Adaptation and learning in postural control

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ADAPTATION AND LEARNING IN POSTURAL CONTROL

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Front cover is an illustration of Oedipus seated on a rock while pondering the riddle of the Sphinx.

Attributed to Oedipus the painter, Classical period.
Attic red-figured kylix ~450 BC,
Room XIX at Museo Gregoriano Etrusco Vaticano,
Vatican City, Italy

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On the road to Thebe in ancient Greece a sphinx posed the following riddle: ***What is it that walks on four feet in the morning, two at noon, and three at dusk?*** Not knowing the true answer was equal to instant death, Oedipus, the only one who passed the test, answered: ***Man, who crawls on four limbs as a baby, who walks upright on two as an adult, and who walks with the aid of a stick in old age***.

Sophocles ~450 B.C.

"One of the reasons people stop learning is that they become less and less willing to risk failure."

John W. Gardner (1912-2002)

For Lina, Ebba, Erik and Nils

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---------- DEFINITIONS

Adaptation A process whereby an organism becomes better suited to handle a new or changed environment.

Habituation When, in an organism, a stimulus or environment will induce a learned set of responses acquired through adaptation processes.

Internal model A neural representation of all the dynamics and kinematics involved in a specific task, stored within the central nervous system.

Long-term adaptation Changes of postural adjustments in response to a perturbation that become refined and executed with more ease on a day-to-day basis.

Perturbation A disturbance causing the body to deviate from its regular movement.

Plasticity The capability of the brain to change both in physical structure (anatomy) and functional organization (physiology).

Postural control adaptation Induced change of postural adjustments in order to withstand the same perturbation and control movements with more ease. In this thesis defined as a decrease in energy expenditure as a function of time exposed to the perturbing stimulation.

Reweighting A process that changes the relative importance of an individual sensory system for maintaining postural control.

Sensory conflict/mismatch A sensory conflict can be induced when the information about posture or movements that the sensory systems convey is, or is perceived to be, divergent.

Short-term adaptation Changes of postural adjustments in response to a perturbation induced within each test situation during exposure to stimulation.

---------- THESIS AT A GLANCE

	Question	Methods	Results	Conclusions
I	How does the postural control system adapt to repeated somatosensory perturbation?	Vibratory somatosensory perturbation 5 consecutive days + after 3 months	Torque variance decreased both during the test and from day to day	Adaptation occur in 2 distinct phases mimicking motor memory formation to generate long-term memory
II	How does the postural control system adapt to repeated galvanic vestibular perturbation?	Galvanic vestibular perturbation 5 consecutive days + after 3 months	Torque variance decreased on the first part of the 1st day, but after that only from day to day	After an initial quick decrease of torque variance does the major adaptation to galvanic perturbations take place from day to day, and generate long-term memory
III	Does the interval between repeated somatosensory perturbations affect the adaptation processes?	Vibratory somatosensory perturbation 5 times with 3 different intervals + after 3 months	The torque variance decreased equally in the groups, but > 3 hours interval had better results after 3 months	Adaptation is most affected by the amount of exposure, but longer intervals benefit long-term retention.
IV	Do antagonistic postural tasks performed in close proximity affect postural responses adaptation processes?	Vibratory somatosensory perturbation to posterior calf and/or Tibialis Anterior muscle	Exposure to posterior calf vibration prior to Tibialis Anterior vibration affected torque values as well as postural strategy	Postural responses can be transferred between different perturbations, provided they have different amplitudes.
V	Does postural adaptation differ between children and adults?	Vibratory somatosensory perturbation 5 consecutive days + after 3 months in children and adults	Children used 38% less torque i the beginning of the second day than they finished with on the first day	Children seem to have more efficient adaptation process due to central nervous plasticity but also due to playful learning.
VI	Is postural adaptation different in patients suffering from Phobic Postural Vertigo?	Vibratory somatosensory perturbation to patients with PPV and healthy controls	PPV patients reduced torque variance less in eyes closed condition and more in eyes open condition.	PPV patients adapt to a lesser extent and do not use visual information as efficiently to modulate postural control.
VII	Does pre-surgical deafferentation with gentamicin + concomitant vestibular training in vestibular schwannoma patients improve postural control and the ability to resolve sensory conflicts?	Vibratory somatosensory perturbation to patients subjected to schwannoma surgery	Patients receiving vestibular PREHAB + gentamicin prior to surgery used less torque variance at the 6 month follow-up	Vestibular PREHAB + gentamicin benefit vestibular compensation if patients have remaining vestibular function prior to surgery

The importance of the ability to use bipedal stance and gait cannot be underestimated in everyday life. Bipedal stance is learned during childhood and constantly adapted to changing circumstances throughout life. Failure to attain and maintain the control of upright posture can have catastrophic consequences. Among elderly in Sweden, deaths related to falls are 10 times more common than to traffic accidents[1]. Postural competence needs to be recovered in a multitude of illness, in developmental disorders as well as in age related decreasing function. To meet this end, health professionals utilise a multitude of techniques, mainly based on sensory based training exercises.

The overall ambition of this thesis was to enhance knowledge on adaptive behaviour and motor learning of human postural control with the aim to identify new therapeutic concepts for training and rehabilitation. This knowledge led to the development of a new therapeutic concept of 'prehabituation' prior to a sensory lesion which was implemented and studied.

Studies I-IV investigated how the postural control system adapts to sensory perturbations in a short and long-term perspective, with the specific aim to assess whether interval (spaced) or congregated training benefits learning. Study V compared children's (7-9 years of age) and adults' ability to adapt to a postural perturbation. Study VI investigated how anxiety affects postural control adaptation, as unsteadiness and dizziness can induce a state of anxiety also in otherwise healthy subjects[2]. The final study (VII) investigated the possible beneficial aspects on postural control by performing a gradual sensory deafferentation concomitant with careful sensory training.

Since the biomechanics of human standing is naturally unstable constant neuro-muscular actions are needed in order to adjust and maintain upright bipedal stance. Postural control is achieved by combining feed-forward and feed-back mechanisms generating forces toward the supporting surface[3,4], adjustments of body position and of body segments (head/trunk/legs)[5, 6]. It could be proposed that feed-forward control constitutes the frame or the grand-plan for postural control and locomotion, whereas feed-back control constitutes reactions and corrections to any deviation from the plan.

FEED-FORWARD CONTROL

Feed-forward mechanisms involve the concept of "*internal models*" or postural strategies, the output of which consists of preformed neuromuscular programs to be activated in given situations. Either automatically, voluntarily or both according to previous postural experience. The classical example for feed-forward has been the postural preparations involved prior to climbing an escalator[7]. However, it is not long since postural control was believed to be solely reflex mediated and that feed-forward control was limited to anticipation of external constraints (supplied primarily by vision)[8].

Direct evidence for feed-forward postural control is provided by studies demonstrating that anticipation influences automatic postural responses to unexpected perturbations[9, 10]. There are also indications that *internal models* are employed in postural control[11]; if subjected to the same repeated perturbation with different amplitudes, the responses are scaled to the previous amplitude indicating preformed ways to respond[12-14].

Cerebellar lesions influence the scaling of the magnitude in postural responses[15], as well as adaptation to postural challenges[16]. The basal ganglia have, through studies on patients with Parkinson's disease, been implicated in the selection of postural programs together with the premotor and supplementary motor cortex[17].

FEED-BACK CONTROL

Feed-back control of posture consists of reactions to sensory cues from the vestibular apparatus, vision and somato-sensation, conveying information about own movements as well as those of the surroundings[18] (figure1). It has been hypothesized that a map of the body's configuration and its relationship to the surroundings exists within the central nervous system[5, 19, 20], to which feed-back information is added to generate corrective postural movements and forces.

Sensory information is integrated and processed within the central nervous system at different levels[8, 21]. Direct evidence of central nervous involvement in the feed-back loop is the fact that the timing of postural adjustments are longer than simple spinal reflexes, though more rapid than voluntary movements[22-25] and that large group of muscles in different body segments are activated[26]. This negates simple spinal reflexes although they seem to be sufficient to control unperturbed stance[27]. The brainstem, cerebellum, basal ganglia and cerebral cortex have all been implicated in feed-back postural control[8].

SENSORY SYSTEMS

Vestibular system

The vestibular contribution to postural control lies in the detection of head movements in space, specifically rotation and translation, and at rest to sense the pull of gravity and thus determine the earth vertical[28]. The derived functions of the vestibular organs include gaze control (i.e. through a reflex loop known as the vestibulo-ocular reflex keeping visual cues sharp on the fovea during head movements), stabilizing the head to the rest of the body and in space (vestibulo-collar reflex), and postural control in low frequency movement range (feed-back and vestibulo-spinal reflexes)[29,30].

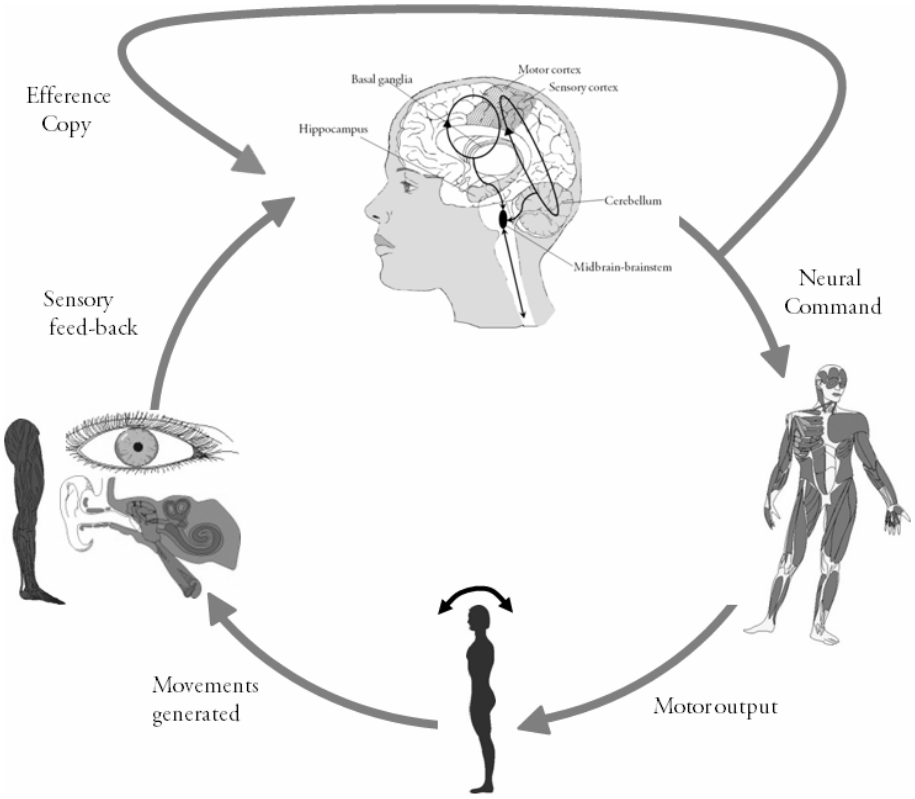


Figure 1. Schematic of feed-back postural control. The sensory systems identify movements of the body and convey that information to the central nervous system. The primary motor cortex initiates the neural command and utilizes information from the sensory, premotor and supplementary motor cortex[31]. The command is then carried to the brainstem and spinal cord[31]. A copy of the command is re-fed to the postural centre in order to control that the intended postural adjustments correspond to the actual postural adjustments, when those are perceived by the sensory systems[32].

There are a lot of convergences of input on the vestibular nucleus in the brain-stem; from the contralateral vestibular system, visual pathways, cerebellum, spinal cord, reticular formation, sensory and motor cortices[33, 34], necessitating sensory integration already at brain-stem level. From the vestibular nuclei are numerous projections throughout the brain[30]. Attempts have been made to identify a vestibular cortex in humans and multiple locations have been found, including parieto-insular cortex (PIVC), hippocampus, pre-motor regions in the frontal lobe and superior temporal gyrus[35-41] which corresponds to what is known through studies on primates[42]. These locations, however, are not committed to vestibular input only, but also to somatosensory and visual input, thus constituting sensorimotor cortices[36].

Vision

Visual cues exert their effect on posture both through feed-forward information on postural demands and feed-back information of the own body's movement as well as that of the surroundings. Visual acuity as well as peripheral vision contributes to stabilizing posture[43-46], though they have different thresholds to detect motion[43]. Postural responses to visual cues are dependent on the size of the visual field (distance to visual cues)[45,47], contrast sensitivity and visual acuity[48]. Vision primarily detects slow body movements <0.1 Hz[49].

Somatosensation

The sense of the relative position of the individual body-segments (proprioception) is mediated through specialized neuromuscular devices within the muscles, tendons and joints[31, 41]. *Proprioception* is mainly possible, due to the actions of the muscle-spindles situated within the skeletal muscle fibers, reacting to muscle length changes and muscle contraction[31, 50], but also from tendon and joint receptors[31, 41]. All these receptors systems adapt to a given stimulus. However, they do so with different time-constants (slow-rapid), which enables proprioception to detect the body's position both at quiet upright stance and during postural perturbations.

The sense for the body's relation to surfaces or external objects is mediated by pressor receptors in the skin including, and especially important for postural control, receptors in the soles of the feet[31, 51-53].

The working range of movement sensation of the somatosensory system is probably wider than the other postural senses, muscle spindles above 1 Hz. and exteroceptors and joint receptors less than 1 Hz[18]. Neuropathies, whether of peripheral or central origin, have great impact on postural function rendering among others an impaired ability to scale the responses to velocity and amplitude, especially if concomitantly visually deprived[54, 55].

SENSORY INTEGRATION

The sensory systems act synergistically to each other and information from one does not always suffice to provide the necessary information to the brain. Vision alone, for instance, cannot without vestibular and/or proprioceptive cues distinguish between self-movements and that of the surrounding, and the vestibular system provides no information when the body is moving at constant velocity and is incapable of determining without visual cues whether an acceleration takes place in one direction or a deceleration in the opposite direction[21]. Proprioceptive information also helps the vestibular system to distinguish between passive and active head movements[28]. It has been demonstrated that the sensory systems expand the working ranges (even detection of movement frequencies) of each other[21]. The systems can also suppress each other, e.g. suppression by vision of the vestibulo-ocular reflex demonstrated by rotation of the head while looking at an object that moves with the body, a task that, if not suppressed, would yield vestibular

induced eye-movements and make visual fixation impossible[36, 56].

Postural sway is influenced by the availability and reliability of the different sensory systems. Visual cues reduce the increased body sway during vibratory proprioceptive calf stimulation (compared to tests with eyes closed), primarily in the high-frequency range (>0.1Hz)[57]. This illustrates that visual cues can reduce the effect of inappropriate proprioceptive information. The same stabilization can be produced by touching a stationary object during similar proprioceptive perturbations[41, 58]. Vestibular cues, however, do not stabilize posture to visually induced sway, unless the stimulation is large enough or if proprioceptive cues are unreliable[59, 60].

