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Neurological aspects in real and simulated weightlessness

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MONIMIR was used onboard the MIR space station 1991-96 to study the influence of prolonged microgravity on eye-head-arm co-ordination and on the interaction and processing of visual, vestibular and proprioceptive input. Spatial, temporal and kinematic parameters of pre-programmed movements were studied before, during and after one short-term (7 days), eight long-term (4-8 months) and one 14-month space flight. 3-dimensional recordings of visually and acoustically prompted head and arm position and eye movements were performed. This chapter presents data of 3 out of 8 experiment parts: One investigated the effect of visual control on fast pre-programmed arm movements. We analyzed the kinematics of pointing arm movements towards visual targets in the horizontal and vertical plane. The second examined the influence of neck reflexes on spatial arm movement parameters; pointing movements were learned with eyes open, head straight and reproduced with eyes closed at different head-to-trunk positions. Third, motor short-term memory was investigated by analyzing spatial and kinematics parameters of memorized pointing arm movements.

Terrestrial control experiments were done with healthy control subjects with an extended experimental design. Disturbed motor patterns in their spatial and temporal characteristics suggest that microgravity exposure changes motor programming in a profound way and modifies the influence of visual feedback and of head-to-trunk position on the accuracy of pointing arm movements. It also alters the efficiency of motor short-term memory trained by proprioceptive and visual feedback during head and arm movements.

In ground based experiments we used the dry water immersion model to simulate microgravity. Healthy subjects lay nearly motionless on a thin foil on the surface of a water- filled tank for 48 or 72 hours, respectively. We investigated the influence of simulated microgravity on neurological functions by clinical examination and by performing arm-matching tests. To learn about muscle atrophic processes, we analyzed muscle enzymes. Changes in cortical activation of the sensorimotor cortex during motor tasks pre- and post-immersion were investigated by functional magnetic resonance imaging (f-MRI). Disturbances in the body scheme and incorrect estimation of limb position were found in- and post-immersion due to degraded proprioceptive feedback and the lack of updating of the sensorimotor system. Investigations with f-MRI showed that post-immersion higher motor control centers were necessary to perform simple motor tasks. At the time the developed devices, methods and software are used in clinical practice for diagnosis of disturbed eye-, head- and arm co-ordination after injuries of the cervical spine and in the course of neurological diseases. The dry water immersion model proved to be an excellent and powerful tool to simulate microgravity effects and to investigate the underlying mechanism of the bed rest syndrome observed in long-term coma (apallic syndrome) and in patients during long-term immobilization.

The outcome of these studies is important for control of therapy and rehabilitation. In further space experiments the interaction of visual / vestibular / proprioceptive information in the perception of trunk-to-head position should be investigated in more detail. Of special interest is the question how different motor tasks change the strategies in sensory information processing and which steps of adaptive processes to microgravity are developed.

Introduction

Since postural and movement control is deeply shaped by gravity, exposure to microgravity helps to gain more insight into neurophysiology, e.g. concerning internal standards. Microgravity alters orientation and movement control in cosmonauts and reduces work efficiency and capacity during space missions. Weightlessness modifies central interpretation of afferent signals from the otolithic organ, from proprioception and exteroception; the reference system used for spatial orientation based on gravity is lost. In contrast, visual information as well as signals from skin and joint receptors are not modified and are preponderant at the beginning of space missions for the recalibration of other sensory cues affected by weightlessness. However, the perception of the position of head, trunk and arms relative to each other and to the environment is somewhat impaired (9, 11, 42, 50). This can be explained by a need of frequent sensory update of the 'body scheme', a hypothetical internal cognitive image of the body (44) that establishes the central motor control of maintenance of a given posture. Such a postural control system may be rather resistant to a loss of environmental information (11).

