Mode of hand training determines cortical reorganisation: A randomized controlled study in healthy adults

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Objective: To evaluate two commonly used forms of hand training with respect to influence on dexterity and cortical reorganization.

Subjects: Thirty healthy volunteers (mean age 24.2 years).

Methods: The subjects were randomized to 25 min of shaping exercises or general activity training of the non-dominant hand. The dexterity and the cortical motor maps (number of excitatory positions) of the abductor pollicis brevis muscle were evaluated pre- and post-training by the Purdue Peg Board test and transcranial magnetic stimulation, respectively.

Results: After shaping exercises the dexterity increased significantly ($p \leq 0.005$) for both hands, mostly so in the non-dominant hand. The cortical motor map of the abductor pollicis brevis muscle shifted forwardly into the pre-motor area without expanding. After general activity training, no significant improvements in dexterity were found for the non-dominant hand. The cortical motor map of the non-dominant abductor pollicis brevis muscle expanded significantly ($p = 0.03$) in the posterior (sensory) direction.

Conclusion: These results indicate that shaping exercises, but not general activity training, increase dexterity of the trained non-dominant hand in parallel with a shift of location of active transcranial magnetic stimulation positions. Shifts of active cortical areas might be important for the interpretation of brain plasticity in common behavioural tasks.

Key words: dexterity; hand training; healthy subjects; transcranial magnetic stimulation; plasticity; cortical shift.


INTRODUCTION

Reorganization of cortical areas of the adult human brain can occur short- and long-term after injuries, exercises, immobilization and sensory stimulation. Increased use/tactile stimulation of the hand in animals (1, 2) and humans (3–5), may enlarge and/or shift representational cortical areas, whereas long-lasting immobilization (6) or deprivation of sensory feedback (7) has been shown to decrease representational cortical areas. Neural plasticity can occur quickly, and simple repeated thumb movements may induce cortical representational changes and changes in motor performance after only 5–30 min of exercising (8, 9).

In patients, rehabilitation of the upper extremity after stroke can induce cortical reorganization in parallel with an improvement in motor function (10, 11), especially after a forced-use technique called constraint induced movement therapy (CIMT) (12), in which the motor output area of the contralateral (injured) hemisphere has been shown to increase (5, 13–15), as examined by transcranial magnetic stimulation (TMS). TMS is a non-invasive method that has been used increasingly to map motor cortical organization in humans (16) and to measure reorganization, e.g. after stroke (17).

CIMT consists of intensive, repetitive training of the more affected arm/hand for several hours per day and of wearing a restraint on the less affected arm 90% of waking hours for a period of 2–3 weeks (12, 18–20). The exercises in CIMT consist of shaping, i.e. practice of adaptive tasks, whereby behavioural goals are attained in small steps with a gradual increase in difficulty and clear feedback (number of repetitions or time spent) as well as of general activity training, e.g. practice of household tasks. Taub and co-workers have emphasized that shaping exercises are of utmost importance in the CIMT concept (21) and this has been confirmed by others (22). On the other hand, some groups (13, 23) have reported that forced-use therapy (FUT) without shaping also improves upper extremity function in chronic stroke. Since the shaping exercises require a one to one relationship between patient and therapist it is important systematically to examine the efficacy of shaping vs general activity training, both on motor performance and on cortical reorganization.

The aim of the present study was to compare how a brief period of shaping exercises or of general activity training, commonly used in stroke rehabilitation, influences dexterity as well as the size and location of the cortical motor area of the abductor pollicis brevis (APB) muscle. Since it is extremely difficult to assemble a large group of patients with homogenous stroke lesions, we chose to use the function of the non-dominant hand of healthy humans as a model for hand training and for cortical plasticity, employing TMS of the contralateral cerebral hemisphere to explore possible cortical reorganization.
SUBJECTS AND METHODS