SENSORY WEIGHTING

The sensory systems overlap and can replace each other's functional capacity to a certain extent, though not completely[18]. If a sensory deficit is congenital or develops very early in life, the other sensory systems overcome the functional deficits to a greater extent than if the sensory loss is acquired[61-63].

The impact that each of the individual sensory components exerts on postural control is context-dependant and in that sense 'weighted' to their relative importance[61, 64, 65]. The weighting of individual sensory components in a normal population varies, e.g. visual dependent people are more easily perturbed by visual cues and generate more body sway when their eyes are closed than with eyes open[66, 67]. The compensatory processes after unilateral vestibular loss involve 'reweighting' of the other sensory inputs[68-70]; e.g. the visual influence on postural control in some patients can be altered from visual dependence to independence and vice versa[71, 72]. Reweighting processes have also been demonstrated on sensory intact healthy subjects[73-77].

Patients with bilateral vestibular deficits do not alter (or adapt) their body sway, as healthy controls do, while subjected to visual[78] or proprioceptive perturbations[79]. This indicates deficits in the adaptive capacity of the remaining postural control system, which has been attributed to the absence of the vestibular role as an orientational and internal reference to other conflicting sensory input[59, 80]. The same conclusions have been drawn from studies on astronauts, returning to earth after a transient period of decreased vestibular influence due to weightlessness[81, 82].

---------- DEVELOPMENT OF POSTURAL CONTROL

The learning of postural control during early childhood through to what is considered adulthood is still a controversial subject for research in neurobiology and psychology. Whether the role of nature or nurture is most important has been contested, i.e. if all motor programs are expressions of what is stored in the genome (nature) or if motor programs are only driven through experience (nurture). Given the evidence, both nature and nurture are complimentary to each other and not antagonistic in any respect.

Nature and postural control

Predetermined motor programs are operational at the time of birth – known as *ontogenesis*[6, 83-86]. It has been shown that motor programs are trained in utero [83, 87, 88], and reflexes present at birth, such as the placing or walking reflex, that later disappear, are indubitable proofs of the existence of ontogenetic processes in postural setting[88]. Furthermore the early postural responses are characterized by more or less coordinated direction-specific activations and inhibitions of muscle groups[89, 90] that exist before the functional ability of a skill has precipitated. For example postural

adjustments to perturbations while sitting are the same whether the child has acquired the ability to sit or not[84, 91] – again indicating the existence of innate postural programs rather than that all postural reactions are driven through experience[92].

The continuing postnatal modification of motor programs as well as development of new motor programs is labelled *epigenesis,* where environment or exposure is thought to act on the genome to induce expression of morphological and behavioural characteristics of an individual throughout the entire life-span [6, 91, 93].

Nurture and postural control

The concept of nurture was well formulated by Asaiante in 2005: "the first step is to build repertoires of postural strategies" and the "second step consists of learning to select the most appropriate strategy depending on the ability to anticipation of environmental and bodily constraints"[85].

The generation of coordinated movements involved in postural control emerges through a series of states of stable and unstable movements with large variability in freedom degrees (joint stabilization)[89, 94]. In short, motor development is driven by practice and follows a pattern where learning of one skill precedes achievement of another; e.g. head stabilization precedes reaching in infants[95]. Reference frames, either from gravitational cues or information from supporting surfaces, are believed to be used leading stabilization of the body in functional stages at different ages[85, 90, 96, 97].

SENSORY DEVELOPMENT

Sensory weighting in children

During growth the sensory systems appear to contribute differently at different ages. Vision seems to be the most important input during early childhood[96, 98, 99] up to 4 years of age, since children above that age do not sway more when their eyes are closed[100]. Somatosensory information has the main impact between 3 and 6 years of age[98, 101, 102], and vestibular cues are regarded to be fully efficient around the age of 7, when the head can be stabilized while walking on a narrow supporting surface (beam)[90, 96]. The ability to ignore irrelevant information and resolve sensory conflicts develops as early as 3 years of age[102], although it seems as if the use of vestibular cues as reference frame does not emerge until the age of 7[101]. Children have been found to be able to reweight to many sensory inputs from the age of 4[103].

Vestibular function

Semicircular canal function has been assessed in infancy and considered operational at an age of 8-16 weeks[104, 105], although there seem to be maturation effects at least up to 7 years of age[106, 107]. Central vestibular responses develop as a function of brain maturation through early childhood to the age of 10-12, and then further to adulthood[108]. Preterm delivery delays the vestibular responses[109], and absent/hypoactive vestibular function at birth often leads to considerable delays in postural and locomotion development[110-112]. Research on the otolith function in children is scarce. Studies on otolith and canal interaction have proposed that responses mature with age and that the integration of vestibular information is different if a postural skill, such as independent walking, has developed[113, 114].

Vision and posture

Visual cues are considered to be operational in a postural setting very soon after birth (3 days)[115]. Most studies have shown that the children's postural muscles (involved in standing) react with direction and velocity specificity[99, 115] to visual stimuli even before children are capable to stand[116-118]. Electromyography recordings (EMG) of the postural muscles while subjecting infants to optic illusions, conclude that muscle responses are largest in children 11-14 months old[119, 120], although responses were detected

even in the youngest subjects that were tested (5 months)[118]. Congenital blindness does not lead to an impaired postural control, but acquired blindness or blurred vision does[62, 63, 121].

Somatosensory function

The somatosensory receptors are functional at birth[99, 122], and spinal and supra-spinal reflexes are present[123] but an adult pattern in reflex latency and reflex suppression is not reached until the age of 6-10[124]. It is possible for 6-year olds, but not younger to discriminate and adjust posture to such somatosensory information as velocity[125]. It is possible to maintain sitting at the age of 6 months by the use of somatosensory input alone[122], but the capacity to control upright posture with legs only is not attained until age 6-7[126].

The feet undergo physical as well as loading changes during childhood and acquisition of standing and walking ability[127, 128], and with increasing age (3-11 years) the centre of gravity moves toward the toes[128], which may have impact on the biomechanics of sway around the ankle joint as well as use of exteroception.

FEED-FORWARD IN CHILDREN

Studies on locomotion indicate that infants use feed-forward models even when crawling on the floor[129], and anticipatory control has been demonstrated in children just over 1 year of age[130], although other studies claim that anticipatory strategies mature and do not become functional until 4 years of age[96, 131, 132].

---------- MOTOR MEMORY PROCESSES

The understanding of formation of motor memories has expanded substantially, but has scarcely been applied to analysis of changes in postural control. The present thesis investigates adaptation of postural control and the potential parallel to motor learning in general. The following sections review some aspects on motor learning.

Adaptation and habituation are fundamental concepts involved in movement control and from a postural control perspective, essential to be able to cope with internal and external demands on posture[13]. Adaptation of posture has been observed during stimulation of each sensory system[56, 73].

MOTOR MEMORY FORMATION

Modern theories on memory processes date back to the late 19th century, when it was proposed that newly learned information can be disrupted by head trauma and by learning of several things in close proximity to each other[133]. This was further developed by Hebb in 1949[134], proposing that newly learned memories are fragile and need to be consolidated in order to become more stable and long-lasting.

The medial temporal lobe and hippocampus have traditionally been viewed as essential to memory processing[135], but are probably not vital to development of all motor skills and habits[136]. Structures like the hippocampus and cerebellum and sub-cortical structures like the thalamus have an abundance of synapses capable of forming long-term-potentiation and are probable structures involved in memory formation[137, 138]. Where different types of memory (motor, conscious memory etc.) are processed and stored with all probability varies[136, 139].

CONSOLIDATION PROCESS

The process of solidifying memories has been coined 'consolidation'. Consolidation takes place after a learning session, during inactivity, and can thus be

regarded as a separate process from short-term learning[140]. It has been shown that different regions of the brain are involved at different stages of memory formation[141-143]. After the completion of learning a motor task, activity shifts from the prefrontal cortex to the pre-motor, posterior parietal and cerebellar cortices[143]. The mechanism for consolidation is not fully understood, but is considered to involve several aspects of synaptic function, such as synaptic connections and long-term potentiation or depression of synapses[144]. The stimuli (or learning) are required to be of sufficiently large amplitudes to induce these alterations at synapses[145]. Sleep is generally regarded as beneficial to the consolidation processes[146, 147], and specifically during slow-wave sleep neuronal activities from preceding behaviour are re-expressed in the hippocampus[148, 149].

The time frame within which the newly formed memory is vulnerable has been estimated to a couple of hours[135, 150-153], and cellular events such as protein synthesis and gene translations are generally held to be required[151, 154]. Motor memories have been shown to be disrupted if a 2nd task is trained immediately before (negative transfer) or up to 3 hours after (retrograde interference)[150, 155] the completion of training a specific motor task. However, consolidation can occur in seconds if failure to learn has catastrophic consequences[156, 157]. This indicates that motor memories are processed in different time-frames given the circumstances (high impact of stimulus – fast consolidation[145]), and that different neuro-modulators (e.g. adrenaline) acting on the synapses[158] may be involved in different situations. A possible mechanism for faster consolidation processes are thought to consist of disinhibition of already existing synaptic connections[140].

INTERNAL MODELS

Learning of motor tasks results in strategies or 'internal models' that are activated consciously or sub-consciously when required. Internal models are regarded to be neural representations of all dynamics and kinematics involved in a task[159, 160]. An example of such a model is the task of lifting an object, where object weight, forces needed, selection of muscle involvement and postural adjustments are calculated prior to the lifting. Internal models are generated through memory processes and are continuously shaped and adapted through experiences[161], an ability that is attributed to central neural plasticity[162].

PLASTICITY

Plasticity is the capability of the brain to change both in physical structure (anatomy) and functional organization (physiology)[162], and as such incorporates both internal modelling and memory processes. If a function disappears due to lesion in the brain, other areas will take over that function to a certain extent, a feature ascribed to plasticity[162]. The adult brain has traditionally been regarded as a fixed hard-wired system, but this view has been challenged during the last decades, and replaced by the opinion that all areas in the brain are plastic and prone to change[163, 164], though generation of new neurons to the current knowledge is restricted to the hippocampus, the olfactory bulb and the cerebellum[165].

During the development from infancy to adulthood, 'critical periods' have been discerned, in which cortical circuits and systems specialize their selective responses, a functional capacity that does not reappear in the same sense[166]. The plasticity of a neonate is regarded as greater than that of adults[167]. With aging, the traditional view is that a functional decline is unavoidable as direct function of brain degeneration. New observations however argue that the decline in elderly is due to domination of plasticity processes that have negative consequences[168]. It is suggested that the

reduced physical activity lead to behavioural changes with further physical inactivity, which in turn lead to reduced brain activity and weakened neuro-modulatory control. It has been hypothesized, and to an extent proven, that the outcome of training older adults can significantly be improved by intensifying training programs with more demanding sensory, motor and cognitive activities[168] - in a sense driving brain plasticity to positive results.

---- PSYCHOLOGICAL INFLUENCE ON POSTURAL CONTROL

The connection between fear and dizziness, "fear to move" (sedere volentibus tremor) was reported as early as the 5th century A.D. by the Roman Caelius Aurelanius[169]. Postural reactions and adaptation depend on the interpretation of the context in which postural control is exerted. Postural behaviour is influenced by anxiety and a fear of falling, which may be a considerable factor among falls in the elderly population[170]. Increased levels of anxiety are very common during the acute stages when suffering from sudden unilateral vestibular loss[169, 171]. Anxiety levels normally decrease through desensitization or habituation[172]. However, sometimes anxiety persists and restricts daily life. It has been hypothesized that the visceral symptoms (nausea, vomiting) induced by acute unilateral vestibular loss serve as conditioning stimuli for later avoidance of situations that may evoke the same sensations[169]. This in turn leads to inactivity and fear of movements yielding ineffective desensitization process, which in turn leads to decreased opportunities for adaptation and learning processes[172], thus completing a vicious cycle.

The links between vestibular dysfunction and panic disorders, such as anxiety and agoraphobia, have been under intense investigation during the last decades. Only one third of the patients in a retrospective study on patients suffering from "psychogenic dizziness" were neuro-otologically intact[173], and the prevalence of psychiatric morbidity is generally high in patients with organic vestibular dysfunction[174, 175]. Similarly vestibular dysfunction is common among patients with panic disorders[176], especially with agoraphobia[177]. Just introducing a postural threat in form of different heights to healthy controls modulates the control of upright stance[178, 179]. The neural interface between vertigo and affective disorders has been ascribed to the connections between somato-sensory, vestibular and visual input in the brainstem and the parabrachial nucleus network, a structure implicated in affective disorders, specifically regulation of anxiety and avoidance behaviour as well as receiving visceral sensory information[169].

PHOBIC POSTURAL VERTIGO

Brandt and co-workers have suggested the concept of somatoform or Phobic Postural Vertigo (PPV)[180] that combines the subjective feeling of dizziness or disturbance of balance, with psychiatric characteristics, though stressing that the only symptom is a feeling of imbalance (see criteria in appendix 1). PPV may follow upon a period of emotional stress or an organic vestibular disorder and is common (up to 16%) among patients seeking consultation for dizziness[181]. The hypothetical theory behind the mechanisms of PPV is that a sensory conflict is caused by mismatch between the anticipated and the actual movement[180], due to a decoupling of the efference copy signal (figure1). The decoupling may be caused by a constant anxious control of balance performance[180]. This theory corresponds well to the models on executive function in emotional disorders[182].

POSTURAL CONTROL IN PHOBIC POSTURAL VERTIGO

The postural performance of PPV patients has shown several aberrations compared to healthy subjects, although the differences decrease when the postural challenge becomes more difficult[183]. PPV patients execute more high-frequency movements in order to correct posture[183-185], and their postural responses to vibratory proprioceptive stimulation are greater than healthy controls[185]. It has been hypothesized that PPV patients have a malfunctioning central programming where they seem to rely more on, or are more sensitive to, proprioceptive information[185].

Querner et al. tested the influence of vision on a subclass of PPV patients and found that they did not seem to be able to transform visual cues to a specific postural strategy[186]. The interpretation the authors made was that PPV patients were oversensitive to any afferent information to the postural control system and labelled it "anxious control".

It has also been suggested that PPV patients have a different focus of attention when exposed to a postural challenge and subsequently do not use the available sensory information in an optimal fashion[185]. This is supported by the facts that anxiety increases the demand for attention when walking[187] and that diversion of attention affects postural responses[188, 189].

---------- ASSESSING POSTURAL CONTROL

A systematic approach to assess upright postural performance began to develop with Moritz von Romberg[54], in the mid-19th century. The test, eponymed 'Romberg's test', consists of observing the ability to stand erect with arms folded on the chest with eyes either open or closed. This examination was further refined by letting patients stand on a platform that recorded shifts of the centre of pressure, and the examination was thus labelled 'posturography'[80, 190, 191]. Posturography is traditionally divided into static and dynamic, with the former being recorded quiet stance and the latter when stance is perturbed. Perturbation can be achieved by altering the conditions of each sensory system individually or together. In this thesis we use individual perturbations to either the proprioceptive system or the vestibular system. The advantage of using individual stimuli is that it is easier to interpret the adaption processes for each sensory system. With the application of posturography it is possible to detect specific diagnoses[192-194] although its clinical value mostly comes from estimating postural function.