Early inflight mismatch of vestibular, visual and proprioceptive input (25, 26, 37) leads to spatial illusions vegetative dysregulation, movement disorders (hypermetry, dysmetry), optomotor dysregulation and slight proprioceptive input disturbances. With prolonged microgravity exposure without sufficient countermeasures, polyneuropathy-like symptoms may develop; deficits range from impairment of simple sensorimotor skills (19, 31, 50, 51) to changes in postural control (1, 11, 40), musculoskeletal functional disorders and disturbed coordination (3-5, 33).

Cooperation between the Institute of Biomedical Problems (IBMP) Moscow and the University Hospital of Neurology Innsbruck started with an agreement on the „development of neurological approaches to study acute and chronic effects of microgravity on the human body" in 1986. Investigating sensorimotor disturbances during different inflight and post-flight phases could be important for the selection of cosmonauts, and for the elaboration of training and rehabilitation programs that would prevent or reduce such deficits.

Experiments in real microgravity

The MONIMIR equipment for 3-dimensional monitoring of head and arm position, and eye movements in response to visual and acoustic cues was part of the 1991 AUSTROMIR project. This equipment allowed to consecutively study the processing between vestibular, proprioceptive and visual input during long-term missions as well. A total of 10 cosmonauts (9m, 1f, 31-47 yr) were investigated pre-, in- and postflight; flight time ranged from 1 week to 14 months. Inflight measurements were performed monthly during long-term flights, and on days 2 and 5 postflight.

Arm movements were to be aimed towards visual targets, presented on a LED-matrix in front of the subject (about 12° to the left and to the right in the horizontal plane, distance 1.6 m). The arm pointer was placed on the right hand; all subjects were right-handed. A laser beam provided visual feedback of pointing accuracy in the eyes-open condition. LEDs flashed every 2 s in a pseudorandomized sequence in the horizontal plane with a 4° and 16° left-right deviation from the subject's visual center. Subjects were instructed to point with the arm-rod pointer at each target as fast and accurately as possible and to remain at the target until the next target appeared. They performed 24 pointing movements per session pre-, in- and postflight. Arm position was measured using the MONIMIR 3-D registration system, consisting of a triple IR- LED lamp, and two IR scanning cameras (sampling rate 25 Hz). The subject carried an IR- LED equipped helmet for 3-D head movement monitoring. On Earth, the subjects sat upright on a chair; in MIR they were fastened to the floor by pelvic / thoracic belts in supine position with the head moving freely (**Fig. 1**). In the following, results from these investigations are presented.

Fig. 1: The MONIMIR experiment as performed in the MIR simulator: Cosmonaut strapped to the floor, pointing laser beam to flashing LED's on the ceiling matrix. Infrared markers and infrared scanner cameras record head and arm position / movements.

- *Kinematics of pointing arm movements*

We recorded accuracy and kinematics of horizontal arm pointing movements to visual targets to study sensorimotor adaptation to microgravity. Movement accuracy remained constant but movement duration increased in all inflight sessions compared to preflight; peak velocities and acceleration / deceleration peak values decreased (**Fig. 2**).

