B), was used to take quantitative measurements during cycling. Strain gauges with a bridge circuit were mounted on the levers of the two pedals to allow torque measurement on both sides independently (only the sum of the left and right torque can be measured with the motorized ergometer according to the current consumed by the motor). Gliding contacts transmit the torque signals and the power supply between the turning levers and the body of the ergometer. The axes of both levers were connected to an angle encoder (12 bit resolution) in order to measure the angle of the pedals. In order to modify the difficulty of pedaling, the two pedals can be disconnected so that they turn independently. In addition, both pedals are equipped with a mechanical breaking system (friction), which increases the cranking resistance.

The electromyogram (EMG) of the biceps and triceps muscles of both arms was recorded during some sessions with surface electrodes. Care was taken to place the electrodes in the same positions during the various sessions in order to obtain comparable results.

The EMGs were low-pass filtered at 1 kHz to avoid aliasing and then, as the signals from the ergometer, fed into the ADC (3 kHz/channel) of a PC.

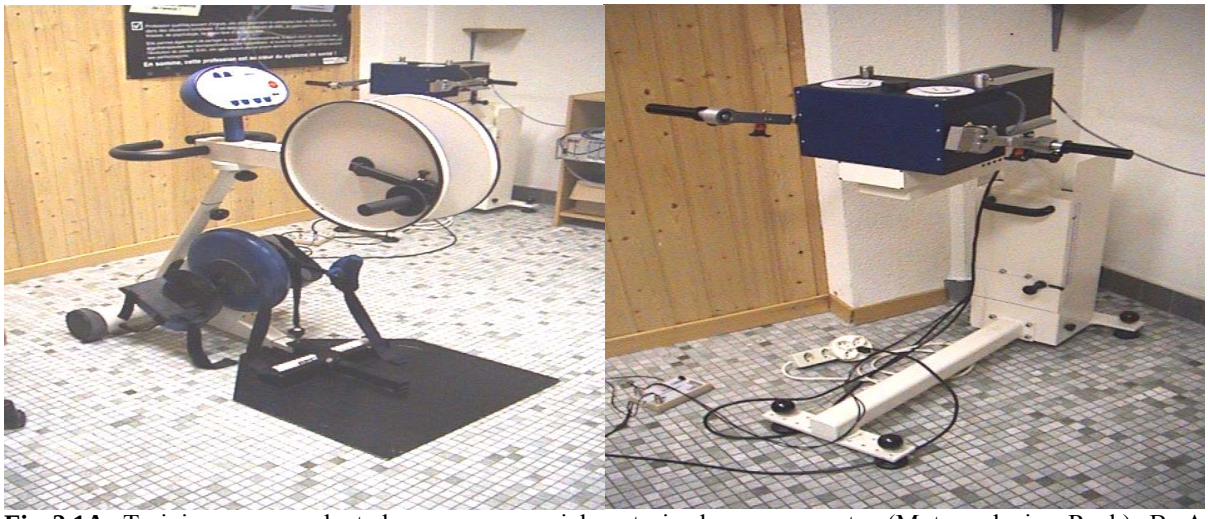

Fig 2.1A. Training was conducted on a commercial motorized arm-ergometer (Motomed viva Reck), B. A second scientific ergometer, developed by the Fachhochschule für Technik und Architektur, Freiburg, was used to take quantitative measurements during cycling.

2.2.3. Experimental Protocol

An A-B-A protocol consisting of the following 3 stages was used:

- A base line (or reference line), which assesses the state of the patient prior to any treatment (pre-training Phase A). In the present investigation, this lasted one week (patients in chronic condition).
- A treatment phase with a therapeutic procedure (Phase B) lasting 3 weeks.
- A follow-up phase, during which the behavioral changes resulting from the treatment (post-training Phase A) were studied (duration 2 weeks).

The patients were positioned in front of the ergometer, either seated in their wheelchair or on an armless chair, so as not to hinder cycling movements. They performed the arm training on the motorized ergometer for 30 minutes daily, 5 days a week and over the 3 weeks of Phase B. The sessions took place in a room specially reserved for the present study, where a physiotherapist took care of the patients.

Each training session comprised 15 min of arm cycling in the forward direction and 15 min in the backward direction with a 5 min break in between. The training was performed without an activated motor (the motor would increase the cycling resistance). Patients were not assisted in any way during the exercise apart from verbal encouragement from the therapist. For patients with severe paralysis, the contralateral arm performed the movement practically by itself.

Each patient was tested during 4 sessions: (1) at T0, the beginning of the pre-training phase A; (2) at T1, one week later, at the end of the pre-training phase; (3) at T2, 3 weeks after T1, at the end of the training period B; and (4) at T3, 2 weeks after T2, at the end of the post-training phase A. The tests included quantitative measurements on the scientific ergometer and a clinical assessment.

2.2.3.1. Recordings on the ergometer

All the subjects cycled in the same direction during the test sessions. The hand moved away from the body on the upper half-circle of the movement trajectory (extension phase), and moved toward the body on the lower half-circle (flexion phase). The pedal torque and the angular position were recorded independently on both sides, usually during 40 sec of continuous pedaling. Since the pedals always remained interconnected, position signals on both sides were equal except for a phase shift of 180^0. The surface EMG of the biceps and triceps muscles was recorded on both sides in some of the sessions.

2.2.3.2. Clinical Assessment

The same person performed all the following tests on a patient.

Rivermead Motorik Assessment (RMA; Lincoln and Leadbitter 1979; Collen et al. 1990): Physiotherapists use RMA to measure gross motor function, upper limb control, and lower limb and trunk control. In this study all 3 sections were evaluated, but only data concerning the upper limb control are presented under Results.

Ashworth Scale: Spasticity was clinically evaluated by the modified Ashworth Scale (Sloan et al. 1992).

Motricity Index (MI); Demeurisse et al. 1980; Collen et al. 1990): The force of the elbow and shoulder flexors and extensors was tested manually. Grading is derived from Medical Research Council grades ranging from 0 (no movement and no contraction can be palpated) to 5 (movements with normal power). The patients' performance was evaluated on the lesioned side by taking the sum of the quotation on the elbow flexors, elbow extensors, shoulder flexors and shoulder extensors.

Range of motion: The range of active movements of the elbow and shoulder of both sides was measured with a goniometer. In order to quantify the performance of a patient, the sum of the angles on the lesioned side was taken: (1) for shoulder flexion and abduction (up to 180^0), (2) for elbow flexion (up to 140^0) and (3) elbow extension (up to 0^0).

Maximum cycling force: The maximum cycling force was measured on the lesioned side. The resistance to cycling could be adjusted on the scientific ergometer. The maximum force was evaluated at which the patient was able to cycle for 10 seconds at a constant frequency.

2.2.4. Data Analysis

Data acquisition, as well as processing, was performed using the LabView programming language (National Instruments), data were saved using the data base Access (Microsoft), and statistical analysis was performed using the statistical package SPSS (SPSS Inc.).

2.2.4.1. Cycling torque

In order to compare quantitatively the forces the patients exerted on the pedals before and after the training, the data obtained during a recording session were averaged across cycles. Since the cycle duration varied from cycle to cycle within a recording session, and even more from session to session and from patient to patient, the data were normalized by computing the torque as a function of the angle, which was obtained by eliminating time from the angle - time and torque - time relations. After the transformation, each cycle had the same length

(from 0^0 to 360^0) and concomitant signals could be averaged. The minimum torque on the lesioned side was measured for each trial on the averaged torque signal. These values were averaged across the trials recorded at one date.

2.2.4.2. Cycling speed

It was computed by dividing the cycles performed during a trial by the duration of the trial.

2.2.4.3. EMG.

In order to quantify the EMG activity, it was high-pass filtered (cut-off frequency 2Hz) in order to eliminate DC shifts and eventual slow movement artifacts, full-wave rectified and then low-pass filtered (cut-off frequency 5Hz) in order to obtain the activation level. Similarly to the torque recordings, the cycles were normalized and the EMG activation level as a function of angle could then be averaged across the cycles. In order to obtain the EMG modulation, a time window during which the muscle was active and another window during which it was inactive were determined manually on a display of the curves of the EMG activation level. The curves were integrated between the windows and the relation between the two integrals was computed (mean activity during the active phase divided by the mean activity during the inactive phase).

2.2.4.4. Spasticity and muscular force

Both of them were estimated in different ways. The spasticity was measured by (1) the Ashworth scale (Tab. 2.2), (2) the maximum active extension of the biceps, and (3) the minimum torque on the lesioned side during arm cycling, and the muscular force was measured by (1) the RMA, (2) the MI (Tab. 2.3) and (3) the cycling force. There were thus 3 data sets related to spasticity and another 3 related to muscular force. Both groups of data have been analyzed in the same way. The Pearson correlation coefficient between the data sets and its significance were computed. The 3 data sets cannot be combined directly to test the effect of training since they are measured in different units.

Therefore they were transformed. The mean of all observations was subtracted from each observation and the resulting values were divided by their standard deviation (z-transformation). The data sets, which have then a mean of zero and a standard deviation of one, were pooled and an analysis of variance (ANOVA) was performed with the factors time of testing and patient.

2.2.4.5. Range of movement:

The range of active movement of the elbow and the shoulder was evaluated by goniometry. A physiotherapist measured the degree of possible flexion and extension. Since the elbow and shoulder are involved in cycling movements, both were weighted identically to evaluate mobility. Angles of possible movements were thus added which resulted in a number ranging from 0 to 500^0. 0^0 corresponding to an immobile subject and 500^0 to a normal subject performing a shoulder flexion of 180^0, a shoulder abduction of 180^0, an elbow flexion of 140^0 and an elbow extension of 0^0. As above, an ANOVA was computed with the factors time of testing and patient.

Tab. 2.2: An ANOVA of the spasticity of the patients. The spastictiy was evaluated by the Ashworth Scale, the active movement range of the biceps and the minimum force during cycling (see text). The data were pooled after normalization (z-score). The differences between the dates of testing are just not statistically significant, the differences between the patients, however, highly significant

Source		Sum of Squares	df	Mean Square	F	Sig.
Dates of testing	Hypothesis	2.200	3	.733	2.584	.076
	Error	6.964	24.539	.284		
patient	Hypothesis	71.495	8	8.937	31.491	.000
	Error	6.964	24.541	.284		
time * patient	Hypothesis	6.810	24	.284	.983	.499
	Error	19.338	67	.289		

Tab. 2.3: An ANOVA of the force of the patients. The force was evaluated by the RMA, the MI and the maximum pedaling force. The data were pooled after normalization (z-score). The differences between the dates of testing and the patients are highly significant.

Source		Sum of Squares	df	Mean Square	F	Sig.
Dates of testing	Hypothesis	1.550	3	.517	17.260	.000
	Error	.718	24	.030		
patient	Hypothesis	98.084	8	12.261	409.593	.000
	Error	.718	24	.030		
time * patient	Hypothesis	.718	24	.030	.464	.981
	Error	4.647	72	.065		

Tab. 2.4: Modulation of the biceps and triceps muscles during cycling for a subject. The mean EMG activity during the ranges was computed. The modulation ratio is the mean activity when the muscle is active divided by the mean activity when the muscle is inactive.

Muscle	**Range**		**Modulation Ratio**	
	active	inactive	control	test
Biceps	100^0 - 325^0	345^0 - 70^0	6.58	1.18
Triceps	265^0 - 75^0	75^0 - 265^0	3.42	0.70

Tab. 2.5: An ANOVA of the range of active movement. The differences between the dates of testing are statistically significant, the differences between the patients highly significant.

Source		Sum of Squares	df	Mean Square	F	Sig.
Dates of testing	Hypothesis	2935.417	3	978.472	5.786	.004
	Error	4058.333	24	169.097		
patient	Hypothesis	1274375.00	8	159296.87	942.043	.000
	Error	4058.333	24	169.097		
time * patient	Hypothesis	4058.333	24	169.097	.	.
	Error	.000	0	.		

2.3. Results

2.3.1. Pedaling

2.3.1.1. Minimum pedal torque on the lesioned side

The torque signals vary during a cycle in a normal pedaling subject (Fig. 2.2A). The signals from the left and right side, which are 180^0 out of phase, add up to the total torque corresponding to the breaking force of the ergometer. If a subject is cycling with relatively little force as the subject presented in Fig. 2.2A (and all the patients), the torque of either arm approximates zero when it was closest to the body. At this position, pulling on the lower half circle stops and pushing on the upper half circle starts the movement. At the moment of zero torque, the contralateral side comes up with full force. In contrast to the torque signals of normal subjects, the torque signals of patients who are partially paralyzed in the arm contralateral to the stroke are lower on the paralyzed than on the normal side (Fig. 2.2B). The patients are not able to relax spastic arm flexor muscles during the extension phase. Since the two pedals are linked together, the intact arm can come up for the missing force in the paralyzed arm and correspondingly develops more torque. During the extension phase, the contracted flexor muscles can even result in a negative torque on the spastic side when the

force is greater in the flexors than in the extensors (Fig. 2.2B), reflecting the spastic flexors, which the subject cannot relax. The EMG signals on Fig. 2.2C confirm that the biceps, one of the flexor muscles was constantly active on the affected side and scarcely modulated during cycling.

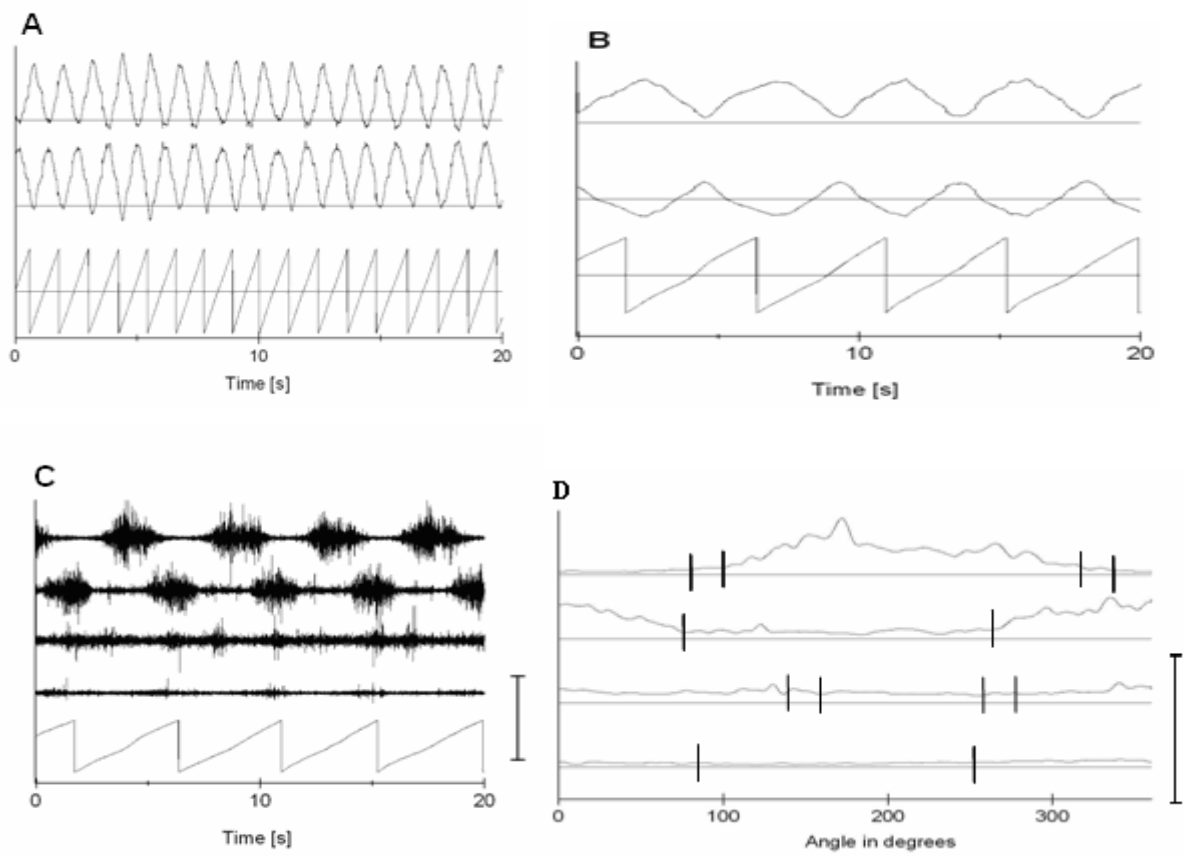

Fig. 2.2A. Torque and position signals of a normal subject during 20 s of pedaling. From top to bottom: torque signal on the left side (calibration: 3 Nm), torque signal on the right side (calibration: 3 Nm) and position signal of the left pedal (calibration: 360^0). The position signal is reset with the stretched left arm. The horizontal lines indicate level 0. Torque signals are nearly symmetrical in a normal subject. **B**. Torque, position and EMG recordings from a subject with a paretic right arm. From top to bottom: torque signal on the left side (calibration: 3 Nm), torque signal on the right side (calibration: 3 Nm) and position signal on the left side (calibration: 360^0). The position signal is reset with the left stretched arm. The horizontal lines indicate level 0. **C**. Subject with paretic right arm, from top to bottom: EMG of the left biceps (calibration: 3.6 mV), EMG of the left triceps (calibration: 3.6 mV), EMG of the right biceps (calibration: 3.6 mV), EMG of the right triceps (calibration: 3.6 mV), and position of the left pedal (calibration: 360^0). The EMG signals on the right side are nearly not modulated during cycling. **D**. Rectified and averaged EMG signals from a subject with a paretic right arm. From top to bottom: EMG of the left biceps, EMG of the left triceps, EMG of the right biceps, EMG of the right triceps, and position of the left pedal. Limits on the left side are used to define time window during muscle activation and relaxation. Corresponding limits on the right side are used to compute muscle activity modulation during cycling (see text). Calibration: 1 mV. The EMG signals on the right side are nearly not modulated during cycling.

2.3.1.2. Cycling speed

Since the patients were not able to maintain a fixed cycling speed, they were free to choose their speed, even though it is obvious that the cycling speed is important when judging

performance. As the biceps and triceps muscle are alternatively shortened and stretched during each cycle, we can expect that spasticity in the stretched muscles increases with cycling speed. Although the patients could chose different speeds, there was not a consistent relation between the time of testing and the cycling speed and we were not able to identify a significant relation between spasticity and cycling speed (not documented). The cycling speed was considered in the further presentation of the results.

2.3.2. Spasticity

The level of spasticity in the arm muscles, which differed from patient to patient, was evaluated by (1) the Ashworth scale, (2) the maximum active extension of the biceps, and (3) the minimum torque on the lesioned side during arm cycling. As expected the 3 data sets are correlated: The correlation between the Ashworth scale and the biceps extension was -0.634 (Fig. 2.3A), between the Ashworth scale and the minimum torque -0.578 (Fig. 2.3B), and between the biceps extension and the minimum torque 0.760 (Fig. 2.3C). We used all these data to test whether training on the arm ergometer decreased spasticity. The data were transformed (z-transformation) pooled and an ANOVA was performed (Tab. 2.2). The differences of spasticity from patient to patient were highly significant ($p < 0.001$) but the differences due to the date of testing were just not significant ($p = 0.076$). The numerical data with the confidence limits (Fig. 2.3D) confirm this finding. Due to the data transformation, the average of all values is 0 and the ordinate is dimensionless. It can clearly be seen that before the training (test times 0 and 1) spasticity was larger than after the training (test times 2 and 3), the confidence limits are, however, large and the differences are not significant.

Having identified spastic movements on the lesioned side, we analyzed EMG recordings in order to identify the involved muscles. The EMGs from the biceps and triceps muscle (Fig. 2.2D) were analyzed in a patient with the Ashworth scale 2, a maximum active extension of the biceps of -20^0 (0^0 corresponding to full extension) and a mean minimum torque during cycling of -.04 Nm. A time window during the active and during the inactive period was determined manually on a display of the average EMG curves of the biceps and triceps of the intact side (the two lower curves of Fig. 2.2D). The relation of the mean EMG activity during the two windows quantifies the degree of modulation of muscle activity during arm cycling. In the present example, the relation was 6.6 for the biceps and 3.4 for the triceps (Tab. 2.4), i.e. the biceps was 6.6 times more active during the flexion than during the extension phase, and the triceps was 3.4 times more active during the extension than during the flexion phase. The same limits were applied to the contralateral side, but 180^0 out of phase. A similar

relation would result in a normal subject. In this patient, the relation was 1.18 for the biceps and 0.70 for the triceps muscle (the two upper curves of Fig. 2.2D). The patient was practically unable to modulate the activity of biceps so as to assist the cycling movements. The condition of the triceps was even worse; the activity was modulated in such a way as to hinder the cycling.

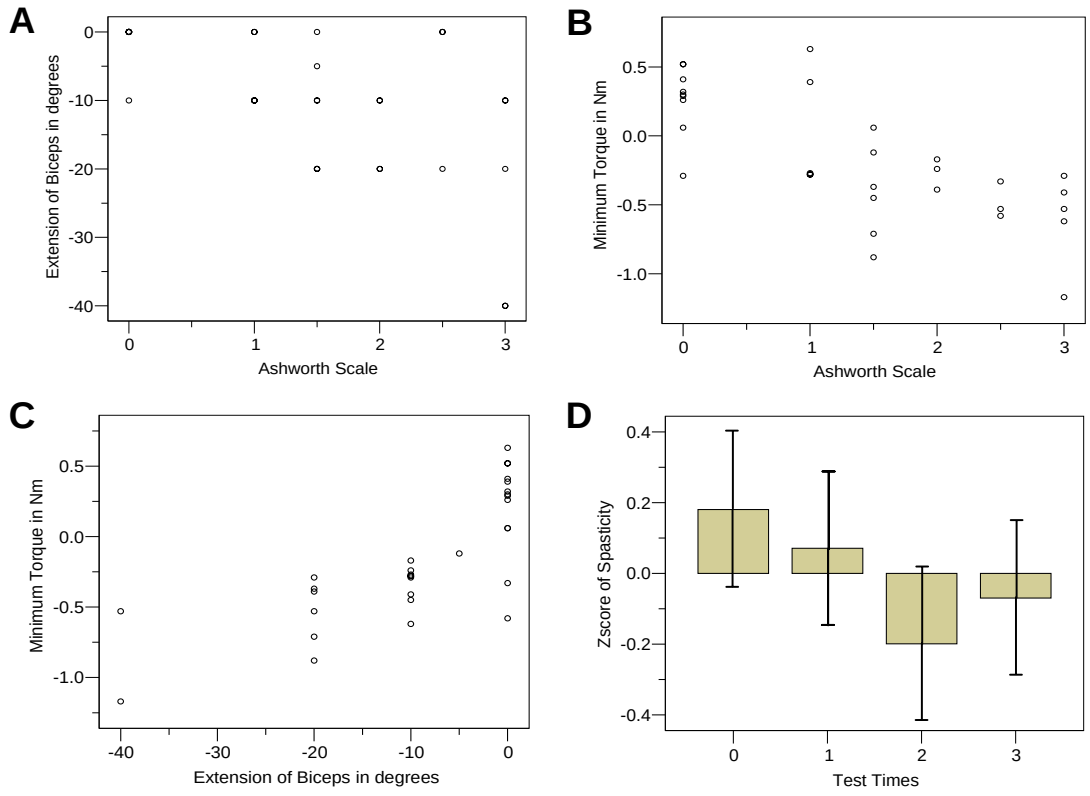

Fig. 2.3. Training effect on the spasticity of all the patients. The Ashworth Scale, the range of active extension of the biceps and the minimum torque on the paretic side during pedaling were assumed to be related to spasticity. Correspondingly they were correlated: The dots corresponding to the patient performance with corresponding relation values. Ashworth Scale – extension of biceps (**A**): $r^2 = -0.634$, $p < 0.001$; Ashworth Scale – minimum torque (**B**): $r^2 = -0.578$, $p < 0.001$ and extension of biceps – minimum torque (**C**): $r^2 = -0.768$, $p < 0.001$. The 3 variables were normalized (z-score) pooled in order to obtain a measured for spasticity, an ANOVA was performed and confidence limits were computed (in **D**). D: Average spasticity 3 weeks before (0) at the beginning (1) at the end (2) and 3 weeks after (3) the training. Bars are confidence limits ($p = 0.05$). The differences are not significant.

2.3.3. Muscular Force

Muscular force was estimated by the Rivermead Motorik Assessment (RMA), the Motricity Index (MI) and the cycling force. Similar as with spasticity, the 3 data sets are correlated. The correlation RMA – MI was $r = 0.939$ (Fig. 2.4A), the correlation RMA – cycling force $r = 0.945$ (Fig. 2.4B) and the correlation MI – cycling force $r = 0.91$(Fig. 2.4C). All of them were highly significant ($p < 0.01$). As for the spasticity, the data were normalized, pooled and an ANOVA with the factors of time of testing and patient was performed. The differences

between the patients and between the recording times were highly significant ($P < 0.001$, Tab. 2.3). The force of the patients remained constant during the base line and during the following up period, but increased significantly over the period of training (Fig. 2.4D). The confidence limits are not overlapping, illustrating thus significant training effect. The patients are sorted according to decreasing force in Fig. 2.5 providing the details of the individual patients. All the patients gained force during the training and this force increase remained during the following 3 weeks.

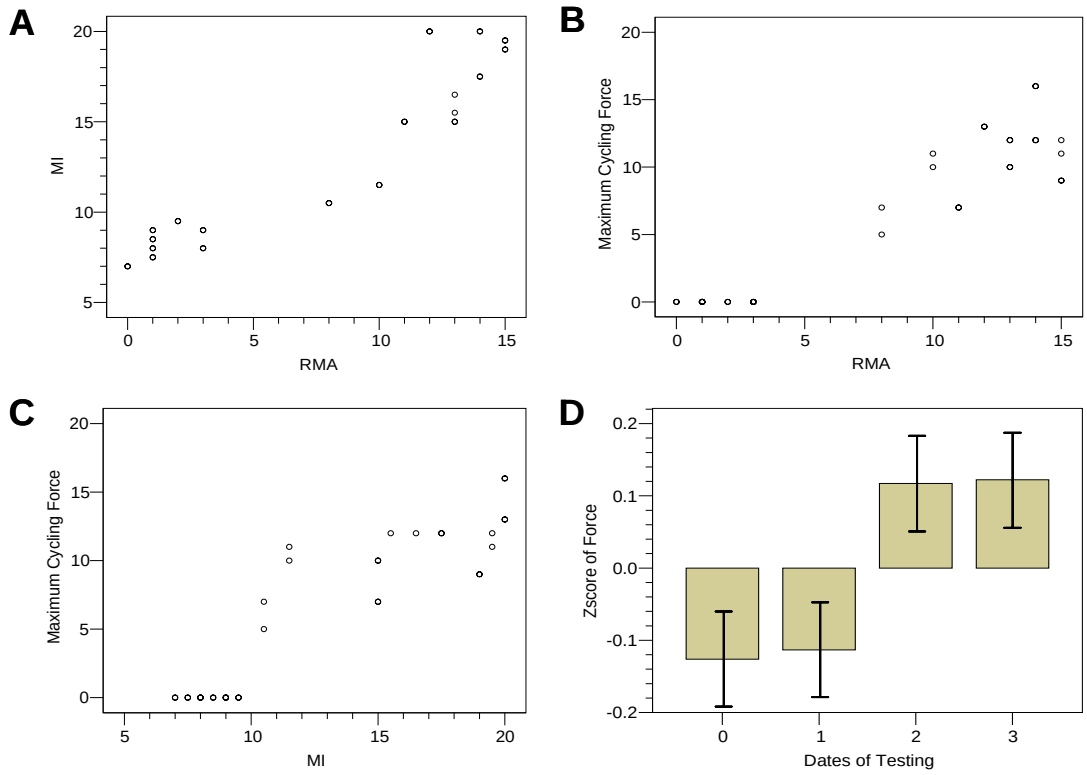

Fig. 2.4. Training effect on the arm force. The RMA, MI and the maximum cycling force during pedaling were assumed to be related to the arm force. Correspondingly they were correlated: The dots corresponding to the patient performance at with corresponding relation values, **A**. RMA – MI: $r^2 = 0.939$, $p < 0.001$; **B**. RMA – cycling force: $r^2 = -0.945$, $p < 0.001$ and **C**. MI – cycling force: $r^2 = -0.917$, $p < 0.001$. The 3 variables were normalized (z-score) pooled in order to obtain a measured for arm force, an ANOVA was performed and confidence limits were computed (in **D**). D: Average arm force 3 weeks before (0) at the beginning (1) at the end (2) and 3 weeks after (3) the training. Bars are confidence limits ($p = 0.05$). The differences are significant ($p < 0.001$). Due to the normalization, values can be negative. There was a significant increase of arm force after the training.

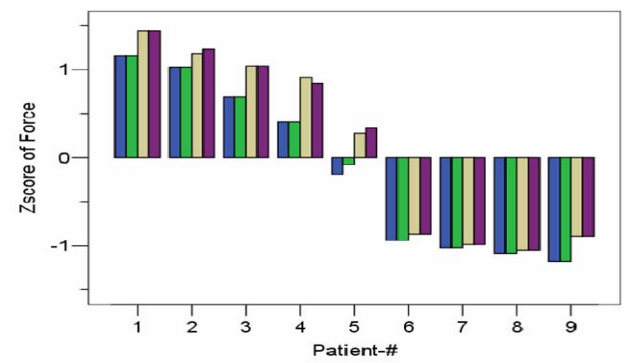

Fig. 2.5. Training effect on the relative arm force in the individual patients. Blocks of bars represent data of individual patients who are arranged according to decreasing forces. Due to the normalization, there are negative force values. Bars within a block show, from the left to the right, the average force before (0) at the beginning (1) at the end (2) and 3 weeks after (3) the training. The arm force was larger after than before the training in all the patients.

2.3.4. Range of Movement

The range of movement was evaluated as the sum of the angles at a maximum shoulder flexion, shoulder abduction, elbow flexion and elbow extension. All patients had approximately normal values on the non-lesioned side (not presented here). On the lesioned side, the variability was very large ranging from 20^0 to 500^0 with a mean range of 288^0. In the ANOVA, the F value obtained for the differences between the subjects was extremely high (F = 942, Tab. 2.5). The average range of possible movements during the 3 weeks before the training and during the 3 weeks after the training remained nearly the same, however, there was a marked increase of 18^0 ($p < 0.005$, Fig. 2.6) due to the training on the ergometer.

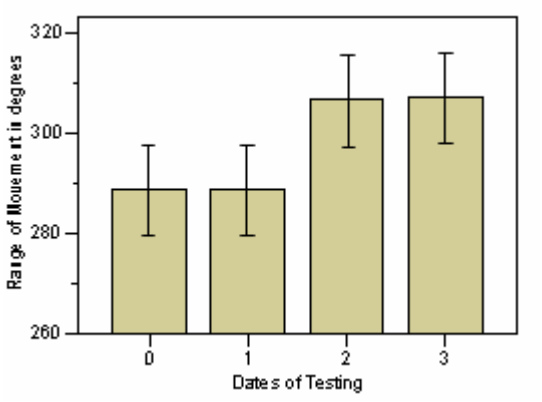

Fig. 2.6. Training effect on the range of active movements. The maximum flexion and extension movements of elbow and shoulder were measured in degrees and the values were added, resulting in mean values around 300 (see text). The 4 bars with confidence limits represent the data at the testing dates as in A and B. The differences between the values before and after the training are significant ($p < 0.001$).

2.4. Discussion

2.4.1. Arm Ergometer

An ergometer is suitable for training stroke patients who usually are paralyzed unilaterally. The intact side can help pedaling the affected side, which often is not able to perform the rotating movements itself. In sophisticated ergometers, the difficulty of the task can be varied by increasing the pedaling resistance or by disconnecting the two pedals and the torques acting on the right and left side can be measured separately. The performance of the affected limb can then be investigated quantitatively. An alternative solution for quantitative studies, EMG recordings, would require the presence of a specialist and the analysis of EMG recordings is more complicated and time-consuming than the analysis of torque recordings.

The situation is more favorable when cycling is performed with the legs rather than with the arms. Subjects push the pedals downward with the legs and usually no pulling forces can be observed during the upward movements (except during bicycle race sprints). In this situation, forces from the right and left leg can be separated since at one time only one leg is developing torque. The arms, however, pull and push during circular movements and these torques have to be measured independently in order to quantify the contribution of each arm. However, even in the legs, the situation is more complicated if a spastic limb slows down the movement.

2.4.2. EMG

Being able to measure torques separately on both sides allows comparing the performance of the intact side with the performance of the lesioned side. The activation of individual muscles cannot, however, be studied since, at each joint, several muscles contribute to the torque. The aim of the present investigation was to test whether the EMG can be used to quantify spasticity of individual muscles during arm cycling. We assumed that spasticity during arm cycling can be quantified by comparing the modulation of the muscle activation on the lesioned side with the modulation on the unaffected side. A typical example in *Results* illustrates the technique, which we could not systematically apply due to methodological restrictions. The EMGs were rectified, normalized in relation to cycle duration, averaged across cycles and low-pass filtered in order to obtain the activity pattern as a function of the angle. On the unaffected side with normal cyclic muscle activation, a time window was defined during which the muscle under investigation was active and a second window when the muscle was relaxed. The relation between the mean activities during these two windows was taken as the value for the modulation of muscle activity (biceps: 6.6, triceps: 3.4). The

same calculations were performed with the EMGs on the lesioned contralateral side, but with the windows shifted by 180^0 in relation to the unaffected side (biceps: 1.2, triceps 0.7). We propose as index for the spasticity of a muscle the relation between the two values. We obtain then for the biceps 4.2 and for the triceps 4.9. The corresponding values in a normal subject would be close to 1. This spasticity index was found to be efficient to quantify the spasticity of a muscle and it has the main advantage not to be affected by amplitude variations due to different electrode positions and other factors. If a patient is partially paralyzed but does not show signs of spasticity the different activation levels of the affected muscles are reduced by the same factor and the spasticity index would be similar as on the unaffected side, i.e. close to 1. We can thus conclude that the value of the index is mainly dependent on the spasticity of the corresponding muscle. The final goal is to estimate how paralyzed and spastic muscles affect adversely pedal torque. Of main importance in this context is co-contraction which can cancel forces of agonists and antagonists. Knowing EMG activities, relative muscle forces can be estimated. In steady-state contractions, the relation between EMG and force is approximately linear (Lawrance and De-Luca 1983; Woods and Bigland-Ritchie 1983). Relative values can, therefore, be obtained as long as dynamic components are of minor importance. Absolute forces cannot be obtained from EMG recordings since their amplitude is influenced by (1) the type of electrodes; (2) the distance between them and, (3) their position in relation to the muscle, and furthermore it does not reflect anatomical characteristics of the muscle (Tate and Damiano 2002). The EMG – force relation of fast time-dependent muscle contractions is highly non-linear. In the case of arm cranking at constant speed, movement patterns are similar at each cycle and, in consequence, useful information about muscle force might be derived.

From the present results, we can conclude that EMG recording is a valuable tool to estimate the motor performance of muscles, their spasticity, and relative forces in cycling subjects.

2.4.3. Patient Performance

2.4.3.1 Spasticity

The biceps to assist the cycling after regeneration of the motor end-plates. This could be expected sinced Botulinum toxin injection changes the cortico-motor representation (Byrnes et al. 1998). Aspects of spasticity were assessed by (1) the Ashworth scale; (2) the range of active elbow extension, and (3) the minimum torque during cycling (negative values indicate that the movement was slowed down). All 3 of them were correlated at a significant level,

indicating they are indeed related to spasticity and they were therefore used to test whether training reduced spasticity. The results clearly showed that training was beneficial for the patients, but the data were statistically just not significant due to their high variability (within a date of recording but also during the pre- and post-training period). These first quantitative results regarding the effect of repetitive training by an arm-trainer on spasticity are corroborated by Durner et al. (2001), who evaluated spasticity by the Ashworth rating scale immediately after training on an arm-trainer. Furthermore, Roesche et al. (1997) reported that the mean F-wave amplitude, the mean F-wave/M-response ratio and the maximum F-wave/M-response ratio were significantly lower after leg training with a motorized exercise-bicycle, documenting a decrease of spasticity.