Subjects

Subjects were recruited mainly among students and employees from Umeå University, Sweden. One subject was an industrial worker. Information about the study was given in verbal and written form. Before entering the study the subjects completed a questionnaire concerning sex, age, occupation, handedness, possible impairments of the non-dominant hand, intake of medication, pregnancy and activities of fine motor practise with both hands. Criteria for inclusion were: (i) being healthy and (ii) age range 18–40 years. Exclusion criteria were: (i) epilepsy, (ii) cardiac pacemaker, (iii) pregnancy, (iv) metal objects implanted in the skull, (v) fixed tooth brace, (vi) reduced joint motion or sensory impairment of the non-dominant hand, (vii) inefficient typing, (viii) regularly playing musical instruments (such as piano, violin, saxophone, etc.) or playing video games > 30 min per day (to avoid the effects of regular hand exercises outside the study) and (ix) cortical motor threshold > 80% of the maximal intensity of our TMS stimulator (see below).

Thirty-three healthy persons were recruited and 30 volunteers (25 women, 5 men; mean age 24.2 years) fulfilled the study criteria after pre-screening. Subjects per group, with a total of 28 subjects, allowing a mean difference of 6.4; Statistical power calculation (a power of 90%, an alpha of 0.05, 14 pairs). This difference in active positions represents 60% of previously published data from training effects in patients with stroke (14).

Protocol and randomization

Immediately before the hand training, the subjects underwent cortical mapping of the APB motor area of the contralateral (non-dominant) hemisphere by TMS, followed by dexterity testing (see below) by investigators (FWJ, FN), who were blinded with regard to the hand training indicated (see below). After hand training, cortical mapping (CB) opened the next numbered envelope and initiated the type of training (see below). When a new subject arrived for training, the trainer (the same person) avoided the effects of regular hand exercises outside the study) and (ix) activity training with both hands. Criteria for inclusion were: (i) being healthy and (ii) age range 18–40 years. Exclusion criteria were: (i) epilepsy, (ii) cardiac pacemaker, (iii) pregnancy, (iv) metal objects implanted in the skull, (v) fixed tooth brace, (vi) reduced joint motion or sensory impairment of the non-dominant hand, (vii) inefficient typing, (viii) regularly playing musical instruments (such as piano, violin, saxophone, etc.) or playing video games > 30 min per day (to avoid the effects of regular hand exercises outside the study) and (ix) cortical motor threshold > 80% of the maximal intensity of our TMS stimulator (see below).

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During cortical mapping the coil was moved systematically over the grid positions on the lateral aspect of the non-dominant hemisphere and kept in the rostro-caudal direction with the grip pointing backwards. The stimulation was performed with biphasic pulses of 280 µs width at 0.5 Hz stimulus rate. It was started with 20% of the maximal initial magnetic pulse field intensity (dB/dt:38 kiloTesla/s) and was increased progressively in steps of 5% to identify the position(s) with the minimal excitability threshold (EThr) for the APB muscle. The EThr was defined as the lowest intensity producing discernible MEPs with constant latency from the surface recordings in 5 out of 10 stimulations (27) and its location constituted the Hot Spot (HS). Thereafter, at an intensity of 20% above the motor threshold of the APB muscle, a map was obtained, delivering 5 stimuli at 0.5 Hz for the positions surrounding the HS. If at least 1 out of the 5 stimuli gave a MEP response with an appropriate latency, the position was considered positive. The MEP at each positive position was photographed for further analysis using a digital camera mounted on a tripod. The area around the HS was searched systematically in grid steps of 10 mm until negative positions were found in all directions. The mapping sessions before and after training were identical (each using about 200–300 stimuli) and lasted between 45 and 60 min.

