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Research report

# Changes in cortical, cerebellar and basal ganglia representation after comprehensive long term unilateral hand motor training



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# HIGHLIGHTS

- Long term hand motor training and changes in performance and fMRI representation in healthy volunteers.
- Differential transfer of unilateral training performance gain for the non-trained hand.
- Differential increase in cerebellar-cortical and striatal-cortical loops during training of different tasks.

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## ABSTRACT

We were interested in motor performance gain after unilateral hand motor training and associated changes of cerebral and cerebellar movement representation tested with functional magnetic resonance imaging (fMRI) before and after training. Therefore, we trained the left hand of strongly right-handed healthy participants with a comprehensive training (arm ability training, AAT) over two weeks. Motor performance was tested for the trained and non-trained hand before and after the training period. Functional imaging was performed for the trained and the non-trained hand separately and comprised force modulation with the fist, sequential finger movements and a fast writing task. After the training period the performance gain of tapping movements was comparable for both hand sides, whereas the motor performance for writing showed a higher training effect for the trained hand. fMRI showed a reduction of activation in supplementary motor, dorsolateral prefrontal cortex, parietal cortical areas and lateral cerebellar areas during sequential finger movements over time. During left hand writing lateral cerebellar hemisphere also showed reduced activation, while activation magnitude was a predictive value for high training outcome of finger tapping and visual guided movements. During the force modulation task we found increased activation in the striate.

Overall, a comprehensive long-term training of the less skillful hand in healthy participants resulted in relevant motor performance improvements, as well as an intermanual learning transfer differently pronounced for the type of movement tested. Whereas cortical motor area activation decreased over time, cerebellar anterior hemisphere and striatum activity seem to represent increasing resources after long-term motor training.

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# 1. Introduction

Most of motor training performed during life time can be classified as long-term training procedures. However, imaging studies investigating effects of long-term motor training are rare. Long-term motor training procedures are especially important for regaining motor skills after damage of the central nervous system. Knowledge about processes going on during long-term training in healthy individuals might help to understand changes in patients after brain damage.

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In general, motor skill learning is indicated by performance improvement of the sensorimotor system and changes in associated cerebral and cerebellar activation maps. With long-term practice performance becomes more precise and automatic including the suppression of associated movements of the other hand during unilateral movement execution [1]. Such behavioral modifications have been found to be reflected by structural and functional changes in the brain. Especially professional instrumentalists, who undergo extremely intensive long-term motor training, showed reduced functional representation sites for motor and sensorimotor processing in comparison to less trained subjects. During the performance of sequential finger movements this has been particularly evident for the ipsilateral primary motor cortex (iM1), ipsilateral primary somatosensory cortex (iS1), bilateral supplementary motor area (SMA), bilateral dorsal premotor cortex (dPMC), and bilateral superior parietal lobe (SPL) [2–5].

Decreased cognitive effort after long-term motor training results in a decreased activation magnitude in representation sites for processing (e.g. working memory [6]). The prefrontal cortex is involved during acquisition of new motor skills, but not during automated performance [7]. The lateral prefrontal cortex is involved in the support of cognitive control operations [8,9]. However, processing of cognitive aspects is not restricted on cortical areas, but is also seen in latero-posterior cerebellar hemispheres [10]. Other loops in the anterior-medial cerebellar hemisphere are associated with early motor learning, especially with sensorimotor integration [11]. In addition, automatization of movement performance is mirrored in changes of striatal activation [12]. Depending on the stage of motor skill acquisition several studies reported increased activation after finger sequence training in the basal ganglia [13,14], whereas others found a decrease in basal ganglia structures, such as the putamen (unilateral) and caudate (bilateral movements) during sequence learning over several days with 3 h of overall training time [9]. It has been suggested that the putamen and pallidum are primarily involved in performance of motor skills, whereas the caudate is involved in acquiring the motor sequence knowledge [15]. Using incidental learning, Grafton and colleagues described increases in putamen, but decreases in the caudate with skill development [16]. With respect to training of memory tasks a very detailed model integrating striatal activation increase has been proposed recently [17]. The complex changes in the interactions of motor areas during training have been integrated in different models. Doyon and colleagues [18] assumed a distinct contribution of the cortico-striatal and cortico-cerebellar systems to different motor skill learning phases in dependence on the type of learning, i.e. motor sequence learning or sensorimotor adaptation. Robertson suggested that both paradigms activate the striatum and cerebellum, but that sensorimotor paradigms are more dependent on cortical motor areas while motor sequence learning is more associated with prefrontal activation [12]. By applying a statistical metaanalysis approach it has been shown that activity in the basal ganglia and cerebellum might be more frequently associated with sensorimotor tasks, while activity in cortical structures (SMA, dPMC, SPL) and the thalamus seems to be stronger for serial response time tasks. Furthermore the left dorsal premotor cortex is suggested as a key structure in the network of brain areas that underlie motor learning [19].

