



Brain functional differences in visuo-motor task adaptation between dominant and non-dominant hand training

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Abstract

Although learning and adapting to visuo-motor tasks is critical to child development and health conditions requiring rehabilitation, the neural processes involved in learning a new visuo-motor task and adapting it to novel conditions such as execution with an untrained limb are not fully understood. Therefore, we trained 27 healthy, right-hand-dominant individuals aged 18–35 years to perform a multidirectional point-to-point visually rotated aiming task with a joystick during functional magnetic resonance imaging, with 13 participants learning the task with the dominant (D) and 14 with the non-dominant (ND) hand. All individuals performed the task with the trained and untrained hand before and after training. As expected, performance of both the trained and the untrained hand improved significantly over the course of task acquisition. Brain functional changes associated with adaptation to the demands of the task, and execution differed significantly between D and ND groups. In particular, the ND group showed greater recruitment of visual and motor regions (left middle occipital and left precentral gyri) than the D group during task acquisition. In addition, the D group exhibited greater recruitment of motor planning regions (left precuneus) that contribute to performance with the trained hand, even after bilateral transfer—switching from the trained to non-trained hand. The D group showed more persistence of activation in sensorimotor regions—greater activation when returning to the rotated task after a switching to a simpler, non-rotated aiming task for a short interval. Finally, the D group showed more activation after-effects—increases in simpler task activation after training on the visually rotated task. The findings suggest that brain functional changes associated with adaptation to a visuo-motor skill may differ substantially depending on whether the dominant or non-dominant hand is trained, with non-dominant-hand training associated with greater activation during acquisition, and dominant-hand training associated with greater activation during bilateral transfer, persistence, and after-effects.

Keywords Bilateral transfer · Functional MRI · Handedness · Motor learning · Motor acquisition

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Introduction

Because a variety of highly prevalent medical events reduce motor skills (Canizares et al. 2009; Kremers et al. 2015; Mozaffarian et al. 2016; Stevens and Burns 2015), large numbers of adults are also faced with a critical need to engage in motor skill learning; learning how to adapt coordination and control of physical movements to new motion limitations. Motor skill learning and adaptation to motor task demands is a central component of post-hospitalization physical rehabilitation (Kosse et al. 2013), because the ability to learn or re-learn motor skills or to adapt to new demands has an important impact on independence and quality of life (Jansson and Granath 2011; Opara et al. 2010; Stevens and Burns 2015). Greater independence and quality of life in turn are associated with lower health care costs and

a variety of better long-term outcomes (Guralnik et al. 2002; Lippa et al. 2010).

Although the neural basis of motor skill learning phenomena has been investigated extensively (Hikosaka et al. 2002; Lisberger 1988; Willingham 1999), the neural basis of specific phenomena is under-explored in the context of visuo-motor aiming tasks. Brain activity during learning of sequential finger tapping tasks has been studied in depth (Catalan et al. 1998; Gerloff et al. 1998; Harrington et al. 2000; Hlustik et al. 2002), but this information is difficult to generalize to visuo-motor aiming because tapping tasks lack the spatial accuracy constraints that characterize visuo-motor aiming. Visuo-motor aiming has been studied behaviorally (Sainburg and Wang 2002), and brain regions involved in acquiring such tasks (Seidler et al. 2006) and adapting from one new task to another (Seidler and Noll 2008) have been identified. However, the neural basis of bilateral transfer of visuo-motor tasks—task performance improvement in an untrained limb after training of the contralateral limb—has not been investigated thoroughly although this phenomenon has been observed repeatedly in behavioral studies (Kumar and Mandal 2005; Teixeira 2000) and its neural basis has been studied in the context of hole-in-peg tasks (Uggetti et al. 2016). The neural basis of persistence (continued high performance on a newly learned motor skill after a break in performance) is not well explored either in the context of visuo-motor aiming, and neither is that of after-effects (changes in performance on a seemingly unrelated motor skill after learning of a new motor skill). Although these phenomena are well studied behaviorally in several settings, studies that assess neural correlates have not received much attention (Kami et al. 1995; Kelly and Garavan 2005). Understanding the neural bases of bilateral transfer, persistence, and after-effects after learning to adapt to the demands a visuo-motor aiming task could lead to greater understanding of inter-individual differences in visuo-motor skill-learning performance as well as neural biomarkers of motor skill-learning success.