Trying to objectively quantify spasticity is a well-known problem (Kakebeeke et al. 2000). Several clinical tests carried out to assess spasticity correlate only poorly, suggesting that such tests evaluate different aspects of spasticity (Priebe et al. 1996). Spasticity is defined by the velocity-dependent response to passive muscle stretching. Accordingly, Kakebeeke et al. (2000) used isokinetic dynamometry, which proved to be an adequate technique to assess spasticity in leg muscles. We have developed a quantitative method based on the surface EMG to assess spasticity during arm cycling. The spasticity index is of interest since during cranking arm movements are more complex than leg movements and a relation between spasticity and torque is more difficult to establish. In contrast to arm movements, leg movements are within a plane orthogonal to the pedal axis. Furthermore, at relatively high forces, arm muscles develop torque during the extension and flexion phase, leg muscles, however, only during the extension phase. The spasticity index can easily be assessed during routine studies since (1) it is independent of the electrode properties (it is computed with the EMG activities recorded from one electrode pair during one session) (2) it can be performed on each muscle of interest, and (3) it requires standard techniques and can easily be computed. Spasticity and exaggerated cocontractions are often the main reason for a functional reduction of arm movements and proved also to hinder arm-cycling in the patients participating in the present study. The question arises whether a cycling training after Botulinum toxin injection would prolong effect of the injection or even enable.

2.4.3.2 Force

After the training, all patients were able to cycle against a higher resistance and performed better in the clinical tests related to force. A force increase due to the training could be expected on the control side since the patients did not experience any arm cycling before they participated in the

investigation. It was, however, not known whether training can produce a force increase on the lesioned side. The observed increase can be due to training mechanisms as on the control side or/and other special mechanisms, such as plasticity. Independent of the mechanisms, it is clear that the force increase is favorable not only for arm cycling but also for activities of daily life, which is finally the principal aim of rehabilitation. This is also reflected by the RMA, which covers the shoulder, elbow and hand function with and without manipulation of objects as well as the MI reflecting elbow and shoulder function.

2.5. Conclusions

Although the stroke of the patients participating at this investigation occurred on average nearly 2 years before the study and their condition remained stable, an additional adequate training can expected to be effective since recovery can occur over the course of several years (Bard and Hirschberg 1965; Heller et al. 1987; Broeks et al. 1999). This finding was corroborated by our study, confirming that arm cycling significantly improved the force of the patients, increased the range of active movements and decreased spasticity, and by Sunderland et al. (1989) and Collin and Wade (1990) who observed a parallel improvement in several tests during recovery after a stroke. Repetitive movements seem to be particularly effective in rehabilitation and motor learning (Bütefisch et al. 1995). The major mechanisms are attributed to synaptic plasticity and synaptic efficacy in existing neural circuits (Asanuma and Keller 1991). Alternative descending pathways, secondary and ispsilateral motor areas and other brain areas implicated in motor control can also contribute to motor recovery (Freund and Hummelsheim 1985; Aizawa et al. 1991; Chollet et al. 1991; Fries et al. 1993, Weiller et al. 1993; Rossini and Dal Forno 2004). This investigation confirmed that simple repetitive movements are suited for functional recovery (Bütefisch et al. 1995; Hesse et al. 2003a). Patients, who are motivated to continue training, can do it themselves, which is an alternative to the hand-to-hand therapy, often limited by budget constraints. Cycling is one of the easiest trainings to achieve. It just requires a bicycle. A new field, robot-assisted motor rehabilitation, has emerged for other repetitive movements, such as walking, which are more complex to achieve (Hesse et al. 2003).

3. Climbing as therapy for the patients with cerebellar disorder (pilot study)

3.1. Introduction

In addition to the motor cortex and the basal ganglia, the cerebellum is considered as one of the 3 important brain areas contributing to motor control. It receives not only information from other modules of the brain related to the programming and execution of movements, but also sensory feedback from receptors about ongoing movements. Many neural pathways link the cerebellum with the motor cortex—which sends information to the muscles causing them to move—and the spinocerebellar tract—which provides feedback on the position of the body in space (proprioception). The cerebellum integrates these pathways, using the constant feedback on body position to fine-tune motor movements. Because of this 'updating' function of the cerebellum, lesions within it are not so debilitating as to cause paralysis, but rather present as feedback deficits resulting in disorders in fine movement, equilibrium, posture, and motor learning (Fine et al. 2002).

Patients with cerebellar lesions (injuries) typically exhibit deficits during movement execution. For example, they show "intention tremors"—a tremor occurring during movement rather than at rest, as seen in Parkinson's disease. Patients may also show dysmetria, i.e., an overestimation or underestimation of force, resulting in overshoot or undershoot when reaching for a target. Another common sign of cerebellar damage is an inability to perform rapid alternating movements (Bastian et al. 1996).

The anterior and medial aspects of the cerebellum represent information ipsilaterally; thus, damage to this region on one side affects the movement on the same side of the body. The posterior and lateral aspects of the cerebellum represent information bilaterally; damage to this region has been shown to impair sensory–motor adaptation, while leaving motor control unaffected. In certain instances, a patient experiences a focal lesion. Such localized lesions cause a wide variety of symptoms related to their location in the cerebellum. A striking example is archicerebellar lesions, which cause motor symptoms not unlike those seen during intoxication: uncoordinated movements, swaying, unstable walking, and a wide gait (Ivry et al. 1988).

A lesion to the paleocerebellum causes severe disturbance in muscle tone and bodily posture, resulting in weakness to the side of the body opposite the lesion. A neocerebellar lesion is associated with deficits in skilled voluntary movement, such as playing the piano. A lesion to the intermediate zone causes problems with fine-tuning and corrective movements. Patients

with this type of lesion who hold their fingers in front of them have great difficulty in moving those fingers together. Patients with a lesion to the lateral zone have difficulty in controlling fine muscle movements and exhibit symptoms similar to those of patients with an intermediate zone lesion (Hallett and Massaquoi 1993).

Lesions of the cerebellum interfere with voluntary movement and produce a characteristic cluster of neurological signs, as impairments of balance and gait. Balance abnormalities are characterized by increased postural sway, either excessive or diminished responses to perturbations, poor control of equilibrium during motions of other body parts, and abnormal oscillations of the trunk (titubation). Gait ataxia has distinctive features including variable foot placement, irregular foot trajectories, a widened base of support, and abnormal interjoint coordination patterns (Hallett and Massaquoi 1993; Crowdy et al. 2000; Bastian et al. 2000).

Many studies have investigated potential mechanisms for cerebellar limb ataxia (Bastian et al. 1996; Brown et al. 1990; Goodkin et al. 1993; Hallett and Massaquoi 1993; Hore et al. 1991; Massaquoi and Hallett 1996; Topka et al. 1998a, b). One strategy has been to study a specific aspect of ataxia (e.g., hypermetria, dysdiadochokinesia) using a single joint movement paradigm (Brown et al.1990; Hore et al. 1991). Spatial errors are a fundamental clinical sign in cerebellar ataxia, yet there have been few studies of these aspects of movement in human cerebellar disease.

Furthermore, arm movements are impaired. The ataxic arm is slow to start moving, moves slowly once under way, develops oscillations and jerky movements during movement (kinetic tremor) and towards the end of movement as the target is approached (intention tremor), with past pointing (dysmetria). Even while maintaining a posture the ataxic limb may begin to oscillate (postural tremor). The rapid alternating movements may be fragmented and clumsy (dysdiadochokinesis, Thach and Bastian 2004).

We chose climbing on a wall as a rehabilitation paradigm because it is a complex task for the motor system, which probably demands the integrative function of the whole cerebellum, and all the sensory systems. It requires precise pointing movements of the feet and the hands to the grips, planning of movements in advance in order to avoid impossible body positions within the climbing wall. The main purpose of this pilot study was to investigate whether different tests (partly on the climbing wall partly independent of it) are adequate to quantify an eventual improvement of the motor performance by climbing wall training. In particular, we wanted to investigate the effects of climbing on: (1) a reduction of the dismetria, (2) a reduction of the tremor, (3) an improved ability to maintain

of the clumsy, impaired ability to perform the rapid alternation movements, (5) a decrease of reaction time (RT) and (6) an improved performance on the climbing wall.

3.2. Methods

3.2.1. Patients

Five patients (one female and 4 male, between 19 and 52 years old) participated in this study. The patients were diverse in terms of pathology, duration of illness and age. Clinical details of these patients are summarized in Tab. 3.1. Patient A had cerebellar ataxia (i.e. loss of muscle coordination caused by disorders of the cerebellum) as the result of an accident and noticeable motor problems in some every-day life activities with respect to fine motor control and production of steady muscular force. Patient B had a cerebellar lesion and an eye movement defect (ocular dysmetria: abnormality of ocular movements in which the eyes overshoot on attempting to fixate an object), and difficulties moving the upper and lower limbs. Patients C and E had multiple sclerosis. Patient D had a tumor in the frontal part of the brain and exhibited minor motor problems in every-day life activities and sustained a metabolic encephalopathy with cerebellar component from unclear origin eight months before study onset. All patients had bilateral motor disorders. The patients were cognitively and physically able to take part in the training program and experiments. Patient performance during the experimental sessions was compared to that of a group of 4 healthy subjects. All subjects, except one control, were right-handed. All subjects gave informed consent before participating in the study. The local research ethics committee approved the experiments.

Tab. 3.1: Patient data and clinical signs; F: female; M: male; CT: cranial trauma; AE: anoxic encephalopathy (failure of oxygen to be delivered to the brain resulting in brain dysfunction) ; MS: multiple sclerosis; MEC: metabolic encephalopathy with cerebellar component (encephalopathy characterized by memory loss, vertigo, and generalized weakness, due to metabolic brain disease); FP: frontal part of the brain.

Subject	Gender/age	Diagnosis	Duration of disease(years)	Case	Part of the brain affected
A	M/19	CT	2	Accident	All
B	M/22	AE	22	Anoxia	All
C	M/39	MS	14	Inflammation	All
D	M/42	MEC	4	Infection	FP
E	F/52	MS	8	Inflammation	All

3.2.2. Material and methods.

Movement paths were recorded with a 3-dimensional movement system CMS30S (ZEBRIS®, Isny, Germany) consisting of a sensor and a basic unit (Fig.3.1). The measurement principle is based on the travel-time of ultrasound pulses from transmitters (i.e. 3 markers attached to the hands) to 3 microphones built into the sensor. The pulses are

transmitted to the sensor and the 3-dimensional position of each marker is obtained in real-time by triangulation. The direction in front of the patient is defined as the X-coordinate, the left-right direction as the Y-coordinate and the up-down direction as the Z-coordinate.

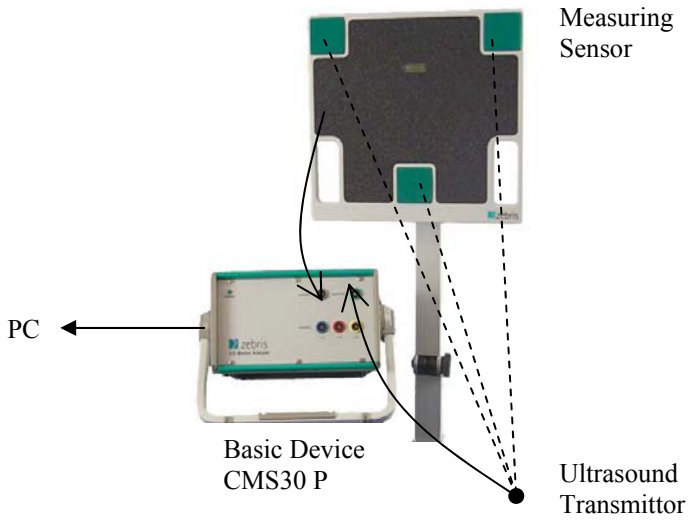

Fig. 3.1 Motion measuring system CMS30 P (Zebris Medizinaltechnik GmbH, Isny).

The positional data of the ultrasonic transmitters is affected with spatial and temporal errors. The resulting error in the positional data is then a combination of all and these systematic and unsystematic errors. Generally the resulting error is not determined by the spatial resolution of the measuring system (CMS-system: about 0.1 mm), but is better described by the accuracy of the system under static and dynamic conditions (CMS-system: about 1 mm). The standard deviation σ of the velocity and acceleration signal resulting from errors in the spatial coordinate x is given by

$$\sigma[v_x] = \sqrt{2} \cdot \mathrm{N} \cdot \sigma(x)$$
$$\sigma[a_x] = 2 \cdot \mathrm{N}^2 \cdot \sigma(x)$$

where N is the sampling rate, v is the velocity and a is the acceleration

The program Windata of the Zebris system recorded 9 coordinates (3 of each of the 3 markers) and in addition a 4 bit digital input at a sampling frequency of 50 Hz. The data were saved on files with the extension a. text and a name was given by 3 digits with the following meaning (Tab. 3.2): digit 1 encoded the experiment, digit 2 the date of the experiment (4 dates: 0, 1, 2 and 3), and digit 3 the mode for the experiment (i.e. code 101 was defined as a pointing movement with the left hand at first experimental date). The file contained a table with the columns: time, digital input and X-, Y- and Z- coordinates of the 3 markers. Each

digit in the digital input channel corresponds to an input bit 0 or 1. The program 3DAwin of the Zebris system suppresses missing data points by interpolation (see below) and enables to display data in various ways.

Tab. 3.2: Codes of the 3-digit data file names

	Digit 1	Digit 3	
Calibration	0	Right Left	0 1
Pointing task	1	Right Left	0 1
RT task	2	Simple – right Simple – left Complex -right Complex - left	0 1 2 3
Flexion/extension task	3	Right Left	0 1

For the experiments the markers were positioned on the patients. On the left hand, the first marker was placed on the nail of the index finger, the second marker left on the first joint of the index finger and the third marker near the wrist. On the right hand, for the flexion/extension condition, the 3 markers were on the palm, at the positions corresponding to those on the back of the left hand.

The subjects were seated at a table with the height of the chair adjusted such that when the arms rested on the table, the forearms were parallel with the table surface. The chair was pushed towards the table until the subject's chest was in contact with the table edge, in order to prevent any trunk motion pointing to the targets.

In the first task, the subjects pointed to 4 targets on the table, initiating each movement from the same starting position directly in front of the subject's midline, 14 cm from the table edge. The target balls of a diameter of 1 cm were marked in the middle with a point. They were suspended on stands at the height of 20 cm from the table surface. The 4 balls were arranged such that target 1 was located 60° to the left of the midline, 31 cm from the starting position, target 2 was 45° to the left of the midline, 28 cm to the starting position, target 3 was 45° to the right of the midline, 30cm from the starting position and target 4 was 60° to the right of the midline, 26 cm from the starting position.

For the RT task, a box with two lights (red and green) and two buttons was placed on the table. The movement started from the starting position directly in front of the subject's midline, 18 cm from the table edge. The distance of the box from the starting position was 42 cm and between buttons 10 cm. The lights could be turned on with switches on a trigger box. The light and trigger box were connected to the digital input of the Zebris system. The green

light with its switch was connected to bit 0, the red light with its switch to bit 1, the response button for the green light to bit 2 and the response button for the red light to bit 3. The patients performed (1) a simple RT task, where always the same light was turned on and they had to press the corresponding button, and (2) a complex RT task, where either of the buttons turned on in a pseudo-random sequence.

3.2.3. Experimental protocol

An A-B-A protocol with the following 3 stages was used:

- A base line (or reference line) of 3 weeks, which assessed the state of the patient prior to any training (pre-training Phase A).
- A training phase of 3 weeks during which the patients were trained for 45 minutes daily on 5 days a week) on the climbing wall (Phase B) lasting 3 weeks.
- A follow-up phase, during which the behavioral changes resulting from the training (post-training stage A) were studied (duration 3 weeks).

Each patient was tested for the RT, the pointing movements and flexion/extension movements of the upper limbs and the climbing performance on the climbing wall during following 4 sessions. (1) at T0, the first day of the pre-training phase, (2) at T1, 3 weeks later, at the end of the pre-training phase, (3) at T2, 3 weeks after T1, at the end of training period and (4) at T3, 3 weeks after T2. The subjects practiced trials in order to familiarize themselves with the apparatus and the experimental protocol. Control subjects did not run through the training phase and were tested only once.

3.2.4. Climbing training

For the climbing training two climbing walls of a height of 2.5 m with different degrees of difficulty were used. The inclination of one wall could be adjusted from 0° vertical to 45°, (Fig. 3.2B) enabling to adapt the climbing difficulty to the abilities of the patient. The training was accompanied by at least two persons, one of them being a physiotherapist. During climbing, they were secured with a climbing harness.

The frequency and the duration of the training sessions on the climbing wall were scheduled in consideration of the state of health and the physical performance of each patient (up to maximally 45 minutes during 5 days over a week). Climbing tasks were prepared as manifold as possible in order to facilitate a transfer of learned motor patterns in everyday life and to keep the training interesting for the patients. Each patient performed exercises which challenged (1) the body equilibrium, (2) the movement accuracy in pointing and grasping, (3) the planning of movement sequences, (4) the smoothness of movement performance, (5) the

integration of sensory information and (5) the velocity of single movements and movement sequences. For example, the patients were climbing as fast as possible, in slow motion, bottom-up, diagonally, horizontally, with the face to the wall, laterally and using specific grips or using only the structure of the wall. The rope with which the patients were secured was used to unload the body weight according to the climbing abilities and the strength of the patients who rested whenever they felt tired.

A **B**

Fig. 3.2 Climbing training. **A** wall for advanced climbers with rough surface. Patient in lateral position performing precise pointing movements to all reachable grips. **B** adjustable wall. Patient climbing to the top.

3.2.5. Tests

3.2.5.1. Climbing tests

Climbing performance was investigated with the following tests.

- The subjects were asked to touch as many grips as possible within 30 sec. They were allowed to move their whole body except their feet. The test was carried out separately for the left and the right arm.
- The subjects were required to touch alternatively two selected grips as fast as possible during 30 sec. The test was carried out separately for the left and the right arm.
- The subjects were required to touch alternatively two selected grips as fast as possible during 30 sec. The test was carried out separately for the left and the right foot.
- The subjects were asked if they could touch grips shown by the investigator without moving their feet. They had first to specify they can reach them and then to verify it. 10 grips were selected in a random order. 5 grips were selected out of reach and 5 grips in the range of the patient.
- The subjects had to climb as fast as possible over a specified track of 5 grips. The subjects had to use the specified grips with their hands but they were free to choose the grips for the feet.

3.2.5.2. Pointing task

Before the onset of the experiment, the position of the 4 targets and the starting position were calibrated for each subject. The subjects were instructed to start slow regular movements from the starting position to one of the 4 balls, to stay there for 3 sec, and to end the movement at the starting position. The subject made 5 movements to each target in a pseudo-random sequence.

3.2.5.3. RT task

As for the pointing task, a calibration was performed before the experiment onset. On the starting position, the subject's arm was slightly flexed at the elbow, the wrist was in a neutral position and the index finger was extended while the remaining fingers were flexed. This position was maintained as stable as possible throughout the RT measurements. When a light turned on, the subject had to press the corresponding light button as fast as possible and to return to the starting position. During the simple RT condition, only one of the two lights (for the right hand red light and for the left hand green light) was switched on in an irregular time sequence. During the complex RT condition, both lights were switched on in a pseudo-random sequence and in an irregular time sequence. We recorded 20 trials for each condition.

3.2.5.4. Flexion/Extension movements

The subjects started the movements in a position, where the elbow was on the table and the forearm in a vertical position in front of them. The subjects were required to flex and extend their forearms from the vertical to nearly the horizontal position. The movements were carried out in a regular rhythm given by the instructor. We recorded 20 flexion/extension movements.

3.2.6. Data analysis

The data of the ultrasonic transmitters (markers) can be affected, when the markers were orientated in such a direction that the sensor can not receive the ultrasonic pulses. Such missing data were replaced by NaN in the data file a. text. The program 3DAwin which is part of the Zebris system can input the data files with extension a. text and replaces the missing data in each dimension separately by interpolation. If one data point is missing, this data point was interpolated by a straight line between the two neighboring points. If two subsequent data points were missing, the velocity before and after the missing points was calculated, then the velocity was interpolated using the information on the covered distance (this corresponding to a constant acceleration of 2 data points) and the interpolated data

replaced the NaN values in the b. text file. The data with the interpolated values were saved in files b. text.

Some movement parameters which were sensitive to the time course of the movement path could not be computed on the basis of data with the interpolated values. For these parameters, the data in the files b. text were treated with a program developed in LabView. The program imported the data from the file b. text and detected accelerations bigger than 25 m/sec^2 which were assumed to be too large to be of physiological origin. The data values that gave rise to these high accelerations were replaced by 10,000 (a value which can be detected by the data analysis programs) and the ensuing data were saved in files c. text.

Since errors were more frequent in data from the first then from the second and third marker, only data from the first marker are further analyzed.

3.2.6.1. Parameters of the pointing task

Parameters from the pointing task were saved in a table of the data base Access (Microsoft). The table contained the following columns: (1) series, (2) subject, (3) day, (4) side, (5) target, (6) interval, (7) start, (8) end, (9) file path, next 21 columns for the 3 coordinates of three markers and their relation (e.g. X1, Y1, Z1,…, X1Y1…..X3Y3Z3) and direction changes for the coordinates of the first marker. A program computes the pointing movements of the data written in Labview and imported the data from files b. text. The program displayed the data for the X-, Y- and Z-direction. The pointing movement has four targets and for each target four positions (rest, go, holding and return periods).

In the Labview program, you put the cursor on the start and end position of each position of the targets and click on saves as rest period etc. It saved the data in access table, which was created for the pointing task. The saved data for the interval (go and holding period) from the data base Access was analyzed for the tremor as the number of the direction changes from the go signal to the holding period of the pointing movements.

Direction changes X-, Y- and Z-direction were detected on the velocity signals which were obtained by subtracting succeeding position signals. Each change of sign in the velocity signals was taken as direction change. In order to eliminate the influence of velocity and the distance between the initial position and the target, the number of direction changes was divided by the movement time.

3.2.6.2. Parameters of the RT task

The RT task data were saved in a table of the data base Access. The table contained the following columns, (1) series, (2) subject, (3) day, (4) side, (5) file path, (6) target, (7)

reaction time, (8) simple/complex, the next 9 columns for the response to the target position for the 3 coordinates of the 3 markers and 21 columns for the relation of the 3 coordinates for 3 markers. A program computes the RT of the data written in Labview and imported the data from files b. text. The program displayed the data for the XY, YZ and ZX direction. The RT was defined as the interval between the 'go' signal (light) and the response to the corresponding light button. If the subject pressed the wrong button in the complex RT condition, data table filled with error (yes) in the table. It saved the data in an Access table, which was created for the RT task. The trials were rejected if the RT was <100 msec or >2 sec. We determined simple RT and the complex RT from each subject.

The dispersion of endpoint errors (hitting and sliding into a target, or hitting the target and sliding out) was measured in the RT experiment. The endpoint error was defined as the distance between the movement end point and the target position.To test how the movement variability changed after the training, we first computed the standard deviation (eq.1) for the dispersion of the endpoints. Then we computed the confidence limits (eq.2) for dispersion of the endpoints of the first marker for the 3 coordinates (X, Y and Z)

$$\sigma = \sqrt{\frac{\sum_i \left(X_i - \overline{X}\right)^2}{N-1}} \qquad \text{(eq.1)}$$

$$CL = X \pm t_{(\alpha/2,N-1)}\, \sigma / \sqrt{N} \qquad \text{(eq.2)}$$

where σ is the standard deviation, $\overline{X}$ the sample mean average (number1, number2,…etc), N the sample size, X the sample mean, α =0.05 and t (α /2 is the upper critical value of the t distribution with N-1 degrees of freedom. The stored data values in the data base Access were transferred to the SPSS statistical program (SPSS inc. Chicago, IL. USA) for subsequent analysis. We applied analysis of variance (ANOVA) with the fixed factors (1) dates before (T0 and T1) and after the training (T2 and T3), (2) subject, (3) side, and (4) simple/complex RTs. The means of the patients and the controls were compared using Student Student's t test.

3.3. Results

3.3.1. Global results

All the tests were measured (1) at T0, the first day of the pre-training phase, (2) at T1, 3 weeks later, at the end of the pre-training phase, (3) at T2, 3 weeks after T1, at the end of the training period and (4) at T3, 3 weeks after T2. Since the two means for the climbing performance, RT, endpoint variability and tremor before and after the training were not significantly different, the data before the training (T0, T1) and after the training (T2, T3) were pooled.

3.1.1.1. Climbing performance.

The climbing performance was evaluated by the number of times the patients could touch alternatively 2 prescribed grips. The mean number (no) was 11 before and 17 after the training within 30 sec (Fig. 3.3A). The training had a significant effect on the patients ($p < 0.05$; Tab. 3.3).

The no of grips that could be touched was about a twice larger for the controls than the patients. The difference between the arm and leg was significant ($p \leq 0.01$; Tab. 3.3, Fig. 3.3B). The controls could touch 18 grips more with the arm and 12 grips more with the leg than the patients.

Tab. 3.3: Significance of F values obtained with an ANOVA of the climbing performance of the patients with the fixed factors and their interaction. The significance levels are ***= $p \leq 0.001$, **= $p \leq 0.01$ and *= $p \leq 0.05$.

Source	Significance of the climbing performance
Subject	.000***
Day	.034*
Side	.068
Arm/leg	.004**
Subject*day	.068
Subject*side	.124
Day*side	.144
Subject*day*side	.678
Subject*arm/leg	.028*
Day*arm/leg	.016*
Subject*day*arm/leg	.012*
Side*arm/leg	.050*
Subject*side*arm/leg	.473
Day*side*arm/leg	.240
Subject*day*side*arm/leg	.192

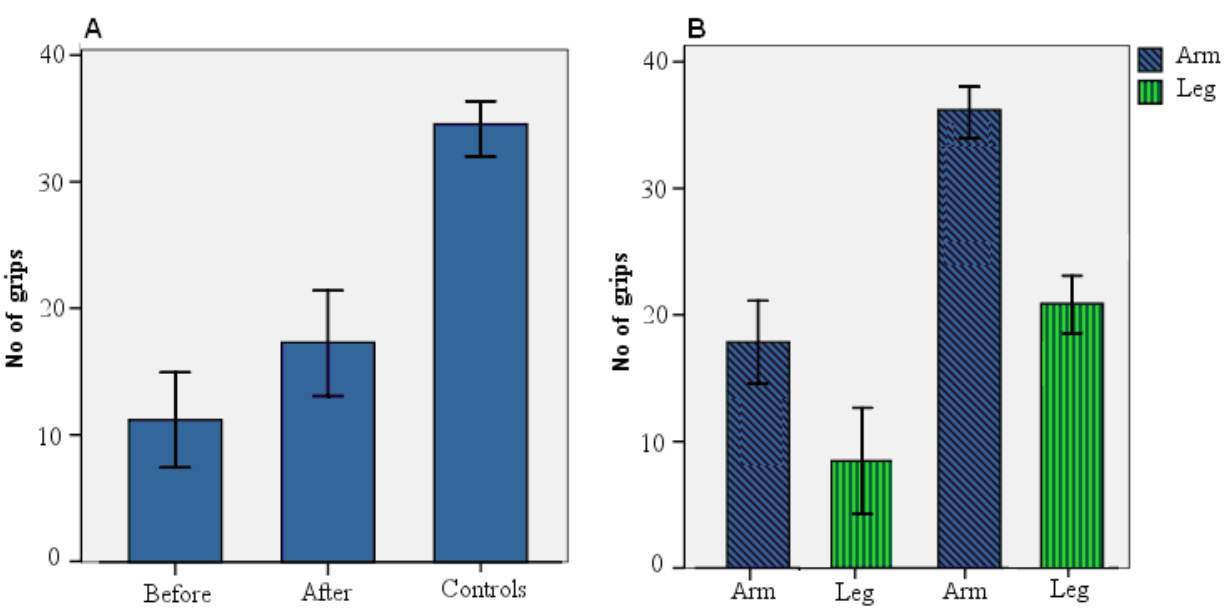

Fig. 3.3. Mean no of times the grips could be touched. **A**: patients before training (left column), patients after training (medium column) and controls (right column). **B**: patients (left 2 columns) and controls (right 2 columns) with arm and leg. Bars are confidence limit (p=0.05).

There was a significant interaction between the arm/leg and the training effect. The mean no of the grips that could be touched was 15 (arm) and 9 (leg) before, and 22 (arm) and 13 (leg) after the training (Fig 3.4). The patients improved thus by 7 for the arm and 4 for the leg ($p < 0.05$, Tab. 3.3), which was a significant difference. However, even after the training they could touch 15 with the arm and 10 with the leg less than in the controls who did not have any training

The mean no of grips that could be touched in the patients was 15 and 21 for the left and the right arm, and 8 and 11 for the left and right leg where as in the controls, it was 35 and 37 in the arm, 21 and 23 in the leg (Fig. 3.5). The difference of 6 between the left and right arm and the difference of 3 between the left and right leg in the patients were significant ($p \leq 0.05$, Tab. 3.3). The controls could touch about twice the no of grips of the patients.

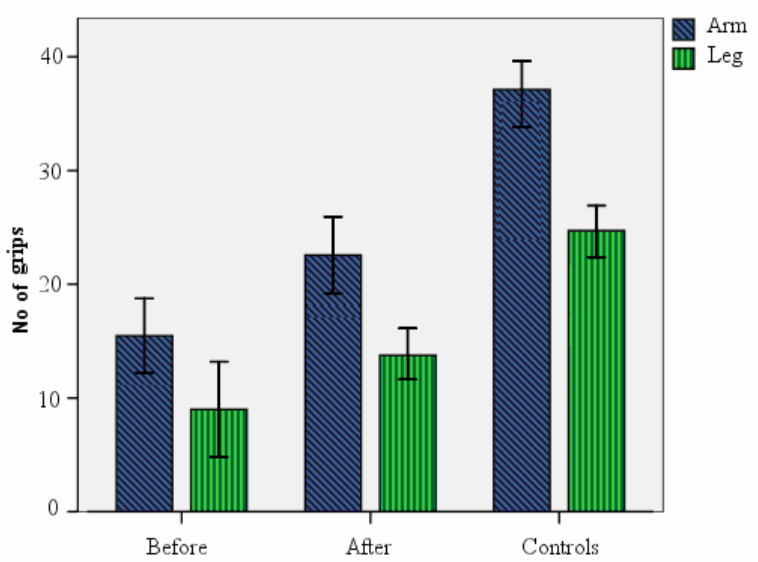

Fig. 3.4. Mean no of times the grips could be touched during the climbing performance on the dates before and after the training by the arm and the leg of the patients and controls without training. Bars are confidence limit (p=0.05).

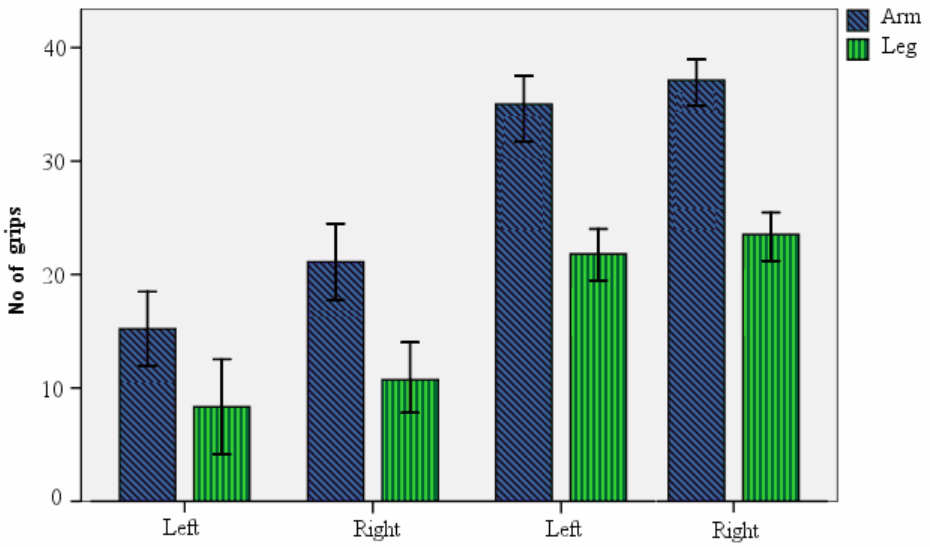

Fig. 3.5. Mean no of times the grips could be touched by the left and the right arm and the leg of the patients (left 2 columns) and controls without training (right 2 columns). Bars are confidence limit (p=0.05).

3.3.1.2. Simple RT

The subjects performed the RT tasks during 4 sessions. After a light turned on, they had to press the corresponding light button as fast as possible. Tab. 3.4 shows the significance level for the fixed factors and for the interaction between the factors for the patients. The mean simple RT was 816 ms before and 807 ms after the training. The patients improved thus by 9 ms, which is highly significant ($p \leq 0.001$; Tab. 3.4). However, even after the training they had a mean RT which was 271 ms larger than in the controls who did not have any training.

Since all the patients and all except one control (bimanual) were right handed, RTs from the right and left hand were compared. The mean RT was 865 ms for the left and 756 ms for the right side of the patients, and 559 ms for the left and 523 ms for the right side of the controls. The

difference of 109 ms in the patients was significant ($p < 0.001$; Tab. 3.4), as well as the difference of 36 ms in the controls ($p < 0.05$; Tab. 3.5). The internal difference was longer for the patients than the controls (109 ms respectively 36 ms).

Tab. 3.4: Significance of F values obtained with an ANOVA of the RT and the dispersion of the endpoints for the 3 coordinates (X, Y and Z) in the patients. The significance levels are ***= $p \leq 0.001$, **= $p \leq 0.01$ and *= $p \leq 0.05$.

Source	RT	X	Y	Z
Subject	.000***	.000***	.000***	.013*
Day	.000***	.549	.001***	.067
Side	.000***	.208	.018*	.708
Simple/complex	.012*	.000***	.018*	.004**
Subject*day	.000***	.480	.195	.100
Subject*side	.000***	.001***	.291	.133
Day*side	.005**	.061	.285	.069
Subject*day*side	.662	.072	.430	.435
Subject*simple/complex	.000***	.297	.114	.714
Day*simple/complex	.001***	.073	.875	.462
Subject*day* simple/complex	.757	.933	.935	.941
Side* simple/complex	.000***	.450	.328	.512
Subject*side* simple/complex	.226	.922	.396	.413
Day*side* simple/complex	.595	.134	.459	.365
Subject*day*side*simple/complex	.241	.540	.349	.948

Tab. 3.5: Significance of F values obtained with an ANOVA of the RT and the dispersion of the endpoints for the 3 coordinates (X, Y and Z) in the controls. The significance levels are ***= $p \leq 0.001$, **= $p \leq 0.01$ and *= $p \leq 0.05$.

Source	RT	X	Y	Z
Subject	.000***	.021*	.031*	.007**
Side	.017*	.254	.215	.548
Simple/complex	.159	.023*	.048*	.034*
Subject*side	.015*	.064	.080	.218
Subject*simple/complex	.432	.428	.389	.524
Side* simple/complex	.416	.793	.320	.314
Subject*side* simple/complex	.652	.688	.457	.621

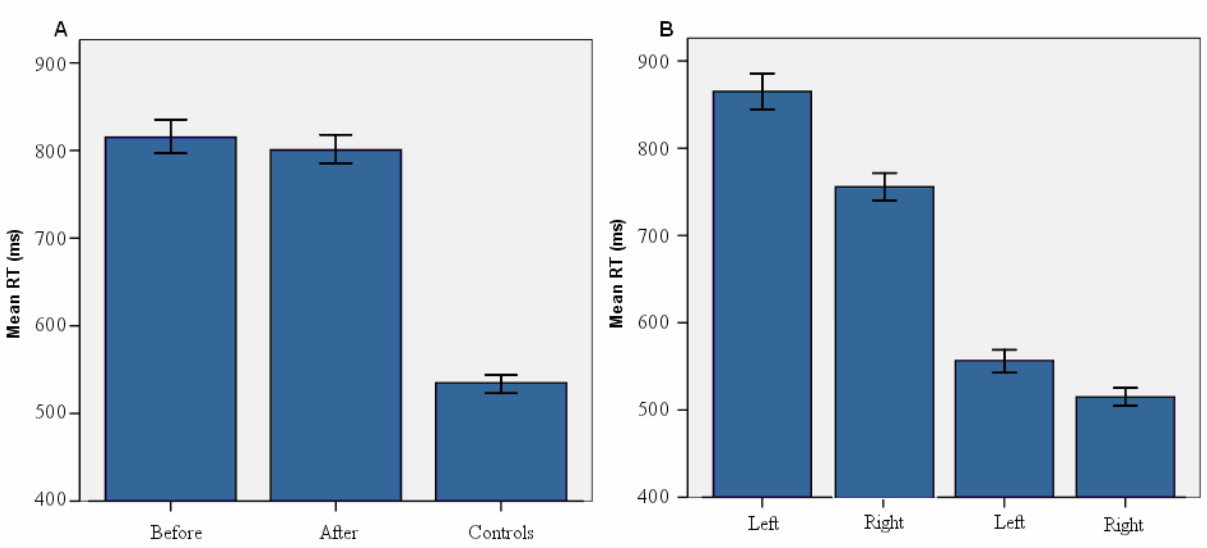

Fig. 3.6. Mean simple RTs for the dates before and after the training (**A**). The average RTs for the left, and the right hand of the patients (left 2 columns) and controls without training (right 2 columns, **B**). Bars are confidence limit (p=0.05).