VIBRATORY PROPRIOCEPTIVE STIMULATION

Vibration applied to a muscle or a muscle tendon increases the firing of the muscle spindles, thus signalling that the muscle is being stretched[23]. The stimulated muscle responds with a reflexive contraction (tonic vibratory reflex)[195, 196] in the agonist muscle and a subsequent relaxation in the antagonistic muscles[197]. It is primarily the type Ia fibers of the muscle spindles that are most sensitive to vibratory stimulation[198], although the Golgi tendon organs are also affected. Beside the physical effects, the stimulation generates a powerful illusion of self-motion that contributes to the postural correctional movements[195, 199, 200].

GALVANIC VESTIBULAR STIMULATION

Galvanic vestibular stimulation has proved to be an effective way to model postural disturbances due to the vestibular system[201]. Although some of the effects have been known since the 18th century,

when Volta experienced vertigo while putting his newly invented battery to his skull[202, 203], the physiological mechanisms behind the evoked postural reaction are still unclear[204]. It is a well established fact that the galvanic stimulation does not act on the vestibular receptor level, but rather on the vestibular nerve or Scarpas ganglion itself[205-207]. The stimulation results in an increased electrical firing rate of the nerves on the side to which the negative cathode electrode is applied, and an analogous decrease on the anodal side[203]. The net sum from bipolar galvanic vestibular stimulation, while standing, signals a roll with a small yaw component towards the cathodal electrode[203]. The stimulation results in an ocular torsion towards the anodal side[208-210] and a change of postural sway towards the anodal side, which results in lateral (right-left) sway when the head is faced forward, and anteroposterior sway if the head is turned 90 degrees in the horizontal (yaw) plane[211-214].

In addition to automatic postural reactions, the stimulation conveys a powerful illusion of movement that influences postural adjustments[215]. The effect seems to be highly context-dependent and does not elicit any responses in the leg muscles (vestibulo-spinal reactions) when applied on seated subjects[215].

---------- AIMS OF THE THESIS

The overall aim of the thesis was to explore both short and long-term perspective of learning processes involved in maintaining postural control during perturbation and to resolve sensory conflicts.

The studies upon which this thesis is based were designed to achieve the following aims:

- To determine how the postural control adapts and habituates when exposed to daily repeated vibratory proprioceptive stimulation and to find out whether previous experience of vibratory proprioceptive disturbance is transferred from one sensory context to another (**paper I**)

- To determine how the postural control adapts and habituate when exposed to daily repeated galvanic vestibular stimulation (**paper II**)

- To ascertain whether the consolidation process in postural control habituation to vibratory proprioceptive disturbance is affected by the length of interval between consecutive tests (**paper III**)

- To examine the effects on postural control learning when subjected to consecutive antagonistic postural tasks (**paper IV**)

- To evaluate how children adapt and habituate when exposed to daily repeated vibratory proprioceptive disturbance (**paper V**)

- To investigate whether patients diagnosed with Phobic Postural Vertigo adapt differently than healthy subjects do when exposed to vibratory proprioceptive disturbance (**paper VI**)

-To study if pre-treatment with gentamicin and pre-habitual vestibular training ‘PREHAB’ of patients scheduled for surgery for vestibular schwannoma, affected perturbed postural control (**paper VII**)

SUBJECTS

The subjects in papers I-V constituted of healthy volunteers. The subjects used in paper I are also included in papers III and V.

The children in paper V were recruited from the families of friends and co-workers. The age selection was chosen to be when the postural reactions could be interpreted as adult-like[110], the sensory systems involved were developed[96, 98, 126] and the ability to weight sensory cues had transpired[101], at least according to the literature.

In paper VI 39 consecutive patients diagnosed with phobic postural vertigo[180], were compared to 24 healthy subjects. The PPV patients did not have any neuro-otological malfunction at the time of the inclusion assessment and constitute as such a subset within the PPV population.

The subjects in paper VII were 41 patients subjected to trans-labyrinthine schwannoma surgery. They were divided into 4 groups depending on the ipsi-lesional vestibular function before surgery and whether they were pre-treated with gentamicin or not. The last group consisted of patients showing signs of central nervous dysfunction.

POSTUROGRAPHY

Postural adaptation was evaluated by the use of a custom-built force platform that recorded the forces and torques actuated by a standing subject's feet with 6 degrees of freedom, with an accuracy of 0.5N. The data was sampled at 50 Hz by a computer equipped with an AD converter. A customized computer program controlled both the sampling and the perturbing stimulation used in the studies.

PROCEDURE

All subjects were instructed to stand erect and relaxed with bare feet and the arms folded across the chest. The subjects' heels were 3 cm apart and feet positioned at an angle of 30 degrees open to the front along guidelines on the platform. Care was taken that the subjects with their legs in valgus position had free space between their knees and feet. The children tested in paper IV were allowed to hold the vibrators before the first test, in order to reduce startling responses. Two tests were conducted on each test-occasion, one with the subjects' eyes closed and the other with eyes open and fixating on a mark on the wall at a distance of 1.5 m. The subjects listened to music through headphones in order to reduce possible movement references from external noise sources. In study II an additional trial was performed for 12 of the subjects, with the head turned 90 degrees in the yaw-plane and eyes closed in order to produce anteroposterior sway[212].

There were 5 repeated trials (I-III and V), with different time intervals, 1 day interval (I, II, V) and 1 day, 20 minutes and 3 hours (III). The timing on the day was consistent throughout the tests with 1 day intervals. In paper III, which contained shorter intervals, care was taken that the subjects had eaten or in other ways fortified themselves before each test. In addition there was also a test performed 3 months after the initial trial (I-III and V). The order for eyes open or closed was randomized and maintained throughout the trials. Half of the test subjects started each trial occasion with the eyes-open test, and the other half with the eyes-closed test.

In paper IV vibratory stimulation was applied to the calf and/or to m. Tibialis Anterior. The subjects were divided into 4 groups where two only received one type of vibration. The remaining two groups either started with posterior vibration and then received Tibialis Anterior vibration or vice versa. The only visual condition tested in paper V was closed eyes.

In papers VI and VII one measurement with eyes open and one with eyes closed was conducted, in a consistent order, according to our standard clinical procedure.

VIBRATORY PROPRIOCEPTIVE STIMULATION

Vibratory stimulation was applied to the belly of the gastrocnemius muscles of both legs simultaneously[216], by two cylindrical vibrators (0.06 m long and 0.01 m in diameter). The vibrators were held in place with an elastic strap around each leg. The vibration amplitude was 1.0 mm amplitude at a constant frequency of 85 Hz. Before the vibratory stimulation started, spontaneous sway was recorded for 30 seconds, labelled as quiet stance. The vibratory stimulation was executed according to a computer controlled pseudorandom binary sequence (PRBS) schedule[217] for 200 seconds by turning on/off the stimulation. Each test lasted 230 seconds including the quiet stance preceding the stimulation. The PRBS schedule was composed of stimulation shift periods (on) with random duration between 0.8 – 6.4 seconds, which yielded an effective bandwidth of the test stimulus in the region of 0.1-2.5 Hz, covering a broad power spectrum[196]. The randomization of the stimulation reduced the opportunity to make anticipative and pre-emptive adjustments.

GALVANIC VESTIBULAR STIMULATION

The galvanic stimulation was applied on the mastoid processes through plates (3.5x4.5 cm) of carbon-based rubber glued in place with conductive glue. The electrical signal was alternating bipolar with strength of 1mA. The stimulation was executed according to a computer controlled pseudorandom binary sequence schedule[217], as described for the procedure with vibratory proprioceptive stimulation.

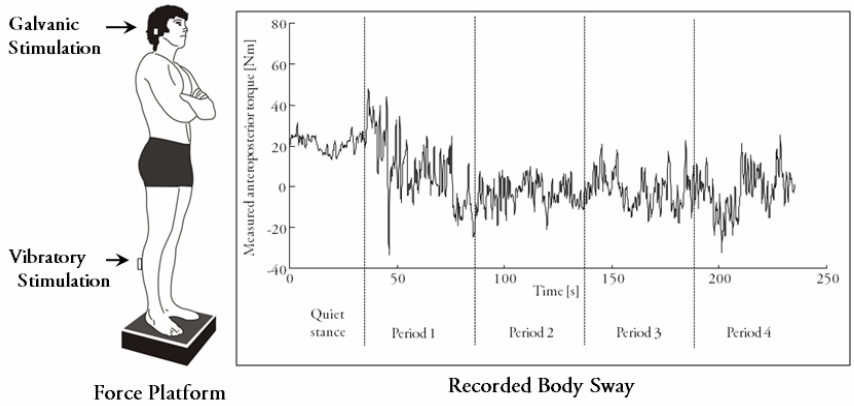


Figure 2 Division of each recorded test into quiet stance and four perturbation periods. Each test lasted for 230 seconds, with an initial 30s recording of quiet stance before any perturbing stimulus was applied, and subsequent 200s of perturbing stimuli. The perturbation periods were split into four periods during the stimulation (30–80, 80–130, 130–180, and 180–230 seconds, respectively). Each of the perturbation periods contained the same amplitude and duration of perturbing stimulus.

DATA ANALYSES

Torque variance

Torque variance was analyzed in the plane where the stimulus was most dominant, i.e. anteroposterior sway for vibratory stimulation and lateral (right-left) sway for galvanic vestibular perturbations.

Postural stability while standing is commonly analyzed using force platforms and the movements of the centre of pressure (CoP), i.e., the point of application of the ground reaction force. We measured torque and analyzed the variance of the torque values. Torque corresponds to Centre of Pressure (CoP); torque τ is calculated from the formula $\tau = CoP \cdot Fz$; where $Fz \approx m \cdot g$; where m = the assessed subjects mass (in kg) and g = gravitational constant 9.81 (in meter/s^2), see figure 1. Fz will fluctuate slightly due to present body leaning and when the subject applies additional forces to the surface to accelerate/decelerate a movement. Hence, changes in recorded torque are equivalent to changes in CoP [218]. The formula for variance is given by;

$$\bar{\tau} = \sum_{i=1}^{n} \frac{\tau(i)}{n}$$

$$\operatorname{var}\tau = \frac{1}{n-1}\sum_{i=1}^{n}\left(\tau(i) - \bar{\tau}\right)^2$$

i=sample, n=number of samples recorded during an analysed period.

One benefit with presenting torque variance values is that the calculated value corresponds directly with the energy used towards the support surface to maintain stability [219]. Regression analysis of the torque variance showed dependence to the test subjects' squared weight and height, so the data were therefore normalized by squared weight and squared height[220].

Frequency separation

Torque variance was divided into three categories; total, low frequency (<0.10 Hz), and high frequency (>0.10 Hz) torque variance (I, II, VI). A fifth-order digital Finite duration Impulse Response filter[221], with filter components selected to avoid aliasing, was used for spectral separation. The frequency cut-off level of 0.1 Hz was based on Fast Fourier Transformation analysis of the sway composition under eyes closed and eyes open conditions[222]. The frequency limit at 0.1 Hz was also based upon empirical trials on recorded body sway, which have shown that this frequency limit is efficient, when separating between fast corrective movements to maintain balance, and the smooth corrective changes in the overall stance.

Statistical methods

The applied statistical methods in all papers were non-parametric since some values were not normally distributed even after log-transformation. In all analyses p-values <0.05 were considered statistically significant.

To determine whether torque variance changed as the test progressed through period 1-4 (I, III, IV, VI) we used linear and exponential regression statistics[223]. The same statistics was applied to determine whether torque variance changed between the test-occasions (I, III, IV). The day and period within the test sequence was used as independent variables to find the relative dependency of period the tests were performed, and the dependency of test-occasion during the stimulation.

The changes in torque variance were further evaluated using Wilcoxon's non-parametric test[223] within the same subject population (I-VII) and Mann-Whitney (Exact sig. 2-tailed)[223] was used between the different populations (V-VII).

In papers II, IV, VI we also analyzed the effects of stimulation, vision, period, day

and their interactions, using a GLM univariate ANOVA (General Linear Model univariate Analysis of Variance)[223] test on log-transformed values. The accuracy of the GLM model was evaluated by testing whether the model residuals were distributed normally. Accordingly, the torque variance values were log-transformed to obtain normal distribution of the GLM ANOVA residual.

Definition of adaptation

Adaptation, in this thesis, was defined as a decrease in energy expenditure as a function of time exposed to the perturbing stimulation.

----------THE PRESENT INVESTIGATIONS

ADAPTATION AND HABITUATION TO VIBRATORY PROPRIOCEPTIVE STIMULATION (PAPER I)

Subjects: Twelve healthy volunteers (six male, six female) age range from 15 to 32 years (mean 26).

Study design: Vibratory perturbation daily on 5 consecutive days and once after 3 months, in two randomized test conditions; eyes open and eyes closed.

Results: No differences in torque variance could be found during quiet stance. The induced torque variance decreased linearly within each test in both visual conditions ($p<0.05$), except for the high frequency range (figure 3). An exponential reduction could be found within the test in all frequency ranges for eyes closed ($p<0.05$). Between the tests the torque variance decreased both exponentially and linearly in all frequency ranges ($p<0.001$ total and high frequency, $p<0.01$ low frequency).