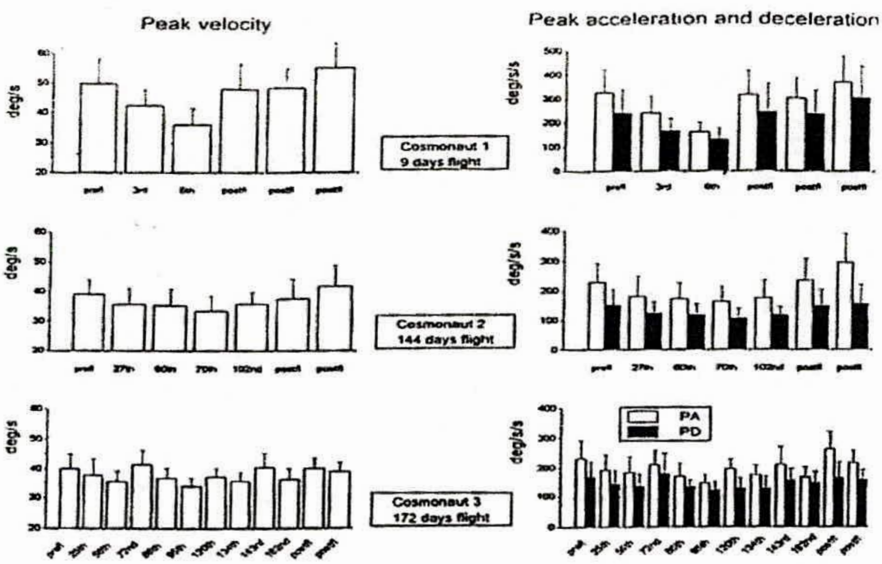

Fig. 2: Kinematics of the arm pointing movements prior to, during and after space flights of different duration. Peak velocity in deg/s (left), peak acceleration (PA) and peak deceleration (PD) values in deg/s/s (right) for 3 cosmonauts, mean values and standard deviations for every session.

We found no evidence of an increased role of direct visual guidance in movement execution in microgravity (6). Movement deceleration in microgravity may be caused by changed control strategies employed by the CNS. To avoid microgravity-induced motor problems, e.g. exaggerated or whole body countermovements, additional control and feedback and modified neural strategies are necessary for accurate motor activities, usually resulting in reduced amplitude of arm movements. Such small movements need more time to be exerted, apparently because of an increased duration to get all necessary sensory information.

- *Modification of spatial parameters of goal-directed arm movements during changed head- to-trunk position pre-, in,- and postflight*

Aim of these measurements was to examine the impact of head-to-trunk position on arm movements under normal gravity and during prolonged space flight (7). The awareness of body posture and movement is based on the processing of sensory input, particularly muscle proprioception. The central nervous system adapts motor command corresponding to changed environmental conditions: Since microgravity modifies central interpretation of afferent input from the vestibular system and from proprioception (41), arm pointing in microgravity with altered head-to-trunk position can be used to study adaptation of sensorimotor control.

Afferents from the neck contribute to the ideotropic body reference by monitoring head-body position. Altering that position affects the perception of vertical and horizontal references (15, 34, 45). With yaw (rotated) or roll (side-bended) the visual or postural subjective vertical is difficult to precisely adjust (18, 49), consequently we used microgravity to study its influence on the spatial localization of arm pointing following head yaw or roll.

Horizontal arm movements were executed with three head positions: Head straight (HS), head rotated to the right shoulder (≥50° yaw), and head tilted to the right shoulder (≥30° roll). Each 45-s test was divided in two parts: after a learning phase of six fold horizontal pointing to LEDs (eyes open, head straight) the subject closed his eyes, changed head position if required and repeated the movement 10 times (performance phase). Pointing arm movements were done sequentially, with left coined as 'negative', right as 'positive'. The sequences were driven by vectors, defined as the difference between laser spot final and initial position on the target. Metric parameters were movement amplitude and duration, spatial parameters the angle between horizontal LED-line and arm movement plane (slant), amount of vertical and horizontal offset, and movement curvature (7). The data demonstrate that head side bending (roll) and rotation (yaw) pre- and postflight (eyes closed) is correlated with considerable counterclockwise slant of the movement plane of the arm **(Fig. 3).**