3.3.1.3. Complex RT

The mean complex RT was 877 ms before and 797 ms after the training of the patients and 552 ms for the controls who were not trained (Fig. 3.7A). It was 80 ms smaller after than before the training of the patients, a highly significant difference ($p \leq 0.01$, Tab. 3.4). The mean RT was 245 ms larger in the patients than in the controls without training.

In the patients, the overall mean RT was 850 ms for the left and 824 ms for the right side. In the controls, it was 564 ms for the left and 546 ms for the right side. The difference between right and left RTs was significant (26 ms smaller, $p < 0.001$) which was smaller than for the simple RT task (109 ms) but more than in the controls (18ms, $p < 0.05$; Tab. 3.5). The mean RT on the left side was 286 ms and on the right side 278 ms longer in the patients than in the controls. These differences were similar as in the simple RT.

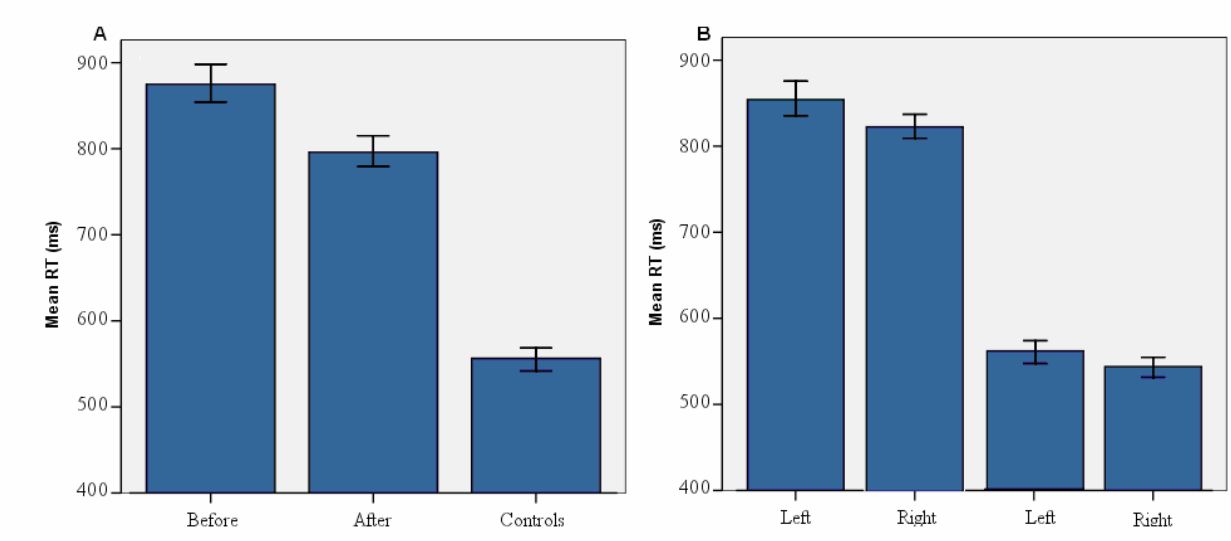

Fig. 3.7. Mean complex RTs before and after the training. (**A**). RTs for the left and the right hand of the patients (left 2 columns) and controls without training (right 2 columns, **B)**. Bars are confidence limit (p=0.05).

3.3.1.4. Interaction of fixed factors shown by RT.

An ANOVA of the RTs was computed with the factors subject, day of training, side and simple/complex RT. There was a significant interaction between these factors. The most striking feature was that all interactions between the subject and factors were highly significant ($p < 0.001$, Tab. 3.6). This suggests, that there are important differences between the subjects. This is a reason, why the subjects are considered individually below.

Tab. 3.6: An ANOVA of the RT with the fixed factors and the interaction between the factors of the patients. The differences between the dates of testing and the patients, patients and side and patients with RT conditions are highly significant.

Source	Sum of squares	df	Mean square	F	Sig.
Subject	27.005	4	6.751	155.483	.000
Day	.809	1	.809	18.463	.000
Side	1.814	1	.1.814	41.777	.000
Simple/complex	.274	1	..274	6.313	.012
Subject*day	2.358	4	.590	13.577	.000
Subject*side	2.670	4	.667	15.371	.000
Day*side	.343	1	.343	7.911	.005
Subject*day*side	.104	4	.026	.601	.662
Subject*simple/complex	1.226	4	.307	7.060	.000
Day*simple/complex	.515	1	.515	11.871	.001
Subject*day* simple/complex	.082	4	.020	.471	.757
Side* simple/complex	.696	1	.696	16.037	.000
Subject*side* simple/complex	.246	4	.062	1.417	.226
Day*side* simple/complex	.012	1	.012	.82	.595
Subject*day*side*simple/complex	.238	4	.060	1.372	.241
Error	70.773	1630	.043		
Total	1209.777	1670			

There was a significant interaction between the side and the training effect ($p < 0.01$; Tab. 3.6, Fig. 3.8A). The training reduced the RT by 15 ms on the left and by 74 ms on the right side.

There was a significant ($p < 0.001$; Tab. 3.6) interaction between the RT condition and the side in the patients. There was a difference between the right and the left hand of 109 ms in the simple and 26 ms in the complex RT condition (Fig. 3.8B).

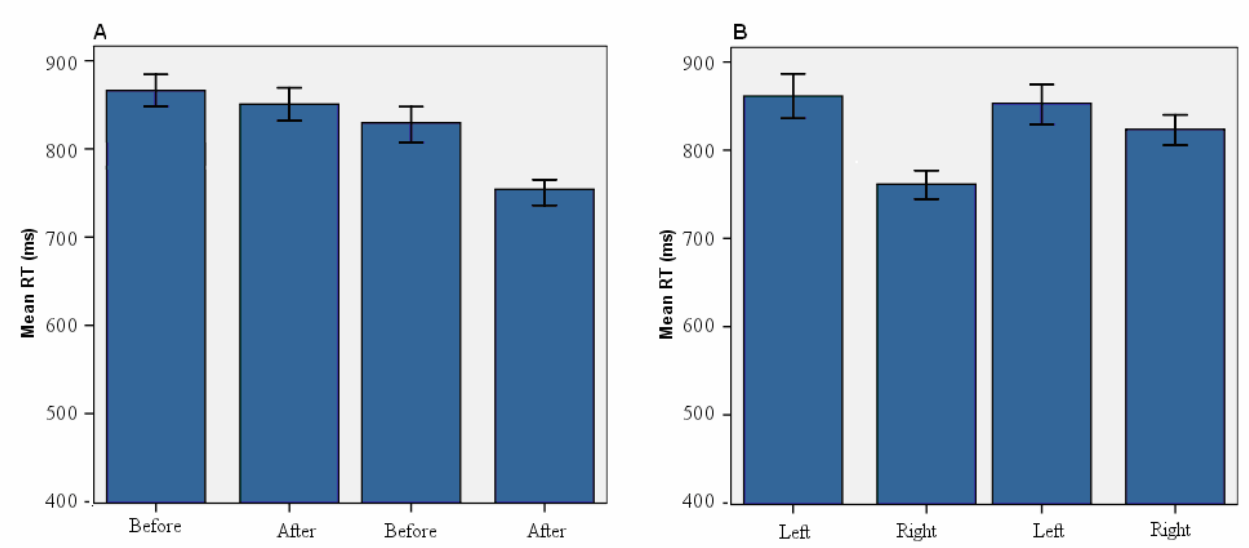

Fig. 3.8A. .Mean RTs for the dates before and after the training for the left (left 2 columns) and the right (right 2 columns) hand of the patients. **B**. Mean RTs of the left and right hand for the simple RT (left 2 columns) and complex (right 2 columns) RT in the patients. Bars are confidence limit (p=0.05).

3.3.1.5. End point variability

Since the precise coordinates of the push buttons in the RT task were not known, the variance and confidence limits of the end points of the movements to the buttons were computed in the X-, Y- and Z-direction. A significant reduction of the endpoint dispersion due to the training was only found in the Y-direction. The confidence limits of the variability in the Y-direction were 31 mm before and 24 mm after the training of the patients and 21 mm for the controls (Fig. 3.9A). The training effect of 7 mm was significant ($p \leq 0.001$; Tab. 3.4). The movements of the controls were more precise than those of the patients (the variability was 10 mm smaller).

The mean confidence limit of the endpoint variability in the Y-direction was 30 mm in the left and 25 mm in the right hand and in the controls 19 mm and 22 mm respectively (Fig. 3.9B). The difference of 5 mm of both sides was significant in the patients ($p < 0.05$; Tab. 3.4). The endpoint variability in the patients was 11 mm on the left side and on the right side 3 mm larger than in the controls.

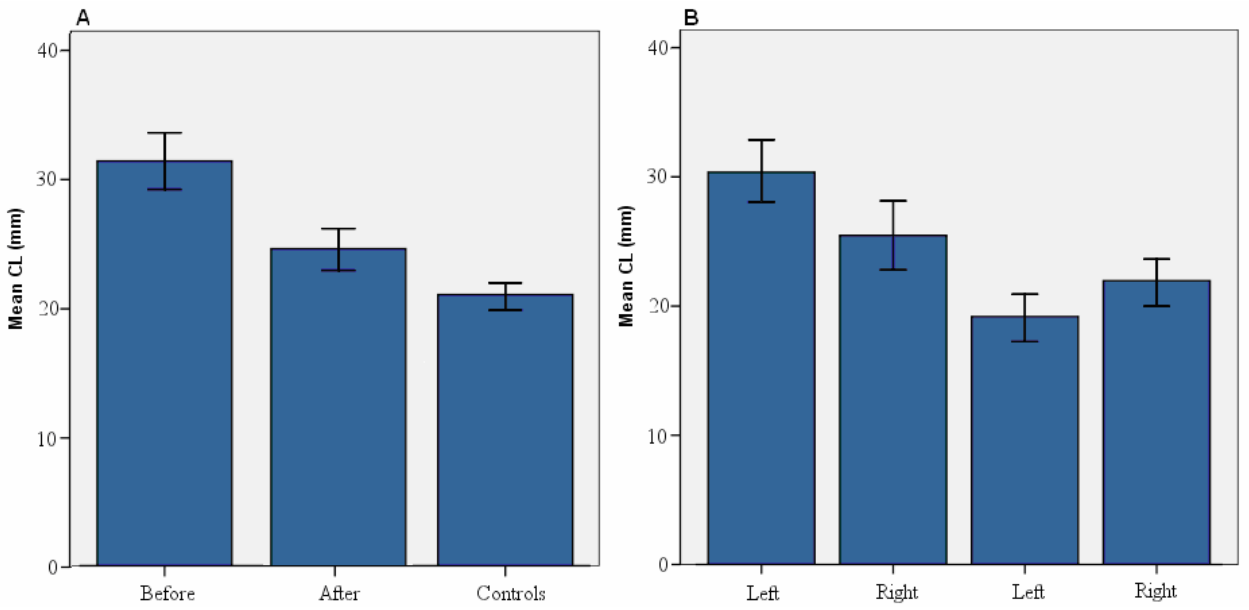

Fig. 3.9A. Mean confidence limits of the end point variability in the Y-direction for the dates before and after the training in the patients and controls without training. **B.** Mean confidence limits of the end point variability in the Y-direction for the left and the right hand of the patients (left 2 columns) and controls without training (right 2 columns). Bars are confidence limits (p=0.05).

In the patients, the mean confidence limit of the endpoint point variability in the X-, Y- and Z-direction was 33 mm, 25 mm and 30 mm in the simple and 42 mm, 30 mm and 43 mm in the complex RT condition in the controls 21 mm, 19 mm, 23 mm and 22 mm, 21mm and 24 mm respectively (Fig. 3.10). The differences of 9 mm ($p < 0.001$), 5 mm ($p < 0.05$) and 13 mm ($p \leq 0.01$; Tab. 3.4) in the patients were significant in the RT conditions. The endpoint variability differences were larger in the patients for the simple and the complex RT condition than in the controls.

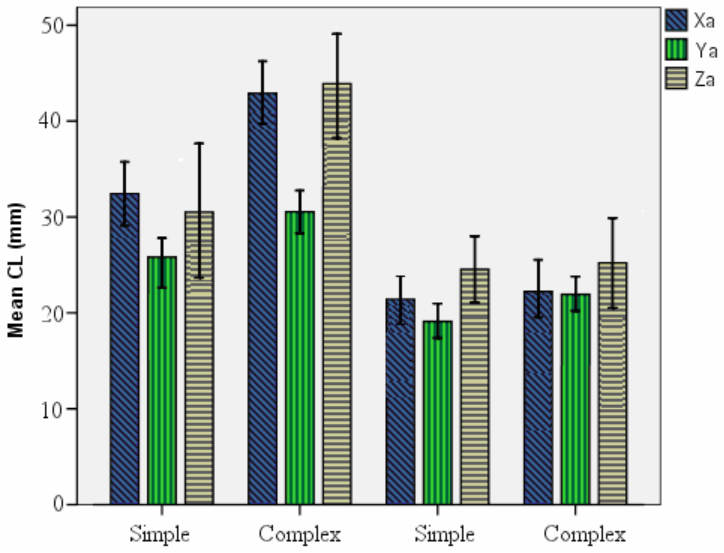

Fig. 3.10. Mean confidence limits of the end point variability in the X, Y- and Z-direction for the simple and the complex RT conditions of the patients (left 2 columns) and controls without training (right 2 columns). Bars are confidence limits (p=0.05).

3.3.1.6. Tremor

The tremor was computed in the X-, Y- and Z- direction on the basis of the recordings from the pointing task. It was defined as the number of direction changes per sec (1) from the beginning of the movement till the patient reaches the target (go period) and (2) during the period he pointed to the target (holding period, Fig. 3.11). Tab. 3.7 shows the significance levels for the factors subject, day of training, side and simple/complex RT and interaction between the factors for the patients.

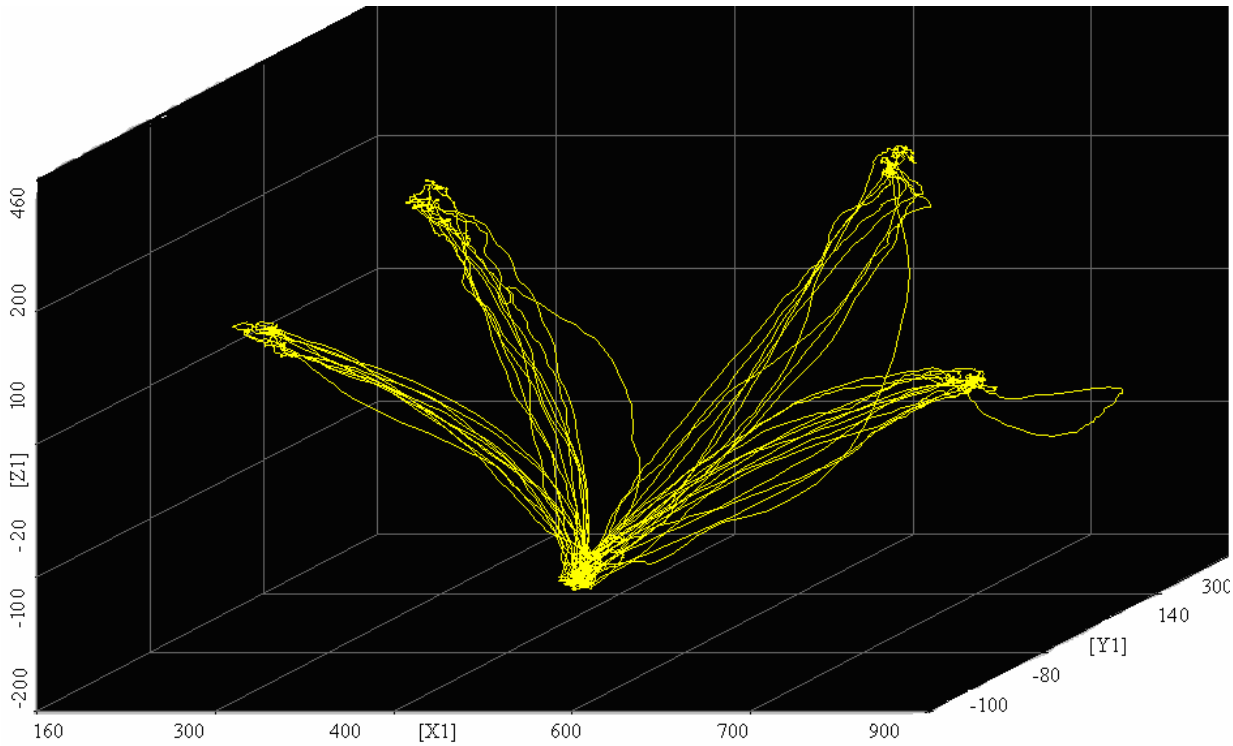

Fig. 3.11. The pointing movement towards the 4 targets in the 3 coordinates (X-axis, Y-axis and Z-axis)

Tab. 3.7: Significance of F values obtained with an ANOVA of the tremor during pointing movements for the fixed factors (subject, day of training, side and simple/complex RT) and their interaction in the X, Y and Z coordinates in the patients. The significance levels are ***= $p \leq 0.001$, **= $p \leq 0.01$ and *= $p \leq 0.05$.

Source	Direction change in the X-axis	Direction change in the Y-axis	Direction change in the Z-axis
Subject	.203	.001***	.000***
Day	.000***	.000***	.000***
Side	.001***	.035*	.003**
Interval	.000***	.000***	.000***
Subject*Day	.000***	.000***	.000***
Subject*Side	.045*	.008**	.003**
Day*Side	.619	.220	.052
Subject*Day*Side	.042*	.050*	.002**
Subject*Interval	.624	.000***	.000***
Day*Interval	.000***	.000***	.000***
Subject*Day*Interval	.000***	.096	.090
Side*Interval	.244	.066	.945
Subject*Side*Interval	.017*	.001***	.036*
Day*Side*Interval	.392	.455	.032*
Subject*Day*Side*Interval	.056	.263	.004**

Tab. 3.8: Significance of F values obtained with an ANOVA of the tremor during pointing movements for the fixed factors (subject, day of training, side and simple/complex RT) and their interaction in the X, Y and Z coordinates in the controls. The significance levels are ***= $p \leq 0.001$, **= $p \leq 0.01$ and *= $p \leq 0.05$.

Source	Direction change for the X-axis	Direction change for the Y-axis	Direction change for the Z-axis
Subject	.000***	.000***	.030*
Side	.000***	.001***	.114
Interval	.000***	.000***	.000***.
Subject*side	.000***	.002**	.100
Subject*interval	.000***	.006**	.001***
Side*Interval	.837	.545	.110
Subject*Side*Interval	.169	.068	.175

In the patients as well as in the controls, the tremor was slower in the X-direction, slightly faster in the Y-direction and fastest in the Z-direction (most differences are not significant). The training had a beneficial effect on the patients. The effect was larger in the X- and Y-direction (from 4.3 movements/sec to 3.4 and from 4.6 to 3.5) than in the Z- direction (from 5.1 to 4.5). All these changes were highly significant ($p < 0.001$, Tab. 3.7). However, even after the training, the tremor was significantly faster in the patients with training than in the controls without training patients (X-, Y- and Z- direction): 3.4 movements/sec, 3.4 and 4.5, controls: X-, Y- and Z- direction: 2.7, 2.9 and 3.0).

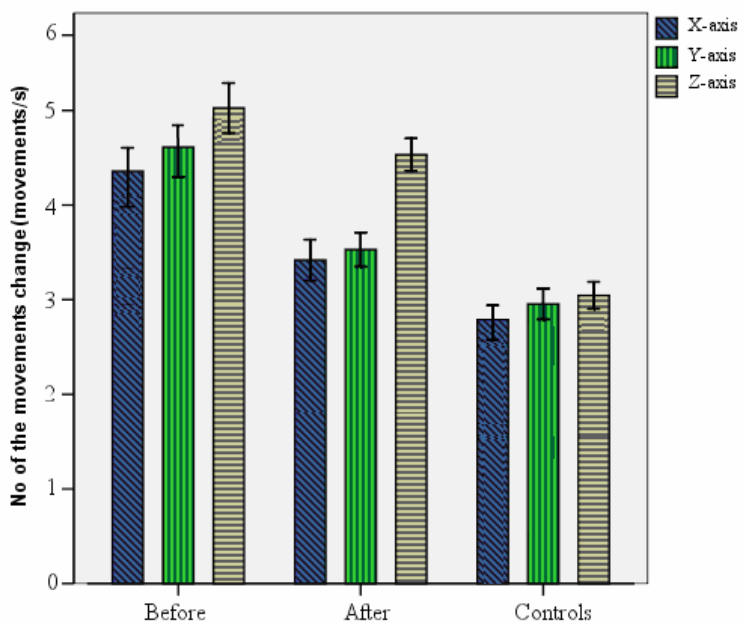

Fig. 3.12. Mean no of the movement changes in the X-, Y- and Z directions on the dates before and after the training of the patients and controls without training. Bars are confidence limits (p= 0.05).

The tremor was faster on the left than on the right side (Fig. 3.13). In the patients, the difference between the left and right side was 0.4 movements/sec in the X-direction ($p \leq 0.001$), 0.2 in the Y-direction ($p < 0.05$) and 0.6 in the Z-direction ($P \leq 0.01$; Tab. 3.7). The corresponding values in the controls were 0.8 movements/sec, 0.4 and 0.1 ($p < 0.001$; Tab. 3.8).

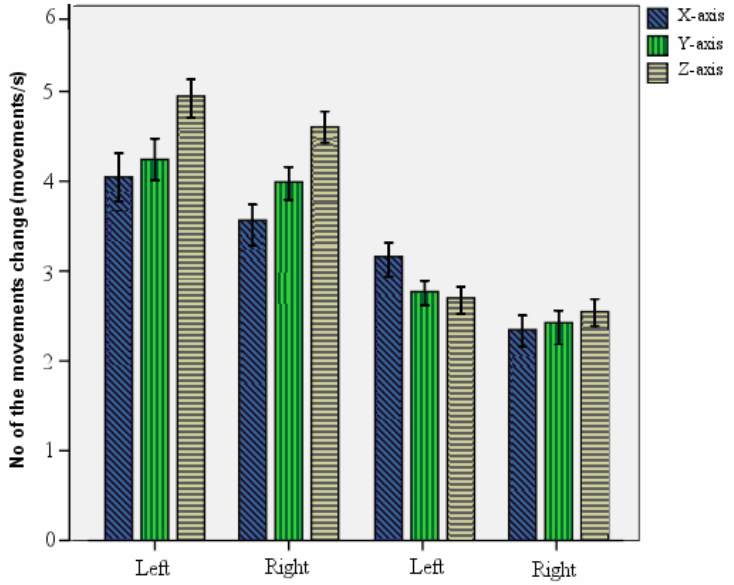

Fig. 3.13. Mean no of the movement changes in the X-, Y- and Z- direction on the left and the right hand of the patients (left 2 columns) and controls without training (right 2 columns). Bars are confidence limits (p=0.05).

In the patients as well as in the controls, the tremor was about twice faster during the holding than during the go period (Fig. 3.14). In the patients, the difference was 4.6 movements/sec

in the X-direction, 3.7 in the Y-direction and 2.3 in the Z-direction. In the controls the corresponding values were 2.7 movements/sec, 2.4 and 1.8 and all these difference were highly significant ($p < 0.001$; Tab. 3.8).

There was significant interaction between the intervals during which the tremor was measured and the training effect ($p < 0.001$; Tab. 3.7). The reduction in tremor was much less during the go period than during the holding period (Fig. 3.15). During the go period, it was 0.24 movements/sec in the X-, 0.18 in the Y- and 0.12 in the Z-direction, during the holding period it was 1.3 movements/sec in the X-, 1.04 in the Y- and 1.02 in the Z-direction. But even the relative decreases were much larger during the holding than during the go period; 12.5%, 8.2% and 3.3% verses 19.3%, 16.9% and 16.6%.

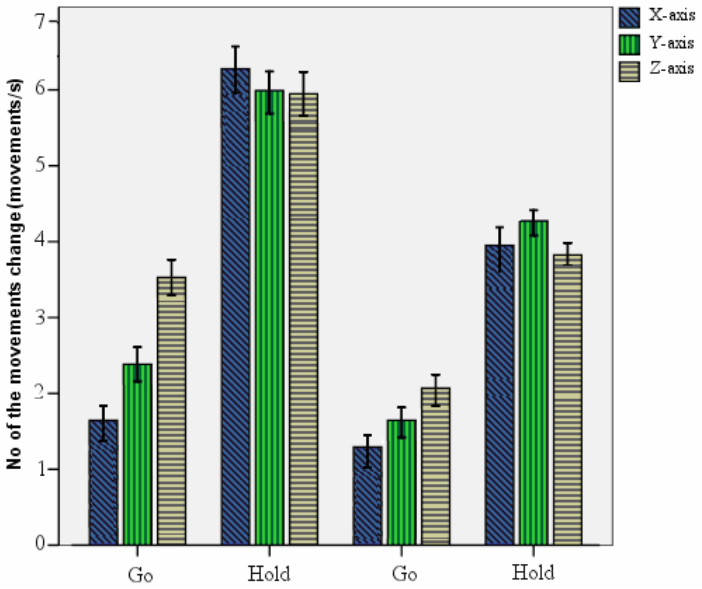

Fig. 3.14. Mean no of the movement changes in the X-, Y- and Z- direction for the go and the holding period of the patients (left 2 columns) and controls without training (right 2 columns). Bars are confidence limits (p=0.05).

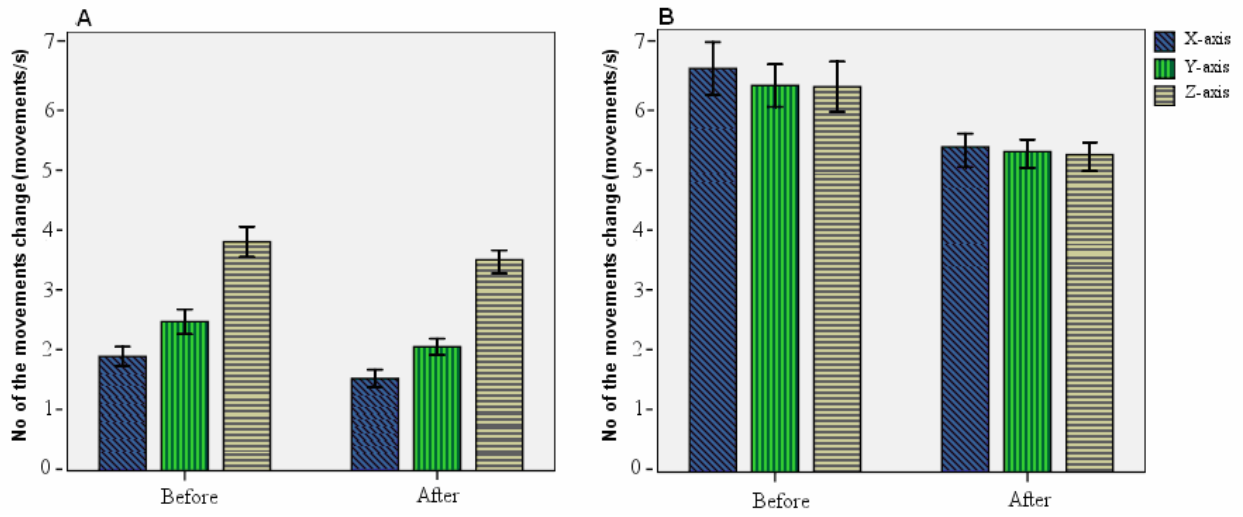

Fig. 3.15. Mean no of the movement changes in the X-, Y- and Z- directions on the dates before and after the training for the go (**A**) and the holding (**B)** period of the patients. Bars are confidence limits (p= 0.05).

3.3.1.7. Non analyzable tests

The main purpose of this pilot study was to evaluate how the performance in motor tasks can be tested in cerebellar patients who underwent a training on a climbing wall. It turned out that some of the tests mainly the tests on the climbing wall, were inadequate for this purpose. The following tests were concerned:

- Body perception. The patients should tell whether they can touch a specified grip with a hand without changing the support of the legs. This could not be evaluated because different grips have to be chosen for each patient. Furthermore the same grips should be chosen at each session to be able to compare results. This, however, depends on whether the patient could remember the results from the preceding session. The results from this test could not be used for further analysis.
- The patients should climb as fast as possible along an indicated track to the top of the climbing wall. The same track was used for all the patients. It turned out that the task was too easy for one patient and for others it was too difficult so that they depended on external help to reach the top. It was therefore not possible to measure the climbing speed as a function of their capabilities.
- There were no striking differences in the shape of the movement paths in the pointing task due to the training.
- The patients were required to perform regular flexion – extension movements of the forearm in a given rhythm. The task was too difficult for some patients and learning effects could not be excluded. The results were therefore not further analyzed.

3.3.2. Results from individual patients

Due to the inhomogeneity of the patients, the results obtained from the different patients were also inhomogeneous. The performance of the patients improved in general, however, the tests in which their performance improved were different from subject to subject. It seemed to us therefore reasonable to present the results individually for each subject.

The results of the 5 patients are summarized in Tab 3.9. The effect of the training can roughly be estimated by the number of asterisks attributed to a patient. There are two groups of patients. There are many asterisks (10 to 14) in one group and zero to one in the other one. The patients in the second group, in which the training had no or nearly no effect, suffer from MS. Patients C and E are therefore not further considered in the presentation of the individual results.

Tab. 3.9: Significance of the training effect evaluated by an ANOVA of the climbing performance, the RT, the end point variability and the tremor in the patients A, B, C, D and E. The significance levels are ***= $p \leq 0.001$, **= $p \leq 0.01$ and *= $p \leq 0.05$. The total number of asterisks was taken as estimation of the global training effect.

	Direction	A	B	C	D	E
Climbing performance		.743	.000***	.589	.002**	.254
RT		.962	.000***	.422	.000***	.144
End point variability	X	.905	.154	.181	.474	.814
	Y	.040*	.733	.224	.322	.424
	Z	.490	.062	.148	.358	.648
Tremor	X	.000***	.003**	.081	.000***	.021*
	Y	.000***	.001***	.234	.000***	.344
	Z	.001***	.000***	.086	.000***	.186
Number of asterisks		10	14	0	14	1

3.3.3. Patient A

This patient has deficiencies due to a car accident (see section patients). His global performance improved less than in other 2 patients (B and D, Tab. 3.9).

3.3.3.1. Climbing performance

The climbing performance which was evaluated by the number of times the patient could touch alternatively 2 prescribed grips, did not increase due to the training (Tab. 3.10)

Tab. 3.10: Significance of F values obtained with an ANOVA for the climbing performance and the RT for the fixed factors and their interaction. The significance levels are ***= $p \leq 0.001$, **= $p \leq 0.01$ and *= $p \leq 0.05$.

	Patients		
	A	B	D
Climbing performance	.743	.000***	.002**
Day	.078	.000***	.055
Side	.068	.062	.052
Arm/leg	.756	.001***	.062
Day*side	.654	.056	.125
Day*arm/leg	.868	.235	.204
Side*arm/leg	.862	.124	.488
Day*side*arm/leg			
RT			
Day	.166	.000***	.000***
Side	.503	.919	.978
Simple/complex	.000***	.067	.156
Day*Side	.458	.030*	.201
Day*simple/complex	.033*	.001***	.170
Side*simple/complex	.000***	.152	.018*
Day*side*simple/Complex	.002**	.695	.957

3.3.3.2. Reaction time task

The mean RT did not significantly decrease by the training (Tab. 3.10). There was, however a significant difference between the simple and the complex RT of 52 ms ($p < 0.001$; Tab. 3.10, Fig. 3.16). The training did not decrease the mean RTs in simple, but the mean RTs decreased from 830 ms to 780 ms in the complex RT condition ($p < 0.05$; Tab. 3.10). It decreased 50 ms in complex RT (Fig. 3.17A)

There was a significant difference between the simple and the complex RT of 40 ms in the left and 60 ms in the right side ($p < 0.001$; Tab. 3.10). The mean RT was 773 ms in the left and 733 in the right side in the simple, and 775 ms and 835 ms in the complex RT (Fig. 3.17B).

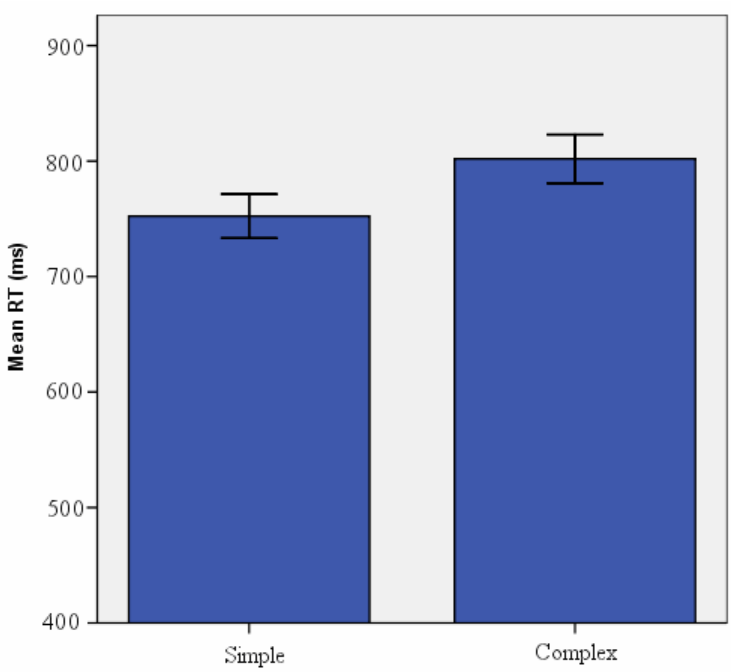

Fig. 3.16. The average mean RTs (the left and right hand) in the simple and complex RT condition in patient A. Bars are confidence limits (p=0.05).

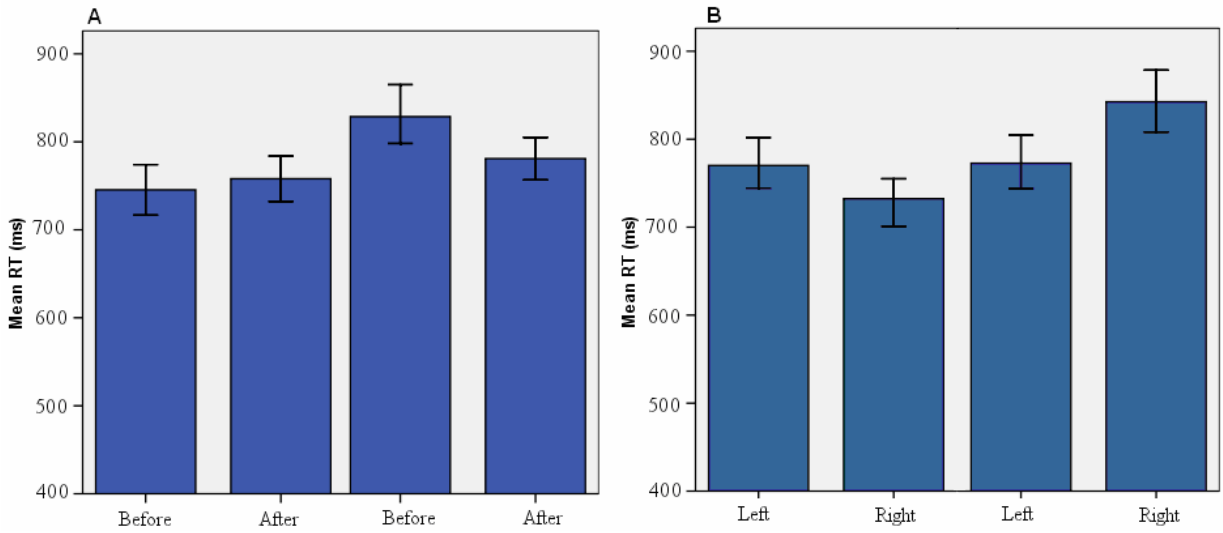

Fig. 3.17A. Mean RTs for the dates before and after the training in the simple (left 2 columns) and the complex (right 2 columns) RT for both hands (**B**). the average mean RTs by the left and the right hand in simple (left 2 columns) and the complex (right 2 columns) RT conditions in patient A. Bars are confidence limits (p=0.05).