Hikosaka and colleagues [20] developed a model of motor sequence learning based on behavioral and physiological experiments with monkeys and humans using sequential button-press tasks that require very limited sensorimotor feedback processing. They assume that during the course of sequential skill acquisition two representations of a motor sequence (spatial and motor) are acquired independently parallel by two sets of cortex-basal ganglia and cortex-cerebellum loop circuits. The authors hypothesize that the acquisition of an effector-unspecific representation in spatial coordinates is predominant in the early stage of learning. This early stage includes rapid changes in areas such as parietal and premotor cortical regions, the caudate, and associative cerebellar regions. In contrast, when the performance becomes automated after long-term practice, the procedure is thought to be acquired predominantly as an effector-specific sequence involving predominantly M1, dPMC, SMA, the putamen, and the cerebellum. In motor adaptation, the cortico-striatal-cerebellar systems contribute to motor learning in another manner than in sequential motor learning, namely with a predominant role of the cerebellum especially in the late phase of learning [18,21].

Motor skill learning involves an effector-dependent and an effector-independent component [22]. It does not only comprise acquisition of the trained motor patterns but also the ability to transfer what has been learned to new conditions [23]. Positive effects of a specific training have been demonstrated for healthy participants not only on the trained but also on the non-trained extremity [24–27] as well as for performing another not specifically trained motor task with the same extremity [28]. Furthermore, similar findings have also been reported after stroke resulting in mild arm paresis for learning transfer on non-trained tasks [29,30] as well as from the healthy to the paretic hand [31]. In fact, training time in a range of weeks to months is essential to understand the effects observed in motor rehabilitation.

Nevertheless imaging-studies investigating longer periods of motor training are rare. Therefore we applied a comprehensive long-term motor training (arm ability training, AAT [29,32]) for the non-dominant hand over two weeks to investigate behavioral and imaging effects for the trained and non-trained hand in healthy adults. We selected the non-dominant hand since we intended to apply a training procedure developed for stroke patients and longterm training of the dominant hand might show a ceiling effect. We were interested in (1) motor efficiency changes for the trained arm characterized by less cortical activation in association with increased performance, (2) intermanual learning transfer on the non-trained arm, and (3) cortical, striatal and cerebellar activity changes associated with these processes.

### 2. Materials and methods

### 2.1. Participants

Fifteen subjects (mean age  $\pm$  standard deviation:  $24 \pm 3.7$  years; 6 women) participated in this study. All were strongly right-handed (mean laterality quotient (LQ) in the Edinburgh Handedness Test [33]:  $93.53 \pm 5.5$ ; range: 88-100). All participants were healthy, without any neurologic or cardio-vascular disease and were not taking any regular medication. They were recruited by an announcement posted at the university. Full written consent was obtained from all participants in accordance to the Declaration of Helsinki. The study was approved by the ethics committee of the Medical Faculty, University of Greifswald.

# 2.2. Training

All participants underwent a two-week arm ability training (AAT) for their left, nondominant hand for one hour per day (11 training days). The AAT had previously been developed for patients after cerebral damage such as stroke [32]. It consists of eight motor tasks: aiming (Ai), tapping (Ta), crossing circles (Cr), turning coins (Tu), labyrinth (La), bolts and nuts (Bo), placing small objects (Ps), placing large objects (Pl)[32]. The AAT targets different sensorimotor abilities such as aiming (i.e. ability to perform quick goal-orientated movements), arm-hand steadiness (i.e. ability to make

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