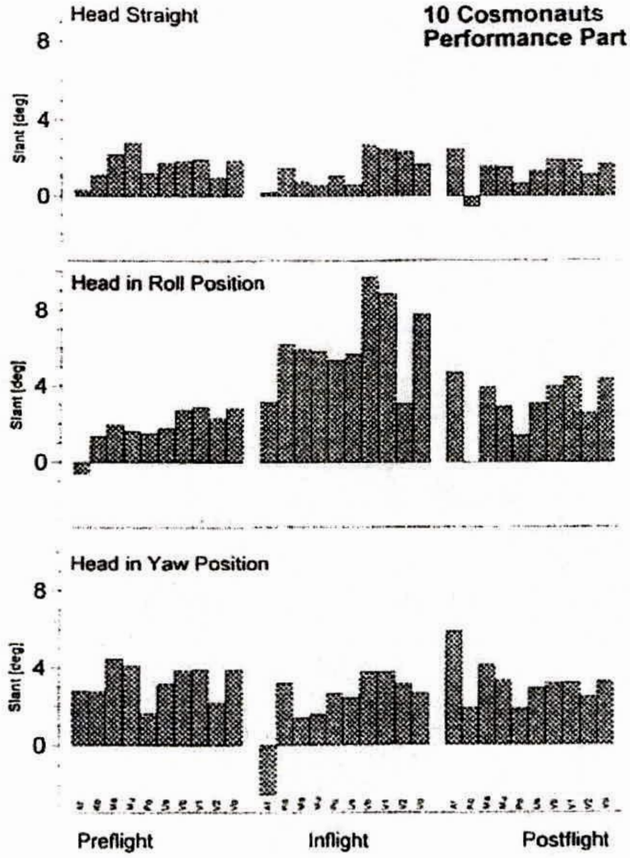

Fig. 3: Slant of the movement plane of the arm for each of 10 cosmonauts (pre-, in-, postflight) in three head-to-trunk positions. Positive values correspond with counterclockwise slant of the movement plane during horizontal pointing with eyes closed.

Long-duration cosmonauts (B) showed optimization of visually controlled arm movements but no improvement without visual guidance. In the short-term flight (A) significant effects were seen with almost no remaining effect seen in the investigation on the 2nd day after landing (**Fig. 4 A, B**).

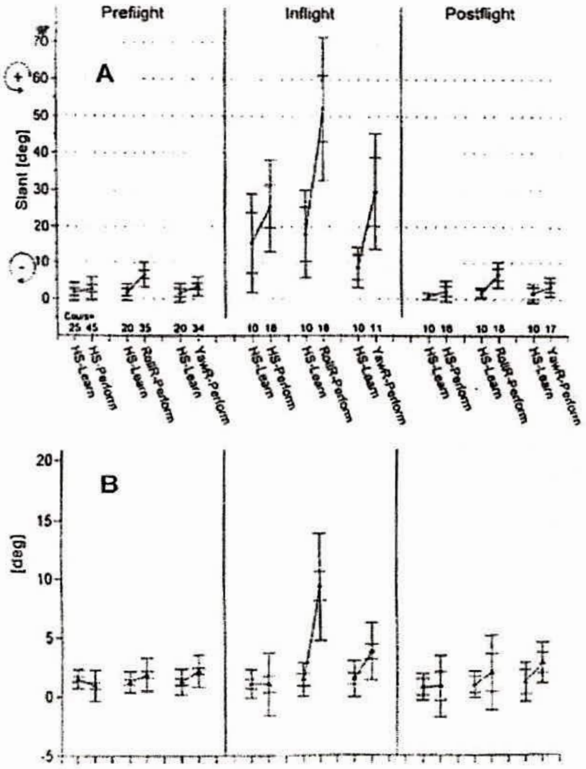

Fig. 4: Slant of arm movement plane in different head-to-trunk positions in one short-term (A, 7 days) and one long-term flight (B, 14 months). Learn = learning phase; Perform = performing phase; HS = head straight; YawR = head rotated to the right; RollR = head bent to the right; slant in deg. Note different scales in A and B. Inflight measurements were performed on the 2nd and 5th day (A), in long-term flights approximately every month (B). Postflight tests were on the 2nd and 5th day after landing.

Thus, head position with respect to the trunk plays an important role in encoding target position. It seems that without visual guidance the distortion induced by rotation or lateral bending of the head disturbs the hypothesized „body scheme" for different reasons, and significant contralateral tilt of the internal representation of the horizontal co-ordinate occurs. Loss of background information due to reduced proprioception inflight causes the development of a changed strategy for movement control even with the eyes open. Amount and direction of the horizontal offset of arm movements seem to depend on the head-to-trunk position as well. Depending on experimental conditions, we also observed changed arm movement amplitude and duration, in the vertical offset and in the curvature of the movement paths.