3.3.3.3. End point variability.

The end point variability when pushing on the buttons in the RT tasks decreased due to the training only in the Y- direction (right-left). It was 26 mm, before, and 20 mm after the training (Fig. 3.18A). The difference of 6 mm was significant ($p < 0.05$; Tab.3.11).There was a significant difference of 13 mm ($p < 0.05$; Tab. 3.11, Fig. 3.18B) between the simple and the complex RT condition in the Z-direction.

Tab. 3.11: Significance values of F obtained with ANOVAs for the endpoint variability during the RT task with the fixed factors and their interaction. A separate ANOVA was performed for each direction and each patient. The significance levels are ***= $p \leq 0.001$, **= $p \leq 0.01$ and *= $p \leq 0.05$.

Source	Patients		
	A	B	D
End point variability			
X-axis.			
Day	.905	.154	.474
Side	.386	.144	.015*
Simple/complex	.349	.005**	.509
Day*side	.517	.279	.921
Day*Simple/complex	.196	.348	.222
Side*simple/complex	.292	.691	.995
Day*side*simple/complex	.148	.041*	.829
Y-axis.			
Day	.040*	.733	.322
Side	.350	.918	.010*
Simple/complex	.105	.108	.019*
Day*side	.958	.530	.944
Day*Simple/complex	.727	.540	.570
Side*simple/complex	.207	.184	.688
Day*side*simple/complex	.314	.888	.664
Z-axis.			
Day	.490	.062	.358
Side	.291	.951	.050*
Simple/complex	.018*	.174	.078
Day*side	.099	.736	.434
Day*Simple/complex	.616	.941	.878
Side*simple/complex	.996	.937	.618
Day*side*simple/complex	.350	.914	.672

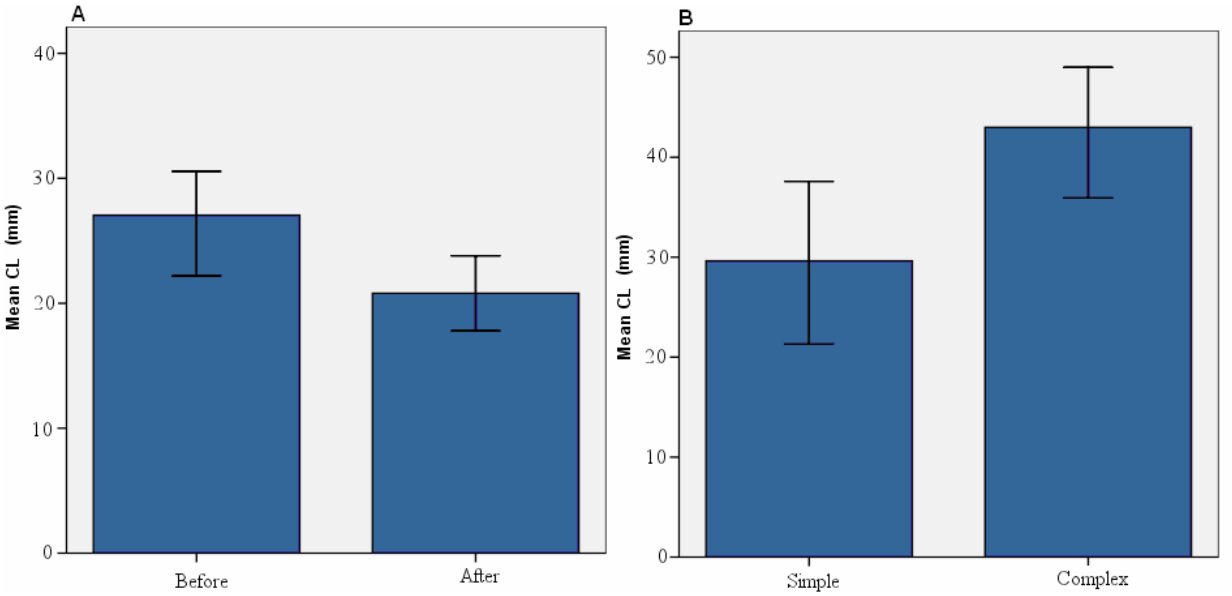

Fig. 3.18. Mean confidence values of the dispersion of the endpoints in the Y-direction before and after the training (**A**) and in the Z- direction for the simple and the complex RT condition (**B**) in patient A. Bars are confidence limits (p=0.05)

3.3.3.4. Tremor

The tremor was computed in the X-, Y- and Z- during the go and holding period in the pointing task.

Tab. 3.12: Significance of F values obtained with ANOVAs test for the tremor during pointing movements with the fixed factors and in their interaction. The significance level are ***=p≤ 0.001, **= p ≤ 0.01 and *=p ≤ 0.05.

Source	Patients		
	A	B	D
Tremor for the three axes.			
X-axis. Day	.000***	.003**	.000***
Side	.109	.771	.385
Interval	.000***	.000***	.000***
Day*side	.180	.770	.573
Day*interval	.000***	.094	.007**
Side*interval	.251	.063	.538
Day*side*interval	.553	.754	.458
Y-axis. Day	.000***	.000***	.000***
Side	.509	.078	.573
Interval	.000***	.000***	.000***
Day*side	.529	.215	.233
Day*interval	.000***	.002**	.007**
Side*interval	.427	.203	.766
Day*side*interval	.195	.471	.972
Z-axis. Day	.001***	.000***	.000***
Side	.303	.193	.697
Interval	.000***	.000***	.000***
Day*side	.313	.462	.878
Day*interval	.000***	.012*	.009**
Side*interval	.437	.188	.643
Day*side*interval	.669	.350	.786

The tremor decreased from 4.3 movements/sec to 2.9 in the X-, from 4.2 to 3.1 in the Y- and from 4.7 to 3.6 in the Z-direction (Fig. 3.19). The differences of 1.4, 1.1 and 1.10 were highly significant ($p < 0.001$; Tab.3.12).

The tremor was about twice faster during the holding than during the go period (Fig. 3.20). The differences were 4.4 movements/sec in the X-direction, 3.4 in the Y-direction and 2.4 in the Z-direction. All these differences were highly significant ($p < 0.001$; Tab. 3.12).

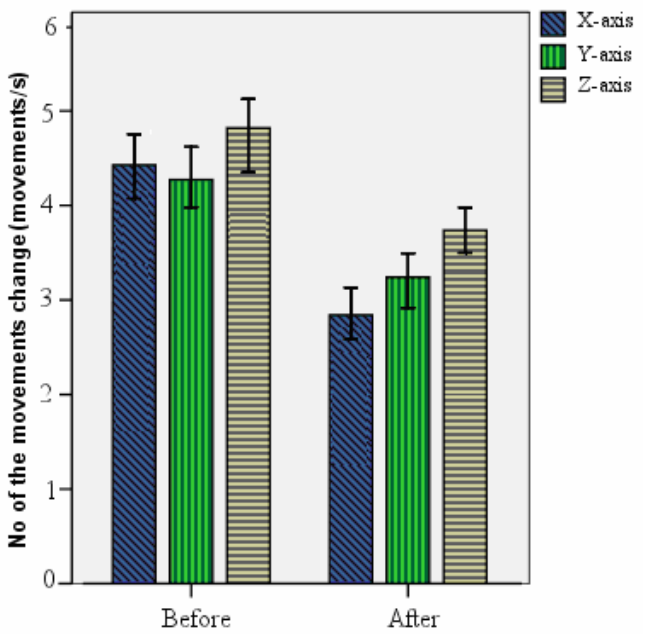

Fig. 3.19. Mean no of movement changes in the X-, Y- and Z- direction for the dates before and after the training in patient A. Bars are confidence limits (p=0.05).

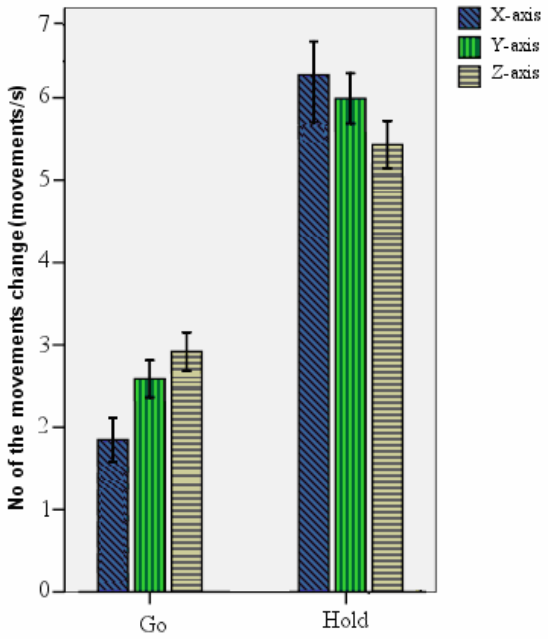

Fig. 3.20. Mean no of the movement changes in the X-, Y- and Z- direction for the go and the holding period in patient A. Bars are confidence limits (p=0.05).

There was a significant interaction between the training effect and interval (go and holding period) ($p < 0.001$; Tab. 3.12). During the go period, the tremor decreased 0.5 movements/sec in the X-, 0.3 in the Y- and 0.3 in the Z-direction, during the holding period it decreased 0.4 movements/sec in the X-, 0.6 in the Y- and 0.40 in the Z-direction (Fig. 3.21).

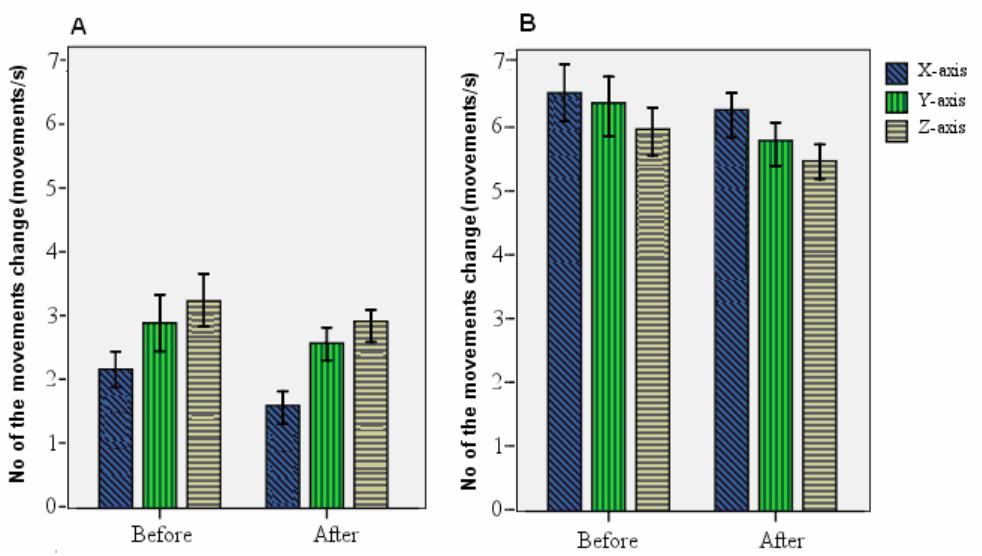

Fig. 3.21. Mean no of the movement change in the X-, Y- and Z- direction for the dates before and after the training for the go (**A**) and the holding (**B**) period in patient A. Bars are confidence limits (p=0.05).

3.3.4. Patient B

This patient had a car accident resulting in several brain lesions resulting e.g. in memory deficiencies.

3.3.4.1. Climbing performance

The number of times patient B could touch alternatively two indicated grips improved by 9 which was highly significant ($p < 0.001$; Tab. 3.10, Fig. 3.22A). There was a significant difference of 3 between the left and right hand ($p \leq 0.001$; Tab. 3.10, Fig. 3.22B).

The mean no times two grips could be touched improved significantly from 13 to 20 on the left and from 14 to 24 on the right hand (Fig. 3.23). The increase was significantly larger on the left than on the right side ($p \leq 0.001$; Tab. 3.10)

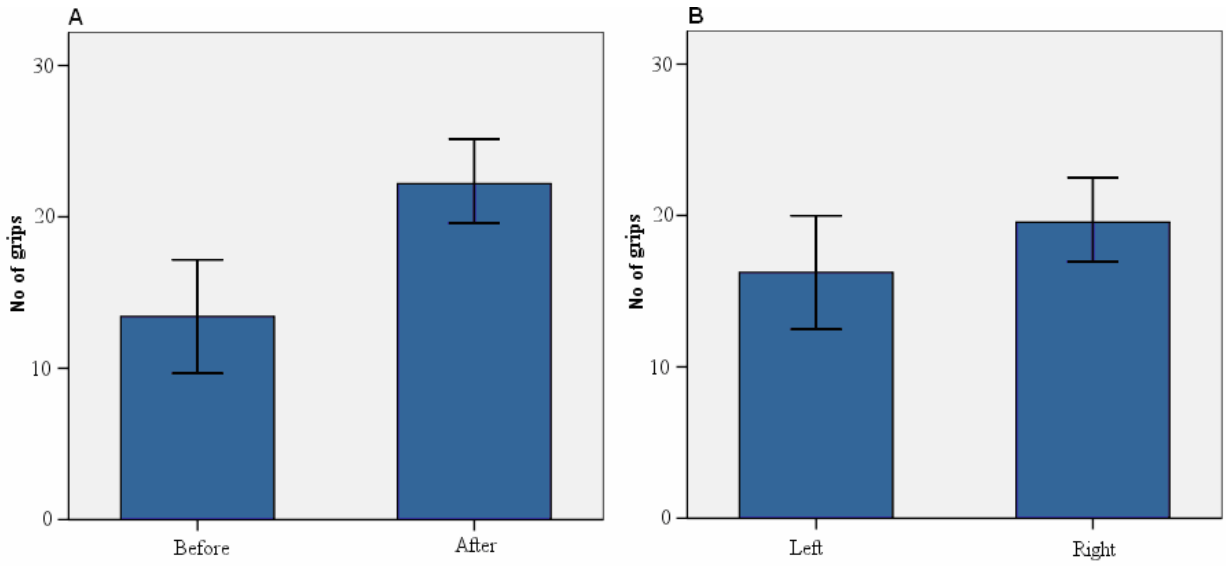

Fig. 3.22. Mean no of times two grips could be touched in 30 sec for the dates before and after the training (**A**) and for the left and right hand (**B**) in patient B. Bars are confidence limit (p=0.05).

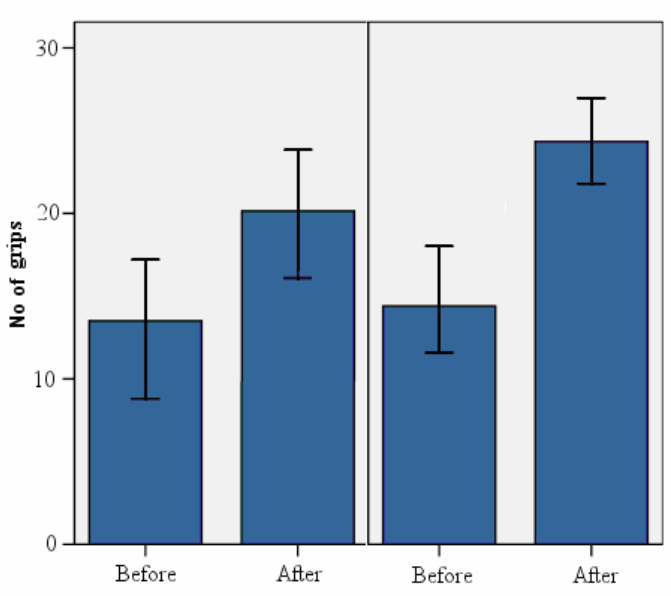

Fig. 3.23. Mean no of times two grips could be touched for the dates before and after the training by the left (left 2 columns) and right (right 2 columns) hand in patient B. Bars are confidence limit (p=0.05).

3.3.4.2. Reaction time task

The training decreased the mean RT by 158 ms ($p < 0.001$; Tab. 3.10, Fig. 3.24).

There was a significant interaction between the side and the training effect ($p < 0.05$, Tab. 3.10). The mean RT decreased from 901 ms to 779 ms in the left and from 939 ms to 745 ms in the right hand (Fig. 3.25A)

The training decreased the mean RTs from 906 ms to 806 ms in simple and from 933 ms to 718 ms in the complex RT conditions ($p \leq 0.001$; Tab. 3.10). It decreased 100 ms in the simple and 215 ms in the complex RT conditions (Fig. 3.25B)

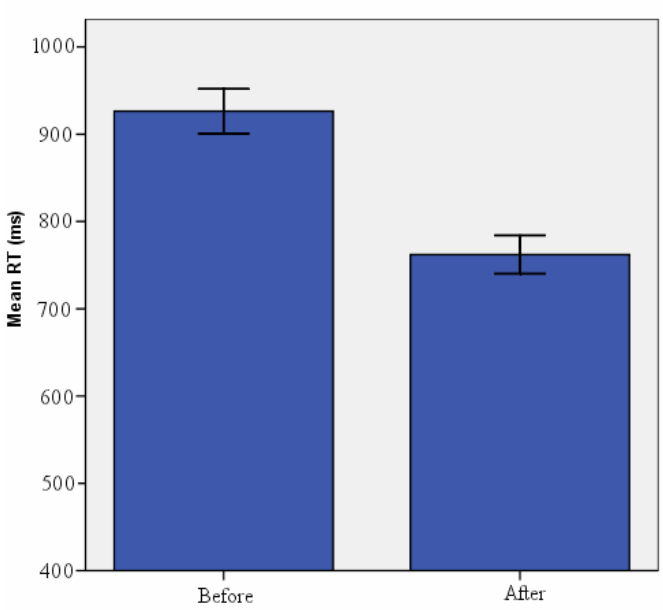

Fig. 3.24.The average mean RTs (the left and right hand) for the dates before and after the training in patient B. Bars are confidence limits (p=0.05).

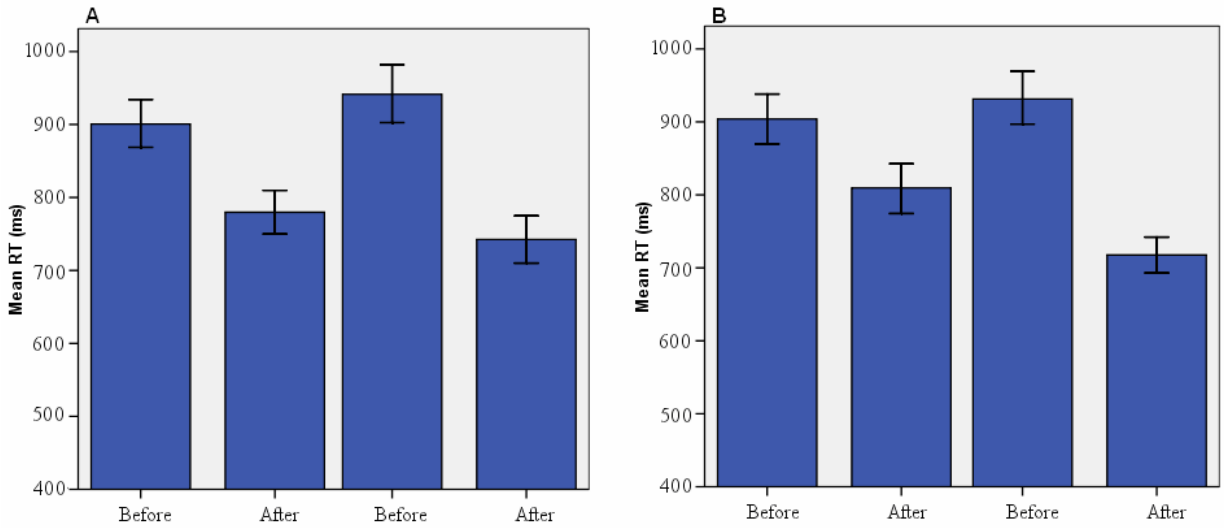

Fig. 3.25. The average mean RTs for the dates before and after the training by the left (left columns) and the right (right columns) hand (**A**) and in the simple (left 2 columns) and the complex (right 2 columns) RT condition (**B**) for both hands in patient B. Bars are confidence limits (p=0.05)

3.3.4.3. End point variability

There was a significant difference 13 mm ($p \leq 0.01$; Tab. 3.11, Fig. 3.26) between the simple and the complex RT condition.

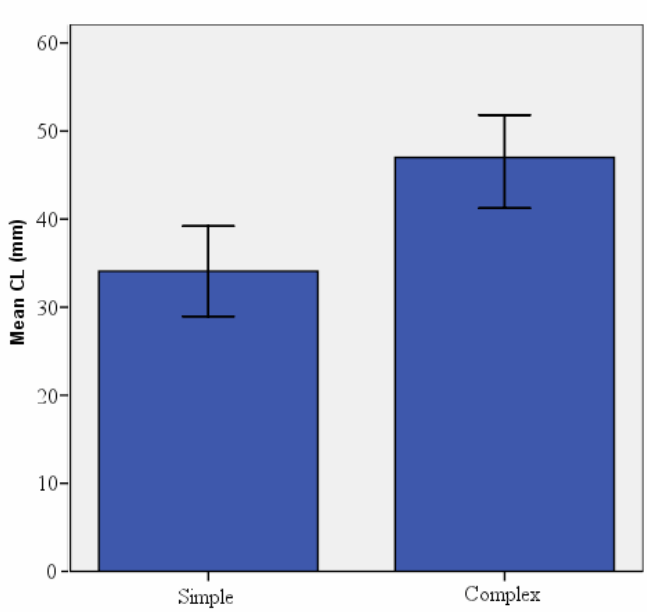

Fig. 3.26. Mean confidence limits values of the dispersion of the endpoints in the X- direction for the simple and the complex RT condition in patient B. Bars are confidence limits (p=0.05).

3.3.4.4. Tremor

The tremor decreased significantly after the training by 1.06 movements/sec ($p < 0.01$), 0.96 ($p \leq 0.001$) and 0.82 ($p < 0.001$) in the X-, Y- and Z-direction (Tab. 3.12, Fig.3.27).

The differences between the go and the holding period were 4.3 movements/sec in the X-direction, 2.9 in the Y-direction and 2.3 in the Z-direction. All these difference were highly significant ($p < 0.001$; Tab. 3.12, Fig. 3.28).

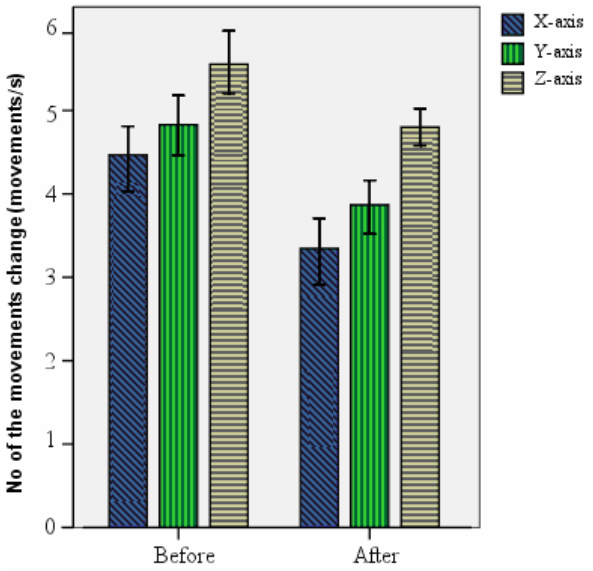

Fig. 3.27. Mean no of the movement changes in the X-, Y- and Z- direction for the dates before and after the training in patient B. Bars are confidence limits (p=0.05).

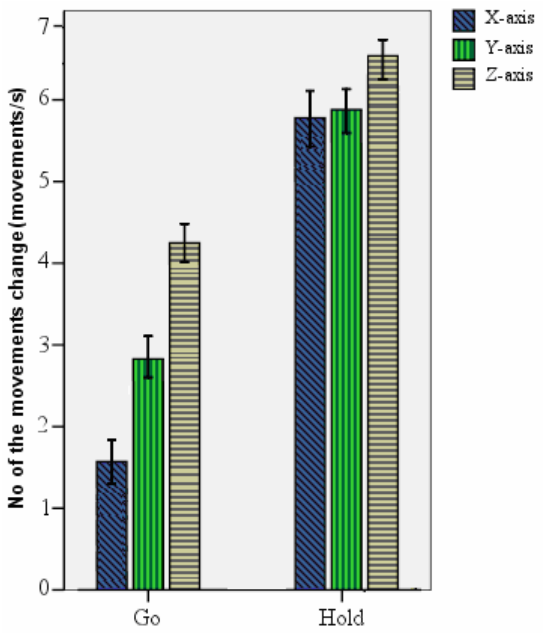

Fig. 3.28. Mean no of the movement changes in the X-, Y- and Z- direction for the go and the holding period in patient B. Bars are confidence limits (p=0.05).

The tremor in the X-, Y- and Z-direction during the go period was 1.9 movements/sec, 3.1 and 4.6 before, and 1.4 movements/sec, 2.7 and 4.1 after the training, and during the holding period 6.4 movements/sec, 6.4 and 6.6 before and 5.2 movements/sec, 5.4 and 6.1 after the training (Fig. 3.28). The differences before and after the training (0.5, 0.4 and 0.5 for the go and 1.2, 1.0 and 0.5 for the holding period) were significant ($p < 0.05$; Tab.3.12).

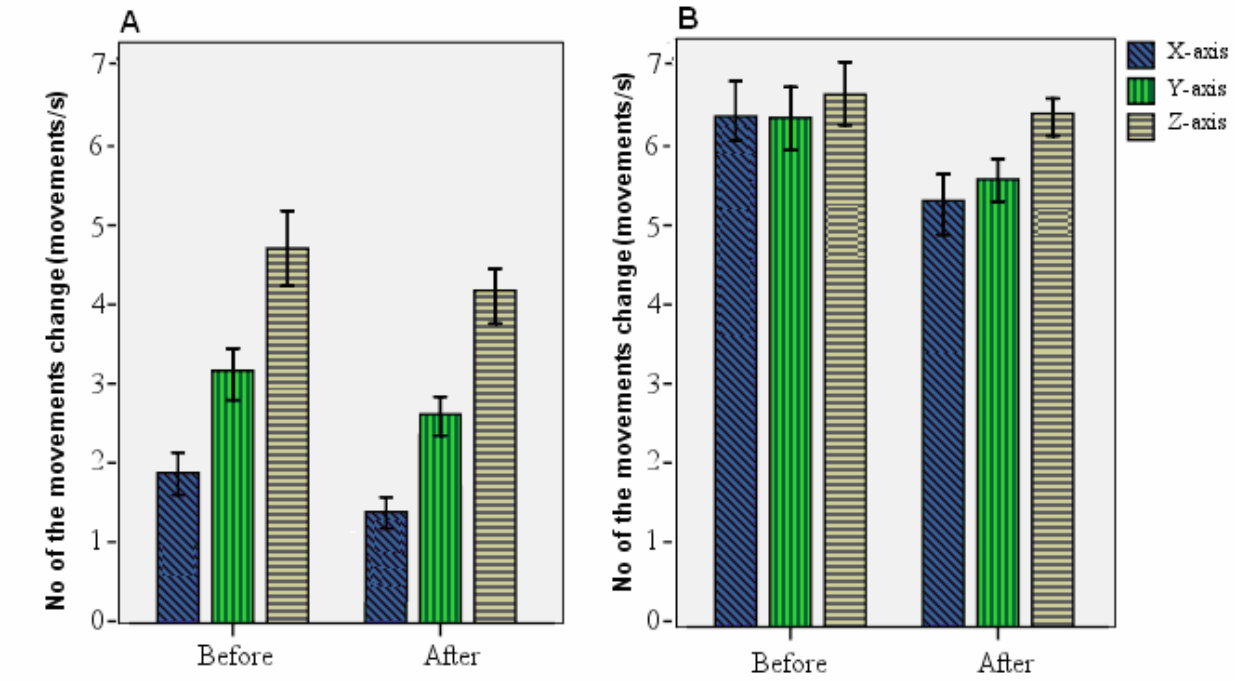

Fig. 3.29. Mean no of the movement changes in the X-, Y- and Z- direction for the dates before and after the training for the go (**A**) and the holding period (**B**) in patient B. Bars are confidence limits (p=0.05).

3.3.5. Patient D

This patient has a tumor in the frontal part of the brain and reaching deficits

3.3.5.1. Climbing performance

The number of movements between 2 grips he could perform within time 30 s increased significantly (from 31 to 38, $p \leq 0.01$; Tab. 3.10, Fig. 3.30).

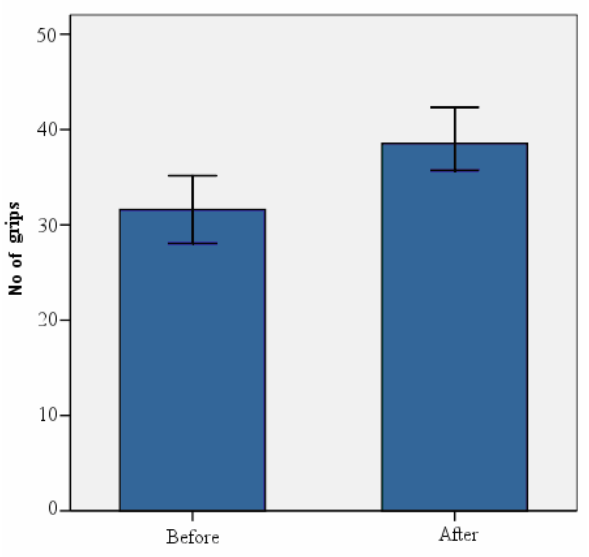

Fig. 3.30. Mean no of times two grips could be touched for the dates before and after the training in patient D. Bars are confidence limit (p=0.05).

3.3.5.2. Reaction time task

The training effect of 90 ms in the RT was significant ($p < 0.001$; Tab. 3.10, Fig. 3.31A). The mean RT was 606 ms in the left and 589 ms in the right hand for the simple and 618 ms and 636 ms in the complex RT condition (Fig. 3.31B). There was a significant difference between the left and right hand of 17 ms in the simple and 18 ms in the complex RT ($p < 0.05$; Tab. 3.10).

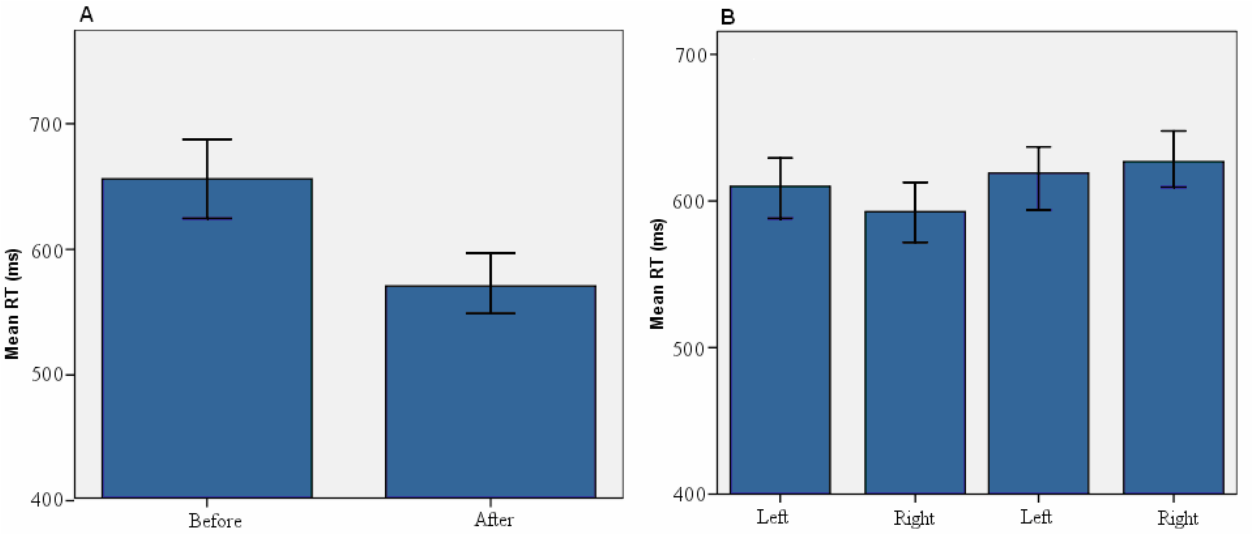

Fig. 3.31A. The average mean RTs (the left and right hand) for the dates before and after the training. **B**. The overall mean RTs for the left and the right hand in simple (left 2 columns) and the complex (right 2 columns) RT condition in patient D. Bars are confidence limits (p=0.05)

3.3.5.3. End point variability

The mean confidence limits of the end point variability was 38 mm, 27 mm and 34 mm for the left and 27 mm, 19 mm and 24 mm for the right hand in the X-, Y- and Z direction (Fig. 3.32). The differences of 11 mm, 8 mm and 10 mm between the left and the right hand were a significant ($p \leq 0.05$; Tab. 3.11).

There was a significant difference of 7 mm ($p < 0.05$; Tab. 3.11, Fig. 3.33) between end point variability in the simple and the complex RT condition in the Y-direction.

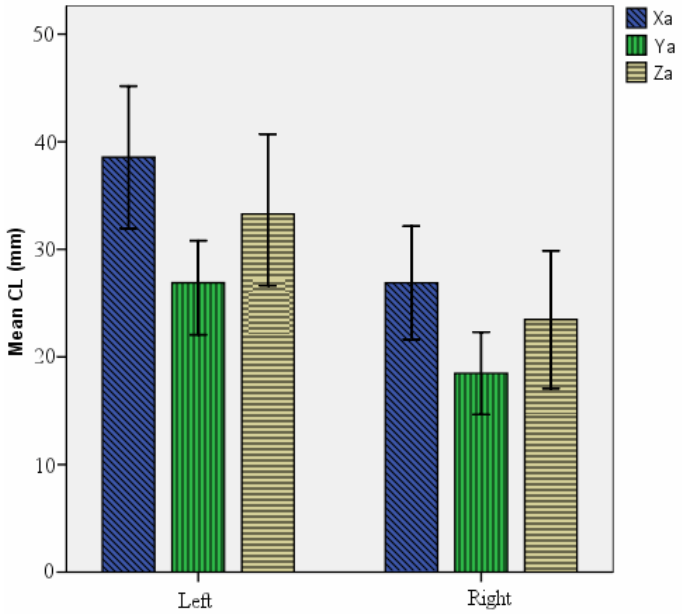

Fig. 3.32. Mean confidence limits values of the dispersion of the endpoints in the X-, Y- and Z-direction for the left and the right hand in patient D. Bars are confidence limits (p=0.05).

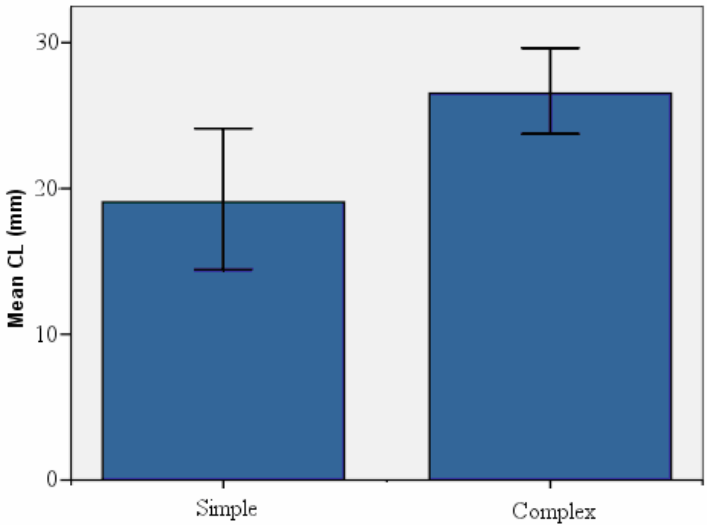

Fig. 3.33. Mean confidence limits values of the dispersion of the endpoints in the Y- direction for the simple and the complex RT condition in patient D. Bars are confidence limits (p=0.05)

3.3.5.4. Tremor

The tremor decreased after the training. The effect was faster in the Y- and Z direction from (4.6 movements/sec to 2.8 and from 4.9 to 3.3) than in the X-direction from (4.1 to 3.4). All these changes were highly significant ($p < 0.001$; Tab. 3.12, Fig. 3.34)

The differences between the go and the holding period were 3.6 movements/sec in the X-direction, 2.9 in the Y-direction and 2.7 in the Z-direction. All these difference were highly significant ($p < 0.001$; Tab. 3.12, Fig. 3.35).