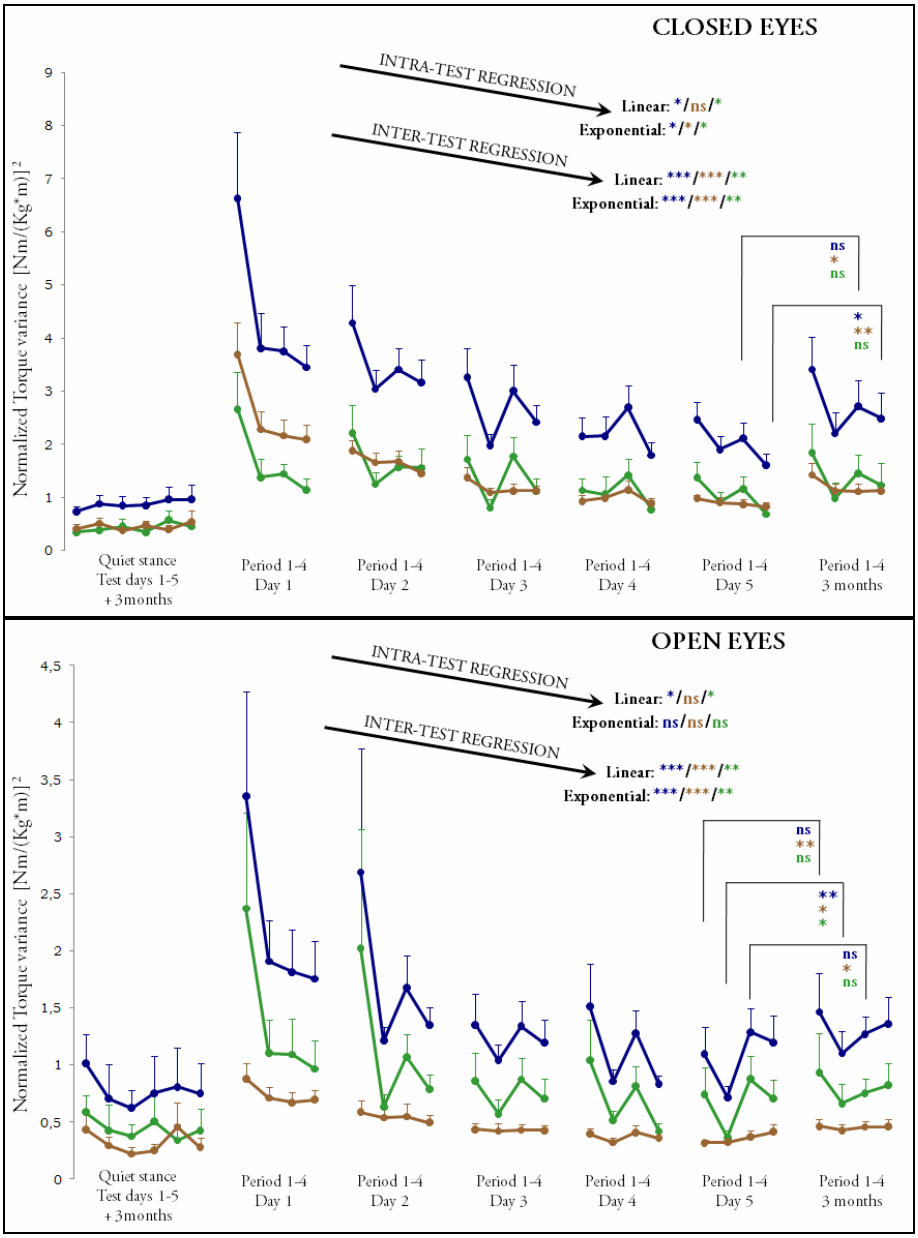
The induced torque variance remained low when retested after 3 months. Although an increase was found compared to the 5th day, they never reached the levels of day 1.

No differences could be found in torque variance values between the subjects that started with their eyes open or closed to the subjects that finished with eyes open or closed.

Conclusion: The perturbation must be sufficiently strong to instigate an adaptive process.

Postural adaptation to vibratory proprioceptive stimulation occurs in two steps; one fast (during the test) and one slow (between the tests) and the learned reactions are consolidated to last 3 months.

Adaptation seems to be restricted to sensory context and experience in one sensory condition is not necessarily transferable to another.



Total torque variance, > 0.1 Hz, < 0.1 Hz

Figure 3 Anteroposterior torque variance (mean and standard error of mean). Note the decrease in elicited torque variance by the use of visual cues, especially in the high-frequency range, as well as the general reduction both during the tests and between the consecutive test occasions. Regression statistics are presented at the top of the figure * p< 0.05, ** p< 0.01 *** p< 0.001.

ADAPTATION AND HABITUATION TO GALVANIC VESTIBULAR STIMULATION (PAPER II)

Subjects: The experiments were performed on 24 healthy volunteers, 1 subject (male) discontinued on the cause of severe malaise, and 2 due to discomfort. The age distribution of the remaining 21 subjects (8 male, 14 female) ranged from 17 to 41, mean 29 years.

Study design: Posturography during galvanic vestibular stimulation was performed daily on 5 consecutive days and once after 3 months in 3 test conditions; 'Head turned-eyes closed' (head turned 90° yaw plane) yielding mainly anteroposterior body movements, and 'Head forward eyes closed' and 'open' yielding mainly lateral body movements.

Results: '*Head turned-eyes closed'* condition yielded increased torque variance between quiet stance and the perturbation periods on almost all days in total and high frequency range, but not until the 5th day and after 3 months in low frequency range (figure 4). The induced torque decreased between the 1st and consecutive periods on day 1 but not on any other day. From day to day the torque variance decreased in high frequency range. There was a tendency to increase the torque variance in low frequency range though not statistically significant.

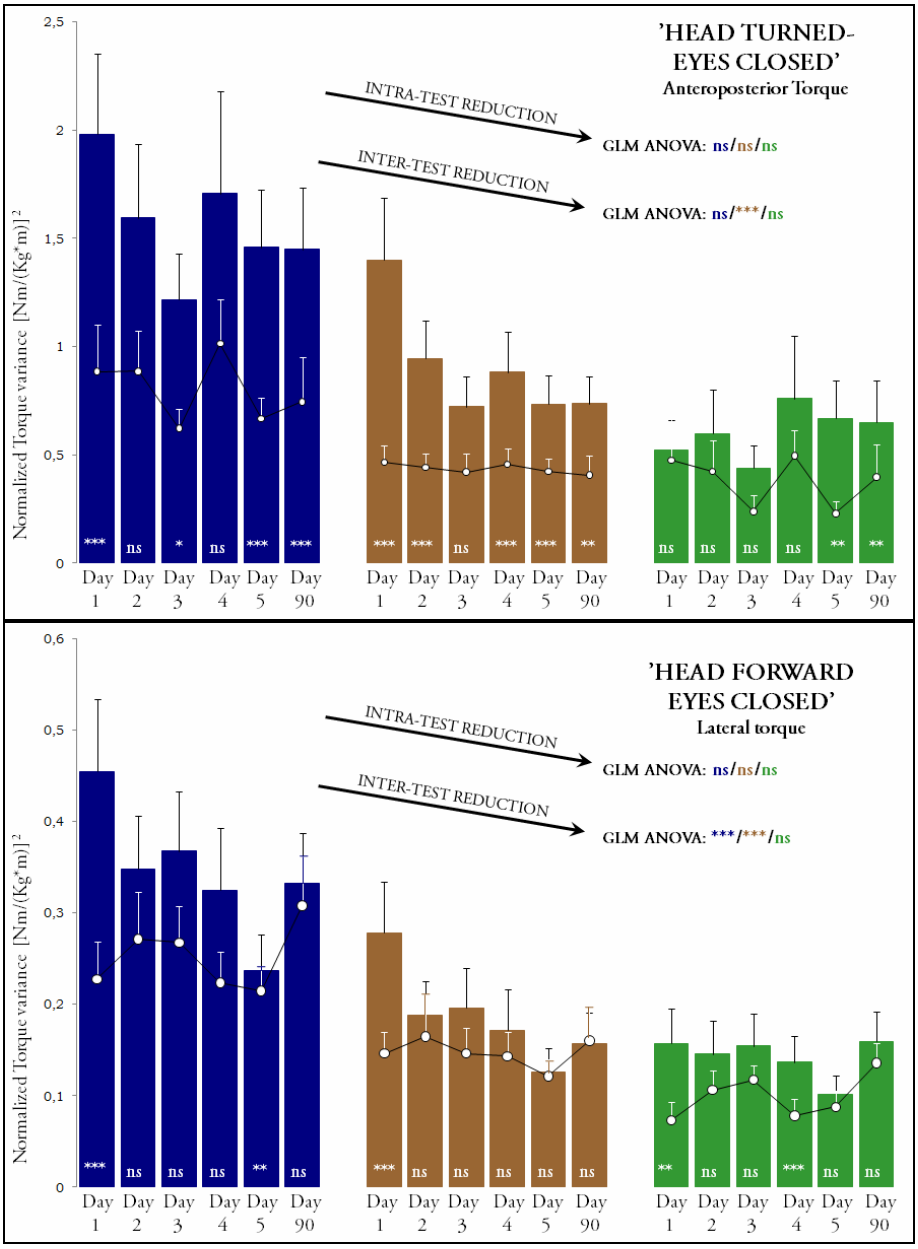
'Head forward eyes closed/open' condition yielded increased torque variance between quiet stance and the perturbation periods on the 1st day, but not on the consecutive days (figure 4). The induced torque decreased between the 1st and consecutive periods on day 1 but not on any other day. From day to day the torque variance decreased in total and high frequency range.

The induced torque variance remained on a low level in all 3 conditions after 3 months.

Conclusion: The induced responses to a galvanic perturbation immediately adapt during the first 50 seconds, after which further exposure yields no continued adaptation of postural responses – immediate sensory reweighting.

There is a major adaptation to galvanic vestibular perturbation that takes place after the exposure to the stimulation, from day to day – similar to the concept of the consolidation process involved in motor learning.

The perturbation induced a change of postural strategy in 'Head turned-eyes closed' condition, from decreasing high to increasing low frequency movements as the test progressed through the days. The same postural strategy appeared to be present after 3 months, which suggests that the strategy consists of a consolidated changed response to galvanic vestibular stimulation and as such constituting an internal model used in feed-forward control postural responses.



Total torque variance, > 0.1 Hz, < 0.1 Hz

Figure 4 Torque variance (mean and standard error of mean).White circles denote the quiet stance period and the coloured bars denote mean of the perturbation periods. The results from 'Head forward-eyes open' condition were similar to that with eyes closed. GLM ANOVA is presented at the top of the figure. Inside the figure are the Wilcoxon statistics between quiet stance period and the first perturbation period.
* p< 0.013, ** p< 0.01 *** p< 0.001.

THE EFFECT OF DIFFERENT INTERVALS BETWEEN TEST SESSIONS ON THE CONSOLIDATION PROCESS (PAPER III)

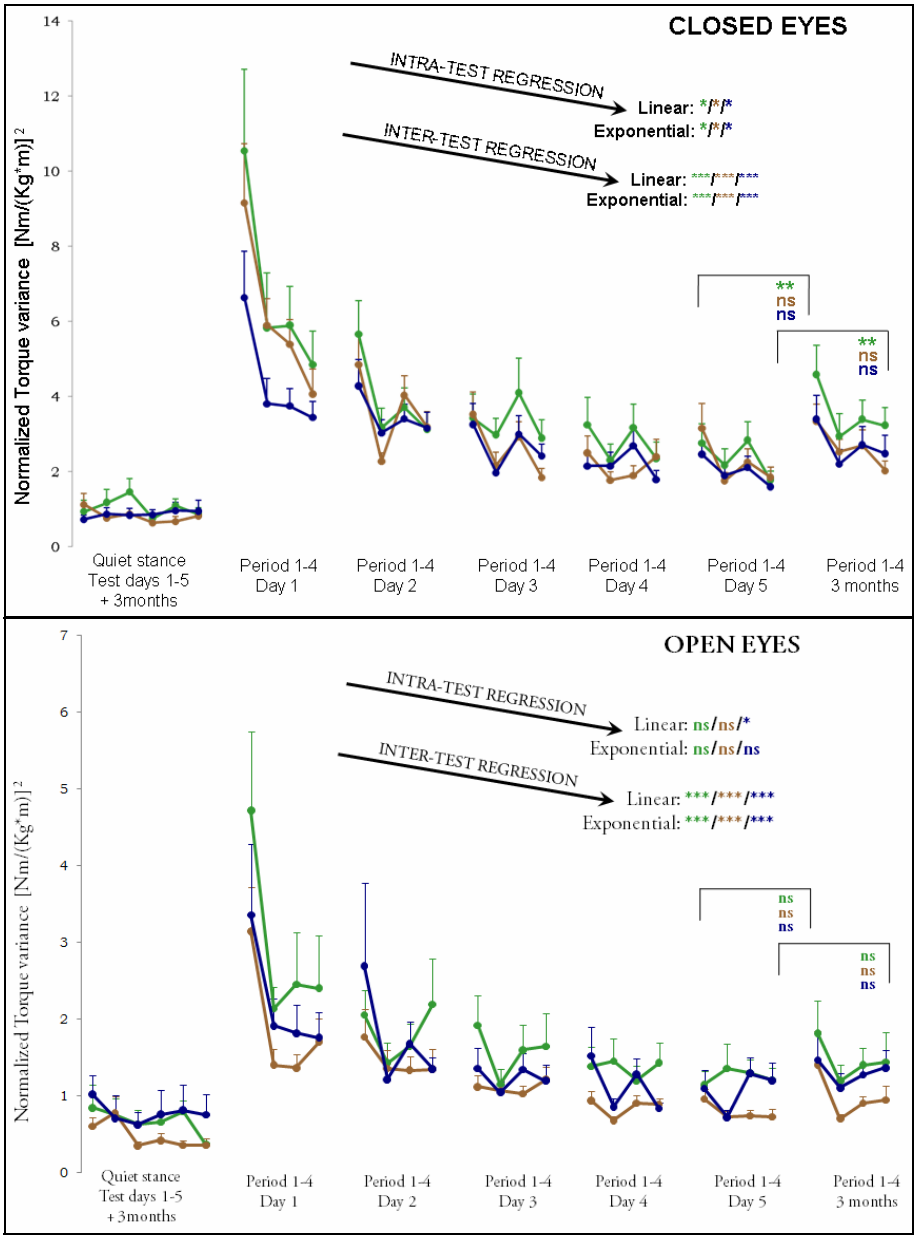
Subjects: Thirty-six healthy volunteers (17 male, 19 female) aged 15-38 years (mean 25) divided into 3 groups.

Study design: Posturography during vibratory proprioceptive stimulation in two randomized test conditions; eyes open and eyes closed, was performed daily on 5 test sessions with different time-intervals (20 min., 3 and 24hrs.), and once again after 3 months.

Results: All three groups displayed the same adaptation pattern (figure 5). The torque decreased linearly and exponentially within each test with eyes closed ($p<0.05$), but only in the 24 hour group when the eyes were open ($p<0.05$ linearly). Retrieval after 3 months was least successful in the group with 20 minutes interval with eyes closed, but no difference could be discerned between the other two groups.

Conclusion: Postural adaptation to vibratory proprioceptive stimulation occurs in two steps; one fast (during the test) and one slow (between the tests) and the learned reactions are consolidated to last 3 months.

It is primarily the amount of training performed that governs habituation, although the consolidation seems to be more efficient if the intervals are >3 hours, which provide ample time for the theoretical mechanisms involved in consolidation processes.



20 min interval, 3 hour interval, 24 hour interval

Figure 5 Anteroposterior torque variance (mean and standard error of mean) recorded while perturbed with vibratory proprioceptive stimulation. Note the significant differences between day 5 and 3 months in the 20 min interval, closed eyes. Regression statistics are presented at the top of the figure.
* p< 0.05, ** p< 0.01 *** p< 0.001.

EFFECT OF TWO CONSECUTIVE ANTAGONISTIC POSTURAL TASKS ON POSTURAL CONTROL (PAPER IV)

Subjects: Forty-six healthy subjects (24 males, 22 females) aged 19-44 years (mean 26).

Study design: Vibratory perturbation performed on two consecutive days with vibration stimulus to Tibialis Anterior or posterior calf muscles, or both in different order, generating 4 groups; 'Calf only'. 'Tib only', 'Calf-Tib' and 'Tib-Calf'.

Results: Tibialis anterior vibration instigated postural adaptation during exposure to the vibration, but did not induce long-term adaptation from day to day, contrary to posterior calf vibration (figure 6).