Data analysis

The data were analysed using the Statistical Package for the Social Sciences (SPSS) version 12.0 Software for Windows (SPSS, Chicago, IL, USA). The number of responsive scalp positions (map size) of the APB muscle were analysed as well as possible shifts in direction of responsive positions after hand training. Shifts were analysed from grid positions of new as well as eliminated positions after training in relation to the HS position. The mean and standard deviations (SD) for the neurophysiological data as well as for the pooled dexterity data (Purdue Peg Board test) were calculated within and between the groups. The 1-sample t-test was used to analyse the treatment effect on dexterity between the groups, respectively in steps of 5% to identify the position(s) with the minimal excitability threshold (EThr) for the APB muscle. The EThr was defined as the lowest intensity producing discernible MEPs with constant latency from the surface recordings in 5 out of 10 stimulations (27) and its location constituted the Hot Spot (HS). Thereafter, at an intensity of 20% above the motor threshold of the APB muscle, a map was obtained, delivering 5 stimuli at 0.5 Hz for the positions surrounding the HS. If at least 1 out of the 5 stimuli gave a MEP response with an appropriate latency, the position was considered positive. The MEP at each positive position was photographed for further analysis using a digital camera mounted on a tripod. The area around the HS was searched systematically in grid steps of 10 mm until negative positions were found in all directions. The mapping sessions before and after training were identical (each using about 200–300 stimuli) and lasted between 45 and 60 min.

Ethics

The research protocol was approved by the Medical Ethics Committee of Umeå University, Sweden (No. 05-0294M).

RESULTS

Training effects on dexterity

The pooled data of the Purdue Peg Board test for the two groups before and after hand training are presented in Table I. After the shaping exercises the participants in group A significantly increased their dexterity in all 4 tasks. The mean difference in placing pins with the non-dominant hand increased by 1.27 pins (CI 0.69–1.84; p < 0.001); with the dominant hand by 1.22 pins (CI 0.44–2.01; p = 0.005); with both hands by 1.00 pins (CI 0.58–1.42; p < 0.001) and for the assembly by 4.82 units (CI 2.89–6.76; p < 0.001).

After the general activity training (group B) no statistically significant improvement in dexterity was found in the trained non-dominant hand (mean difference 0.25 pins: CI −0.16 to 0.65; p = 0.213) or in both hands (mean difference 0.11 pins: CI −0.50 to 0.72; p = 0.709), but a small but significant difference was found in the dominant hand (mean difference 0.58 pins; CI 0.02–1.13; p = 0.042). Furthermore, there was a statistically significant improvement in the assembly task (mean difference 3.09 units; CI 1.57–4.61; p < 0.001). Thus, the improvement in dexterity was particularly prominent in group A (after shaping exercises). The mean difference in placing pins for the trained non-dominant hand was also significant between the groups (p = 0.007; Fig. 2A).

Size of cortical motor output area

The change in number of active (responsive) scalp positions over the non-dominant hemisphere for the APB muscle before and after hand training for the two groups can be seen in Fig. 2B. The motor output area was significantly enlarged only after the general activity training (group B). The number of active scalp positions for group B was a mean number of 18.5 (SD = 6.28) before training and 21.4 (SD 5.97) after training
(mean difference 2.93 positions; CI 0.33–5.54; \( p = 0.03 \)). The number of active scalp positions after shaping exercises (group A) was a mean number of 22.0 (SD 6.18) before training and 21.0 (SD 5.78) after training (mean difference –1.0 positions; CI –2.06 to +4.06; NS).

**New and eliminated number of responsive scalp positions**

The HS was located about 30 mm anterior to the vertex-aural line and consisted of 1–2 active positions for both groups. To analyse possible shifts of active (responsive) scalp positions after the hand training we employed sectorial maps in steps of 45 degrees emerging from the HS and with the vertex (medial) direction defined as 0° and that of the nasion (anterior direction) as 90°. The new active scalp positions after shaping (group A, Fig. 3A) were found mainly in the anterior direction. In this group, the HS moved by 10 mm in the anterior direction in 7/15 subjects, downwards in 1 subject but did not change in 7 subjects (mean difference 6.7 mm: CI –0.2 to 13.5; \( p = 0.05 \)).