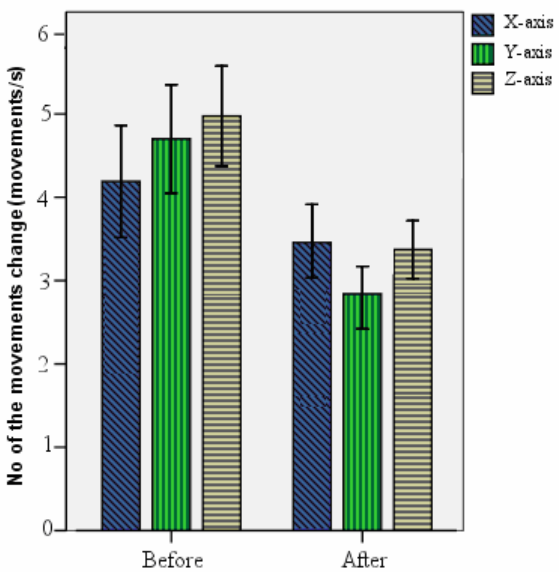

Fig. 3.34. Mean no of the movement changes in the X-, Y- and Z- direction for the dates before and after the training in patient D. Bars are confidence limits (p=0.05).

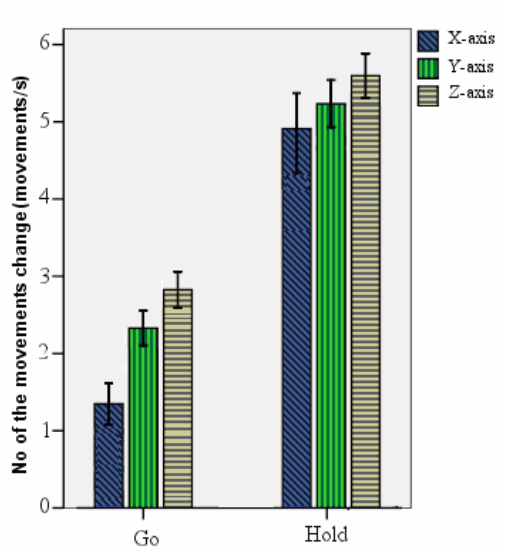

Fig. 3.35. Mean no of the movement changes in 3 coordinates (X-, Y- and Z axis) direction for the go and the hold period in patients D. Bars are confidence limits (p=0.05).

The tremor decreased after the training during the go and the holding period. During the go period, it was 0.4 movements/sec in the X-direction ($p \leq 0.01$), 0.2 in the Y-direction ($p \leq 0.01$) and 0.5 in the Z-direction ($p \leq 0.01$), during the holding period, it was 1.5 movements/sec in the X-, 1.9 in the Y- and 1.2 in the Z-direction (Tab. 3.12, Fig. 3.36). The training was significantly faster during the holding ($p < 0.001$, $p < 0.05$, $p < 0.01$) than during the go period.

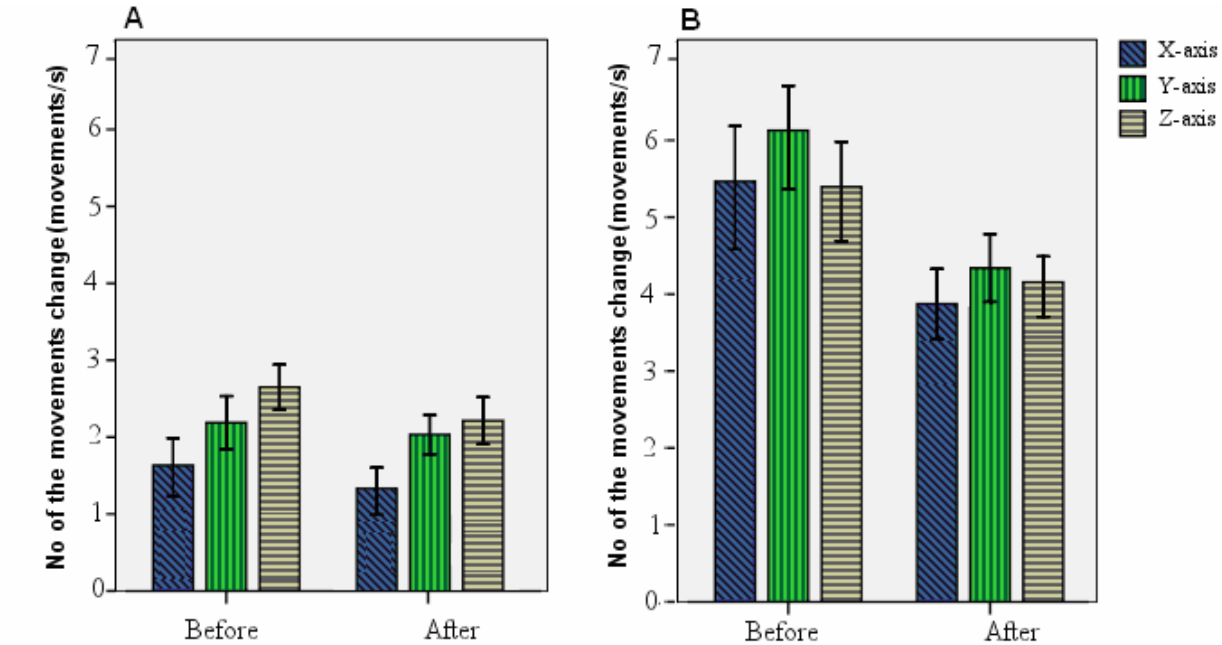

Fig. 3.36 Mean no of the movement changes before and after the training in 3 coordinates (X-, Y- and Z axis) direction for the go and the hold period in patients D. Bars are confidence limits (p=0.05).

3.4. Discussion

Abnormalities of movement execution in cerebellar patients are commonly referred to as limb ataxia. When used to describe limb movement it indicates an irregularity in the direction and range of the movement (Adams and Victor 1993). According to Holmes et al. (1939), this irregularity is always more marked with rapid and complex rather than with simple movements: "Simple actions which require movement at one joint only may be fairly accurately performed, though complex actions are irregular and ataxic; the patient can succeed much better in touching with either his finger or toe an object that he can reach with his limb extended than when movements at the elbow, knee or other joints are also necessary".

It was shown in this study that the climbing wall training improved the performance in all the patients although they had various types of cerebellar disorders. Free, unrestrained reaching and pointing movements of the arm, with emphasis on speed and accuracy, allowed the full expression of ataxia.

The current study demonstrates that some patients improved their motor performance after training. An interpretation of the results from our patients is difficult, since the lesions were diffuse and not precisely localized. In spite of the large variability of the results it was found in the present study, that the RTs were significantly longer in the patients than in the controls. In the present discussion, the increase of RT and the spatial abnormalities, as overshoot, undershoot and indirect movement paths are considered.

RTs

Our finding that the RTs were increased compared to normal subjects, supports the hypothesis that the cerebellum plays a central role in timing control, in terms of setting up the temporal parameters of a motor program (Ivry et al. 1988). This timing control might determine when each of a series of motor responses can be initiated or how long the specific response (such as setting the timing for the reciprocal activation of agonist-antagonist muscles) can last.

The patients had even slower simple and choice RTs than patients with Parkinson's or Huntington's disease and the capacity to maintain a general motor readiness was reduced (Jahanshahi et al. 1993). These findings were supported by Nakamura and Taniguchi (1980) who found, compared with controls, increased RTs in 10 cerebellar patients who performed forearm flexions and supinations. They suggested that the cerebellum is a critical area for the increase in RT and the lengthening of the RT might be the result of loss of excitatory feedback from the cerebellum to the motor cortex.

The patients with limb ataxia took longer to initiate movement and movements were slower than normal, in keeping with the well-documented prolongation of reaction times and slowness of movement in human cerebellar disease (Hallett et al. 1991; Hore et al. 1991; Bonnefoi-Kyriacou et al.1995; Bastian et al. 1996). The slowness of our patients may have been partly due to the instructions, which emphasized accuracy and speed and not just speed. However, this is unlikely the cause of slowness since Bastian et al. (1966) found that subjects, who were asked to perform movements which were (i) slow and accurate, (ii) fast and accurate, or (iii) as fast as possible with no constraint on accuracy, moved slower than normal in all three situations (Bastian et al. 1996).

In the same trend, neurophysiological studies on monkeys indicate that the cerebellum may trigger motor programs elaborated elsewhere (Trouche et al.1980; Ito et al; 1974; Meyer-Lohmann et al. 1977). RTs in monkeys are increased after lesions in the dentate nucleus (Trouche et al.1980; Beaubaton and Trouche. 1982).

3.4.1. Spatial abnormalities

A number of spatial abnormalities were observed in our patients. The spatial paths of the fingertip were more circuitous than normal, leading to longer path lengths. Bastian et al. (1996) found similar results in arm movements of cerebellar patients. It is well known that cerebellar damage affects motor adaptation (error-based learning) of several types of specific arm (Martin et al. 1996; Lang and Bastian 1999) and eye movements (Krupa and Thompson 1997; Takagi et al. 1998). Constant pointing errors have also been observed previously in monkeys after dentate nucleus cooling or ablation (Beaubaton and Trouche 1982). Studies of single jointed movements have revealed several parameters that the cerebellum may control, including timing and/or amplitude scaling in either the agonist, antagonist, or both muscle groups. However, no single deficit uncovered can be generalized across studies to explain the different features of ataxia. Instead, cerebellar damage appears to disrupt different aspects of a movement depending on task conditions. The one common feature across these studies is that the movement deficits were always attributed to an imbalance of agonist-antagonist activity.

3.4.2. Scaling

An important feature of cerebellar control may be in predictively scaling the relative activities of different muscles in relation to the mechanical demands (e.g., inertia, interaction torques) during the movement. If this is the case, then cerebellar ataxia should be more

pronounced during movements that require coordination of many muscles and/or have complex mechanical demands. Evidence from both humans (Bastian et al. 1996; Topka et al. 1998b; Goodkin et al. 1993; Massaquoi and Hallett 1996) and monkeys (Thach et al. 1992a,b) indicate that cerebellar damage impairs multi-jointed movements to a greater extent than would be expected based on single jointed deficits. Goodkin et al. (1993) reported about a cerebellar subject who could make relatively normal single-jointed wrist movements, but had impaired multi-jointed reaching movements. Similarly, monkeys with an inactivated dentate nucleus had only mild impairments of single-jointed wrist movements, but gross impairments of reaching movements (Thach et al. 1992b).

3.4.3. Interaction torques

It has been suggested that the role of the cerebellum may be in generating interaction torques (Bastian et al. 1996; Schweighofer et al. 1998a, b). Interaction torques are the mechanical consequence of moving limb segments that are linked together. During a reaching movement, the elbow movement causes a torque at the shoulder, called interaction toque, and reciprocally a shoulder movement causes an interaction torque at the elbow. Interaction torques may assist or oppose the desired movement at each joint depending on direction, velocity and acceleration of joint movements. A cerebellar ataxia during multi-jointed reaching may be due to an inability to adjust for dynamic interaction torques (Bastian et al. 1996; Topka et al. 1998a, b). This is especially evident during fast, multi-jointed reaching movements. Specifically, the torque produced by the muscles did not counter the interaction torque appropriately, allowing interaction torques to contribute excessively to the generation of the movement. This results in an abnormal pattern of reaching, with the elbow and shoulder joints moving at inappropriate rates relative to one another and the fingertip overshooting the target (Bastian et al. 1996; Topka et al. 1998a,b). Cerebellar deficits, such as dysmetria, should be also be greatly improved when interaction torques are eliminated. Boose et al. (1999) have proposed that this impairment is a result of a generalized inability to quickly generate the appropriate muscle torque levels.

3.4.4. Locomotion and Balance

Human studies of cerebellar involvement in balance and locomotion are more limited than the extensive animal literature. Cerebellar damage and disease occurs relatively infrequently and is often accompanied by injury to other central nervous system regions such as the brainstem or spinal cord. Horak and Diener (1994) studied whether cerebellar subjects could learn to adjust for

predictable postural perturbations during standing. Rand et al. (1998) studied adaptation to sudden but predictable changes in treadmill speed during walking in subjects with cerebellar damage and mild ataxia. Results suggested that the patients can adapt to changes in speed, but they have a considerable variability in the timing and duration of muscle activation patterns and use a strategy that is different from that used by healthy subjects.

4. Climbing as therapy for the patients with cerebellar disorder (Part2)

4.1. Introduction

In addition to the motor cortex and the basal ganglia, the cerebellum is considered as one of the 3 important brain areas contributing to motor control. It receives not only information from other modules of the brain related to the programming and execution of movements, but also sensory feedback from receptors about ongoing movements. After processing this information, it modulates the motor output of the motor cortex and other systems within the brainstem. The functions of the cerebellum can be roughly attributed to 3 distinct zones. The vestibulocerebellum controls the axial muscles for equilibrium control, the spinocerebellum modulates the actual execution of the movement and the muscle tone, and the cerebrocerebellum participates in programming the motor cortex for the execution of movement but also in the coordination of ongoing movements (Shumway-Cook et al. 2001). Cerebellar damage can result in severe ataxia of voluntary limb movements or gait and in high-amplitude tremor. However, the exact function of the cerebellum in motor control is still subject of debate. It was suggested that the cerebellum controls timing or amplitude scaling in the agonists, the antagonists, or both muscle groups or that it may coordinate the relative activity of multiple muscles and adjust movements at a given joint to oppose or assist torques that are caused by other linked segments (Bastain et al. 1996). In addition to its role in motor control processes, the cerebellum seems to be important in cognitive processes and in motor learning. Several human and animal studies have thus dealt with the question whether motor learning is possible when the cerebellum is damaged.

A study investigating multi-joint figure-8 movements in the air found limited but not absent motor learning in the movement task alone. However, in contrast to healthy subjects motor performance deteriorated to prepractice levels when attention was focused away from the movement during dual task trials. They concluded that cerebellar damage impairs the automaticity of a recently practiced movements (Lang and Bastain 2001). Other studies indicate that cerebellar patients can improve their performance in a series of two-dimensional tracing-tasks. Also when tested 24 h later, patients demonstrated significant retention of the acquired skill and tended to improve more rapidly when performing the same skill again (Timmann et al. 1996; Topka et al. 1998a). It has also been shown that patients with cerebellar lesions are able to adapt their gate pattern in response to repeated changes in treadmill speed, but that they do not establish a motor pattern comparable to that employed

by healthy subjects (Rand et al. 1998). In a case report two patients with cerebellar dysfunction demonstrated improvements in postural stability after a six-week balance training. It was concluded that, if the cerebellum is not totally destroyed, adaptation or compensation for the movement impairment occurs perhaps in a neighbouring area of the cerebellum or in another part of the brain (Gill-body et al. 1997). Both preoperative and postoperative trainings of cerebellectomised mice on a rotating rod improved the restoration of the equilibrium (Caston et al. 1995). Furthermore, rats with cerebellar damage improved significantly in motor skills tests, and the thickness of the molecular layer in the paramedian lobule of the cerebellum increased after complex motor skill training. However, motor skill tests showed no improvement after motor conditioning on a flat runway (Klintosva et al. 2002). It seems that, when the cerebellum is damaged, motor learning is impaired and probably different from that in healthy subjects, but nevertheless possible. However, under which training conditions and to which extent motor learning is possible when the whole cerebellum or parts of it are damaged is still unclear and up to now there is no directive for an adequate, efficient and valid treatment of cerebellar patients. Most human studies investigate short-term learning in a specific motor task in response to repetition. Rehabilitation of patients with cerebellar damage, however, requires a long-term learning process and the acquired motor patterns have to be transferred to everyday life. Since there are many parallel motor pathways for carrying out an action sequence, we cannot assume that the training effect will transfer to all other activities requiring the same set of muscles, simply by repeating one single motor task. Thus, further research is inevitable in order to investigate whether long-term learning of motor control in cerebellar patients is possible and in order to determine an adequate treatment for these patients. The aim of this investigation was to evaluate the effect of a six-week climbing training on motor control of patients with cerebellar damage. Measurements taken before, during and after the treatment included 3-dimensional movement analysis of arms and legs, clinical balance and motor skill tests and self-perception of symptoms. We chose climbing for the training of motor control because of its numerous positive aspects. Climbing on a wall is a complex task for the motor system. It involves the coordination of all 4 limbs and challenges equilibrium and body stability. It requires precise pointing movements of hands and feet to the grips, the planning of single movements and movement sequences and for more advanced climbers optimal body positions in order to put the largest possible weight on the feet and the least possible force on the hands. Climbing enables a variety of different movement tasks and the degree of

difficulty can be very well adjusted to the requirements of the patient. Last but not least climbing has a positive effect on strength and endurance.

4.2. Methods

4.2.1 Patients

Four patients with cerebellar damage and 4 control subjects participated in the study. All gave their informed consent prior to participating. The patients were diverse in terms of pathology, duration of illness and age. Motor disorders of all patients were dominant on the right side of both the upper and lower extremities. The exact localisations of the brain lesions were unknown.

Two years before the onset of this study, patient 1 (male, 19) sustained a severe craniocerebral injury with subarachnoid hemorrhage which damaged multiple brain areas and resulted in an ataxic paresis of all 4 limbs. Patient 2 (male, 56) suffered an ischemic stroke (two month before study onset) which damaged the cerebellum and caused ataxia and tremor in upper and lower limbs. In patient 3 (male, 22) an anoxic encephalopathy at birth with lesions in multiple brain areas caused spastic diplegia, visual and perceptive troubles and psychomotor retardation. Patient 4 (male, 42) sustained a metabolic encephalopathy with cerebellar component from unclear origin eight months before study onset. Three and half years earlier, he was diagnosed with cancer in the frontal cortex. Since then he suffered from repeated severe epileptic seizures. Clinically, the patient exhibited only mild motor disorders and no detectable tremor during movements.

Patient performance during the experimental sessions was compared to that of a group of 4 (3 males and one female with mean age of 33.5 years) healthy subjects.

4.2.2 Experimental setup and procedure

The long-run motor learning of the patients as a result of a 6-week climbing training was evaluated in 3 different ways, with (1) an analysis of 3-dimensional pointing movements, (2) clinical balance and motor skill tests and (3) self-perception of symptoms. All measurements and tests were taken 6 times, twice before, during and after the treatment at intervals of two weeks. During the climbing period, the patients were requested to complete a questionnaire at the end of each week.

4.2.2.1. Kinematic and kinetic movement parameters

The 3-dimensional motion measuring system CMS30 P (Zebris Medizinaltechnik GmbH, Isny) was used for data registration (Chapter 3.2.2).

The experimental setup to measure arm movements was as follows: 4 ball targets with a diameter of 2 cm, with red points as precise marks and labelled with numbers were suspended from a fine wire above a table in a semicircle around two starting points. The starting points,

labelled with colours, were positioned on the table, one on the right ipsilateral side of the performing arm (13 cm from the edge of the table) and the other one on the contralateral side (34 cm from the edge of the table). The target positions varied in height (5-35 cm) above the table and horizontal distance to the starting points (14-48 cm), which resulted in 8 different movements. A device similar to a glove was used to fix two transmitters on the tip of the right index finger and on the back of the hand in order to keep them in the same position during all measurements. The cables were fixed with straps around the arm. The patients were comfortably seated on a chair with their right upper arm vertical and in the sagittal plane and their upper body upright. Patient 2 stayed in his wheel chair. The distance to the table was determined in such manner that the ankle of the horizontal lower arm was flush with the edge of the table.

The experimental setup for the leg movements was similar: 4 balls with a diameter of 4 cm and red points as precise marks were suspended from a fine wire above the ground in a semicircle around one starting point. As for the arm movements, the horizontal distances between starting point and targets (25-36 cm) and the heights of the targets above the ground (13-32 cm) varied, which resulted in 4 different movements. An adjustable walking aid provided body stability. The patients stood with both feet on the ground holding the walking aid with both hands. The right big toe was placed on the starting point and the cables were fixed with straps around the leg. Patient 2 was seated on the walking aid with both legs in the air, in a distance to the targets which allowed him to reach them comfortably. Special socks were used to fix two transmitters on the tip of the big toe and on the back of the foot in order to keep them in the same position during all measurements.

The patients performed unconstrained 3-dimensional pointing movements under two different experimental conditions with their clinically more affected right arm and leg. Small trunk movements were accepted, although the distance of the patients to the table was such that all targets could be comfortably reached by the index finger without trunk movements. Each patient performed as many trials as his physical capacity and concentration allowed. These were 24 (6 movements/target from 2 different starting points) to 80 (20 movements/target from 2 different starting points) arm movements and 12 (3 movements/target) to 40 (10 movements/target) leg movements for each experimental condition. Seventy to maximal 240 movements were thus performed during an experimental session, which lasted about 1 h with a 10 min rest in the middle. During a session, the slow-without vision movements followed the fast-accurate movements (see below). The 4 targets and the two starting points (arm

movements) were announced in pseudo-random order. The patient could practice each movement before the measurements started.

4.2.2.2. Fast-accurate pointing movements

The patients were instructed to reach out to an auditory go signal, touch the red dot on the ball target and come back as fast as possible. The target was announced at least 2 s before the acoustic signal. This period between target announcement and the go signal ensured an adequate time for the patients to prepare the movement and to minimize the reaction time. The patients were urged to react as fast as possible. Although the patients were asked to touch the target, the emphasis was clearly put on the speed of the movement.

4.2.2.3. Slow-without vision pointing movements

The patients were instructed to locate the target, close their eyes and move their finger without vision to an auditory go signal to the target and back to the initial position. The go signal was given immediately after they closed the eyes, at the earliest 2 s after announcing the target.

The patients were not urged to react rapidly to the go signal but instead to move slowly and smoothly. The emphasis was put on the smoothness and the end point accuracy of the movement.

4.2.2.4. Balance and manual dexterity

To evaluate the patients' balance abilities and manual dexterity, two clinical tests were performed, the duration of which varied from 15 to 30 min.

4.2.2.5. Box and Block test

A box was divided by a small barrier into two equal sections. About 100 wooden blocks of a diameter of 2.5 cm were placed in the section ipsilateral to the tested hand. The patient was required to grasp one block at a time and transport it to the other section. The number of blocks transported to the other side during 60 s was counted. The test was performed with both hands.

4.2.2.6. Berg test

The patients were asked to perform 14 various functional activities such as standing unsupported, reaching forward while standing, turning 360° and retrieving objects from the floor. A 5-point ordinal scale from 0 to 4 was used to judge the performance of these functional tasks.

4.2.2.7. Self-perception of symptoms

For each patient a specific questionnaire was compiled to evaluate (1) their physical activities (besides the climbing training), (2) the motivation for the climbing training, (3) changes of

specific movement characteristics (e.g. the performance of slow movement sequences, tremor or the movement velocity) and (4) the performance of certain everyday skills (e.g. brushing teeth, cutting food or tying shoes). The patients were requested to complete the questionnaire at the end of each training week. Answers were given written by a nominal scale of 5 categories.

4.2.3 Climbing training

For the 6-week therapeutic climbing training two climbing walls of a height of 2.5 m with different degrees of difficulty were used. The inclination of one wall could be adjusted from 0° to 45°, enabling to adapt the climbing difficulty to the abilities of the patient. The other wall was almost vertical with a structured rough surface, allowing advanced climbers to do exercises without using grips (Fig. 4.1). Adjustable climbing belts, ropes and carabineers were available.

An experienced climber supervised the training. The frequency and the duration of the training sessions were scheduled in consideration of the state of health and the physical performance of each patient (up to maximally 3 sessions a week). In addition, the availability of the climbing wall as well as the patients' transport and personal schedules had to be considered.

Climbing tasks were prepared as manifold as possible in order to facilitate a transfer of learned motor patterns in everyday life and to keep the training interesting for the patients. Each patient performed exercises which challenged (1) the body equilibrium, (2) the movement accuracy in pointing and grasping, (3) the planning of movement sequences, (4) the smoothness of movement performance, (5) the integration of sensory information and (5) the velocity of single movements and movement sequences. For example, the patients were climbing with closed eyes, as fast as possible, in slow motion, bottom-up, diagonally, horizontally, with the face to the wall, laterally, with rice filled balloons on their limbs, using specific grips or using only the structure of the wall.

The rope with which the patients were secured was used to unload the body weight according to the climbing abilities and the strength of the patients who rested whenever they felt tired.

Patient 1:

In the first half of the training period, the patient trained twice 45 min per week. The training frequency was increased in the second half of the training phase to 3 times 45 min per week. Particular emphasis was put into the coordination of the limbs and the speed of single movements as well as movement sequences.

Patient 2.
The patient trained twice 30 min per week at the beginning of the training period. In the second week the duration of the climbing time was increased to 40 min and in the fifth and sixth week the frequency of the training sessions was increased to 3 times per week. Mainly movement accuracy and balance were trained.

Patient 3
In the first half of the training period the patient trained twice 45 min per week. The training frequency was increased in the second half of the training phase to 3 times 45 min per week. One of the training goals was the appropriate turning of the head and the integration of the visual information into the movement strategy.

Patient 4.
Despite the beginning of a chemo- and radiotherapy in the middle of the training period the patient was in good physical condition. He trained 3 times 60 min per week during the whole training period. Due to the fact that he already had experience in climbing he was training at a high level. He performed complex movement tasks which demanded concentration and physical endurance.

A **B**

Fig. 4.1. Climbing training. **A** wall for advanced climbers with rough surface. Patient in lateral position performing precise pointing movements to all reachable grips. **B** adjustable wall. Patient climbing to the top.

4.2.4. Data analysis

4.2.4.1 Kinematic and kinetic movement parameters

The 3-dimensional position data of the movement path and the digital data which encoded the time of the acoustic go signal were stored with the software WinData. Each movement sequence of a specific experimental condition and the superimposed go signals were stored in an ASCII text file for further treatment with several programs developed with the software LabView. Only data from the transmitter positioned on the tip of the index finger was analyzed. In order to enable the calculation of the different parameters, several time markers were set in each movement.

Some markers for the fast movements were computed automatically. The *movement start* was defined as the time where the sum of the absolute velocity values in x, y and z direction was bigger than 7.5 cm/s. The finger was supposed to *reach the target* when the sum of the position coordinates in x, y, and z direction was maximal (the algebraic signs of position coordinates were inverted, if the coordinates decreased towards the target). The *end of the movement* was defined as the time, when the difference between the sum of the position coordinates in x, y, and z direction and the sum of the position coordinates at the time of the go signal was smaller than 5 mm. As before, the algebraic signs of the corresponding position coordinates were inverted when the movement velocities were negative.

With exception of the *movement start*, the time markers for the slow movements were set manually on the basis of a visual display of the movement path in all 3 dimensions. The finger was supposed to *arrive* at the target, when the position coordinates reached their maximal respectively minimal values in all 3 dimensions. It was supposed to *quit* the target when the movement started in at least one dimension. The time marker for the *end of the movement* was set when the finger touched the table. Movements with more than 3 missing values or with accelerations bigger than 25 m/s^2 were excluded from further analysis.

The parameters described below were calculated for each single movement and stored in an Access table from where they were exported to the program SPSS for statistical analysis. An univariate analysis of variance (ANOVA) was performed for each patient with the respective movement parameter as dependent variable and the time (before, after), the target (1-4) and the initial position (left, right) as between-subject factors. The tests showed the influence of the defined between-subject factors on the dependent variable and the interactions for all combinations of between-subject factors. The same statistical analysis was also performed for the healthy control group. A t-test was used to evaluate the difference of movement performance between each patient and the control group. For all parameters of each movement

condition, the means of the control group were taken as reference values. To evaluate the effect of the climbing training, the kinematic movement parameters were analyzed for both the fast and slow movements whereas the kinetic parameters were only analyzed for the fast movements.

4.2.4.1.1. Kinematic parameters

Endpoint error
The endpoint error was defined as the distance between the movement end point and the target position. It was calculated with the equation of Pythagoras and taken as degree of the movement accuracy.

Direction changes
The number of direction changes per s from the movement start to the reaching of the target served as a measure for the smoothness of the movement path. The more direction changes were, the more saccadic the movement was. Direction changes were detected with the velocity signals in the x-, y- and z-direction which were obtained by subtracting succeeding position signals. Each change of sign in the velocity signals counted as direction change. In order to eliminate the influence of velocity and the distance between the initial position and the target, the number of direction changes was divided by the movement time. Since the algebraic sign of the velocity only changes when a movement away from the origin of the coordinate system changes to a movement towards the origin of the coordinate system or vice versa, this movement parameter was only sensitive to pronounced and not to slight direction changes.

Path ratio
The path ratio was defined as the sum of the distances between adjacent data points from the position at movement start until the position where the target was reached divided by the length of a straight line between these two points. In contrast to the number of direction changes the path ratio was also sensitive to slight curves. Data was excluded if the path ratio was larger than 1.5 (fast movements) or larger than 3 (slow movements).

4.2.4.1.2. Kinetic movement parameters

Reaction time
The reaction time was defined as the time interval from the go signal (tone) to the start of the movement. Data was excluded if the reaction time was shorter than 100 ms (the movement was anticipated) or longer than 1 s.

Movement time
The movement time was defined as the time interval between the start of the movement and the end of the movement. Data was excluded if the movement time exceeded 2 s.

Peak speed
To determine the speed of the finger, the derivative of the 3-dimensional movement path with respect to time was calculated. Peak speed was the maximum velocity attained between the start of the movement and the moment when the target was reached. Data was excluded if the peak speed was smaller than 0.4 m/s or larger than 2.5 m/s.

Symmetry of the velocity profile
The symmetry of the velocity profile was calculated by dividing the time interval from the start of the movement to the peak speed by the time interval from the start of the movement to the moment when the target was reached. This ratio provided information about the symmetry of the velocity profile. Data was excluded if the peak speed was smaller than 0.4 m/s or larger than 2.5 m/s.

4.2.4.2 Balance and manual dexterity

Berg Balance Test

The sum of the obtained scores for all movement tasks was calculated for each test and plotted against the time.

Box and Block Test of Manual Dexterity
The number of transferred cubes was plotted against the time, for both the left and the right hand.

4.2.4.3 Self-perception of symptoms
Oral and written reports of the patients and observations during the climbing training and the experiments provided important information that helped to understand better the patients' movement disorders and the effect of the climbing training.

4.3. Results and discussion

This investigation evaluated the effect of a 6-week climbing training with a 3-dimensional movement analysis, clinical balance and manual dexterity tests and a questionnaire for self-perception of symptoms. Since the patients had different aetiologies, durations and symptoms of cerebellar dysfunction, the effect of the climbing training was different from patient to patient. The results and the discussion will be thus presented for each patient separately after a general introduction.

Remarks about data analysis

The location of the target and, in some cases, the initial position influenced most of the kinematic and kinetic movement parameters. However, these factors are not subject of this study. Sometimes the change of a movement parameter over the time depended on the target location or the initial position. In these cases, it could happen that a deterioration of a movement parameter with respect to certain targets hides an improvement with respect to other targets. To evaluate the effect of the climbing training it seemed nevertheless more reasonable to compare the means of the respective movement parameters before and after the training taking all targets and both initial positions together.

In all patients most of the kinematic and kinetic movement parameters differed significantly from the reference values of the control group. They were thus appropriate to investigate the movement deficits of the patients participating in this study. Patient 4 deviated the least from the reference values, which was expected since he showed only slight clinical symptoms.

Interpretation of kinematic and kinetic movement parameters

With healthy subjects, multi-joint pointing movements are straight or slightly curved and show ripples when performed slowly (Fig. 4.2).

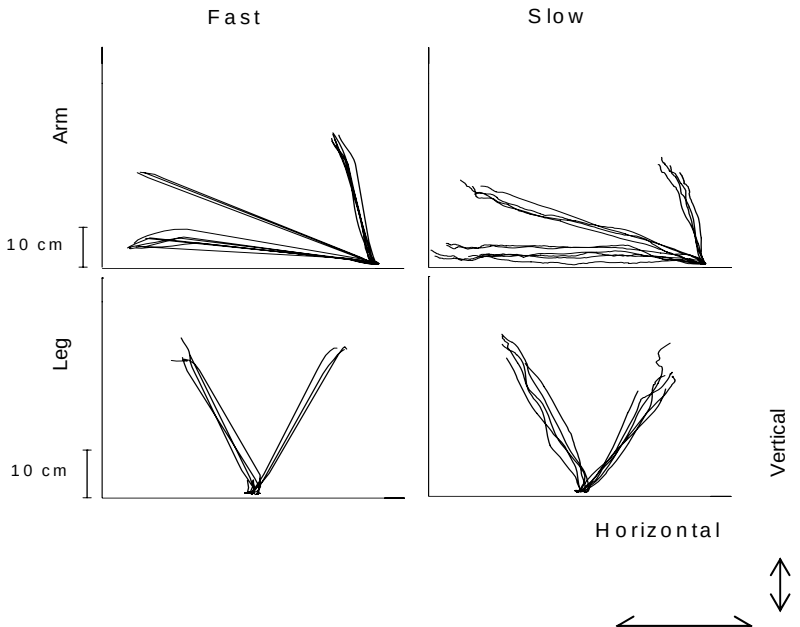

Fig. 4.2. Movement paths of healthy controls in the frontal plane of the body for the fast-accurate (left) and the slow-without vision condition (right). Movements of the right index finger from the right ipsilateral initial position to one target in front and two contralateral targets (above). Movements of the right big toe to one target on the left and one target on the right side of the mid-sagittal plane (below).

Visual inspection of the patients' movement paths showed in addition to the ripples, which were considered as normal, two other types of deviations from the normal movement path: small squiggles or wobbles and curves, which were largely reproduced in every movement to the same target. The small squiggles or wobbles appeared exclusive in the slow movements and there mainly in the deceleration phase, before the reaching of the target (Fig.4.3A, right). They have also been described in another study, were they were considered to result from errors in the visual guidance mechanism (Day et al. 1996). However, since these squiggles appeared also in our movement condition without vision, they may have resulted from a disorder in movement correction due to a general deficient integration of sensory information. They would thus only appear in movements, which are slow enough to enable corrections. The number of calculated *direction changes* was taken as indicator for this kind of movement disorder.

Larger curves, which appeared in both the fast-accurate and the slow-without vision condition, made up the other type of deviation from the normal movement path (Fig.4.3, left). This type of larger curves which are mainly reflected in the *path ratio* were described in another study (Day et al. 1996) and suggested to be either the consequence of inappropriate programming of muscle activity or the result of proprioceptice feedback incorrectly modifying the central commands. It was also suggested that patients with cerebellar disorders have difficulties in scaling muscle activity to overcome inertial characteristics of the limb and to oppose or assist

torques that are caused by other linked segments (Bastian et al. 1996). Others assumed impaired timing or amplitude scaling in the agonists, the antagonists or both muscle groups as cause for difficulties in coordination (Bastian et al. 1996). However, these larger curves were reproduced in nearly every movement to a specific target. We therefore assume that they result from an impaired multi-joint coordination related to a deficient movement planning or a constant error in the execution of the movement plan, rather than to errors in movement correction.

The *end point error* can reflect either a disorder in movement preparation, when the patient pointed consistently to the same wrong position (wrong end point coordination) or a deteriorated movement execution, when the spread of the end points was larger than normal (dysmetria as a consequence of impaired multi-joint coordination leading to target under- or overshoot or impaired integration of somatosensory information). An increased end point error is expected in the slow movements without vision, because the motor instructions to the arm must be either completely determined before the movement start or they must be adjusted during the movement according to the memorized target location (Day et al. 1996). Variable deviations from the normal movement path were suggested to be related to impaired movement regulation (probably to deficient integration of sensory information) and constant deviations rather to impaired movement preparation or consistent errors in the execution of the movement plan.

The patients showed a tendency to longer *movement* and *reaction times*, a lower *peak speed* and a smaller *symmetry* (prolonged deceleration phase) than the healthy subjects. This might be related to a deteriorated timing and/or amplitude scaling of agonist and antagonist what leaded to an overall slowing down of movement velocity (delayed movement initiation, decreased acceleration rate, prolonged deceleration phase, slower inversion at the target). However, we cannot determine whether the overall reduction in movement velocity is a fundamental deficit of patients with cerebellar disorder or whether it is a result from a compensatory strategy that the patients adopt after the lesion, in order to increase precision (Bastian et al. 1996).