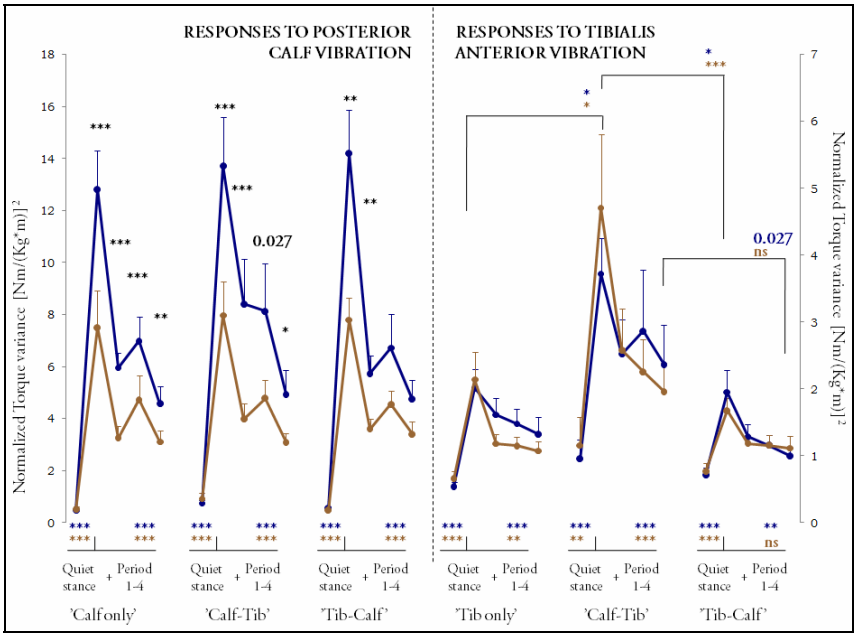
The long-term postural adaptation from day to day when the posterior calf was vibrated was not affected by prior or subsequent tibialis anterior vibration (figure 6).

Exposure to posterior calf vibration prior Tibialis Anterior vibration, led to changes of postural strategies and larger amount of torque variance (figure 6 and 7).

Conclusion: The perturbation must be sufficiently strong to instigate consolidation processes, since Tibialis Anterior vibration did not yield day-to-day reduction, though being sufficiently strong to induce reduction within the test.

The consolidation processes involved in learning to withstand postural perturbations induced by vibration to posterior calf seem to be insensitive to a concurrent postural task – dissimilar to other forms of motor learning.

Experiences or postural strategies can be transferred between postural challenges if they post different demands, implied by the finding that postural strategies initiated by the gastrocnemius vibration were re-employed during the subsequent tibialis anterior stimulation. This may represent the formation of an internal model, used as feed-forward control of posture, possibly consisting of sensory reweighting.



Day 1, Day 2

Figure 6 Anteroposterior torque variance (mean and standard error of mean). Annotations below the graphs refer to differences within each test. Annotations above the graphs refer to differences between the days (calf vibration) and between the groups (Tibialis Anterior). *left figure=p< 0.017, *right figure=p<0.025, ** p< 0.01 *** p< 0.001.

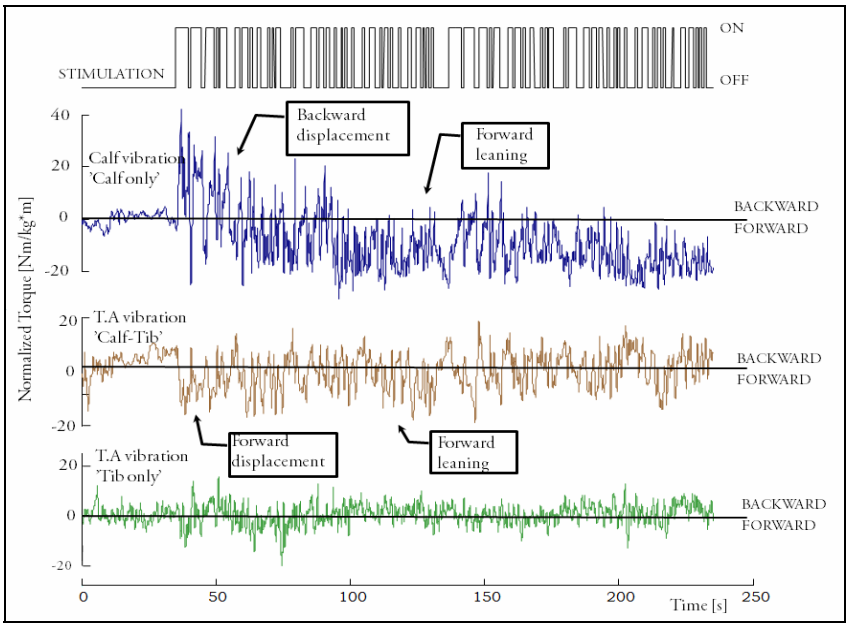


Figure 7 Normalized torque during the 1st day. Note the difference in amount of induced torque and the different body adjustments 'leaning' between 'Calf-Tib' and 'Tib only'.

THE EFFECT OF DIFFERENT CENTRAL NERVOUS PLASTICITY ON CONSOLIDATION AND HABITUATION (PAPER V)

Subjects: A child group consisting of 7 female and 6 male subjects with the following age-distribution: four 9 years old, two 8 years old, and seven 7 years old, and an adult group consisting of 6 male and 6 female subjects, age range 15-32 years were recruited.

Study design: Vibratory posturography performed daily on 5 consecutive days and once more after 3 months, in two randomized test conditions; eyes open and eyes closed.

Results: The children did not reduce their torque variance during each test as the adults did (figure 8). The statistics revealed similar significant decrease of induced torque variance between tests in both groups regardless visual condition ($p<0.001$), though with larger slope coefficients in the children group, indicating a larger reduction of torque. In the children group the mean of elicited torque on the 2nd day was on a much lower level than they finished on day 1, in contrast to the adults. The children seemed to have adapted the most between the 1st and 2nd day, and further training hardly decreased the amount of induced torque variance.

The adults responded to the vibratory perturbation with a forward leaning (figure 9), presumably a better position to withstand the perturbation. No homogeneous strategy to withstand the perturbation could be discerned in the children group, when studying the raw data.

Conclusion: Children have more efficient or stronger postural consolidation processes, which can be attributed to the difference in central nervous plasticity or the nature of the children to learn through exploring the task at hand.

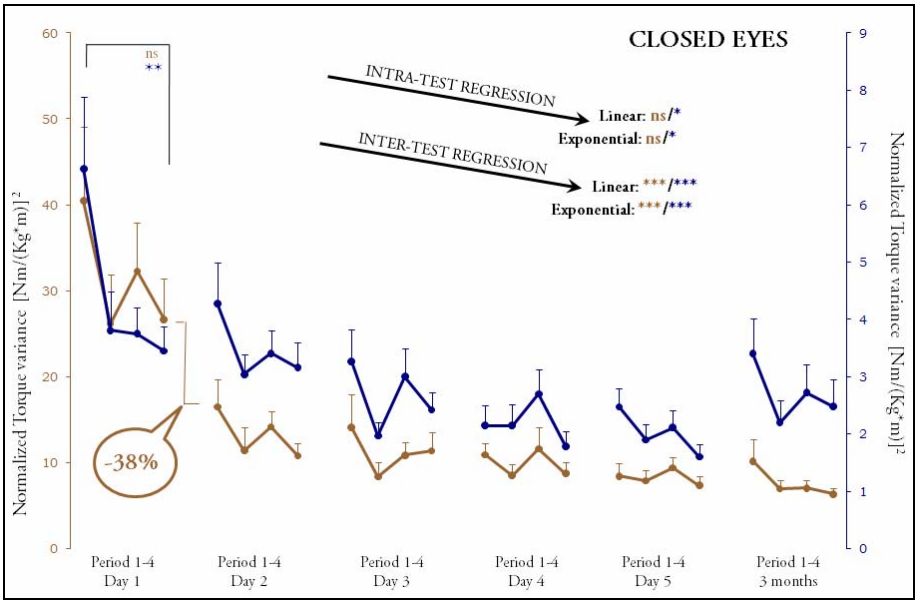


Figure 8. Total anteroposterior torque variance (mean and standard error of mean) for children (left y-axis) and adults (right y-axis). Note the lack of torque reduction in the children group. Note also the first period on day 2 compared to the last period on day 1. Regression statistics are presented at the top of the figure
* p< 0.05, ** p< 0.01 *** p< 0.001.

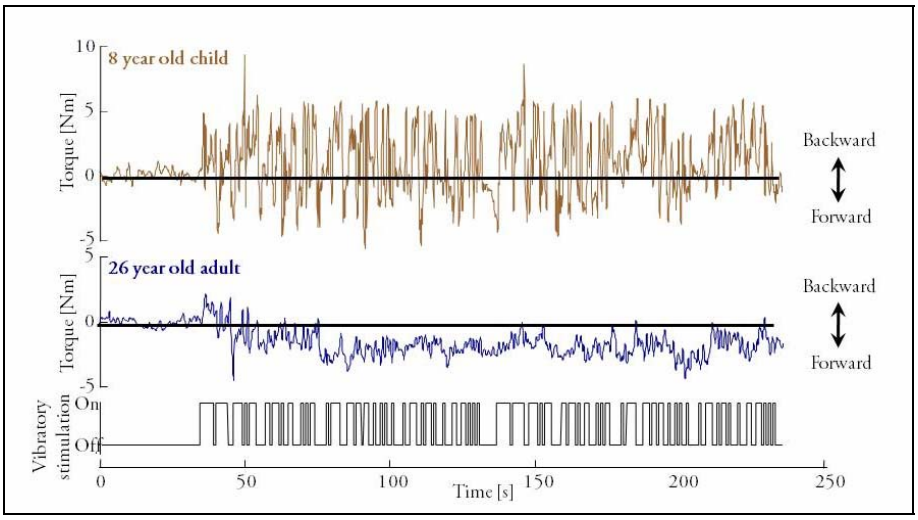


Figure 9. Raw data of torque during one measurement. Note the forward leaning of the adult vs. the non-leaning of the 8-year old child as well as the no apparent reduction of torque over time.

THE IMPACT OF ANXIETY ON THE ADAPTATION PROCESS (PAPER VI)

Subjects: 39 consecutive patients suffering from Postural Phobic Vertigo (PPV) (17 men and 22 women, mean age 49 years) and 24 healthy subjects (14 men, 10 women, mean age 38 years).

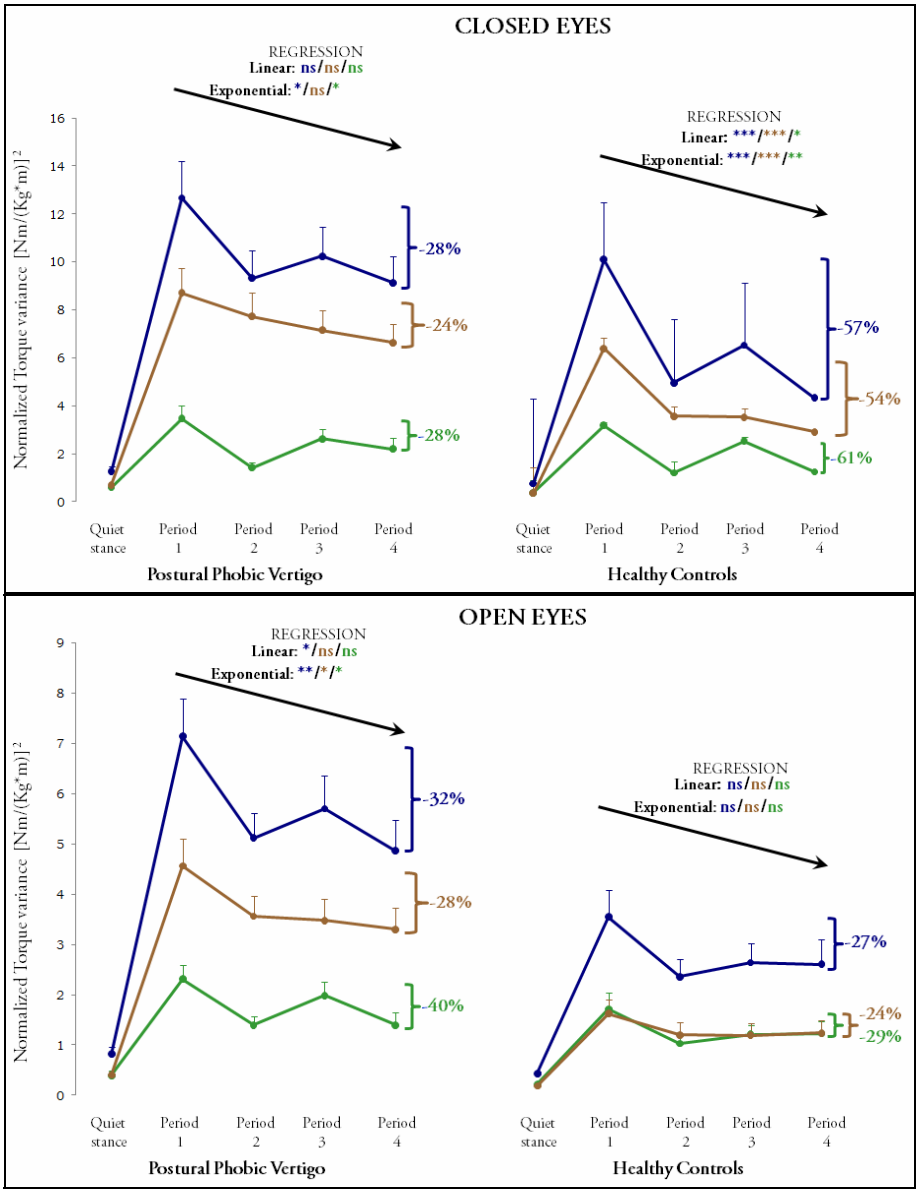
Study design: Vibratory proprioceptive stimulation during two visual conditions (eyes open/closed).

Results: *Closed eyes:* The perturbation induced increased torque variance in both groups to the same levels (table 1 and figure 10), but the PPV patients did not decrease their sway as much as the controls did. *Open eyes:* The induced torque variance was greater in the PPV group than controls ($p<0.001$). There was no decrease of torque variance as the test progressed in the control group, but significant reductions in the PPV group.

Test Condition	Stimulation Period	Total	>0.1 Hz	<0.1 Hz
Closed Eyes	Period 1	ns	$p<0.05$	ns
	Period 4	$p<0.001$	$p<0.001$	ns
Open Eyes	Period 1	$p<0.001$	$p<0.001$	ns
	Period 4	$p<0.01$	$p<0.001$	ns

Table 1. Differences in torque variance between PPV patients and healthy controls in the different perturbation periods. Note that the difference between the groups in torque variance increases as the test progresses during closed eyes (total and >0.1Hz), and decreases when the eyes were open (total).