- *Influence of microgravity on memorized arm movements*

The ability to reproduce defined motor patterns was examined pre-, in-, and postflight under two conditions: First, the cosmonaut's outstretched arm was passively moved in order to trace a visually presented pattern (the shape of an isosceles triangle) three times by the fellow cosmonaut. With the eyes still closed, the test person tried to repeat actively the movement sequence from his memory. Passive learning meant passive limb displacement. The eyes were closed; therefore, only proprioceptive feedback was available for memorizing the movement's features.

Second, the test person actively traced the figure on the LED's matrix three times with eyes open, and then eyes closed. In active learning, the cosmonaut traced the visually presented pattern. This implicated the retention of information from central commands; visual calibration as well as proprioceptive feedback was possible. As in the horizontal pointing tests, the task was learned preflight to a standard performance until no more improvement was seen.

Fig. 5 shows typical results of an inflight test: reproduced triangles, 5 at a time, learned passively (A) or actively (B). In order to quantify spatial characteristics of the movement trajectories, the position of the corners of each triangle, its area, circumference, lengths of the sides, slopes, angles and central point were evaluated.

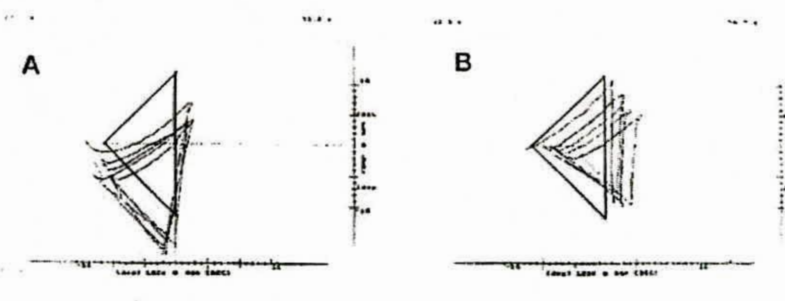

Fig. 5: Typical arm movement trajectories reproduced inflight after passive learning (A: left panel) and active learning (B: right panel).

Effect of different gravity levels: Spatial parameters changed inflight compared to preflight, particularly for passively learned memorized triangles. For example, there was a highly significant offset of the central point of the reproduced triangles, which means that caudal offset occurred immediately after closing the eyes. Inflight the memorized triangles were tilted ($p > 0.01$), due to a clockwise shift of the "vertical" side of the triangle (top-basis line). After 1 week in space, hardly any after-effects were found postflight - the performance was similar to preflight. But after long-term space flight, especially on day 2 after landing, most movements were quite inaccurate, except a remarkable vertical orientation of the reproduced triangles.

Passive versus active learning: As to learning conditions, the analysis of variance showed significant differences in metric parameters as area ($p < 0.05$; circumference $p < 0.01$) and lengths of sides only. Mainly the up- ($p < 0.05$) and down-movements ($p < 0.01$) were larger after active learning, therefore in general, the reproduced triangles constituted reproductions of the stimulus pattern that are more accurate. Inflight and postflight active learning was able to prevent the reproduced triangles from extensively shifting up or down. Thus different learning situations had an effect on metric parameters of the memorized stimulus pattern while the change in the gravitational force operated mainly on spatial characteristics of the reproduced triangles.

After passive learning without a visual reference frame, the deterioration of body awareness in microgravity leads to larger errors in reproducing metric and spatial parameters of pointing arm movements. In spite of this the angles are preserved, consequently so are the shapes of the triangles, for the most part after active preflight, least after passive inflight learning. The coding and retention of selected spatial information is more successful as there exists an internal representation that defines the shape of a triangle. Because of its high redundancy, the triangular shape is more resistant to the reduction of information in the passive learning situation and/or in microgravity. Therefore, in microgravity, it seems to be easier to reproduce this special shape than its size, for shape recognition is a cognitive function - size however is a problem of calibration (46).