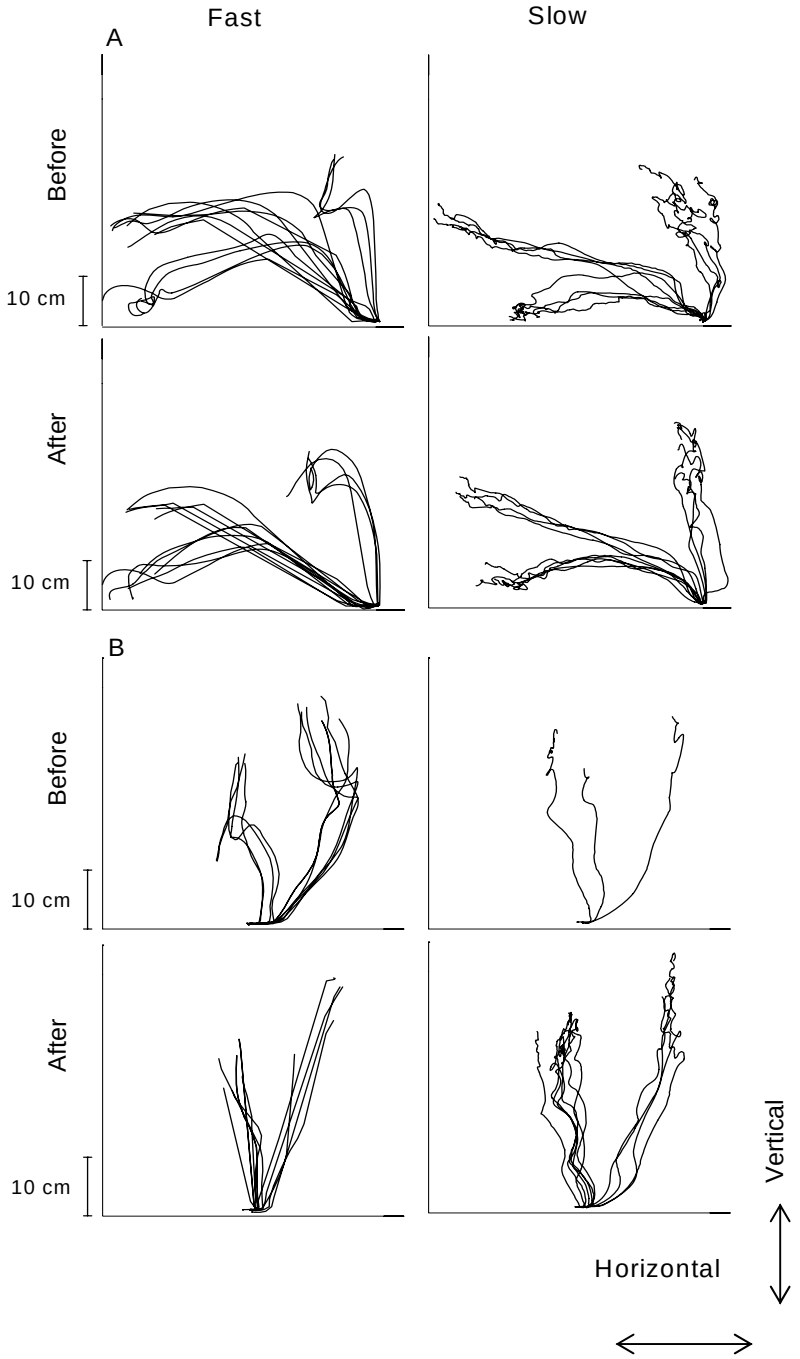

Fig. 4.3. Movement paths of patient 2 in the frontal plane of the body before (above) and after the training (below) for the fast-accurate (left) and the slow-without vision condition (right). Because of fatigue of the patient and noise during data recording only 3 leg movement path are shown in the slow movement condition before training. **A** movements of the right index finger from the right ipsilateral initial position to one target in front and two contralateral targets. **B** movements of the right big toe to one target on the left and one target on the right side of the mid-sagittal plane.

Expectations

Climbing means a permanent challenge of balance control and body stabilisation. The climbing grips provide only small supporting areas for the feet and vary in distance and form what forces the climber into a variety of different body positions. The climber has to repeatedly shift the body weight and to stabilize the trunk in order to reach adequate grips. The ability to control the body's position in space is essential for movement tasks that require balance, as for example locomotion, and for moving one part of the body without destabilizing the rest of the body. Postural deficits have thus also a strong influence on upper extremity function and can affect speed and accuracy of reaching movements (Shumway-Cook et al. 2001). Furthermore climbing requires precise multi-joint pointing movements of hands and feet to the grips, the coordination of all four limbs and the planning of single movements and movement sequences.

We hypothesized that the six-week climbing training would improve multi-joint coordination of upper and lower limbs, the control of the body position in space and the planning of movements.

4.3.1 Patient 1

4.3.1.1. Kinematic and kinetic movement parameters

Most of the kinetic and kinematic parameters (except the end point error) improved significantly for the fast movements (Tab. 4.1) and approached and partly even reached the values of the controls (Fig. 4.4 and 4.6). The parameters for the slow movements did (except the end point error) hardly change.

The path of the fast arm and leg movements changed from a movement pattern with convergent movement paths with ripples to straighter paths with increased end point variability (Fig. 4.5, left). The visual inspection of the slow arm and leg movements showed altogether a decreased variability among different movement paths to the same target (Fig. 4.5, right).

4.3.1.2. Balance and manual dexterity

Patient 1 reached before the training period 54 of 56 possible scores on the Berg Balance Scale. The 6 balance tests showed a constant level of equilibrium control throughout the training period (Fig. 4.7A).

The number of cubes, which were transferred in the Box and Block test increased from 39 to 47 out of 84.5 normal for his age group. The performance of the right more affected hand didn't change, but stayed at about the same level of 39 transferred cubes (Fig. 4.7B).

4.3.1.3. Self-Perception of Symptoms

The patient reported a reduction of tremor and an improvement in handling cups and tying shoes. His motivation for the climbing training was moderate to good. He liked climbing as a change in everyday life.

4.3.1.4. Discussion

The fast arm and leg movements showed a general increase in movement velocity, what was interpreted as improvement in movement coordination (Fig. 4.6). However, considering that the end point error of the fast arm and leg movements was before as well as after the training smaller than that of the healthy persons and that the movement time remained also after the training considerably higher compared to that of the healthy subjects it would also be possible that the patient had reduced a compensatory strategy, which had caused a general slowing down of the movements with for the sake of increased accuracy. We suppose that as a result of the ability to increase movement speed, the patient corrected less during movement execution and adjusted less towards its end what resulted in straighter paths and increased end point variability (Fig. 4.5A, left). The statistical analysis showed a decreased end point error in the slow leg movements and the visual inspection a decreased variability among different movement paths to the same target which could have resulted from an improved integration of somatosensory information.

Dexterity improved considerably in the left less affected hand but stayed at about the same level in the right hand (Fig. 4.7B). Why would the right arm of this patient show improved coordination in pointing movements but not in this specific motor task? Grasping and releasing wooden blocks involves other neural mechanisms than pointing to a target or grasping climbing grips. Presumably this patient improved motor performance in pointing and reaching for grips but not in this specific motor task. However, it cannot be determined whether the unilateral motor learning of this specific motor skill was related to damage in the cerebellum or in other parts of the brain.

The balance abilities remained unchanged (Fig. 4.7A). They were already before the training period at a high level, and no great change was thus expected.

During the climbing training it was noticed that the patient was able to increase the velocity of specific movement sequences within one training session when practiced several times in succession. In the course of the training period the movement paths became smoother and fewer corrections were necessary towards the end of the movements to reach the climbing grips. These observations support the assumption that the patient was able to improve motor

coordination. The performance of complex movements and climbing tasks which demanded concentration caused sometimes difficulties. It seemed as if the patient had to coordinate the movements more consciously than healthy subjects and as if the memory of the initial movement task disappeared very quickly and the patient, therefore, depended much on external feedback. It has been suggested previously that in patients with cerebellar disorder the automaticity of movements is disturbed and movements are performed more consciously (Lang and Bastian 2001). Obviously, this circumstance doesn't inhibit motor learning but may imply a different neuronal mechanism for motor learning.

In this patient the overall increase of movement velocity was considered as the main effect of the climbing training and interpreted as the result of improved coordination.

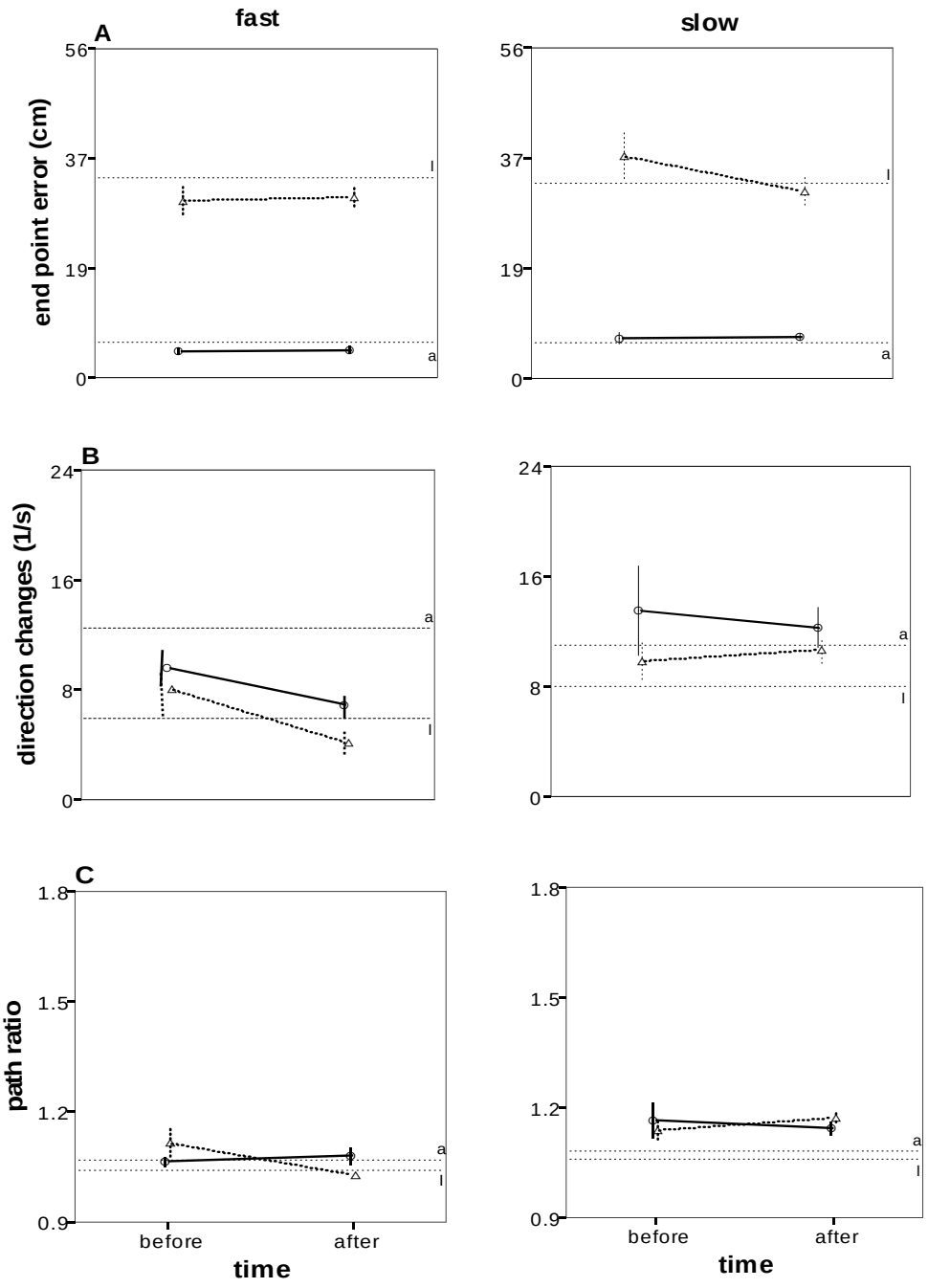

Fig. 4.4. Means with 95% confidence intervals of kinematic movement parameters of patient 1 and means of the control group. Patient data for arm (-) and leg (----) movements before and after the training for the fast-accurate and the slow-without vision condition. Data of the control group are indicated with reference lines (----, a: arm, l: leg). **A**. distances between the endpoint of the movement and the target location (index finger). **B**. sums of direction changes per sec in x, y and z direction. **C**. movement paths of the index finger (relative to the straight line between the initial position and the endpoint).

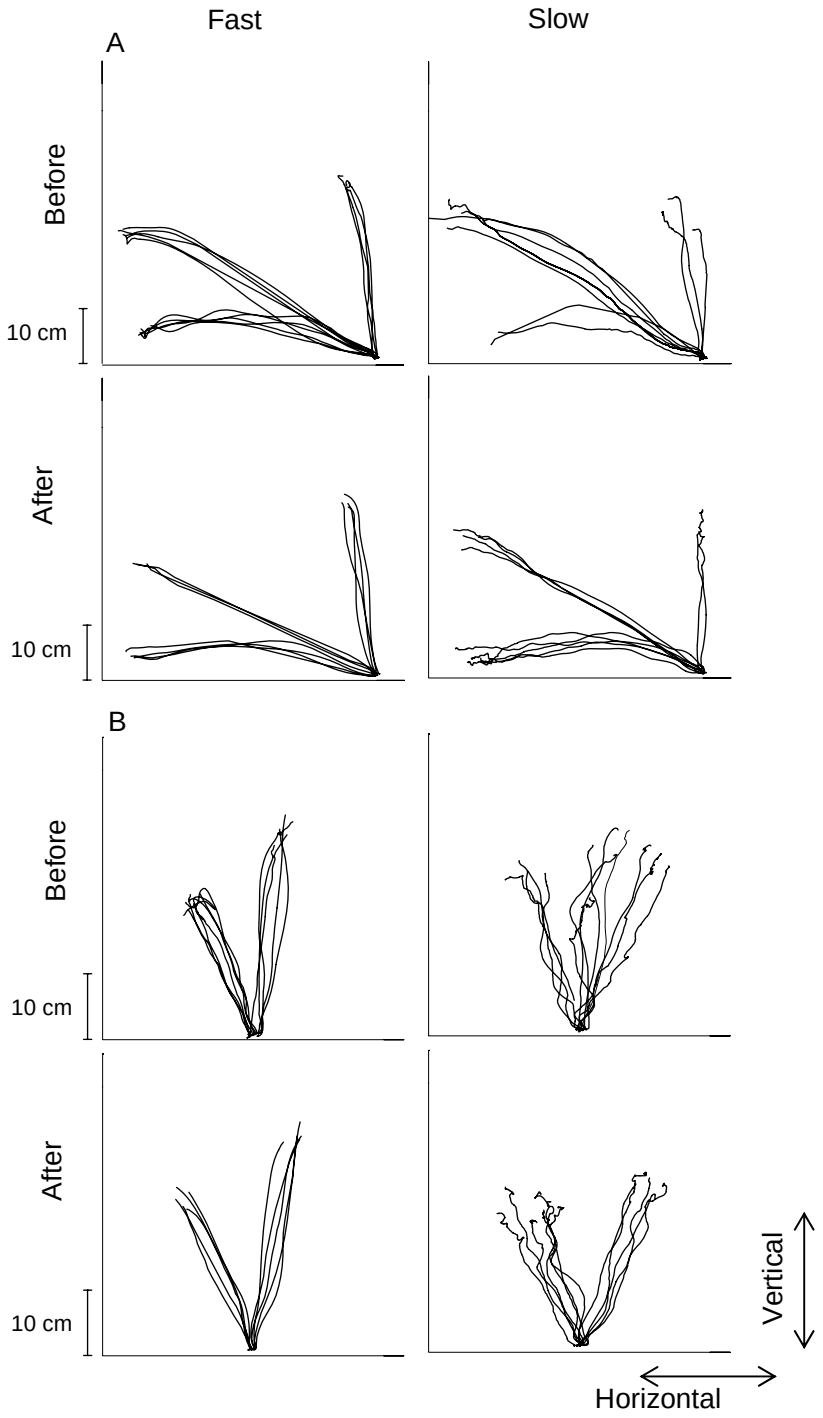

Fig. 4.5. Movement paths of patient 1 in the frontal plane of the body before (above) and after the training (below) for the fast-accurate (left) and the slow-without vision condition (right). Legend as for Fig. 4.3.

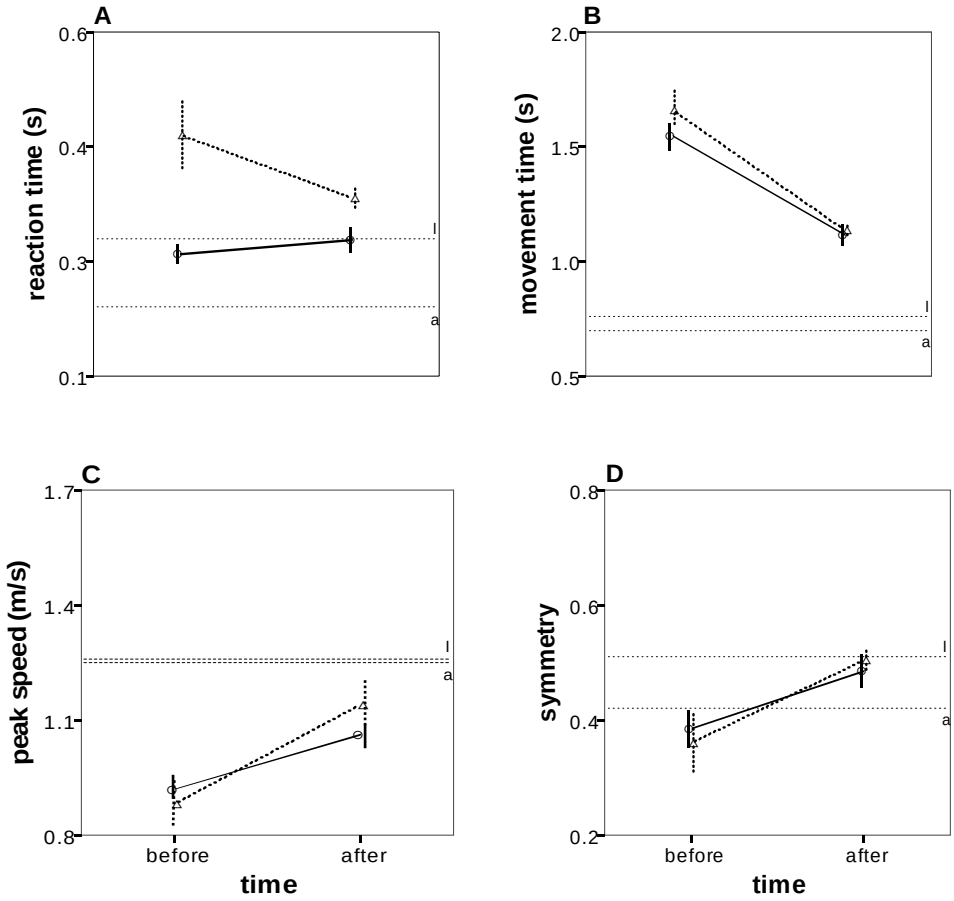

Fig. 4.6. Means with 95% confidence intervals of kinetic movement parameters of patient 1 and means of the control group. Patient data for arm (-) and leg (----) movements before and after the training for the fast-accurate condition. Data of the control group are indicated with reference lines (----, a: arm, l: leg). **A**. time intervals from the acoustic go signal to the initialization of the movement. **B**. time intervals from the start of the movement to the end of the movement **C**. maximal velocities attained in the interval between the start of the movement and the achievement of the target. **D**. durations of the acceleration phases divided by the whole movement times. A velocity profile with equal durations of acceleration and deceleration would show a ratio of 0.5.

Tab. 4.1. Change of kinematics and kinetic movement parameters of patient 1. Values are differences between means before and after training. $p \leq 0.05$: *, $p \leq 0.01$: **, $p \leq 0.001$: ***.

	Fast-accurate		Slow-without vision	
	Arm	Leg	Arm	Leg
Endpoint error (cm)	+0.201	+0.799	+0.431	-1.831 *
Direction changes (1/s)	-2.399**	-3.811 ***	-0.804	+0.673
Path ratio	+0.002	-0.094 ***	-0.076	+0.031
Reaction time (s)	+0.013	-0.095 ***		
Movement time (s)	-0.408***	-0.445 ***		
Peak speed (m/s)	+0.142 ***	+0.261 ***		
Symmetry	+0.107 ***	+0.143 ***		

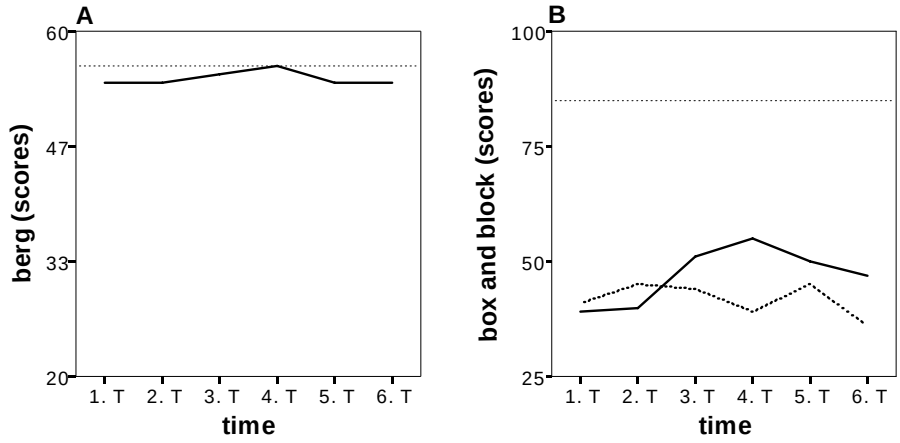

Fig. 4.7. Balance and manual dexterity of patient 1. **A** Berg Balance Scale. The maximal score (56) is indicated by the reference line (----). **B** The number of transferred cubes in the Box and Block Test of Manual Dexterity with the left (-) and the right (----) hand. The reference line (----) indicates the average number of transferred cubes of age matched healthy males (84.5)[9].

4.3.2 Patient 2

4.3.2.1. Kinematic and kinetic movement parameters

Similarly as in patient 1, most of the kinetic and kinematic parameters improved significantly for the fast movements (Fig. 4.8 left and 9). The parameters for the slow movements improved in the arm but not in the leg movements (Fig. 4.8 right). For statistics see Tab. 4.2.

Before the training, the movement pattern of the fast arm movements was dominated by a lift during the initial phase of the lateral deviation. After the training the lift and the lateral deviation were performed more simultaneously what resulted in a less pronounced curve of the movement path (Fig. 4.3A, left). The leg movement paths showed a somehow s-shaped movement pattern before the training, which was reproduced to a large extent in every

movement to the same target. This special shape disappeared after the training (Fig. 4.3B, left). The slow arm movement paths tended to become more convergent towards the endpoint and varied less among the different trials to the same target (Fig. 4.3A, right).

4.3.2.2. Balance and manual dexterity

Patient 2 gained 12 points in the Berg Balance Test from 21 before the training to 33 after the training out of 56 maximal possible points (Fig. 4.10A).

The number of cubes, which were transferred in the Box and Block test increased from 27 (right hand) respectively 31 (left hand) before the training to 31 (right hand) respectively 34 (left hand) after the training out of 74.5 on average transferred cubes in his age group (Mathiowetz et al. 1985). The curve of motor skill performance over the time of the right more affected hand was always lower but in parallel to the curve of the left less affected hand (Fig. 4.10B)

4.3.2.3. Self-perception of symptoms

Patient 2 reported an increasing force and endurance throughout the training period. He felt more stable and gained confidence in his body's capabilities to control equilibrium and dared thus more to shift the body weight to a single leg during locomotion. He felt also a constantly improving accuracy and velocity of his right arm and leg movements in everyday life. In the second half of the training period he noticed slightly smoother movement paths of his right arm and leg and a slight increase of the velocity of movement sequences. In the second and third week, he felt a temporary increase of tremor. His ability to reach high placed objects improved notably, especially towards the end of the training period. The difficulty to brush teeth did not change, but cutting food and tying shoes became easier towards the very end of the training period. The handling of cutlery improved during the first two weeks and stayed stable until the end of the training period. He was always very motivated and appreciated the physical activity and the upright body position during climbing for a change to the sitting position in the wheelchair.

4.3.2.4. Discussion

The overall increase of movement velocity and the decreased path ratio in the fast movements (Tab. 4.2) point at an improved multi-joint coordination. This is supported by the visual inspection of the patient's movement paths, which were conspicuously less curved after the training, indicating that the joints were moved more simultaneously (Fig. 4.3 left). During the training sessions, this became apparent in fewer movement corrections before reaching

climbing grips. The number of direction changes in the slow leg movements increased significantly. It could be assumed that the patient decreased the fixation of hip, knee and ankle joints, that is performed the movements with more degrees of freedom, what leaded to more errors in movement execution. In the slow arm movements the number of direction changes and the end point error decreased (Fig. 4.8 right) and the end points were less variable (Fig. 4.3A right). This was interpreted as an improved ability to perform corrections during movement execution.

We suppose that the improvement in manual dexterity (Fig. 4.10B) was due to an improved multi-joint coordination. This goes in line with our findings of more simultaneous joint movements especially during fast accurate pointing movements. The Berg balance test pointed to an improved balance (Fig. 4.10A), what was also confirmed by the patient, who felt more stable throughout the training period. The equilibrium control also improved during climbing. Difficulties to control the rotation around the longitudinal body axis decreased towards the end of the training period. Due to increasing force and endurance, climbing time could be prolonged and the body weight support decreased.

Altogether, the patient improved considerably balance control, multi-joint coordination and probably the integration of somatosensory information during movement execution. These improvements have been supported by the increased force and endurance.

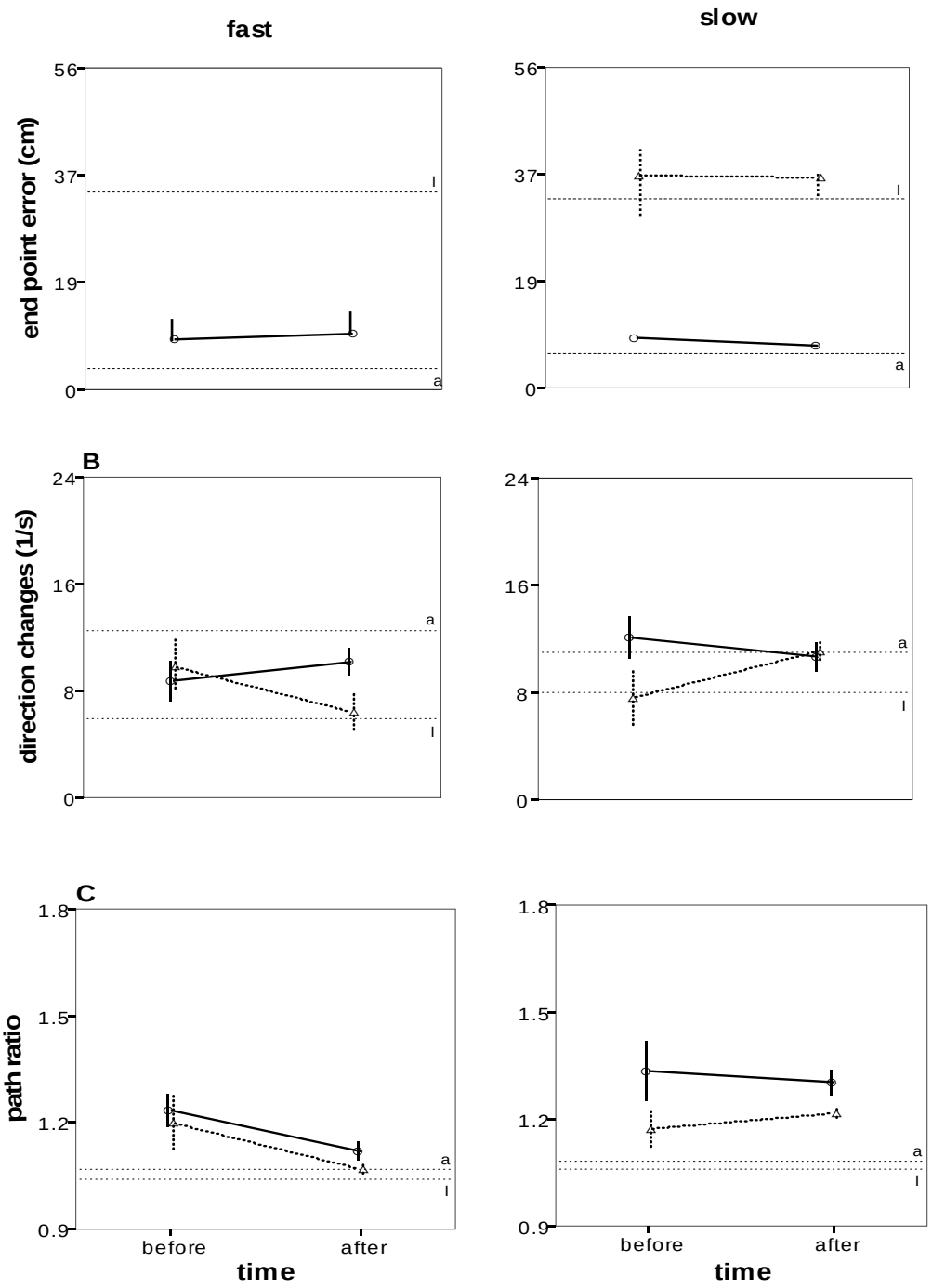

Fig. 4.8. Means with 95% confidence intervals of kinematic movement parameters of patient 2 and means of the control group. Patient data for arm (-) and leg (----) movements before and after the training for the fast-accurate and the slow-without vision condition. Data of the control group are indicated with reference lines (----, a: arm, l: leg). Legend as for Fig. 4.4.

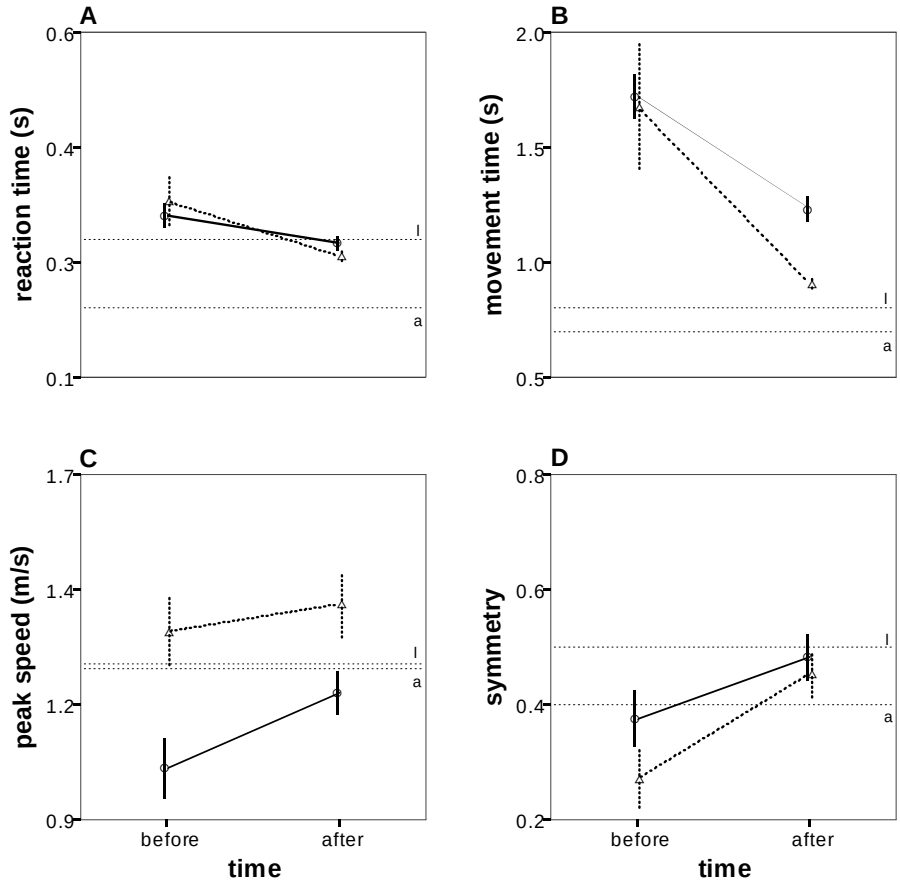

Fig. 4.9. Means with 95% confidence intervals of kinetic movement parameters of patient 2 and means of the control group. Patient data for arm (-) and leg (----) movements before and after the training for the fast-accurate condition. Data of the control group are indicated with reference lines (----, a: arm, l: leg). Legend as for Fig. 4.6.

Tab. 4. 2. Change of kinematic and kinetic movement parameters of patient 2. Values are differences between means before and after training. $p \leq 0.05$: *, $p \leq 0.01$: **, $p \leq 0.001$: ***.
[1]Problems in data processing made analysis impossible.

	Fast-accurate		Slow-without vision	
	Arm	Leg	Arm	Leg
Endpoint error (cm)	+0.926	[1]	-1.510 **	-0.487
Direction changes (1/s)	+1.052	-3.271 **	-2.516 ***	+2.164 *
Path ratio	-0.110 ***	-0.122 ***	-0.057	+0.056
Reaction time (s)	-0.048 **	-0.074 ***		
Movement time (s)	-0.507 ***	-0.743 ***		
Peak speed (m/s)	+0.176 ***	+0.027		
Symmetry	+0.091 ***	+0.178 ***		

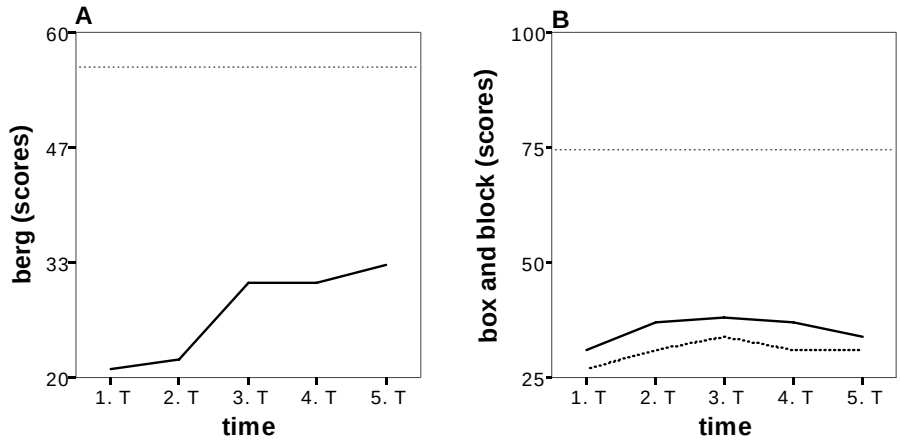

Fig. 4.10. Balance and manual dexterity of patient 2. **A** Berg Balance Scale. The maximal score (56) is indicated by the reference line (----). **B** The number of transferred cubes in the Box and Block Test of Manual Dexterity with the left (-) and the right (----) hand. The reference line (----) indicates the average number of transferred cubes of age matched healthy males (74.5)[9].

4.3.3 Patient 3

4.3.3.1. Kinematic and kinetic movement parameters

In contrast to the two preceding patients, only the path ratio of the fast arm movements and the movement time of the fast leg movements improved significantly whereas the other kinematic (Fig. 4.11) and kinetic parameters (Fig. 4.13) hardly changed (Tab. 4.3).

The paths of the fast arm movements were straighter after than before the training, because the lift and the lateral deviation were performed more simultaneously (Fig. 4.12A left) and the end points of the slow arm and leg movement paths were less spread (Fig. 4.12 right).

4.3.3.2. Balance and manual dexterity

Patient 3 reached before the training 29 out of 56 possible scores in the Berg balance test. He constantly increased the amount of scores up to 37 after the training period (Fig. 4.14A).

In the Box and Block test, the number of transferred cubes increased from 26 before to 40 (left hand) respectively 45 (right hand) after the training. Patient 3 gained thus more points in the more affected right hand than in the left hand. Males in his age group transfer on average 87.3 cubes in 1 min (Fig. 4.14B) (Rand et al. 1998).

4.3.3.3. Self-perception of symptoms

Patient 3 noticed a positive effect of the climbing training on body position and stability, and on the use of the visual system i.e. on the appropriate turning of the head toward movement targets. He also reported a slight increase of the velocity of single movements and movement sequences, and a slight amelioration in dressing, taking a shower and handling cutlery.