Conclusion: PPV patients adapt to proprioceptive perturbation to a lesser extent than normal subjects and PPV patients do not use visual information as efficiently to modulate postural control. The mal-adaptive behaviour of the PPV patients could reflect a general anxiety of not maintaining perfect postural control and thus the PPV patients do not instigate a normal adaptation process to the perturbing stimuli.



Total torque variance, > 0.1 Hz, < 0.1 Hz

Figure 10. Anteroposterior torque variance (mean and standard error of mean) recorded on a PPV population and healthy controls. Note the differences in torque reduction depending on group and visual condition.
Regression statistics are presented at the top of the figure.
* p< 0.05, ** p< 0.01 *** p< 0.001.

THE EFFECT ON POSTURAL CONTROL BY TREATMENT WITH GENTAMICIN AND VESTIBULAR 'PREHAB' PRIOR TO SURGERY OF VESTIBULAR SCHWANNOMA (PAPER VII)

Subjects: 42 patients scheduled for trans-labyrinthine schwannoma surgery divided into 4 groups depending on the vestibular activity before surgery as described in figure 11.

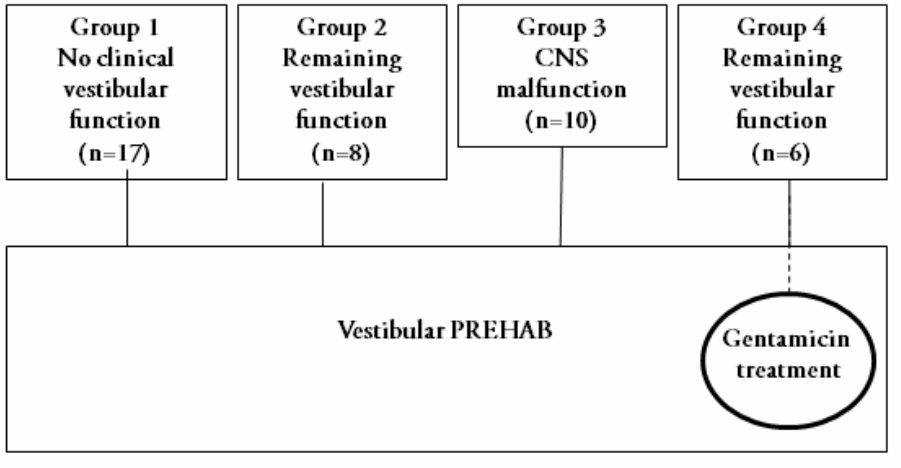
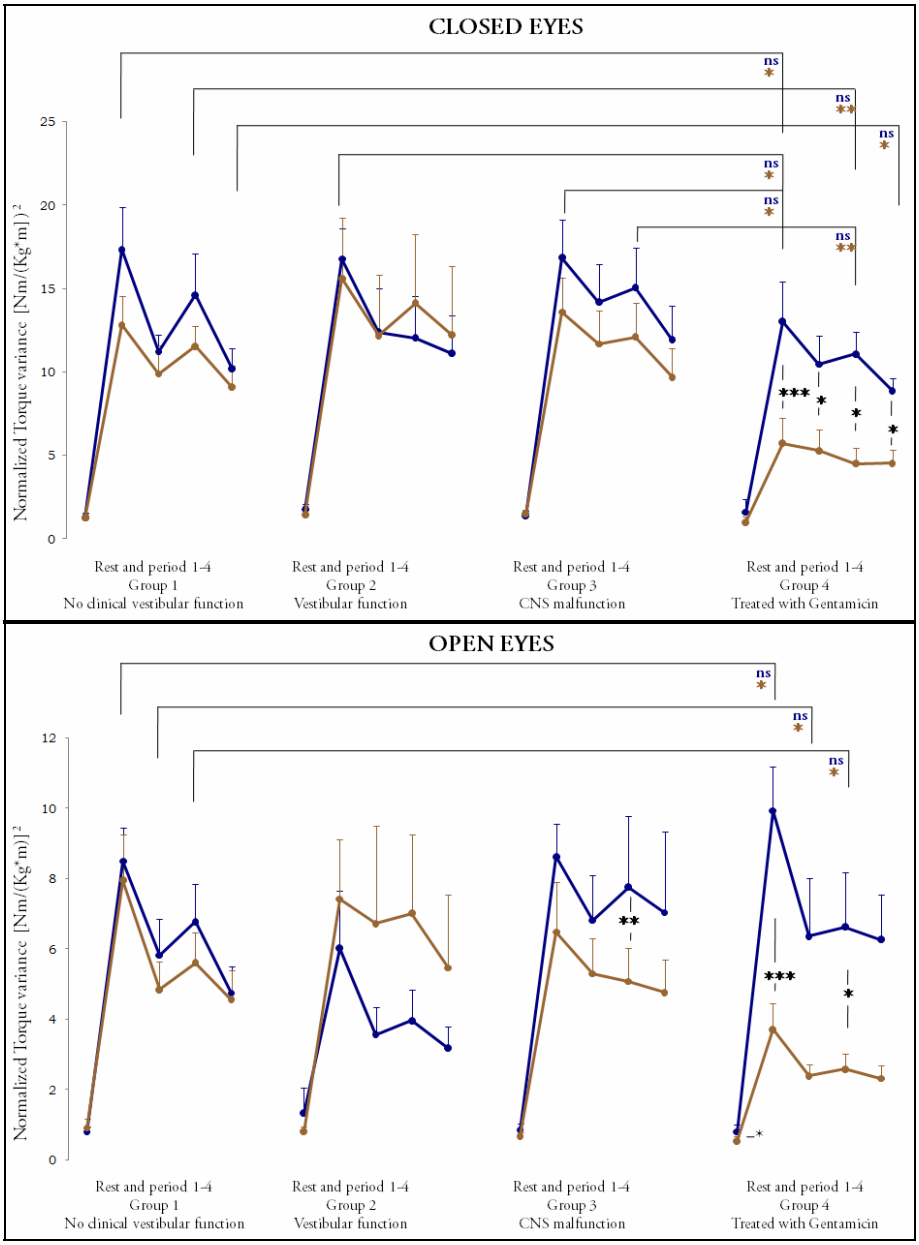


Figure 11. Division of patients scheduled for trans-labyrinthine schwannoma surgery.

Study design: Vibratory proprioceptive stimulation during two visual conditions (eyes open/closed). One test was performed before surgery and another performed at a follow-up 6 months after surgery. All patients received instructions to perform vestibular training (see appendix 1) before and after surgery, and the patients receiving gentamicin were instructed to execute the training before and after the medical vestibular ablation.

Results: The subjects pre-treated with gentamicin had significantly less induced torque variance at the follow-up in both test conditions, both compared to the preoperative recordings and to the other groups after surgery (fig X). The other groups did not reduce their torque to the 6 month follow-up (except the group with central signs, 3rd period open eyes).

Conclusion: It is conceivable that adaptation processes, essential for coping with altered sensory information and resolving arising sensory conflicts, are impeded by performing both sensory deafferentation and major surgery at the same time. Pre-treatment such as extensive vestibular training and the separation of sensory ablation from surgery seem to be of benefit for the patients. Furthermore the sensory training (vestibular 'PREHAB') performed during gradual sensory decline induced by gentamicin, seemed to benefit the ability to resolve later sensory conflicts and withstand somatosensory perturbations.



BEFORE SURGERY, AT 6-MONTH FOLLOW UP AFTER SURGERY

Figure 12 Anteroposterior torque variance (mean and standard error of mean) recorded while perturbed with vibratory proprioceptive stimulation. Note the lower level of induced torque variance in the group that was treated with gentamicin
* p< 0.05, ** p< 0.01 *** p< 0.001.

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GENERAL DISCUSSION

---------- METHODOLOGICAL CONSIDERATIONS

POSTUROGRAPHY

Posturography has been used in both research and clinical contexts. Although induced perturbations are artificial (not necessarily corresponding to natural postural control), they still require the different sensory systems to interact and induce central nervous processes.

All subjects and patients received the same instructions: 'to stand erect but not at attention', except for the children who were allowed to hold the vibrators in their hands prior the first posturography, in order to reduce startle responses. The instructions may theoretically influence the postural performance; however studies measuring posture with different instructions could not find any effect[197].

Postural sway was evaluated with calculated torque variance and correlates to the actual postural adjustments in all body segments to a high degree, elucidated by a concomitant 3D-analysis of postural sway[224].

LEARNING TASKS

The task during the tests in this thesis could be defined as maintaining postural control during sensory perturbations and resolving the corresponding sensory conflict. As torque variance gives an appreciation of the energy that is spent[219, 225], it would seem plausible that a task is handled with more ease if less energy is spent both during and between the tests, and as such corresponds to task-learning.

An obvious goal in perturbation studies is for the subjects to realize on a sub-conscious level that the perturbing stimuli only yield an illusion of movement[195, 200, 215], and reduce the relative importance of this erroneous sensory information.

ANXIETY AND PHOBIC POSTURAL VERTIGO

Anxiety was not quantitatively documented at the time of the measurement in the group that suffered from PPV. However it can be stated, for good reasons, that PPV patients in general suffer from anxiety or anxiety correlated stigmata. The diagnosis includes a medical evaluation comprising assessment of anxiety and dizziness. The anxiety levels and handicap due to dizziness that PPV patients experience have been reported by Holmberg et al.[226] and they score higher on anxiety questionnaires than other patients referred to our clinic on cause of dizziness. It has also been established that, although not all patients present symptoms of anxiety, most patients develop a phobic-avoidance pattern[227]. It can thus be stated that our PPV population can be regarded to have an anxiety-related disorder.

REPEATED MEASUREMENTS AND 'PREHAB'

The 6 patients receiving gentamicin before surgery were subjected to more posturography measurements due to clinical evaluation of treatment efficacy. It is possible that a major part of the performance differences between the groups was caused by the number of executed tests. This assumption would however also favour a consecutive improvement between the tests (similar as in I and III), which does not seem to occur (see figure 3 in paper VII).

SENSORY REWEIGHTING

One possible way to cope with postural perturbations is to change the relative importance of the sensory systems to the ones perceived to be reliable.

The repeated galvanic vestibular perturbation in ***study II*** failed to induce higher torque levels compared to quiet stance toward the end of the 5 days as well as after 3 months. This indicates that by repeating the vestibular stimulation it becomes ignored by the postural control system – i.e. a sensory reweighting.

Furthermore, the responses to galvanic perturbation were reduced as soon as the first 50s on the 1st day, after which further exposure to this perturbation did not result in further reduction of torque variance. This could reflect a fast reweighting to ignore the unreliable vestibular information.

INTERNAL MODELS

Another way to cope with a postural perturbation is to initiate a different automatic program or internal model. When exposed to antagonistic postural perturbation in ***study IV,*** it was obvious that the experience from previous calf vibration induced different responses when Tibialis anterior was vibrated. Both the amplitude of responses and adjustments of body position (figure 6 and 7) differed in comparison to the other groups. This indicates that a preformed automatic program[12] was initiated at the start of Tibialis Anterior vibration, presumably induced by the previous calf vibration – i.e. an internal model.

The higher amplitude of torque variance corresponds to other studies when responses were scaled to the preceding amplitude[18]. The preformed responses have been reported to decrease as the test progresses, related to learning from feed-back information. However, in study IV the responses of greater magnitude and leaning did not decrease to the same levels as the other two groups, which would be the obvious way of dealing with Tibialis Anterior vibration. This could be due to the non-predictable pattern of the pseudo-randomized stimulation pulses as opposed to other studies where the stimulation was constant[18].

Another plausible explanation could be that the internal model or strategy developed by the control system during posterior calf vibration, consisted of sensory reweighting, where the control system relies more on vestibular and other somatosensory cues. This suggests that the feed-back loop conveying sensory information from the vibrated muscle was ignored or at least initially suppressed from the beginning of the stimulation, which corresponds to the hypothesis underlying sensory reweighting processes, in this case instigated by experiencing posterior calf vibration previously.

SENSORY CONTEXT SPECIFICITY

The postural responses when subjected to a perturbation depend on the available sensory systems. It is possible that the experience from performing a postural task in one set of sensory condition e.g. eyes open is transferred to another sensory condition, i.e. eyes closed. The results from such recordings in ***study I*** however do not corroborate this theory. The responses to the perturbation in either visual condition were unaffected whether or not the test had previously been performed in the other visual condition. This implies that the postural responses are specific to the sensory context.

This finding does not correspond to the report by Perrin et al[228] , where the subjects in closed eyes conditions appeared to benefit from previous posturography tests with their eyes open. In contrast to Perrin, we applied external sensory disturbance to cause

perturbations, and the order of eyes open and eyes closed test was randomized.

Furthermore, the significant differences in body sway during eyes open and eyes closed test remained with few exceptions throughout all test days and test periods. This suggests that adaptive processes are context-dependent (i.e. specific for the sensory systems that are stimulated/available)[229], and that postural control is not fully able to benefit from the extra afferent information provided by the visual input.

SENSORY TRAINING IN SPECIFIC CONTEXT

The importance of training in a proper functional sensory context is demonstrated in ***study VII***. The abrupt deafferentation that schwannoma surgery normally results in, rendered less capacity to resolve a conflicting sensory task, such as vibratory posturography, than the group that received a gradual deafferentation due to gentamicin treatment.

The 'vestibular 'PREHAB' regime aims to initiate motor learning at a cellular level before the lesion has become manifest[230, 231], in line with plasticity mechanisms active in cerebellar and hippocampal adaptation[232, 233]. This enabled the postural control system to gradually adapt and build new internal models and internal representation of the importance of the individual sensory systems.

The greater ability to withstand a postural perturbation in gradual deafferentation could also be due to the separation of the surgical and the sensory trauma. It has been shown that even minor surgery interferes with hippocampal function in aged rodents[234]. The cognitive functions and memory function in particular are impaired after surgery[235, 236]. Furthermore, the loss of vestibular input affects hippocampal function and integrity[237, 238]. Hypothetically it is thus not improbable that the trans-labyrinthine surgical trauma in addition to an impaired hippocampal function delays central neural adaptive processing.

---------- SHORT AND LONG-TERM ADAPTATION

The adaptation to perturbing stimuli, at least for vibratory calf stimulation, followed two separate processes, the first being a decrease in stimuli response during active exposure, i.e. *short-term adaptation* (I, III, IV), and the second a further reduction between the test-days, i.e. *long-term adaptation* (I-V). It would be valid to claim that these responses parallel to what is generally regarded as the paradigm of memory formation, i.e. consolidation of short-term into long-term memories. It is plausible that the reduction in energy-expenditure was based on previous experience, driving refinements of strategies to maintain balance and withstand the perturbations. This part of the postural adaptation process could be defined as "consolidation", since postural strategies and motor responses were further improved on a day to day basis[155, 239]. These results are in sharp contrast to previous notions that there is no learning between repeated posturographic tests and great test-retest reliability[197, 240].