It was necessary to administer the tests always in the order passive-active. A possible transfer effect will be small, because during passive learning and reproducing there was not any visual feedback available about the accuracy of performance by which the cosmonauts would profit. Plus, passive positioning of a limb reduces the capability of detecting limb position (10, 17, 22, 35, 38, 39). As long as visual calibration is possible in microgravity, new motor control patterns can be trained and adapted to plan and to execute temporally and spatially accurate movements. The ability to reproduce movement patterns which are learned from visual, afferent and efferent information (active learning) improves inflight. Proprioceptive feedback alone without a visual reference frame (passive learning) is not sufficient to optimize goal-directed arm movements during prolonged space flight.

Experiments in simulated microgravity (dry water immersion)

Neurological microgravity research is largely performed in simulated microgravity in ground based laboratories: Prior to real microgravity exposure, all tests have to be prepared in simulated microgravity, and only few experiments can be carried out in real microgravity. Long periods of head down tilt bed rest are sufficient to induce changes similar to those observed in microgravity (36, 43). We used dry water immersion (DWI), which resembles the unloading effects of microgravity very well (47). The DWI model consists of a water-filled pool covered with a thin foil that prevents volunteers from submerging in supine position and allows for floating movements **(Fig. 6)**.

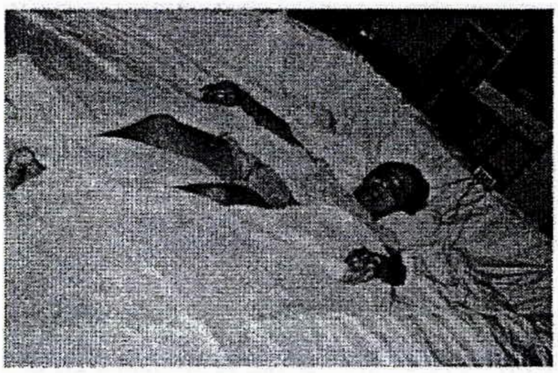

Fig. 6: Dry-water immersion model to simulate microgravity.

- *Neurological findings after 72 hours DWI*

Neurological investigations in healthy subjects were carried out before, and with 24, 48, and 72 hours DWI. Cerebellar dysfunction, signs of deteriorating peripheral neural function as well as of the posterior tract, and frontal lobe symptoms have been observed with DWI (20). Neurological alterations after 72-h DWI were investigated in 6 healthy volunteers (23.3±5.3 yr), and in another 10 (27.9±6.3

yr) in comparison with effects of bed rest. Reflex amplitude, exteroceptive and proprioceptive afferences (afferent input) were changed; signs of disintegrated cerebellar function occurred as well as frontal signs. An increase in reflex amplitude was observed in the first 24-48 hours, but dropped below pre-immersion values after 72 hours in the majority of test subjects ($p<0.02$); muscle tone decreased as well. Altered reflex amplitude has been observed earlier (29, 30) after short- and long-term exposure to real and simulated microgravity and may be due to a change of afferent inputs, influencing a closed control loop of the motor system.

A disturbance in co-ordination, as defined by the occurrence of minor ataxia, was observed first in three persons after 34,2±4,1 hours, in seven after 72 hours, with increasing symptoms within the two hours following DWI. Deficits of co-ordination may be the consequence of decreased afferences to the cerebellar nuclei: after microgravity exposure, increased cell activity was found in nerve cells of the rat Deiter's nucleus. Proprioceptive input from the lower limbs, which decreases during microgravity exposure, may also play a role. Frontal signs were seen in 11 of 16 subjects; an increased stress reaction could be ruled out after examining of the adrenergic system. Sleep profile was unchanged in other DWI subjects (13). Disturbed proprioceptive feedback from the extremities, the trunk and cervical spine in addition to disturbances of the autonomic nervous system serves as a pathophysiological explanation of the bed rest syndrome (23). In its heaviest form, bed rest syndrome in coma patients may be accompanied by other complications and develop into a severe defect stage.