4.3.3.4 Discussion

The statistical analysis of the 3-dimensional movement paths of patient 3 doesn't point at any striking improvement in motor performance (Tab. 4.3). The state of mind and the ability to concentrate on movement tasks had a great influence on his motor performance. Presumably these two factors varied between the different measurements and made it thus impossible to detect an improvement of motor performance. The patient's troubles within the visual system are another possible explanation. He rarely turned his head to look at the climbing grips, but relied more on his sense of touch than on visual information while searching for climbing grips. This rendered the development of an appropriate climbing strategy more difficult and caused also disadvantages in everyday life. In order to reach for an object successfully, we must first locate the object in space. Visual deficits affecting target localization also appear to affect hand motor function (Shumway-Cook et al. 2001). It is thus possible that his visual deficits somehow impaired an improvement of motor performance.

The decrease in the path length in relation to the ideal path (Fig. 4.11C left) may reflect an improved ability to coordinate multi-joint movements, what would also explain the remarkable progress in manual dexterity (Fig. 4.14B). Most of the kinetic parameters tend to a higher movement velocity (Fig. 4.13). The slow arm and leg movement paths converged more and varied less among trials (Fig. 4.12 right) pointing to an improved somatosensory integration. Furthermore the patient made remarkable progresses in balance control (Fig. 4.14A).

We conclude that the six-week climbing training may have improved the ability to control body position in space and multi-joint coordination.

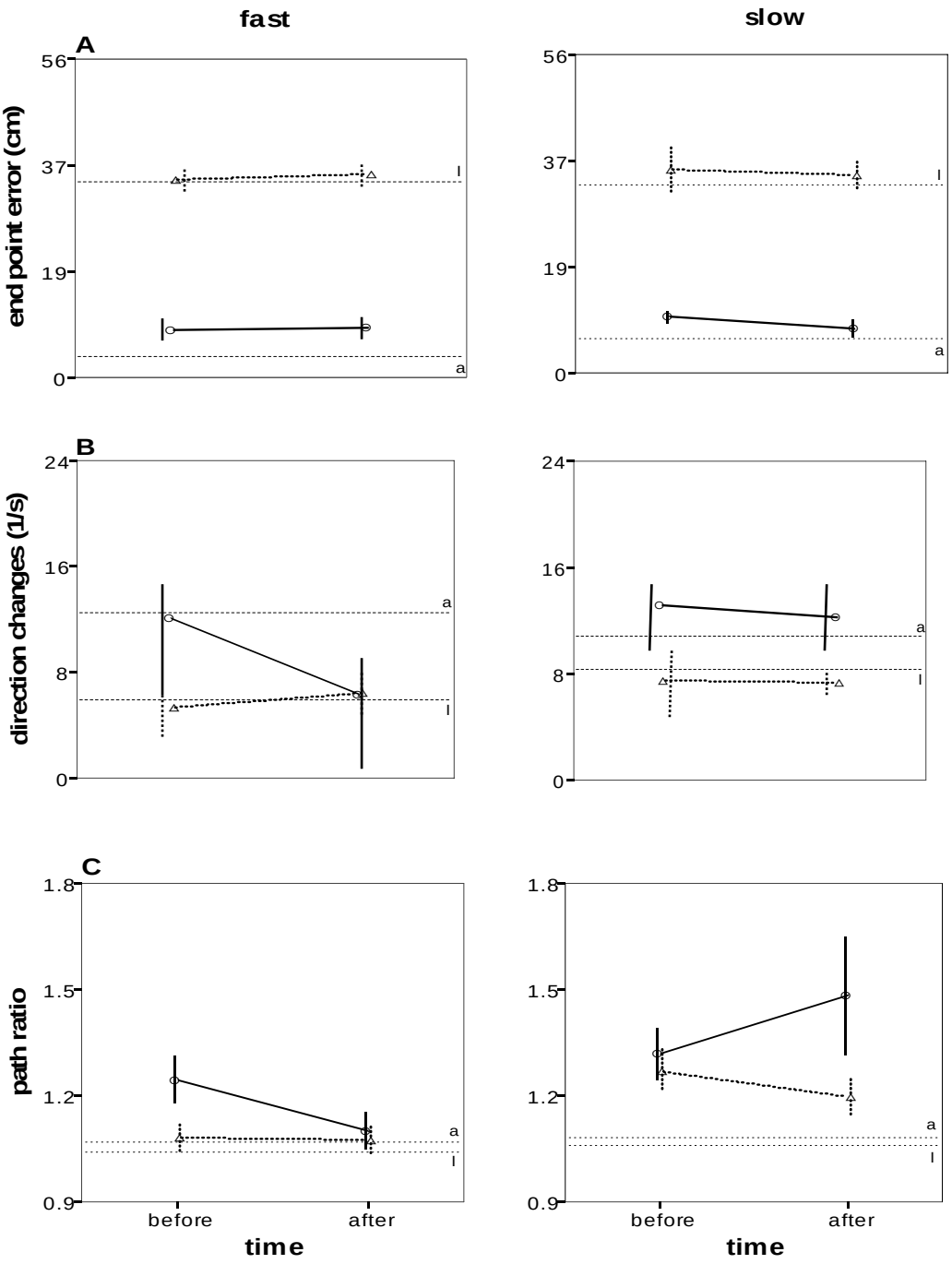

Fig. 4.11. Means with 95% confidence intervals of kinematic movement parameters of patient 3 and means of the control group. Patient data for arm (-) and leg (----) movements before and after the training for the fast-accurate and the slow-without vision condition. Data of the control group are indicated with reference lines (----, a: arm, l: leg). Legend as for Fig. 4.4.

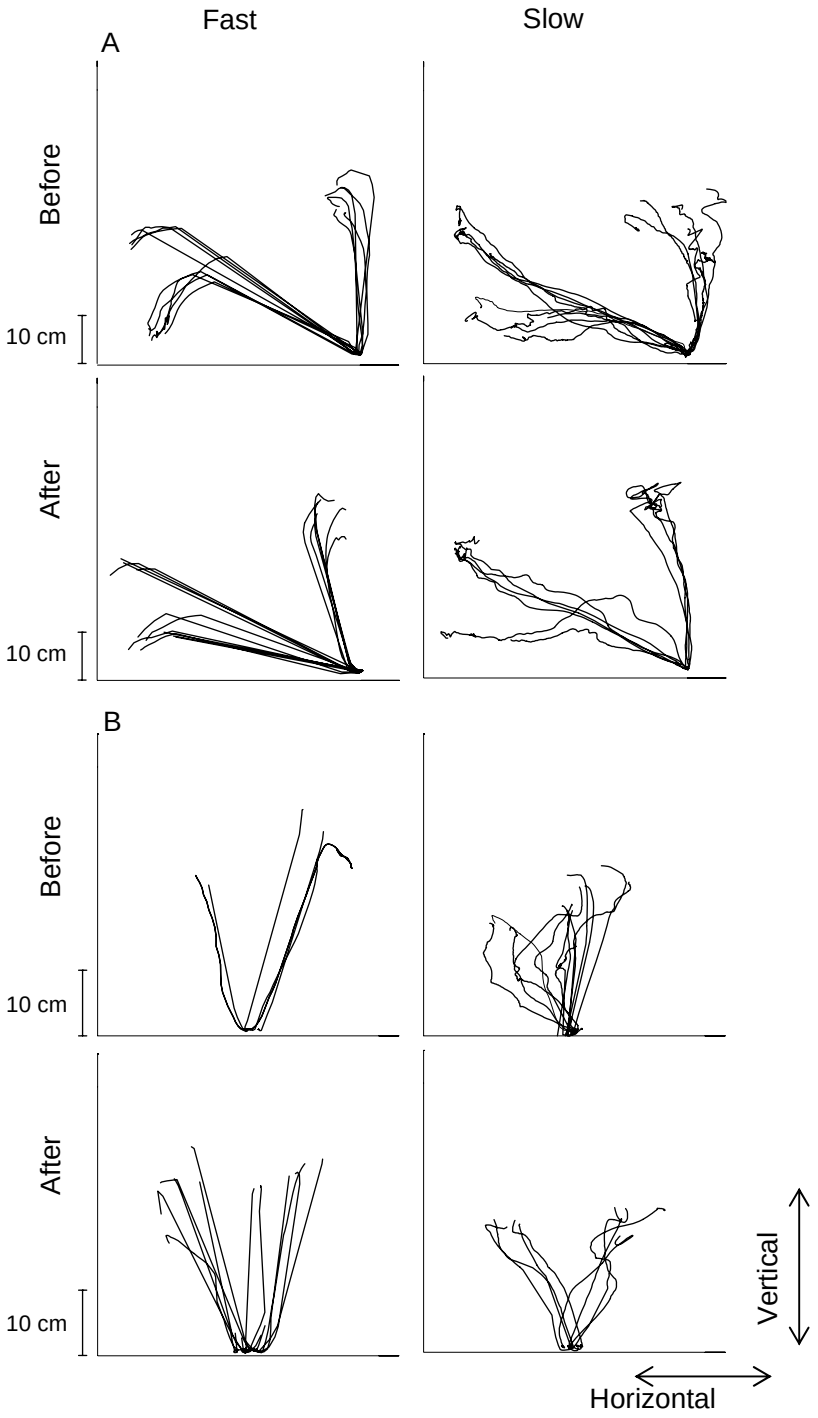

Fig. 4.12. Movement paths of patient 3 in the frontal plane of the body before (above) and after the training (below) for the fast-accurate (left) and the slow-without vision condition (right). Legend as for Fig. 4.3.

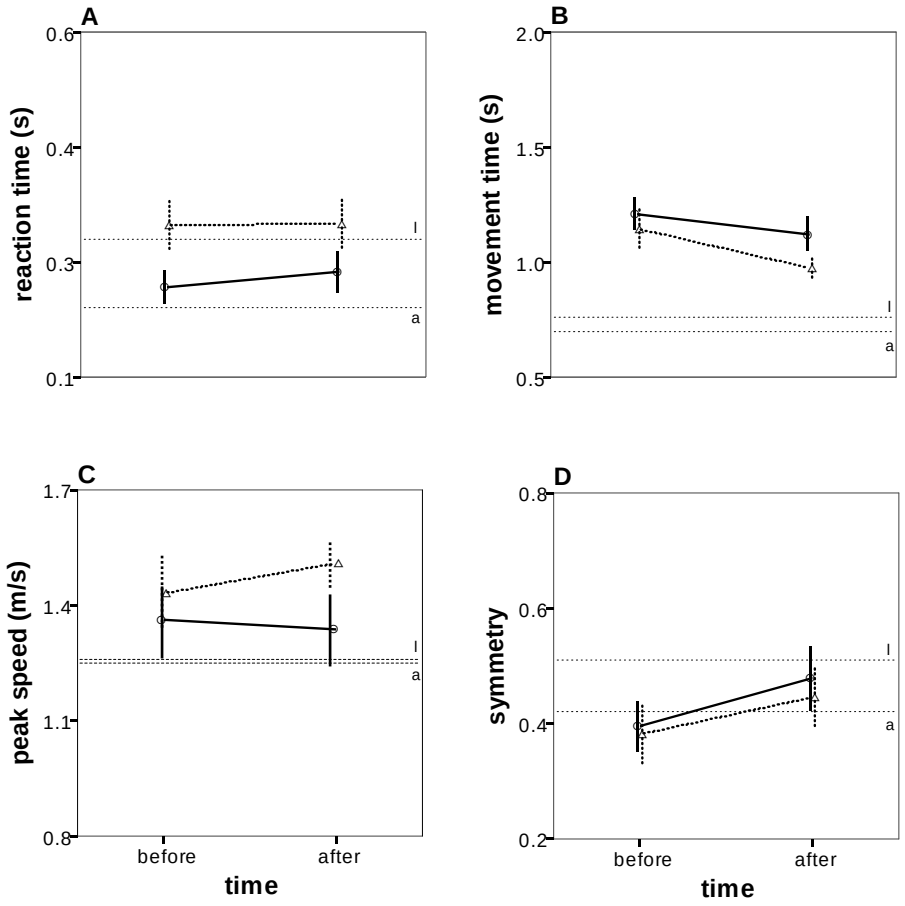

Fig. 4.13. Means with 95% confidence intervals of kinetic movement parameters of patient 3 and means of the control group. Patient data for arm (-) and leg (----) movements before and after the training for the fast-accurate condition. Data of the control group are indicated with reference lines (----, a: arm, l: leg). The lower reference lines always indicate the means of the controls' arm movements. Legend as for Fig. 4.6.

Tab. 4.3. Change of kinematic and kinetic movement parameters of patient 3. Values are differences between means before and after training. p≤ 0.05: *, p ≤ 0.01: **, p ≤ 0.001: ***.

	Fast-accurate		Slow-without vision	
	Arm	Leg	Arm	Leg
Endpoint error (cm)	+0.314	+0.931	-1.449	-1.087
Direction changes (1/s)	-5.753	+1.114	-0.571	-0.804
Path ratio	-0.121 *	+0.009	+0.137	-0.105
Reaction time (s)	+0.017	+0.003		
Movement time (s)	-0.010	-0.179 ***		
Peak speed (m/s)	-0.023	+0.076		
Symmetry	+0.087	+0.068		

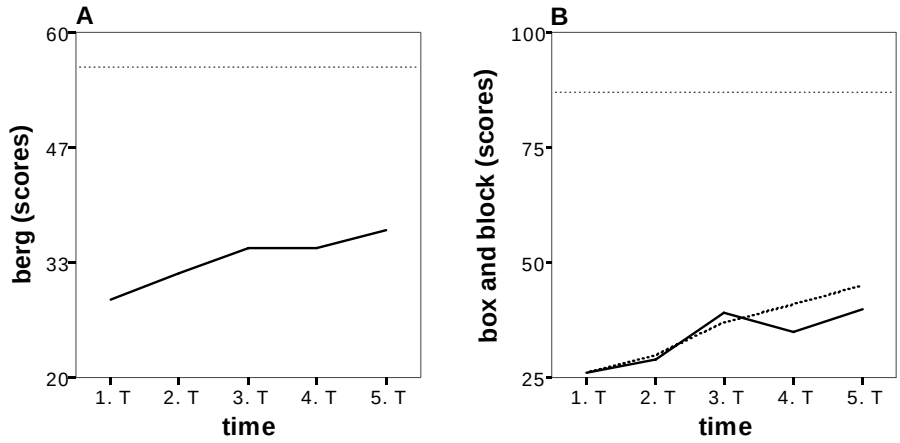

Fig. 4.14. Balance and manual dexterity of patient 3. **A** Berg Balance Scale. The maximal score (56) is indicated by the reference line (----). **B** The number of transferred cubes in the Box and Block Test of Manual Dexterity with the left (-) and the right (----) hand. The reference line (----) indicates the average number of transferred cubes of age matched healthy males (87.3)[9].

4.3.4 Patient 4

4.3.4.1. Kinematic and kinetic movement parameters

In patient 4, mainly the kinematic parameters for the leg movements improved significantly (Tab. 4.4). Changes of the kinematic movement parameters for all movement conditions are visualised in Fig. 4.15, the change of the kinetic parameters in Fig. 4.17.

The fast arm and leg movement paths were less divergent after than before the training (Fig. 4.16 left) and the paths of the slow leg movements were shorter and simultaneously less bent (Fig. 4.16B right).

4.3.4.2. Balance and manual dexterity

Patient 4 didn't show any difficulties to maintain the equilibrium during the different movement tasks. He got already before the climbing training the maximal scores in the Berg balance test.

In the Box and Block test he started with 59 transferred cubes in 60 seconds before the training and did with 89 (left hand) respectively 96 (right hand) transferred cubes after the training which was even better than healthy males in his age group (81.5) (Mathiowetz et al. 1985) (Fig. 4.18B).

4.3.4.3. Self-perception of symptoms

Patient 4 reported that, after a temporary deterioration in the second training week, the ability to perform slow movement sequences improved and the tremor decreased. Slow movements performed without vision became smoother from the third week onwards. Rapid movements became faster and improved constantly in accuracy from the fourth week until the end of the

training period. Despite serious problems of health, the patient noticed that he performed movements more natural and with greater ease. Clumsy movements became rare, also when the patient felt tired and concentrated less on movement execution.

Patient 4 liked climbing as a physical activity and was always very motivated. In addition to the physical aspect, he appreciated climbing as a source of mental calmness and recreation.

4.3.4.4. Discussion

Patient 4 improved climbing strategies rapidly without external feedback in the course of one or several climbing sessions. He had a great power of concentration during the climbing training and the experiments. This observation and reports of himself led to the assumption that he performed movements more consciously than healthy subjects, what may imply a different neuronal mechanism for motor learning than in healthy subjects. Inspite of mild clinical symptoms, he nevertheless improved the ability to correct on-going movements and multi-joint coordination in line with the improved performance in the Box and Block test for manual dexterity (Fig. 4.18B).

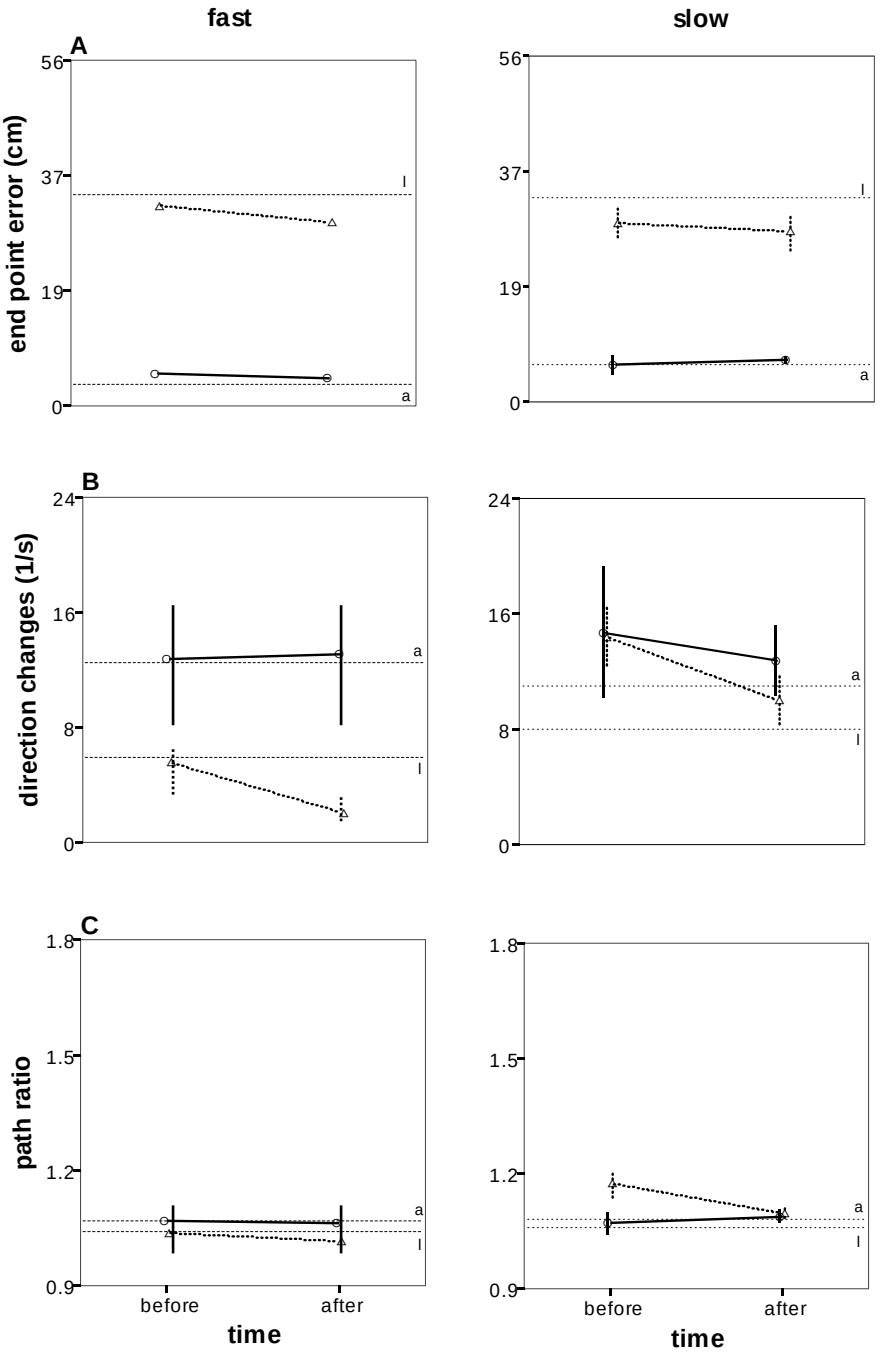

Fig. 4.15. Means with 95% confidence intervals of kinematic movement parameters of patient 4 and means of the control group. Patient data for arm (-) and leg (----) movements before and after the training for the fast-accurate and the slow-without vision condition. Data of the control group are indicated with reference lines (----, a: arm, l: leg). Legend as for Fig. 4.4.

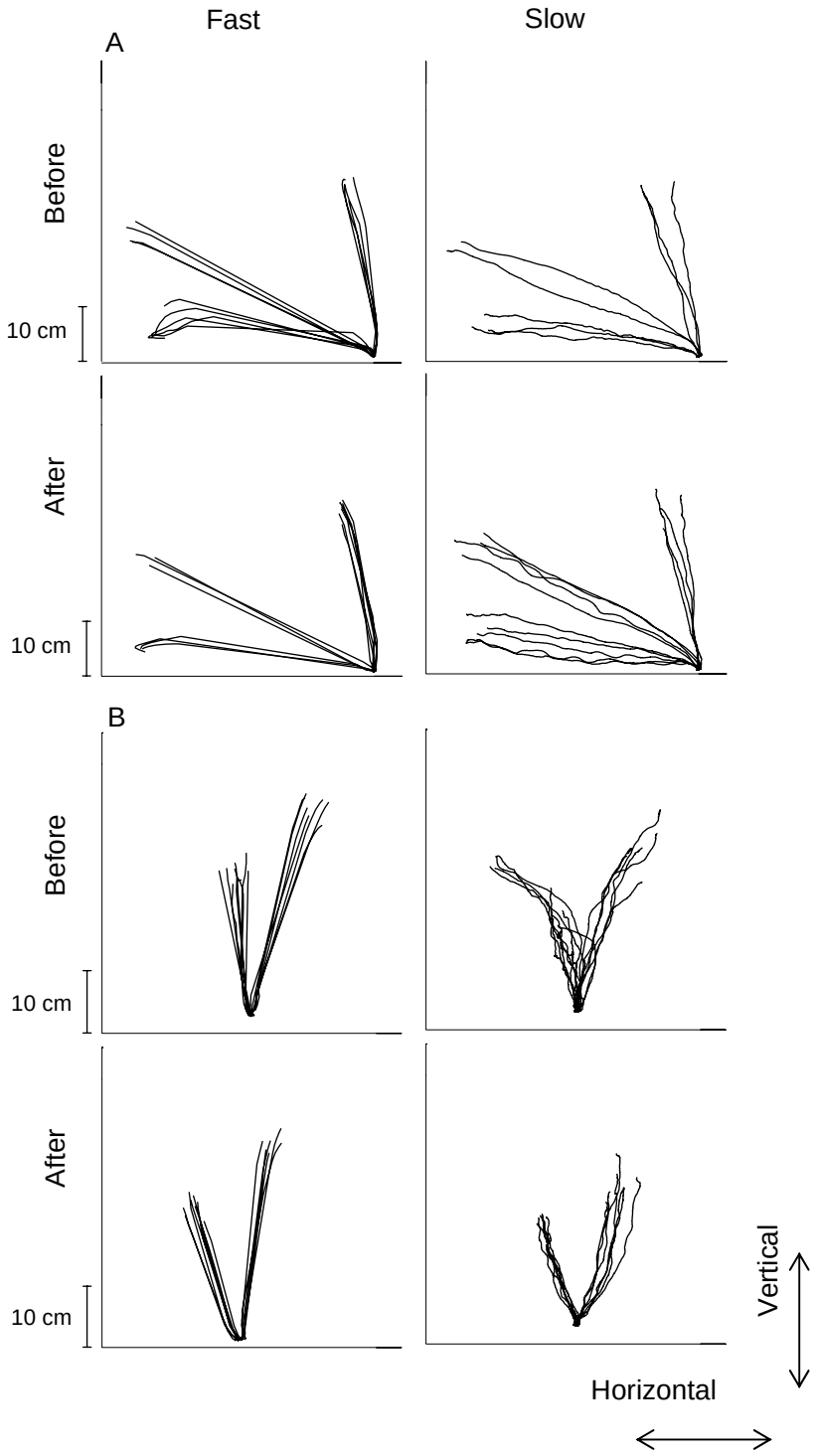

Fig. 4.16. Movement paths of patient 4 in the frontal plane of the body before (above) and after the training (below) for the fast-accurate (left) and the slow-without vision condition (right). Legend as for Fig. 4.3.

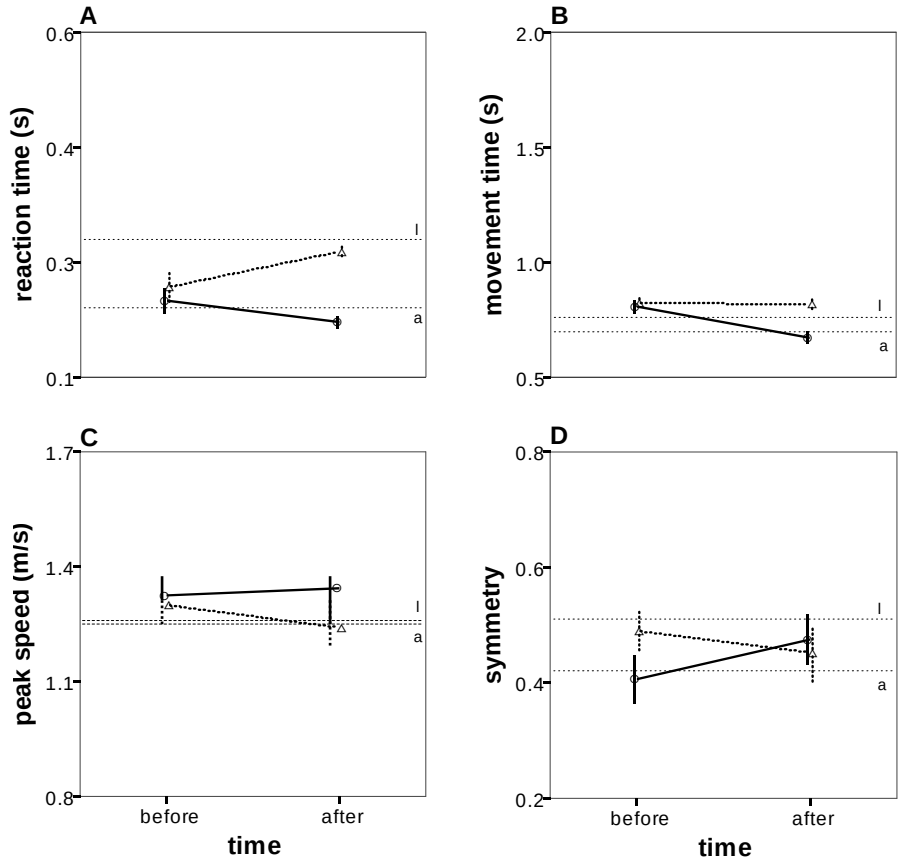

Fig. 4.17. Means with 95% confidence intervals of kinetic movement parameters of patient 4 and means of the control group. Patient data for arm (-) and leg (----) movements before and after the training for the fast-accurate condition. Data of the control group are indicated with reference lines (----, a: arm, l: leg). The lower reference lines always indicate the means of the controls' arm movements. Legend as for Fig. 4.6.

Tab. 4.4. Change of kinematic and kinetic movement parameters of patient 4. Values are differences between means before and after training. $p \leq 0.05$: *, $p \leq 0.01$: **, $p \leq 0.001$: ***.

	Fast-accurate		Slow-without vision	
	Arm	Leg	Arm	Leg
Endpoint error (cm)	-0.673 *	-2.815 ***	+0.928	-1.479
Direction changes (1/s)	+0.360	-3.579 ***	-1.851	-4.705 **
Path ratio	-0.008	-0.024 ***	+0.014	-0.054 *
Reaction time (s)	-0.032 *	+0.053 ***		
Movement time (s)	-0.120 ***	+0.006		
Peak speed (m/s)	+0.018	-0.060		
Symmetry	+0.044	-0.034		

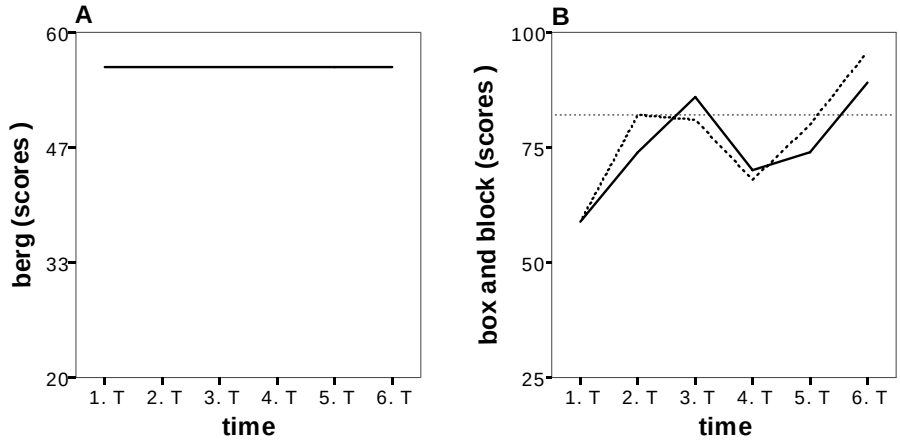

Fig. 4.18. Balance and manual dexterity of patient 4. **A** Berg Balance Scale. No reference line, because the patient reached the maximal score (56). **B** The number of transferred cubes in the Box and Block Test of Manual Dexterity with the left (-) and the right (----) hand. The reference line (----) indicates the average number of transferred cubes of age matched healthy males (81.5)[9].

4.4. Conclusion

A major problem with experiments on patients is that in most cases, as in the present investigation, the patients are different in terms of pathology, duration of illness and age. In addition, factors like motivation, the state of health and mind and climate influence the experimental results and render the interpretation of the results difficult. The patients participating in this investigation did not have lesions that were isolated to the cerebellum. Damage in other parts of the brain may thus have impaired motor learning. In addition, the exact localisation of the lesions was not known. Otherwise the training could have been more focused on the specific deficits of each patient. Nevertheless the 4 patients, who participated in the 6-week climbing training, increased movement velocity in 3-dimensional unrestricted pointing movements. The maximal velocity increased and the deceleration phase, the reaction time and the movement time decreased (Tab. 4.5). We took this as expression for an improved coordination. In addition, manual dexterity improved in all patients and two patients improved balance to a great extent whereas the two others didn't have balance problems initially and therefore did not improve

Because the recordings took place at intervals of two weeks, it is unlikely that the improvements in performance can be attributed to the practice of the experimental tasks. Since there was a parallel improvement of the climbing performance the improved motor performance in the tests was likely the result of the 6-week climbing training. We do not know whether a longer duration of the training would further improve motor performance, since, although we tested the patients each two weeks, we could not investigate the time course of

motor learning due to the too large variability of the data. As could be expected, the potential for spontaneous recovery was greatest in patient 2, whose health problems started 2 months ago.

An overall reduction in movement velocity occured often in patients with cerebellar disorders (Bastian et al. 1996; Day et al. 1998 and Shumway-Cook et al. 2001) and was also obvious in the present patients. Whether this slow-down is a compensatory strategy that the subjects adopt after the lesion in order to be still able to perform the required tasks or whether it is the expression of a fundamental cerebellar deficit remains unclear (Bastian et al. 1996).

We suppose that at least two patients performed the movements much more consciously than healthy subjects which has already been observed in patients with cerebellar damage (Lang and Bastian et al. 2001). Not only movement execution but also motor learning may thus involve different neuronal mechanisms than in healthy subjects, perhaps in brain areas outside of the cerebellum.

The results of this investigation show a positive effect of the climbing training on the coordination of upper and lower limbs during pointing movements and on balance and of patients with cerebellar damage. The patients' feedback supported these findings and at least two of them will continue climbing.

Tab. 4.5. Test results of all patients. Stars indicate significant improvements of movement performance in the pointing movements. $p \leq 0.05$: *, $p \leq 0.01$: **, $p \leq 0.001$: ***. Arrows indicate the change of movement performance in the clinical tests. Improvement:↑, unchanged: →. [1]Problems in data processing made analysis impossible. [2]Significant deterioration.

		Patient 1	**Patient 2**	**Patient 3**	**Patient 4**
Endpoint error					
Fast	arm	-	-	-	*
	leg	-	[1]	-	***
Slow	arm	-	**	-	-
	leg	*	-	-	-
Direction changes					
Fast	arm	*	-	-	-
	leg	***	**	-	***
Slow	arm	-	***	-	-
	leg	-	* [2]	-	**
Path ratio					
Fast	arm	-	***	*	-
	leg	***	***	-	***
Slow	arm	-	-	-	-
	leg	-	-	-	*
Reaction time					
Fast	arm	-	**	-	*
	leg	***	***	-	*** [2]
Movement time					
Fast	arm	***	***	-	***
	leg	***	***	***	-
Peak speed					
Fast	arm	***	***	-	-
	leg	***	-	-	-
Symmetry					
Fast	arm	***	***	-	-
	leg	***	***	-	-
Balance		→	↑	↑	→
Manual dexterity		$\uparrow_{\text{left arm}} \rightarrow_{\text{right arm}}$	↑	↑	↑

5. General. Discussion

In the context of this work, stroke patients have been trained on a hand ergometer and cerebellar patients on a climbing wall for rehabilitation. Specific experiments and tests have been used to quantify whether the training has improved the motor capabilities of the patients. It could be concluded that the motor performance improved significantly in both groups of patients. In spite of the fact that both groups were inhomogeneous and thus had to consider the patients individually, we were able to show statistically significant results.

These positive results should have an influence on the further treatment of patients. Stroke patients should further train on a hand ergometer. The ergometer which has been developed for the present study has the advantage that it allows to quantify the performance of both arms separately since torque and position can be recorded separately on both sides. Ergometer training seems to be more efficient than physiotherapeutic treatments which are to a large extent passive and do correspondingly not require so many active movements by the patients. Such training involves furthermore less presence of a physiotherapist. On the long run it would be cheaper than conventional treatment. Similarly, cerebellar patients should train on a climbing wall. Climbing has the advantage compared to physiotherapy that patients are usually much motivated to achieve a goal, as e.g. to reach the top of the climbing wall, whereas similar goals are less evident in physiotherapy.

The main factors which were used to quantify the motor performance in stroke patients were force, spasticity and range of movements. Spasticity was measured by 3 parameters :(1) the Ashworth scale, (2) the range of active elbow extension, and (3) the minimum torque during cycling (negative values indicate that spastic muscles slowed down the movement). All 3 of them were correlated, indicating they are indeed related to spasticity. In addition to the aim, to test whether arm cranking improves the motor abilities of stroke patients, we wanted to test whether the surface EMG can be used to quantify the spasticity of specific muscles. During arm cranking, movements are more complex than during pedaling with the legs and a relation between spasticity and torque is more difficult to establish. Furthermore, arm muscles develop torque during the extension and flexion phase, leg muscles, however, only during the extension phase. Our results on arm muscles were positive and we have developed the spasticity index, which can be computed on the basis of the surface EMG. It has the advantage that it is independent on the absolute amplitude of the EMG which can vary from patient to patient due e.g. to a different skin thickness. The index is close to one in normal subjects and larger in patients with spastic muscles. In the example we have presented it was

close to 4. The spasticity index is a valuable tool to test the effects of drugs, physiotherapy or training methods on the spasticity of specific muscles.

EMG recordings might also give some indication on how much a muscle contributes to pedal toque. In steady-state contractions, the relation between EMG and force is approximately linear (Woods and Bigland-Ritchie 1983).

After the training, all patients were able to cycle against a higher resistance and performed better in the clinical tests related to force. A force increase due to the training could be expected on the control side since the patients did not experience any arm cycling before they participated in the investigation. It was, however, not known whether training can produce a force increase on the lesioned side. The observed increase can be due to training mechanisms as on the control side or/and other special mechanisms, such as plasticity. Independent of the mechanisms, it is clear that the force increase is favorable not only for arm cycling but also for activities of daily life, which is finally the principal aim of rehabilitation. Positive results have also been obtained in stroke patients who performed aerobic ergometer exercises (Giuliani et al. 1989, Potempa et al. 1995). Significant improvements in maximal oxygen consumption, workload, and exercise time were measured, as well as lowering of the systolic blood pressure during a submaximal exercise test. We also observed a reduction of spasticity, similar as Durner et al. (2001), who evaluated spasticity by the Ashworth rating scale immediately after training on an arm-trainer.