PERTURBING THE VESTIBULAR VERSUS THE SOMATOSENSORY SYSTEM

The nature of the perturbation had impact on the changes of induced torque variance within each test. The vibratory somatosensory stimulation (***study I)*** resulted in significant reduction of torque variance during each test. The same reduction was not induced when galvanic vestibular stimulation was applied (***study II***). Only on the 1st day a reduction of torque could be discerned during galvanic

stimulation.
The difference in adaptive responses between the different stimuli could be due to a greater sensory mismatch caused by the galvanic vestibular stimulation. 3 subjects discontinued the galvanic study compared to none in the somatosensory study, despite that vibration induced torque variance levels close to 10 times that of galvanic stimulation. Galvanic stimulation induces a sensory mismatch between vestibular and visual cues [245] and perhaps also otolith canal mismatch [246]. This could lead to motion sickness, which in turn, is well known to reduce alertness also when there are no overt symptoms[247]. Reduced alertness per se may affect postural control as may the sensory mismatch[218]. This may explain the apparent lack of adaptation of postural responses during galvanic perturbations.
Although the natures of the stimuli are different, they carry the same necessity for adaptation and habituation in processes such as reweighting of sensory information. These processes possibly take place in the same central neural circuits for both stimuli. The reason why the responses are different could be discrepancies in the processing of sensory information itself, and/or differences in stimuli pathways. One may speculate that vestibular information is of such importance, from an evolutionary perspective, that no further depression is allowed, and that we only see the initial part of the adaptive process, which might be an immediate sensory reweighting.

COGNITIVE INFLUENCE ON SHORT TERM ADAPTATION

Patients in ***study VI*** diagnosed with Phobic Postural Vertigo (PPV) differed in adaptation patterns compared to healthy controls in two ways. The first was a decreased adaptation to the perturbing stimuli when the eyes were closed, and the second a greater adaptation when the eyes were open.
The PPV patients appear to select an inefficient postural strategy or internal model to withstand the perturbation. The adaptive process seems also to be inefficient, since they did not abandon their elevated high-frequency content of postural corrections (figure 10) toward the end of the test. Both these responses could be ascribed to misinterpretation of sensory cues, and as such an anxious control of posture[186].

Adaptation of postural control has not been studied on a PPV population before and neither on an 'anxious' population. However, anxiety and adaptation to visuo-vestibular mismatch has been studied, with the result that anxiety induced greater adaptation[248]. The less adaptation exhibited by the PPV patients during closed eyes does not correspond to those findings, but the results are not comparable since there were fundamental differences in the tests set-up[248]. The possible consequences of the perturbations were diverse since, in the previous study the subjects were sitting, vs. standing in our study. Since it is primarily the patients' perception of their own postural performance that induces their symptoms, anxiety related postural adaptation needs to be studied and executed in tasks that involve maintenance of postural control in stance.

The greater torque variance in the PPV population with eyes open corresponds to observations that anxiety diminishes the attention to external surroundings and targets for orientation[249] (egocentric strategy[250]) and that PPV patients do not transform visual cues to specific postural strategies[186]. If the postural control in PPV is egocentric, and external cues induce increased postural sway, then the higher degree of reduction of induced torque during eyes open (figure 10) could be due to a greater sensory mismatch, which constitutes a stronger incentive for adaptation.

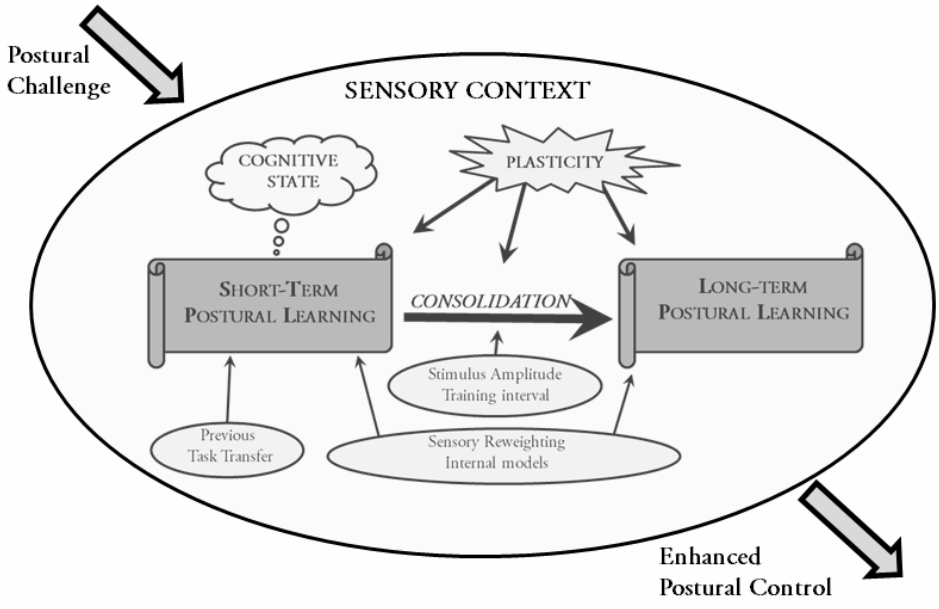

Figure 13. Paradigm for postural control learning and factors affecting the adaptation processes elucidated by the present thesis.
Adaptation could act on several different aspects, sensory perception, integration and neuromuscular output, and the availability as well as perception of 'own movement' are important parameters to the process. In a postural context, proving and modelling adaptation processes separated in time and formation of internal models are novel findings. As to where, within the central nervous system, the process of postural adaptation occurs, is not elucidated by the present thesis. It seems plausible, though, that the cerebellum, motor cortex and basal ganglia are involved in the process[15, 16, 241-244].

STIMULUS AMPLITUDE

The amplitude of the perturbing stimulation or the level of difficulty had a great impact on adaptive responses. Quiet stance alone did not yield any adaptation between consecutive days in either vibratory proprioceptive or galvanic vestibular perturbation (***study I-V)***. This is well in line with the notion of test to test reliability in posturography[197, 240].

When exposed to antagonistic postural perturbation (***study IV***), no adaptive responses from day to day could be discerned when Tibialis Anterior was stimulated. This could be interpreted as vibration to that muscle does not constitute a sufficiently difficult perturbation of postural control in order to necessitate long-term adaptation (between the days). This is well in line with the existing theories on memory processing, since it is generally believed that the stimulus (or learning) is required to be of sufficiently large amplitude to induce alterations at synapses held to be involved in consolidation processes[145].

Furthermore, it correlates well with what has been demonstrated in studies on learning ability, where more challenging tasks yield improved learning performances [168].

However, adaptation to galvanic stimulation ***(study II)*** did not yield significant short-term differences but highly significant day to day reductions of torque. This contrasts to *study IV*, where the opposite was true when Tibialis Anterior was vibrated. Three of the subjects discontinued the galvanic study which is virtually unknown when the somatosensory system is perturbed, and it is probable that galvanic stimulation adds one or more factors facilitating long-term adaptation, and such a factor could be discomfort which would yield a stimulation not necessarily possible to measure on a force-platform

CONSOLIDATION PROCESS IN POSTURAL LEARNING

The manner of how the responses were reduced between the different test-days in ***study I-V*** and was preserved over 3 months (***I-III, V***) argues that adaptation processes to postural perturbations takes place also after exposure to the stimulation – similar to the concept of the consolidation process involved in motor learning [135, 140]. Indirect evidence of the existence of a consolidating process involved in posturography with somatosensory perturbation is the better retrieval of the performance after 3 months when the intervals between the training sessions were 3 hours or more (***III***). This corresponds to similar motor learning with different training sessions where intervals of more than 3 hours resulted in improved outcome[150, 155], suggesting that neural interactions and events specific for consolidation have had ample time to be processed[151, 154]. However, most of the effect on habituation was due to the number of performed tests. This suggests either that consolidation in this context appears to be time-independent, or that the vibratory stimulus used is sufficiently strong to induce fast consolidation[140, 156, 157].

In ***study IV*** we introduced 2 antagonistic postural tasks – posterior calf and anterior leg vibration. One of the hypotheses was that the adaptation (as recorded as reduction of torque variance) would be disrupted from day to day, similar to other motor task training[150, 155]. Our two stimuli proved to yield different amplitude of torque variance and as such of different difficulty. Only posterior calf vibration yielded reductions to the 2nd day but that was seemingly not affected by performing an antagonistic task immediately before or after (figure 6 and 7). One explanation why postural learning differs from other types of motor learning could be that the adaptation involved in maintaining balance is so vital in coping with postural threats, that an unlearning would be unfavourable from a evolutional perspective[161].

PLASTICITY IN CONSOLIDATION

Children adapted to vibratory stimulation very differently compared to adults (***study V***), both during each test and between consecutive days. The major torque reduction took place between the 1st and 2nd day of the trials, which could be interpreted as a stronger or more efficient consolidation process. This could be an effect of the higher degree of neural plasticity that is generally held to exist in younger persons[166, 167, 251].

It could also be attributed to the concept of 'exploratory learning' [129, 252], which hypothesizes that children learn during play and subsequently explore the learning task itself. In our postural setting this would correspond to figure 9, where no apparent strategy to withstand the perturbation was present in children, whereas adults leaned forward. This could be interpreted as if the children tested and explored the stimuli in order to learn as much as possible. The adults seemed to promptly decide how to cope with the perturbations. The contrasts are obvious - stimuli testing enhancing feed-back control vs. limiting through a specific strategy, i.e. feed forward. The same observations have been made when assessing posture in both adults and infants under weight-loading; adults leaned in the opposite direction to the load, while the children leaned with the load[253]. These observations suggest that children have a flexible approach to deal

with new postural challenges, in contrast to previous findings where children are reported to exhibit a fixed control system parallel to that of elderly[53]. This is also corroborated by the fact that children find multiple and variable ways to move over challenging obstacles in their path, rather than a single fixed approach, considering the everyday environment as a playground, filled with possibilities for exploration and amusement[129].

Seemingly children's plasticity or the possible exploratory behaviour has not been taken into account in studies designed to assess postural control maturity and sensory weighting. Some have observed that children respond stronger than adults to whatever perturbation they are subjected to[113], but it has not been considered that these 'immature' responses might be natural inherent ways to deal with novel situations[129]. Our observations suggest that a reappraisal may be warranted of the general view of how children integrate and weight sensory information at different ages.

---------- CLINICAL IMPLICATIONS

The present thesis supports some specific features involved in rehabilitation:

Spaced training Studies I-IV indicate that the learning processes become more stable and long-lasting if conducted repeatedly, and especially so with intervals of 3 hours or more (III). Spaced training seems to be especially important when suffering and rehabilitating from a vestibular deficit (II). It is also important to separate rehabilitation exercises of different intensity to avoid development of inappropriate postural strategies (IV).

Customize rehabilitation Factors like cognitive function and age are important in adaptation processes, which should be taken into account when designing rehabilitation programs. Although vertigo is rare among children, postural problems are more common due to cerebral lesions and developmental disorders[254]. Postural deficiencies might also result from chronic otitis media (fluid in the middle-ear)[255, 256], and, though the impairment is effectively resolved by middle-ear drainage, the children might suffer from sequelae[257] that could be ameliorated by sensory training. To individually tailor postural rehabilitation has shown positive results in a fall-preventive effort conducted on elderly[258], which could be extended to any person suffering from dizziness. However, custom made and perhaps more difficult programs need to be weighed against the efficacy of simplistic and easily available approaches.

Encourage 'plastic exploratory' learning The postural learning of children seems to consist of exploring rather than limiting available strategies. This also led to improved learning, and it is conceivable that rehabilitation training could be improved if playful circumstances were to be introduced. In fact driving plasticity to challenging situations can promote learning[168], although it may be important that circumstances for training are safe.

Aspects on anxious rehabilitation The mal-adaptation found in PPV patients could be an important trait regarding treatment outcome. Theories regarding an optimal treatment have been put forward combining medical and psychological treatment[259, 260] since at least the cognitive treatment alone has been shown to have doubtful long term effects, if not repeated, on the experienced symptoms of PPV patients[260].

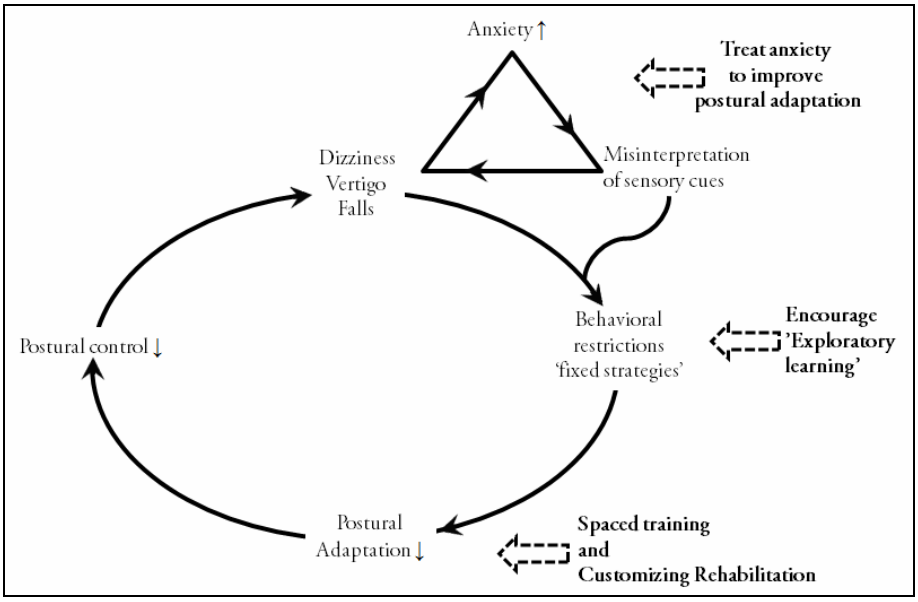

Figure 14 Possible mechanisms from a postural control aspect for 'the vicious cycle' involved in impaired postural control and subsequent falls, as well as reduced independence when suffering from dizziness. Possible targets for improving postural performance elucidated by the present thesis in bold.

Alleviating anxiety symptoms medically could result in an improved learning effect of postural control and thereby impact of cognitive treatment. The cognitive behavioural treatment focusing on knowledge of the mechanisms underlying postural control and methods how to cope with situations perceived as difficult, might be too blunt to induce an adaptive behaviour on its own. The discrepancies between the adaptive responses during the different test-conditions in study VI are interesting. When visual cues were available, more adaptation of postural responses was observed. This could also be rephrased as if increased attention to allocentric cues (outside the own body) affected the inappropriate egocentric view of own body movements, and it may be that rehabilitation of patients suffering from PPV should be exposed to more conflicting sensory stimuli to drive adaptation or plastic learning.

'PREHABITUATION'

It is demonstrated in ***study VII*** that the careful sensory training and the gradual sensory deafferentation, plus separating surgical from sensory trauma, have a huge impact on patients' ability to withstand a postural perturbation after schwannoma surgery. One interesting finding is that the group that was assessed prior to surgery to have no vestibular function left performed worse than the group that received gentamicin treatment. This difference could be due to a better compliance with the sensory exercises in the patients receiving gentamicin, since they visited our department on more occasions. It could also mean that the 'no function' group had vestibular function that was not assessed, although our investigation is thorough and examines both high and low frequency functions, as well as assessing all 5 senses of the vestibular system. These questions highlight the need to secure compliance with all patients for the training before schwannoma surgery and that a study should be executed treating all patients with gentamicin prior to translabyrinthine schwannoma surgery.