- *The influence of simulated microgravity on matched arm position (48 hours DWI)*

We also examined proprioceptive function under simulated microgravity condition. It is well established that movements with proprioceptive loss are more variable than those with normal proprioception (12,14) In an arm-matching test, an incomplete representation of arm position due to degraded proprioceptive feedback would limit the ability to match the setting arm correctly. Four healthy subjects (24-30 yr) underwent DWI for 48 hours as motionless as possible with minimal use of their hands. Arm positions were measured pre-, in-, and post-immersion (immediately before and 1 h after immersion, and every 12 h during immersion, i.e. two times a day) by ZEBRIS CMS-50, an ultrasonic distance measuring system, sampling frequency 50 Hz. Every 12 hours the subject was blindfolded, the ZEBRIS sensors on dorsum and elbow of each arm were fixed. The subject felt the platform during lifting it by a hand wheel. Immediately after checking the device in this position, the first test was started. The experimenter passively and slowly moved the setting arm into one of three arm positions in x-direction (45°, 90°, 135°), which were indicated by a large goniometer positioned close to the subject's arm, its origin close to the shoulder joint. Some random deviation in y-direction was intended and should be reproduced by the subject while matching

Subjects were instructed to 'feel the position of the arm which has been set by the experimenter and try to match the second arm exactly'. Dependent variables were the ZEBRIS-recorded absolute co-ordinates of the moved arms (setting arm, matching arm). The x-direction corresponded to the body-mid-line (head to feet), the y-direction was the direction right (-) to left (+), the z-direction corresponded to the vertical direction (+ means against gravity). Three different errors (angles) were evaluated: the „matching error" in the x-direction, the error in the y-direction (lateral, from the body) and the radial error. This radial error represented the deviation of the measured direction of the matched arm (the absolute angle) from the ideal position. The ideal position represented the position of the setting arm in the moment of matching.

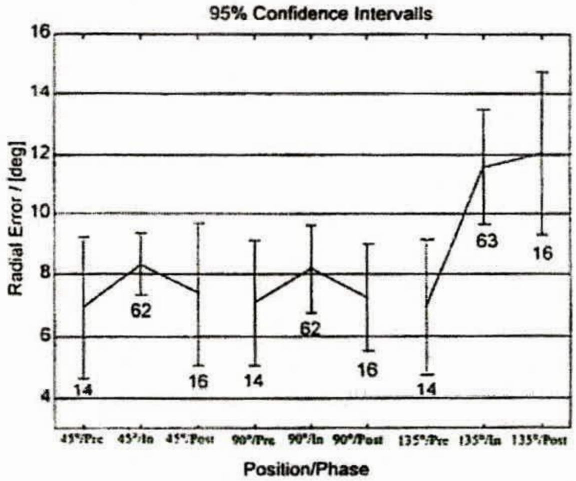

Fig. 7: Radial Error, angle between the ideal direction (corresponding to the position of the setting arm) and the measured direction of the matched arm for each position and phase during DWI.

Most of the significant results were seen with radial error (**Fig. 7** indicates its amount for all positions and phases). Due to the inactivity in DWI and the reduced proprioceptive input, the subject was unable to update the proprioceptive representation of his/her limbs. The inaccurate proprioceptive representation of the initial position of both arms in DWI reduced the capability to accurately program the position of the matched arm. Thus arm matching, a simple task which is also used in neurological examination and which can be performed correctly without difficulty under normal conditions, was impaired as soon as important information was lacking.

- *Sensorimotor cortex functional magnetic resonance imaging before and after 48 hours of DWI*

In this pilot study, 4 healthy subjects were investigated pre- and post-immersion by functional Magnetic Resonance Imaging (f-MRI). The aim of the study was to evaluate the effects of simulated microgravity or immobilization on cortical activation patterns of the sensorimotor cortex. DWI deprives the brain of proprioceptive input, and activity changes can be expected. The on/off motor paradigm was a monitored finger tapping with the left hand. We found increased higher motor control area activity compared to baseline: 1 hour after DWI, the cortical activation during finger tapping changed within the anterior and posterior supplementary motor area (SMA, **Fig. 8**), within the ipsilateral premotor area, the ipsilateral globus pallidus, the left and the right primary motor and primary somatosensory area, and the secondary somatosensory area on both hemispheres. We speculate that higher control centers are necessary to re-establish programs for the performance of known pre-programmed movements to get additional information from other sensory systems and to estimate the magnitude of execution errors.