The main objective of the investigation on the cerebellar patients was to evaluate the effect of a 6-week climbing training. The effect was quantified with a 3-dimensional movement analysis, clinical balance and manual dexterity tests and a questionnaire for self-perception of symptoms. Since the patients had different aetiologies, durations and symptoms of cerebellar dysfunction, the results were different from patient to patient.

The finding that cerebellar patients had even after the training significantly longer simple and complex RTs than the controls, supports the hypothesis that the cerebellum plays a central role in timing control. It was suggested that the lengthening of RT might be the result of loss of excitatory feedback from the cerebellum to the motor cortex. The patients not only took longer to initiate movement but the movements were slower than normal, keeping in line with the well-documented prolongation of RTs and slowness of movements in human cerebellar disease (Hallett et al. 1991; Hore et al. 1991; Bonnefoi-Kyriacou et al. 1995; Bastian et al. 1996). Similar results were found in non-human primates with cerebellar dysfunction (Thach et al. 1995; Meyer-Lohmann et al. 1977; Trouche et al. 1980). The slowness of our patients

may have been partly due also to the instructions, which emphasized accuracy over speed. However, this is unlikely to be the main cause of slowness given the results of Bastian et al. (1996). In their experiments, subjects were asked to produce movements which were (i) slow and accurate, (ii) fast and accurate, or (iii) as fast as possible with no constraint on accuracy. Cerebellar patients moved slower than normal for all 3 instructions. Nevertheless, Bastian et al. (1996) interpreted the slowness as a possible compensatory strategy, and this may also have been the case in the present study. Thus, moving at a slower speed may reduce or minimize other motor deficits.

A number of spatial abnormalities were observed in our patients group. The spatial paths of the fingertip were more circuitous than normal, leading to longer path lengths. This has been described previously for arm movements of monkeys following cerebellar ablation (Gilman et al. 1976) and for human subjects with cerebellar disease (Bastian et al. 1996). Inaccuracy was present in two forms: increased spatial variability between paths to the same target, and the appearance of constant errors at the end of movement when moving in darkness. Constant pointing errors have also been observed previously in monkeys after dentate nucleus cooling or ablation (Beaubaton and Trouche 1982). In all patients, most of the kinematic and kinetic movement parameters differed significantly from the reference values of the control group. Small squiggles or wobbles appeared exclusively in the slow without-vision movements and there mainly in the deceleration phase, before the reaching of the target. They may have resulted from a disorder in movement correction due to a general deficient integration of sensory information. They would thus only appear in movements, which are slow enough to enable corrections. The number of calculated *direction changes* was taken as indicator for this kind of movement disorder.

The differences between the movement patterns in patients and healthy subjects may be due to disruptions in inter-joint coordination reflecting a deficit at the central level of motor control. The right hemisphere is thought to play a greater role in the fine temporal resolution needed for rapid complex movements (Haaland and Harrington 1989) whereas the left hemisphere in the integration of sensory information with movement control and in the selection of an appropriate motor program (Goodale et al. 1988). A further analysis of these deficits is difficult. Studies of single jointed movements have revealed several parameters that the cerebellum may control, including timing and/or amplitude scaling in the agonist, antagonist, or both muscle groups. However, no single deficit can be generalized across studies to explain the different features of ataxia. Cerebellar damage appears to disrupt

different aspects of a movement depending on task conditions. The one common feature is that the movement deficits were always attributed to an imbalance of agonist-antagonist activity.

In the spatial domain, the difference between the vision and no-vision condition was most apparent towards the end of the movement. With vision the variability between paths was reduced as the target was approached and constant errors at the end of movement were eliminated, which was obviously not the case without vision. In the latter situation, the motor instructions to the arm must be either completely determined before movement start or adjusted during movement according to the memorized target location. This internal representation can then be used to compute the appropriate muscle activity to take the finger to the target. The movement errors may arise from errors occurring within these preparatory processes. We assume that they result from an impaired multi-joint coordination related to a deficient movement planning or a constant error in the execution of the movement plan, rather than to errors in movement correction. It was also suggested that patients with cerebellar disorders have difficulties in scaling muscle activity to overcome inertial characteristics of the limb and to oppose or assist torques that are caused by other linked segments (Bastian et al. 1996).

The *end point error* can reflect either a disorder in movement preparation, when the patients pointed consistently to the same wrong position (wrong end point coordination) or a deteriorated movement execution, when the spread of the end points was larger than normal (dysmetria as a consequence of impaired multi-joint coordination leading to target under- or overshoot or impaired integration of somatosensory information). An increased end point error is expected in the slow movements without vision, because the motor instructions to the arm must be either completely determined before the movement start or they must be adjusted during the movement according to the memorized target location (Day et al. 1998).

We do not know how the nervous system encodes final arm position. In the “fast” condition, the delay between the onsets of agonist and antagonist activity becomes so small that feedback from the peak acceleration would “arrive” too late to “correct” the antagonist activity in time, which could lead to an increase in the overshoot. In the framework of the equilibrium point hypotheses, the CNS is proposed to specify a “virtual” trajectory (Flash et al. 1987) or an “equilibrium” trajectory (Adamovich et al. 1997), along which the equilibrium will move.

It has long been suspected that cerebellar kinematics movement abnormalities are more pronounced when subjects perform fast movements as opposed to slow ones (Hallett and Massaquoi et al. 1993; Hallett et al. 1991; Holmes et. al. 1939; Hore et al. 1991; Massaquoi and Hallett 1996; Meyer-Lohmann et al. 1977). However, the suspected relationship between movement velocity and kinematics abnormalities has not been studied systematically. Massaquoi and Hallett (1996), in their detailed study of the initiation of planar multijoint movements, observed that the deviation from linear hand pathways was more pronounced with fast movements than slow ones. In contrast, in their recent study of multi joint pointing movements in cerebellar ataxia, Bastian and colleagues (1996) compared kinematics movement variables during slow-accurate and fast-accurate reaching movements and found that the curvature of the patients movements as measured by the ratio of target distance and the path the hand travelled during the movement was similar or even slightly larger if subjects performed slow-accurate movements rather than fast-accurate movements.

The fast arm and leg movements showed a general increase in movement velocity, what was interpreted as improvement in movement coordination. It would also be possible that the patients had reduced a compensatory strategy, which had caused a general slowing down of the movements for the sake of increased accuracy. We suppose that as a result of the ability to increase movement speed, the patients corrected less during movement execution and adjusted less towards its end what resulted in straighter paths and increased end point variability.

The current study demonstrates that the climbing wall training improved the motor performance in all the patients although they had various types of cerebellar disorders. During the climbing training it was noticed that the patients were able to increase the velocity of specific movement sequences within one training session when practiced several times in succession. In the course of the training period, the movement paths became smoother and fewer corrections were necessary towards the end of the movements to reach the climbing grips. These observations support the assumption that the patients were able to improve motor coordination. It seemed that the patient had to coordinate the movements more consciously than healthy subjects, that the memory of the initial movement task disappeared very quickly and that the patient, therefore, depended much on external feedback. Similarly, it has been suggested that the automaticity of movements in patients with cerebellar disorder is disturbed and movements are performed more consciously (Lang and Bastian 2001).

References

- Adams RD and Victor M (1993). Principles of Neurology (5th edn.), McGraw-Hill, New York, 1394.
- Adamovich SV, Levin MF, Feldman AG (1997). Central modifications of reflex parameters may underlie the fastest arm movements. J Neurophysiol; 77: 1460–1469.
- Aizawa H, Inase M, Mushiake H, Shima K, Tanji J (1991). Reorganisation of activity in the supplementary motor area associated with motor learning and functional recovery. Exp Brain Res; 84 (3): 668-71.
- Asanuma H, Keller A (1991). Neuronal mechanisms of motor learning in mammals. Neuroreport; 2(5): 217-24.
- Asanuma H, Pavlides C (1997). Neurobiological basis of motor learning in mammals Neuroreport; 8:1–6.
- Barbeau H, Wainberg W, Finch L (1987). Description and application of a system for locomotor rehabilitation. Med Biol Eng Comput 25:341-344.
- Bard G, Hirschberg GG (1965). Recovery of voluntary motion in upper extremity following hemiplegia. Arch Phys Med Rehabil; 46: 567-72.
- Basmajian JV, Gowland CA, Finlayson MA, Hall AL, Swanson LR, Stratford PW, Trotter JE, Brandstater ME (1987). Stroke treatment: comparison of integrated behavioral-physical therapy vs traditional physical therapy programs. Arch Phys Med Rehabil; 68(5 Pt 1): 267-72.
- Bastian AJ, Martin TA, Keating JK, Thach WT (1996). Cerebellar ataxia: Abnormal control of interaction torques across multiple joints. J. Neurophysiol; 76: 492-509.
- Bastian AJ, Zackowski KM, Thach WT (2000). Cerebellar ataxia: torque deficiency or torque mismatch between joints? J Neurophysiol; 83: 3019–30.
- Beaubaton D, Trouche E (1982). Participation of the cerebellar dentate nucleus in the control of a goal-directed movement in monkeys. Effects of reversible or permanent dentate lesion on the duration and accuracy of a pointing response. Exp Brain Res; 46: 127–38.
- Bhakta BB Cozens AJ, Chamberlain MA, Bamford JM (2000). Impact of botulinum toxin type A on disability and career burden due to arm spasticity after stroke: a randomized double blind controlled trial. J Neurol Neurosurg Psychiatry; 69: 217–221.

- Bobath B (1990). Adult hemipleg : evaluation and treatment. Heinemann Medical Books. London.
- Bonita R, Beaglehole (1988). Recovery of motor function after stroke. Stroke; 19: 1497–1500.
- Bonnefoi-Kyriacou B, Trouche E, Legallet E, Viallet F (1995). Planning and execution of pointing movements in cerebellar patients. Mov Disord; 10: 171–8.
- Boose A, Dichgans J, Topka H (1999). Deficits in phasic muscle force generation explain insufficient compensation for interaction torque in cerebellar patients**.** Neurosci Lett. Feb; 12: 261(1-2):53-6.
- Borg-Stein J, Pine ZM, Miller JR, Brin MF (1993) Botulinum toxin for the treatment of spasticity in multiple sclerosis. Am J Phys Med Rehabil; 72(6): 364–368.
- Brashear A, Gordon MF, Elovic E, Kassicieh VD, Marciniak C, Do M, Lee CH, Jenkins S, Turkel C (2002). Intra muscular injection of botulinum toxin for the treatment of wrist and finger spasticity after a stroke. N Engl J Med; 347(6): 395–400.
- Broeks JG, Lankhorst GJ, Rumping K, Prevo AJ (1999). The long-term outcome of arm function after stroke: results of a follow-up study. Disabil Rehabil; 21 (8): 357-64
- Brown, SJ, Child RB, Day SH, Donnelly AE (1997). Exercise-induced skeletal muscle damage and adaptation following repeated bouts of eccentric muscle contractions. Journal of Sports Sciences; 15: 215-222.
- Brown SH, Hefter H, Mertens M and Freund HJ (1990). Disturbances in human arm movement trajectory due to mild cerebellar dysfunction. J. Neurol. Neurosurg. Psychiatry; 53: 306-313.
- Bruehlmeier M, Dietz V, Leenders KL, Roelcke U, Missimer J, Curt A (1998). How does the human brain deal with a spinal cord injury? Eur J Neurosci; 10: 3918–22.
- Bütefisch CM, Davis BC, Wise SP, Sawaki L, Kopylev L, Classen J and others (2000). Mechanisms of use-dependent plasticity in the human motor cortex. Proc Natl Acad Sci U S A; 97: 3661–5.
- Bütefisch CM, Khurana V, Cohen LG (2001). Enhancement of use dependent plasticity through rTMS applied to the motor cortex. Aktuelle Neurologie; 28: S98.
- Bütefisch C, Hummelsheim H, Denzler P, Mauritz KH (1995). Repetitive training of isolated movements improves the outcome of motor rehabilitation of the centrally paretic hand. J Neurol Sci; 130: 59-68.

- Byrnes ML, Thickbroom GW, Phillips BA, Wilson SA, Mastaglia FL (1999). Physiological studies of the corticomotor projection to the hand after subcortical stroke. Clin Neurophysiol; 110: 487–498.
- Cao Y, D'Olhaberriague L, Vikingstad EM, Levine SR, Welch KM (1998). Pilot study of functional MRI to assess cerebral activation of motor function after post stroke hemiparesis. Stroke; 29: 112–122.
- Caston J, Jones N, Stelz T (1995). Role of preoperative and postoperative sensorimotor training on restoration of the equilibrium behaviour in adult mice following cerebellectomy. Neurobiol Learn Mem; 64: 195-202.
- Chollet F, Di Piero V, Wise RJS, Brooks DJ, Dolan RJ, Frackowiak RSJ (1991). The functional anatomy of motor recovery after stroke in humans: a study with positron emission tomography. Ann Neurol; 29: 63-71.
- Classen J, Liepert J,Wise SP, Hallett M, Cohen LG (1998). Rapid plasticity of human cortical movement representation induced by practice. J Neurophysiol; 79: 1117–1123.
- Collen FM, Wade DT, Bradshaw CM (1990). Mobility after stroke: reliability of measures of impairment and disability. Int Disabil Stud; 12:63-71.
- Collin C, Wade D (1990). Assessing motor impairment after stroke: a pilot reliability study. Neurol Neurosurg Psychiatry; 53(7): 576-9.
- Cramer SC, Nelles G, Benson RR, Kaplan JD, Parker RA, Kwong KK, Kennedy DN, Finklestein SP, Rosen BR (1997). A functional MRI study of subjects recovered from hemiparetic stroke. Stroke; 28: 2518–2527.
- Crowdy KA, Hollands MA, Ferguson IT, Marple-Horvat DE (2000). Evidence for interactive locomotor and oculomotor deficits in cerebellar patients during visually guided stepping. Exp Brain Res; 135: 437–54.
- Curt A, Bruehlmeier M, Leenders KL, Roelcke U, Dietz V (2002). Differential effect of spinal cord injury and functional impairment in human brain activation. J Neurotrauma; 19: 43–51.
- Day BL, Thompson PD, Harding AE, Marsden CD (1998). Influence of vision on upper limb reaching movements in patients with cerebellar ataxia. Brain; 121: 357-372.
- Demeurisse G, Demol O, Robaye E (1980). Motor evaluation in vascular hemiplegia. Eur Neurol; 19(6): 382-9.

- Deschenes, MR, Maresh CM, Crivello JF, Armstrong LE, Kraemer WJ and Covault J (1993). The effects of exercise training of different intensities on neuromuscular junction morphology. J Neurocrytol; 22: 603–615.
- Dettmers C, Stephan KM, Lemon RN, Frackowiak RSJ (1997). Reorganization of the executive motor system after stroke. Cerebrovasc Dis; 7: 187–200.
- Dickstein R, Hocherman S, Pillar T, Shaham R (1986). Stroke rehabilitation. Three exercise therapy approaches. Phys Ther. Aug; 66(8): 1233-8.
- Dietz V (2000). Spastic Movement Disorder. Spinal Cord; 38(7): 389-393.
- Diserens K, Herrmann F, Perret N, Chatelain S, Filipovic N, Ruegg D, Vuadens P, Bogousslavsky J, Vingerhoets F.(2004) Quantitative evaluation of the effect on post stroke spasticity and motor control of repetitive training with an arm trainer. Neurol Rehabil 4(Suppl):40
- Dobkin BH (1989). Focused stroke rehabilitation programs do not improve outcome. Arch Neurol; 41: 701–703.
- Dombovy, ML and P. Bach-y-Rita (1988). Clinical observations of recovery from stroke. Adv. Neurol; 47: 265–276.
- Donoghue JP, Hess G, Sanes J (1996). Substrates and mechanisms for learning in motor cortex. In Acquisition of Motor Behavior in Vertebrates. Eds. J. Bloedel, T. Ebner and S. P. Wise. MIT Press.
- Duncan PW, Goldstein LB, Horner RD, Landsman PB, Samsa GP and Matchar DB (1994). Similar motor recovery of upper and lower extremities after stroke. Stroke; 25: 1181–1188.
- Durner J, Neumann C, Haase I (2001). Reduktion der Spastik durch Bewegungstrainer. Neurol Rehabil; 7(2):68-70.
- Ebner TJ, Wise SP, editors. Acquisition and mechanisms for learning in motor cortex. Cambridge (MA); MIT Press: 363–86.
- Ernst E (1990). A review o f stroke rehabilitation and physiotherapy. Stroke; 21: 1081–1085.
- Fine EJ, Ionita CC, Lohr L (2002). The history of the development of the cerebellar examination. Semin Neurol 22 (4): 375-84.
- Flanagan JR, Rao AK (1995). Trajectory adaptation to a nonlinear visuomotor transformation evidence of motion planning in visually perceived space. J Neurophysiol; 74(5): 2174-8.

- Flash T (1987). The control of hand equilibrium trajectories in multi-joint arm movements. Biol Cybern; 57: 257–274.
- Flett PJ (2003). Rehabilitation of spasticity and related problems in childhood cerebral palsy. J Paediatr Child Health; 39(1): 6–14.
- Freund HL, Hummelsheim H (1985). Lesions of premotor cortex in man. Brain; 108: 697-733.
- Fries W, Danek A, Scheidtmann K, Hamgurger C (1993). Motor recovery following capsular stroke. Role of descending pathways from multiple motor areas. Brain; 116: 369-82.
- Garhammer J (1979). Periodization of strength training for athletes. Track Tech; 73: 2398–2399.
- Garraway WM, Whisnant JP, Drury I (1983). The continuing decline in the incidence of stroke. Mayo Clin. Proc; 58: 520–523.
- Gill-Body KM, Popat RA, Parker SW, Krebs DE (1977). Rehabilitation of balance in two patients with cerebellar dysfunction. Phys Ther; 534-552.
- Gilman S, Carr D, Hollenberg J (1976). Limb trajectories after cerebellar ablation and deafferentation in the monkey. Trans Am Neurol Assoc ;101:168-70
- Giuliani CA, Haroo CC, Rosecrance JC (1889). The effect of bicycle pedalling on the temporal-distance and EMG characteristics of walking in hemiplegic subjects. Phys Ther; 69: 367-371.
- Goodale MA & Milner AD (1992). Separate visual pathways for perception and action. Trends in Neuroscience; 15: 35–62
- Goodkin HP, Keating JG, Martin TA, Thach WT (1993). Preserved simple and impaired compound movement after infarction in the territory of the superior cerebellar artery. Can. J. Neurol. Sci; 20: S93-S104.
- Haaland KY, Harrington DL, Knight RT (1999). Spatial deficits in ideomotor limb apraxia: A kinematic analysis of aiming movement. Brain; 122: 1169–1182.
- Hakkinen KM, Alen M, Kallinen RU, Newton, Kraemer WJ (2000). Neuromuscular adaptation during prolonged strength training, detraining and re-strength-training in middle-aged and elderly people. Eur J Appl Physiol; 83: 51–62.
- Hallett M, Berardelli A, Matheson J, Rothwell J, Marsden CD (1991). Physiological analysis of simple rapid movements in patients with cerebellar deficits. J. Neurol. Neurosurg. Psychiatry; 53: 124-133.

- Hallett, M, Massaquoi S (1993). Physiologic studies of dysmetria in patients with cerebellar deficits. Can. J. Neurol. Sci; 20 Suppl. 3: S83-S92.
- Heller EJ, Reimers JR, Drolshagen G (1987). Classical and semiclassical approximations for incoherent neutron scattering. Phys Rev A. Sep 15; 36(6): 2613-2627.
- Herman JM (1986). Present and future patterns of stroke care. Clin Geriatr Med; 2: 113–119.
- Hesse S, Schmidt H, Werner C, Bardeleben A (2003). Upper and lower extremity robotic devices for rehabilitation and for studying motor control. Current Opinion in Neurology; 16:705-710.
- Holmes G (1939). The cerebellum in man (The Hughlins Jackson Memorial Lecture). Brain; 62: 1-30.
- Horak FB, Diener HC (1994). Cerebellar control of postural scaling and central set in stance. J Neurophysiol; 72: 479–93.
- Hore J, Wild B, Diener HC (1991). Cerebellar dysmetria at the elbow, wrist, and fingers. J. Neurophysiol; 65: 563-571.
- Hummelsheim H, Eickhof C (1999). Repetitive sensorimotor training for arm and hand in a patient with a locked-in syndrome. Scand J Rehabil Med; 31: 250–256.
- Ito M (1974). The control mechanisms of cerebellar motor systems. In: Schmitt F. O, Worden F. G. The neurosciences, third system program. Cambridge: MIT Press.
- Ivry RB, Keele SW, Diener HC (1988). Dissociation of the lateral and medial cerebellum in movement timing and movement execution. Exp Brain Res; 73: 167-180.
- Jahanshahi M, Brown RG, Marsden CD (1993). A comparative study of simple and choice reaction time in Parkinson's, Huntington's and cerebellar disease. J Neurol Neurosurg Psychiatry; 56: 1169-1177.
- Johansen-Berg H, Dawes H, Guy C, Smith SM, Wade DT, Matthews PM (2002). Correlation between motor improvements and altered fMRI activity after rehabilitative therapy. Brain; 125: 2731–42
- Jorgensen HS, Nakayama H, Raaschou H, Vive-Larsen J, Stoier M and Olsen T (1995). Outcome and time course of recovery in stroke. Part II: Time course of recovery. The Copenhagen Stroke Study. Arch Phys Med Rehabil; 76: 406–412.
- Kakebekke TH, Lechner H, Baumberger M, Denoth J, Michel D, Knecht H (2002). The importance of posture on the isokinetic assessment of spasticity. Spinal Cord May; 40(5): 236-43.

- Karni AG, Meyer P, Jezzard MM, Adams R, Turner, Ungerleider LG (1995). Functional MRI evidence for adult motor cortex plasticity during motor skill learning. Nature; 377: 155–158.
- Klintsova AY, Goodlett CR, Greenough WT (1999). Therapeutic motor training ameliorates cerebellar effects of postnatal binge alcohol. Neurotoxicol Teratol; 22: 125-132.
- Krupa DJ, Thompson RF (1997). Reversible inactivation of the cerebellar interpositus nucleus completely prevents acquisition of the classically conditioned eye-blink response. Learn Mem; 3: 545–56.
- Kunkel A, Kopp B , Müller G, Villringer K, Villringer A, Taub E, Flor H (1999). Constraint-induced movement therapy for motor recovery in chronic stroke patients. Arch Phys Med Rehabil; 80: 624–628.
- Kwakkel G, Wagenaar RC, Twisk JW, Lankhorst GJ, Koetsier JC (1999). Intensity of leg and arm training after primary middle-cerebral-artery stroke: a randomized trial. Lancet; 354: 191–196.
- Lang CE, Bastian AJ (1999). Cerebellar subjects show impaired adaptation of anticipatory EMG during catching. J Neurophysiol; 82: 2108–19.
- Lang CE, Bastian AJ (2001). Additional somatosensory information does not improve cerebellar adaptation during catching. Clin Neurophysiol.;112(5):895-907.
- Langhammer B, Stanghelle JK (2000). Bobath or motor relearning programme? A comparison of two different approaches of physiotherapy in stroke rehabilitation: a randomized controlled study. Clin Rehabil; 14: 361–369.
- Langhorne P, Wagenaar RC, Partridge C (1996). Physiotherapy after stroke: more is better? Physiotherapy Res Int; 1: 75–88.
- Lawrence JH, De Luca CJ (1983). Myoelectric signal versus force relationship in different human muscles. Appl Physiol; 54 (6) : 1653-9
- Lincoln N, Leadbitter D (1979). Assessment of motor function in stroke patients. Physiotherepy; 65: 48-51.
- Liepert J, Miltner WH, Bauder H, Sommer M, Dettmers C, Taub E and others (1998). Motor cortex plasticity during constraint-induced movement therapy in stroke patients. Neurosci Lett; 250: 5–8.

- Martin TA, Keating JG, Goodkin HP, Bastian AJ, Thach WT (1996). Throwing while looking through prisms I: focal olivocerebellar lesions impair adaptation. Brain; 119: 1183–98.
- Massaquoi S, Hallett M (1996). Kinematics of initiating a two-joint arm movement in patients with cerebellar ataxia. Can. J. Neurol Sci; 23: 3-14.
- Mathiowetz V, Volland G, Kashman N, Weber K (1985). Adult norms for the box and block test of manual dexterity. Am J Occup Ther; 39: 386-91.
- Meyer-Lohmann J, Hore J, Brooks VB (1977). Cerebellar participation in generation of prompt arm movement. J Neurophysiol; 40: 1038-1050.
- Nakamura RS, Moriyama Y, Yamada, Seki K (1992). Recovery of impaired motor function of the upper extremity after stroke. Tohoku J. Exp. Med; 168: 11–20.
- Nelles G, Spiekermann G, Jueptner M, Leonhardt G, Müller S, Gerhard H, Diener HC (1999). Evolution of functional reorganization in hemiplegic stroke: a serial positron emission tomographic activation study. Ann Neurol; 46: 901–909.
- Newell A, Rosenbloom S (1981). Mechanisms of skill acquisition and the law of practice. In: J. R. Anderson, Editor, Cognitive skills and their acquisition, Erlbaum, Hillsdale: 1–55.
- Nudo JR, Plautz EJ, Frost SB (2001). Role of adaptive plasticity in recovery of function after damage to the motor cortex. Muscle Nerve; 24: 1000–19.
- Page SJ, Sisto SA, Levine P (2002). Modified constraint-induced therapy in chronic stroke. Am J Phys Med Rehabil; 81: 870–875.
- Prieb S, Kaiser W, Huxley P (1996). Quality of life as a planning and evaluation criterion in psychiatric management. Gesundheitswesen. Jul; 58(1 Suppl): 86-90.
- Potempa K, Lopez M, Braun LT, Fogg L, Tincknell T (1995). Physiological outcomes of aerobic exercise training in hemiparetic stroke patients. Stroke; 26: 101-105.
- Rand MK, Wunderlich DA, Martin PE, Stelmach GE, Bloedel JR (1998). Adaptive changes in responses to repeated locomotor perturbations in cerebellar patients. Exp Brain Res. Sep; 122(1): 31-43.
- Reddihough DS, King JA, Coleman GJ, Fosang A, McCoy AT, Thomason P, Graham HK (2002). Functional outcome of botulinum toxin A injections to the lower limbs in cerebral palsy. Dev Med Child Neurol; 44(12): 820–827.
- Rösche J (1997). The effects of therapy on spasticity utilizing a motorized exercise-cycle. Spinal Cord 35:176-178.

- Rossini PM, Dal Forno G (2004). Integrated technology for evaluation of brain function and neural plasticity. Phys Med Rehabil Clin N am; 15 (1): 263-306.
- Rowland LP (2002). Stroke, spasticity, and botulinum toxin. N Engl J Med; 347(6): 382–383.
- Schapiro RT (2001). Management of spasticity, pain, and paroxysmal phenomena in multiple sclerosis. Curr Neurol Neurosci Rep; (3): 299–302.
- Schweighofer N, Arbib MA, Kawato M (1998a). Role of the cerebellum in reaching movements in humans. I. Distributed inverse dynamics control. Eur. J. Neurosci; 10: 86-94.
- Schweighofer N, Spoelstra J, Arbib MA, Kawato M (1998b). Role of the cerebellum in reaching movements in humans. II. A neural model of the intermediate cerebellum. Eur. J. Neurosci; 10: 95-105.
- Shumway-Cook A, Woollacott MH (2001). Motor control. Lippincott Williams & Wilkins, Baltimore.
- Sloan FA (1992). Adverse selection: does it preclude a competitive health insurance market? J Health Econ Oct; 11(3): 353-6.
- Smith SJ, Ellis E, White S, Moore AP (2000). A double-blind placebo-controlled study of botulinum toxin in upper limb spasticity after stroke or head injury. Clin Rehabil; 14(1): 5–13.
- Staron RS, Karapondo DL, Kraemer WJ (1994). Skeletal muscle adaptations during early phase of heavy-resistance training in men and women. J Appl Physiol; 76: 1247–1255.
- Stein DG (1988). In pursuit of new strategies for understanding recovery from brain damage: Problems and perspectives, in: T. Boll, B.K. Bryant (Eds.), Clinical Neuropsychology and Brain Function: Research, Measurement, and Practice, American Psychological Association, Washington, DC, pp. 13–55.
- Stefan K, Kunesch E, Benecke R, Cohen LG, Classen J (2002). Mechanisms of enhancement of human motor cortex excitability induced by interventional paired associative stimulation. J Physiol (Lond); 543: 699–708.
- Sunderland A, Tinson D, Bradley L, Hewer RL (1989). Arm function after stroke. An evaluation of grip strength as a measure of recovery and a prognostic indicator. Neurol Neurosurg Psychiatry; 52(11): 1267-72.
- Takagi M, Zee DS, Tamargo RJ (1998). Effects of lesions of the oculomotor vermis on eye movements in primate: saccades. J Neurophysiol; 80: 1911–31.

- Tate OJ, Damiano DL (2002). Torque-EMG relationships in normal and spastic muscles. Electromyorg Clin Neurophysiol; 42(6): 347-357.
- Thach WT, Bastian AJ (2004). Role of the cerebellum in the control and adaptation of gait in health and disease. Prog Brain Res; 143: 353-66
- Thach WT, Goodkin HG, Keating JG (1992a). The cerebellum and the adaptive coordination of movement. Annu. Rev. Neurosci; 15: 403-442.
- Thach WT, Kane SA, Mink JW, Goodkin HP (1992b). Cerebellar output: multiple maps and motor modes in movement coordination. In: The Cerebellum Revisited, edited by R. Llinas, and C. Sotelo. New York: Springer-Verlag: 283-300.
- Timmann D, Watts S, Hore J (2000). Causes of left-right ball inaccuracy in overarm throws made by cerebellar patients. Exp Brain Res; 130(4): 441-52.
- Topka H, Konczak J and Dichgans J (1998a). Coordination of multi-joint arm movements in cerebellar ataxia: analysis of hand and angular kinematics. Exp. Brain Res; 119: 483-492.
- Topka H, Konczak J, Schneider K, Boose A and Dichgans J (1998b). Multi-joint arm movements in cerebellar ataxia: abnormal control of movement dynamics. Exp. Brain Res; 119: 493-503.
- Traversa R, Cicinelli P, Bassi A, Rossini PM, Bernardi G (1997). Mapping of motor cortical reorganization after stroke. Stroke; 28: 110–117.
- Trouche E, Beaubaton D (1980). Initiation of a goal-directed movement in the monkey. Role of the cerebellar dentate nucleus. Exp Brain Res; 40: 311–21.
- Wagenaar RC, Meijer OG, van Wieringen PC, Kuik DJ, Hazenberg GJ, Lindeboom J, Wichers F and Rijswijk H (1990). The functional recovery of stroke: a comparison between neuro-developmental treatment and the Brunnstrom method. Scand J Rehabil Med; 22(1): 1- 6.
- Weder B, Seitz RJ. 1994 Deficient cerebral activation pattern in stroke recovery. Neuroreport. 12; 5(4):457-60
- Weiller C, Ramsay SC, Wise RJ, Friston KJ, Frackowiak RS (1993). Individual patterns of functional reorganization in the human cerebral cortex after capsular infarction. Ann Neurol; 33(2): 181-9.
- Whitall JS, McCombe Waller, Silver KH, Macko RF (2000). Repetitive bilateral arm training with rhythmic auditory cueing improves motor function in chronic hemiparetic stroke; 31: 2390–2395.

- Wilson EO (1975). Sociobiology*:* the new synthesis, Belknap Pr, Cambridge.
- Wittenberg G, Chen R, Ishii K, Bushara KO, Taub E, Gerber HL and others (2003). Constraint-induced therapy in stroke: magnetic stimulation motor maps and cerebral activation. Neuro rehabil Neural Repair; 16(4): 1–10.
- Woldag H, Waldmann G, Heuschkel G, Hummelsheim H (2003). Is the repetitive training of complex hand and arm movements beneficial for motor recovery in stroke patients? Clin Rehabil 17; (7): 723-30.
- Woods JJ, Bigland-Ritchie B (1983). Linear and non-linear surface EMG/force relationships in human muscles. An anatomical/functional argument for the existence of both. Phys Med; 62 (6): 287-99.
- Yang TF, Fu CP, Kao NT, Chan RC, Chen SJ (2003). Effect of botulinum toxin type A on cerebral palsy with upper limb spasticity. Am J Phys Med Rehabil; 82(4): 284–289.

Acknowledgments.

I am very grateful to the supervisor of my PhD studies, **Prof. Dieter G. Rüegg**, for his enthusiastic encouragement, kindness of offering me convenient working conditions, and the careful reading and correction of the present dissertation.

I also express my gratitude to **Prof. Eric M. Rouiller** and **Prof. Jean-Pierre Montani** for the helpful advice and moral help through my study period.

Many thanks I owe to my colleague **Marianne Stephan** for her fruitful collaboration and friendly support during the last part of our study and **Monika Bennefeld** for assistance in the experiments.

Furthermore I would like to thank **Prof. Jean-Pierre Gabriel**, **Dr**. **Marc-Adrien Schnetzer**, **Dr**. **Richard Baltensperger**, **Thomas Fournier** and especially **Jerome Pasquier** from the Department of Mathematics of the University of Fribourg for their helpful advice and for writing programs for data analysis.

From the rehabilitation clinic Plein Soleil, I thank **Dr. Karin Diserens** for the medical guidance, in particular **Sylvie Krattinger** for accompanying the work with the patients at the clinic, **Valerie Pillet** for the performance of the clinical tests and the assistance at the climbing training.

I owe much to my dear parents and my dear **Fasial Bashir**, **Ali Bahsir**, **Sumaira Bashir**, **Faiza kousar** and all my friends who stood by me who gave me strength to go on all the way of getting to the end. For all their selfless encouragements and sacrifices, I am ever grateful.

Shahid Bashir

Personal details:

Name: Shahid Bashir
Date of Birth: 2-10-1975
Place of Birth: Lahore
Temporary Address: Rue-st-nicalos-5 1700 Fribourg Switzerland
Permanent Address: House no 28-L Street no 5 New Model Colony Gullberg 3 Lahore Pakistan
Marital status: Married
***Phone*:** 0041-026-323-2242
***Mobil*:** 0041-076-348-1786
E-mail shahid.bashir@unifr.ch

shahidbpk@hotmail.com

Languages

Urdu (fluent); English (fluent); French (good knowledge)

Education and degrees

- ***2006:*** Ph.D**.** degree, University of Fribourg: "*Rehabilitation of stroke and cerebellar patients*"
- ***2000***: *M.sc in Zoology,* University of the Punjab, Lahore, Pakistan
- ***1998***: *B.Sc* (Zoology, Botany, Chemistry) University of the Punjab, Lahore, Pakistan.

Major Research Interests

- Functional restitution after damage of the central nervous system (rehabilitation), Including behavioral assessment of deficits and recovery.
- Control of voluntary movements by the motor system, sensori-motor integration, motor
- Try to develop a new family of techniques, which show to be effective in improving the rehabilitation of movement after stroke and other neurological injuries.

Poster presentation.

- *Estimation of the input-force relation of a muscle by superposition of contraction. in Neurosciences meeting 2003 in Fribourg Switzerland.*
- *The effect of gravity and negative pressure in the lower body on cycling. in USGEB meeting 2004 in Fribourg Switzerland*
- *The effect of gravity and negative pressure in the heart rate on cycling.* in Germany

List of publications

- Echinoucus granulosus , histopathology of naturally infected sheep liver Zaheer, A. Akhtar, T, and Bashir, S. Punjab univ.j.zool.,14:(1999).
- The effect of repetitive arm cycling on post stroke spasticity and motor control. Diserens K , Herrmann F , Perret N , Chatelain S , Filipovic N , Bashir S , Ruegg D , Vuadens, P , Bogousslavsky J , Vingerhoets F (In pres**s)**

Fellowship and membership of societies*:*

- Member of Zoology society Pakistan
- Member of Pakistan Fisheries
- Member of Physiology society of Switzerland
- Member of Neuroscience society of Switzerland

Reference

Prof. D. G. Ruegg (dieter.ruegg@unifr.ch)

Institut of Physiology Rue du Musée 5 1700 Fribourg
Switzerland
1700 Fribourg
Tel.: + 41 26 300 8608
fax: + 41 26 300 9734

Prof. Eric M. Rouiller(eric.rouiller@unifr.ch)

Institut of Physiology Rue du Musée 5 1700 Fribourg
Switzerland

Tel.: + 41 26 300 8609
fax: + 41 26 300 9734