After general activity training (group B, Fig. 3A) the new active scalp positions were mainly found in the posterior direction from the HS. The HS in this group moved posteriorly and/or downwards by 10 mm in 7/15 of the subjects, anteriorly/upwards in 5 subjects and did not change in another 3 (mean difference 2.7 mm: CI –2.2 to 7.6; \( p = 0.262 \)). The elimination of scalp positions (Fig. 3B) was considerable after the shaping exercises, whereas only a few, evenly distributed positions were eliminated after general activity training.

During the cortical mapping 3 participants experienced discomfort, became dizzy, nauseated or developed a headache. Since there were individual landmarks on the caps, these subjects were allowed to remove the cap after the first stimulation session, if it was not possible to keep it on. This usually eased the discomfort.

**DISCUSSION**

The results of our study in healthy subjects indicate that less than 30 min of shaping exercises improved dexterity of the trained non-dominant hand as well as of the dominant hand and of bimanual tasks. After general activity training, we found a statistically significant improvement mainly in the bimanual task (assembly). After (but not before) training, the difference in dexterity in the non-dominant hand between subjects receiving shaping exercises (group A) and those receiving general activity training (group B) was highly significant (\( p = 0.007 \)).

Both shaping exercises and general activity training, commonly used hand training modalities in rehabilitation after stroke, induced rapid cortical reorganization of the APB muscle motor area in the non-dominant hemisphere. The reorganization was not merely an increase in the number of responsive posi-
interhemispheric transfer and/or familiarization with the PPB
dominant hand (even if mainly in group A), indicating that an
perform the assembly task increased, as did the dexterity of the
healthy subjects (34), we enrolled both right- and left-handed
-(33). Since it has been reported that there are insignificant in-
teriorhemispheric asymmetries of hand muscle representations in
areas) (Fig. 3A), and the HS moved posteriorly/inferiorly in
the amputation stump for persons with phantom limb pain found that the sensory
cortical representation of areas surrounding the phantom shrank to
resume a more normal pattern in parallel with an improved sensory function.
Conversely, in those subjects receiving general activity train-
ing, the motor cortical area expanded posteriorly (into sensory areas) (Fig. 3A), and the HS moved posteriorly/inferiorly in
half of those subjects. However, this expansion was not ac-
companied by improved dexterity of the trained non-dominant
hand. It cannot be excluded that the cortical expansion in the
posterior direction represents another dimension of motor
functioning of the paretic arm. Some of the exercises were modi-
ified to a more difficult level since we studied healthy subjects. It
would perhaps have been desirable to perform the hand training
sessions for longer time periods than utilized here. However,
no systematic bias.

We chose to investigate healthy subjects since it would be very
difficult to enrol a large homogenous group of patients with stroke
with the same location, size and type of brain injury necessary
for the TMS component of the study. It might be argued that
the shaping training influenced the functions assessed by the
PPB test more than did the general activity training. It should
be remembered, however, that the 2 types of training used were
selected because they are common in clinical hand training prac-
tise, not because they activate the APB muscle to a similar extent.
Our results cannot automatically be translated to patients with
cortical or subcortical injuries e.g. stroke. It would therefore be
interesting to evaluate the effects of shaping exercises vs general
activity training on dexterity in a group of patients with stroke.
However, it is reasonable from our behavioural and motorcorti-
cal data to assume that shaping exercises, as apart from general
activity training, are effective to improve dexterity, confirming
previous anecdotal evidence from Taub et al. (21).

In conclusion, this study shows that dexterity of hand move-
ments seems to increase after a short period of shaping exercises
rather than after general activity training in healthy adults. The
activity training expands the number of active TMS positions of
the APB muscle into more posterior (sensory) parts of the
contralateral sensorimotor cortex, whereas the shaping exercises
shift the APB motorcortical area into pre-motor areas. Hence,
change of location, not merely the size of motor areas, may be an
important factor in evaluating cortical plasticity in humans.
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