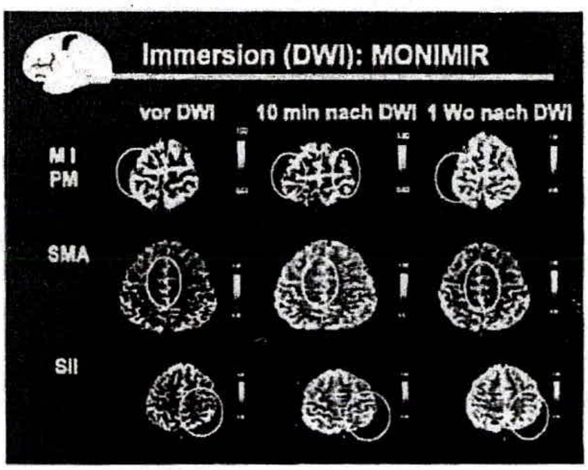

Fig. 8. Cortical activation within the anterior and posterior supplementary motor area (SMA) a) prior to DWI, b) immediately after DWI and c) one week after DWI. There is more than doubling of cortical activation in anterior and posterior SMA. The third examination one week after DWI shows activation back to baseline values.

- *Muscle degradation after DWI*

Of the many disturbances induced by a decrease in gravitational load, the disorders and effects on the function of the musculoskeletal and motor regulatory systems are of major significance. They resemble the symptoms of posterior funicle pathologies, hereditary spinocerebellar degenerations or those of the bed rest syndrome. Prolonged bed rest and immobilization inevitably lead to several musculoskeletal complications such as atrophy, loss of muscle strength and endurance or/and morphological changes (13). All of these complications are much easier to prevent than to treat. These pathologies are well known in long period bedridden patients as well as after prolonged exposure to real as well as to simulated microgravity.

5 days DWI led to diffuse lesions mainly of slow twitch fibers in antigravitational muscles (8), evidenced by an increased muscle enzyme activity such as serum creatine kinase (CK), myoglobin, and myosin heavy chain fragments (MHC) after a defined muscle load of 40 isometric quadriceps femoris contractions. Especially MHC, mostly present in slow muscle fibers (24) of antigravitational muscles, increased dramatically, with a peak 72 h after loading. Maximal efflux of soluble proteins as CK (2) and myoglobin was observed earlier, mostly 16 hours after exercise. The isometric loads 14 days after DWI exposure showed a significantly lower response to loading. The increase of MHC suggested that total immobilization led to a temporary hidden and diffuse lesions of slow twitch fibers, which were found predominantly in antigravitational muscles. The reported changes may be the consequence of a functional adaptation process indicating regeneration rather than permanent damage of slow twitch skeletal muscle fibers. Recent studies showed that similar changes could be expected in patients mobilized after long duration bed rest.

Conclusions

Cortical motor programs are dependent on peripheral input from visual, vestibular, extero- and proprioceptive systems. Interactions of these peripheral inputs were investigated to study the adaptation of the sensorimotor system to gravity and weightlessness. The results help to understand the severe defects in sensorimotor co-ordination after long bed rest and can be used to design new diagnostic and therapeutic programs for certain neurological diseases.

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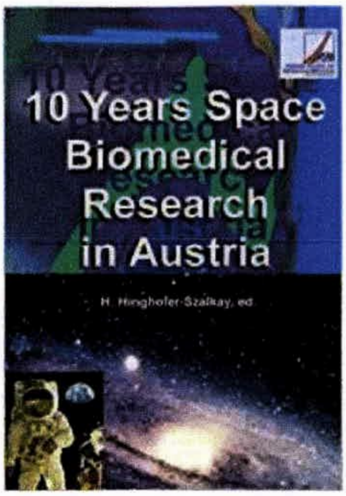

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