CONCLUSIONS

•Postural adaptation to vibratory proprioceptive stimulation occurs in two steps; one fast (during the test) and one slow (between the tests) and the learned reactions are consolidated to last 3 months. (**I**)

•Adaptation seems to be restricted to sensory context, and experience from one sensory condition is not necessarily transferable to another. (**I**)

•Postural adaptation to galvanic perturbation immediately adapts, after which further exposure yields no continued adaptation. By repeating the perturbation at another time however yields further adaptation and the learned reactions are consolidated to last 3 months (**II**)

•Spaced training with intervals >3 hours benefits long-term learning in postural control (**III**).

•Experiences or postural strategies can be transferred between postural challenges if they post different demands (**IV)**

•Children have more efficient or stronger postural consolidation processes, possibly attributed to the difference in central nervous plasticity or the nature of the children to learn through exploring the task at hand (**V**)

•Anxiety leads to a decreased ability to adapt postural control to vibratory proprioceptive stimulation (**VI**)

•Separating surgical trauma and sensory deafferentation in time + careful sensory training as the sensory system gradually attenuates can improve the outcome in postural control (**VII**)

POPULÄRVETENSKAPLIG SAMMANFATTNING
(SUMMARY IN SWEDISH)

Förmågan att hålla balansen är grundläggande för alla de aktiviteter som utgör en normal vardag. Oförmåga att hålla balansen kan få katastrofala följder. Enligt en rapport från Räddningsverket 2007, är dödsfall bland äldre orsakade av fallolyckor 10 gånger vanligare än de relaterade till trafikolyckor. Problem med att hålla balansen kan bero på sjukdomar, utvecklingsstörningar samt i en del fall även normalt åldrande. Förmågan att anpassa balanssystemet och fortlöpande skapa nya reaktionsmönster är därför närmast livsavgörande.

Balansfysiologin, dvs. att kunna hålla balansen är en komplext uppbyggd förmåga. Delvis består den i en återkoppling till hjärnan från balanssinnena som ger information om hur de olika kroppsdelarna rör sig i förhållande till varandra och till omgivningen. Våra olika balanssinnen består av synen, balansorganen i innerörat, led och muskelsinnet, samt tryckreceptorer i fotsulorna. Balansinformationen tolkas i hjärnan och ger upphov till nervsignaler till de olika muskler som behövs för att hålla balansen. Funktionen hos våra olika balanssinnen överlappar delvis varandra, vilket gör att en funktionsnedsättning eller förlust av ett känselsinne delvis kan hjälpas upp av de kvarvarande. Information från de olika balanssinnena ställs ständigt mot varandra och viktas efter vad som är viktigast för stunden. Till exempel har synen mindre betydelse när det är mörkt. Balansen är dessutom beroende av förmågan att medvetet eller undermedvetet kunna förutse de krav som aktiviteter eller omgivningen ställer på balansen. En del muskelprocedurer för att hålla balansen finns förprogrammerade i hjärnan, s.k. interna modeller, redo att aktiveras beroende på situation och behov.

Det är i stort okänt hur nya interna modeller bildas för att hantera olika balansstörningar. När det gäller inlärning av viljemässiga kroppsrörelser så har man visat att erfarenheter från ett träningstillfälle skapar minnen som sedan förstärks under vila och mellan upprepade träningstillfällen. Processen som sker under vila kallas konsolidering och involverar förändringar i engagemang och koppling mellan olika strukturer i hjärnan. Konsolidering leder till att rörelseprogram skapas och bevaras en längre tid – ett minne. Förmågan att cykla är ett utmärkt exempel på en intern modell, då kunnandet är en produkt av upprepad träning och kan utövas trots att många år kan ha förflutit sedan man sist satt på en cykel.

Hjärnan har stor förmåga att omorganisera sig efter behov. Skador i hjärnan eller nya inträngade beteenden leder till att områden av nervceller och deras förbindelser kan få förändrade arbetsuppgifter, s.k. plasticitet. Plasticitet är betydelsefullt för inlärning och rehabilitering, och traditionellt har man ansett att plasticitet är störst i barnaåren och avtar med stigande ålder. Alltmer pekar dock på att äldres mindre plastiska inlärning beror på att nervsystemet inte avsätter tillräcklig tid för att tolka information på ett korrekt sätt. Istället sker ett snabbt val av strategi som underlättar för stunden, men inte skapar någon ny inlärning. För balansinlärning skulle detta kunna innebära att balansinformationen inte tolkas eller undersöks. Istället väljs en strategi för att hålla balansen vilket förhoppningsvis minskar problemet för stunden men inte på längre sikt.

Om balanskontrollen påverkas av känslor såsom ångest och rädsla för att tappa balansen är begränsningen att inte känna av balansinformation potentiellt än mer uttalad. Känslan av ångest påverkar hur man tolkar olika sinnesintryck och när det gäller balanskontroll har man kunnat visa att patienter som lider av ångestrelaterad yrsel använder ofysiologiskt snabba kroppsrörelser för att korrigera balansen.

För att undersöka balansförmågan och förändringar av balanskontroll används en ståplatta (posturografi), som mäter de krafter mot underlaget - energimängden - som krävs för att hålla balansen. Balansen störs antingen genom vibration mot vaden *(delarbete I,III-VII),* vilket stör muskelsinnet och orsakar ett ökat kroppssvaj framåt och bakåt, eller genom att applicera en elektrisk ström riktad mot balanssinnet i innerörat *(delarbete II)* vilket ökar kroppssvajet i sidled. Inlärning eller anpassning av balanskontrollen definieras som betydliga minskningar av energiåtgång.

I *delarbete I* undersöktes om kort- respektive långtidsinlärning kunde dämpa den balansstörning som orsakas av vibrationsstimulering. Resultaten tyder på att inlärning sker i 2 steg; det första medan man utsätts för balansstörningen och det andra mellan testerna när det inte finns något aktivt stimuli. Denna 2-stegs inlärning överensstämmer väl med det generella paradigmet hur rörelseminnen bildas. Resultaten påverkades inte om testet först utfördes med öppna ögon före slutna ögon och tvärtom. Detta betyder att inlärning av balansprogram är specifik för de sinnen som är tillgängliga och inte enbart beroende av balansstörningens natur. Det inlärda reaktionsmönstret behölls vid kontroll efter 3 månader, vilket talar för att ett långtidsminne skapats.

I *delarbete II* undersöktes om kort- och långtidsinlärning kunde motverka störningar av balanssinnet i innerörat. Mycket av inlärningen skedde under de första 50 sekunderna. Efter detta tillförde ytterligare stimulering ingen mer inlärning under själva testen. Däremot ökade förmågan mellan testdagarna. Vidare tyder resultaten på att betydelsen av balansinformationen från innerörat minskade under de första 5 dagarna. Det inlärda reaktionsmönstret var detsamma vid kontroll efter 3 månader, vilket tyder på att ett långtidsminne skapats.

I *delarbete III* analyserades om längden på intervallet mellan olika stimuleringstillfällen påverkade den motoriska långtidsinlärningen. Inlärningseffekten var framför allt beroende av antalet genomförda tester. Om intervallen var 3 timmar eller längre mellan träningstillfällena var det inlärda reaktionsmönstret efter 3 månader bättre bibehållet.

Två olika läromoment anses kunna motverka varandra vilket undersöktes i *delarbete IV*. Om man utsätts för en kraftig störning av balansen före en lättare balansstörning påverkas reaktionsmönstret vid den lättare balansstörningen. Med andra ord återanvänds samma reaktionsmönster eller interna modell, som bildats vid den svårare balansstörningen. Inlärda automatiska program verkar således till viss del vara överordnade återkoppling av känselinformation. Dessutom visades att balansstörningen behöver vara tillräckligt svår att klara av för att reaktionsmönstret ska konsolideras till nästa gång man utsätts för samma störning.

I *delarbete V* studerades inlärningsmönstret hos barn (7-9 åringar) och vuxna. Barnen hade inte någon specifik strategi för att hantera balansstörningen, medan de vuxna lutade sig framåt för att minska risken för fall. Barnen minskade sina reaktioner betydligt mer än de vuxna mellan 1:a och 2:a testtillfället. Skillnaden består således i att barnen tycks utforska balansstörningen (explorativt lärande) vid det första testtillfället, vilket resulterar i en mer effektiv inlärning. Detta stämmer väl överens med uppfattningen av och kunskapen om hur barn lär sig genom lek och genom att utforska olika möjligheter. Dessutom överensstämmer det med barns större förmåga att forma hjärnans funktioner – plasticitet.

Då ångest påverkar förmågan att hantera en balansstörning undersöktes i *delarbete IV* friska kontrollpersoner och patienter med diagnosen fobisk postural vertigo - en yrselsjukdom med stark koppling till ångest och paniksyndrom. Förutom att ha mycket

mer kroppssvaj så lärde var patienterna sämre på att lära sig hantera balansstörningen. När testet genomfördes med öppna ögon minskade patienterna däremot sitt kroppssvaj mer än kontrollerna. Detta kan bero på att synen medförde en ytterligare stimulering för patienterna och således en svårare balansövning som de tvingades att lära sig.

I *delarbete VII* studerades patienter som skulle opereras för en tumör på ena sidans balansnerv, vilket medför en samsidig förlust av innerörats balanssinne. Om funktionen av balanssinnet försvinner hastigt får patienter förutom akut yrsel och illamående dessutom problem med balansen. Denna förlust kompenseras genom att de kvarvarande sinnena tar över, vilket dock kan ta tid. Studier har dessutom visat att förlust av balanssinnet innebär att strukturer i hjärnan som är centrala för inlärningsprocesser (hippocampus) delvis minskar i storlek. Samma strukturer i hjärnan kan också övergående påverkas av kirurgi i sig, oavsett hur och vilken kroppsdel som opereras.
En del av patienterna med kvarvarande balansfunktion på tumörsidan förbehandlades med gentamicin, vilket slår ut det kvarvarande balanssinnet gradvis. Före operationen genomgick alla patienter ett fastställt övningsprogram, framtaget för att träna samspelet mellan synen och det kvarvarande balanssinnet i det andra innerörat.
Resultaten visade att de patienter som förbehandlats med gentamicin hade avsevärt mindre kroppssvaj 6 månader efter operationen jämfört med övriga patienter. Bakgrunden till den bättre förmågan kan vara en sinnesträning samtidigt som ena sidans balanssinne gradvis slås ut, eller att sinnesträning sker med funktionellt intakta hjärnstrukturer, viktiga för inlärningsprocesser.

Slutsatser
Sammanfattningsvis kan man hävda att skapande av balansminnen sker på delvis liknande sätt som för övriga minnen. En plastisk undersökande förhållning till en balanskrävande uppgift är positiv medan ångesttillstånd är negativt för inlärning. Inlärning är som mest effektiv om träningstillfällen sker med lämpligt långa intervall och om övningarna är tillräckligt svåra.
Praktiskt innebär resultaten att vi nu fått en vetenskaplig grund för hur balansrehabilitering bör utformas, och denna kunskap kan förhoppningsvis göra rehabiliteringen av balansstörningar mera effektiv. Rehabiliteringen bör ske som intervallträning (framför allt vid störningar av balanssinnet i innerörat), och övningarna bör vara varierade och med hög svårighetsgrad samt anpassade efter individuella förutsättningar såsom ålder och eventuella ångesttillstånd. Förhoppningsvis kan denna kunskap minska såväl yrsel som fallskador orsakade av balansstörningar. Genom förbehandling av patienter som skulle opereras för tumörer på balansnerven och lillhjärna (meningeom) implementerades kunskapen om utformning av balansminnen, vilket ledde till bestående minskad postoperativ balansstörning.

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APPENDIX 1: Criteria for Phobic Postural Vertigo

1. Dizziness and subjective disturbance of balance while standing or walking despite normal clinical balance tests such as Romberg, tandem walking, balancing on one foot and routine posturography

2. Fluctuating unsteadiness in episodes lasting seconds to minutes or momentary perceptions of illusory body perturbations

3. Although the attacks can occur spontaneously, there is usually a perceptual stimulus (bridge, staircase, empty room, street) or social situation (department store, restaurant, concert, crowd) from which the patients have difficulty withdrawing and they recognize as a provoking factor. There is a tendency for rapid conditioning, generalization and avoidance behavior to develop.

4. Anxiety and distressing vegetative symptoms occur during or after vertigo. Most patients have attacks both with and without anxiety

5. Obsessive-compulsive type personality, labile affect, mild depression

6. Onset of condition frequently follows a period of particular emotional stress, after a serious illness or following an organic vestibular disorder.

APPENDIX 2: Vestibular sensory training PREHAB'

Note! You will experience some dizziness when you do the exercises!

daily3 times

A home-based training program for *Dizziness*

1. Sit down, Fixate on an object 1,5 - 2 m away. Shake your head horizontally from side to side - still fixeating the object. Repeat twice a second for 15 seconds. Count one-thousand-one; one-thousand-two ...one-thousend -fifteen to keep pace and time.

2. Stand up and put a finger on a stabile onject (chair/table), Fixate on an object 1,5 - 2 m away. Shake your head horizontally from side to side - still fixeating the object. Repeat twice a second for 15 seconds. Count one-thousand-one; one-thousand-two ...one-thousend -fifteen to keep pace and time. .

3. Stand up with out support or touching any object, Fixate on an object 1,5 - 2 m away Shake your head horizontally from side to side - still fixeating the object fixate on an object 1,5 - 2 m away. Shake your head horizontally from side to side - still fixeating the object. Repeat twice a second for 15 seconds.

4. Stand up and close your eyes (with and then without support) .
Fixate on an object 1,5 - 2 m away. Shake your head horizontally from
side to side - still fixeating the object. Repeat twice a second for 15 seconds.

5. Stand up, fixate on an object 1,5 - 2 m away. Shake your head **vertically** from side to side - still fixeating the object. Repeat twice a second for 15 seconds.

6. Walk forwards fixate on an object 1,5 - 2 m away. Shake your
head horizontally from side to side - still fixating the object.
Repeat twice a second for 15 seconds.

7. Stand on a pillow from your coach in a corner of the room. Remain there fore *1 minute* then close your eyes and remain standing like this for another minute. If it is difficulte place a chair in front of you and initially you may put a fingertip on the chair.

8. Stand up holding a glass of water which is filled halfways again in a corner of the room. Remain there fore 1 minute than close your eyes and remain standing like this for another minute. If it is difficulte pu a chair in front of you and initially you may put a fingertip on the chair.

9. Take walk outdoor for at least 30 minutes. Try windowshopping which will have you turning your head from side to side when you walk.

How to execute the head movements:
Begin to smoothly shake your head. Increase the speed until vision gets blurred. Decrease speed to regain clear vision, then increase again. The idea is to push the limit were vision gets blurred.