An additional unknown is whether the neural substrates of these visuo-motor skill-learning phenomena depend critically on whether the limb being trained is dominant or non-dominant. The notion of such differences is grounded in the dynamic dominance model of motor lateralization, which suggests that motor functions relevant to skill learning differ by hemisphere, with the dominant hemisphere specialized in limb and task dynamics taking into account current conditions, while the non-dominant hemisphere minimizes potential errors under more static conditions (Sainburg 2014). To date, neural differences by hand of training have been reported in the context of the nine-hole peg task (Uggetti et al. 2016), but not in the context of visuo-motor aiming. If the brain bases for visuo-motor skill acquisition, bilateral transfer, persistence, and after-effects differ between

dominant and non-dominant hand training, there could be implications for personalization of rehabilitation regimens based on laterality of brain injury.

In this study, functional MRI (fMRI) data were collected while healthy young adults were trained to perform a visuo-motor aiming skill, and brain activation changes associated with skill acquisition, bilateral transfer, persistence, and after-effects were quantified. Differences in brain activation and motor performance were calculated between those trained with the dominant and the non-dominant hand. We believe this study may present the first direct quantification of neural correlates of several visuo-motor aiming skill learning phenomena (bilateral transfer, persistence, and after-effects) as well as the first direct comparison of neural correlates between dominant and non-dominant hand training.

Materials and methods

Participants

30 healthy young adults (14 females; mean age 23.6 years \pm 3.3) were recruited for the study via on-line advertisements on the Pennington Biomedical Research Center website. Participants provided informed consent prior to participation. All participants were right handed with handedness laterality quotient of 0.7 or higher as measured by the Edinburgh Handedness Inventory (Oldfield 1971), and had no reported neurological problems or cognitive deficits. Data from 3 individuals were excluded from analysis due to excessive head motion; thus, data from 27 participants are reported. This study was approved by the Pennington Biomedical Research Center Institutional Review Board.

Experimental design

Participants performed a joystick-aiming task while lying supine in an MRI machine (Fig. 1). The joystick was strapped to a plastic table positioned over the abdomen approximately at the level of the navel. Participants viewed a projected computer screen through a mirror attached to the head coil. Participants were instructed to move a joystick so that the cursor on the computer screen moved from a centrally located red dot toward a target green dot located to the right of, left of, above, or below the red dot. Instructions emphasized both speed and accuracy in moving the joystick to make the cursor overlap with the target dot. Each trial began with presentation of the central red dot; when the cursor reached the target green dot, participants clicked the joystick button to complete the trial and advance the task. Failure to click the joystick button within 10 s resulted in automatic cessation of the trial. A fixation cross was

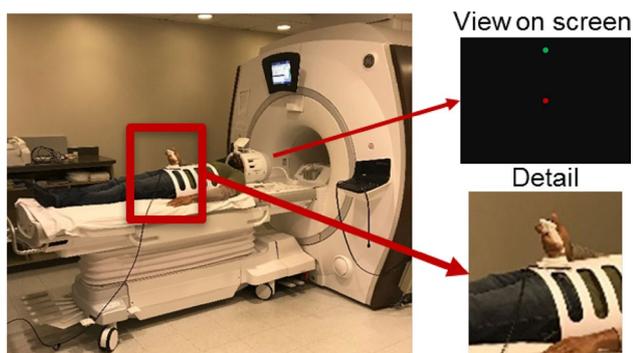


Fig. 1 Left: each study participant completed fMRI scanning while using a table-mounted joystick to complete a fine visuo-motor skill-learning task. A visual display projected onto a scanner bore mounted screen was viewed through a head-coil-mounted mirror. Top right: participant view of the visual display at the start of the typical task trial. The visuo-motor skill-learning task required using the joystick to move a cursor (red) from a starting location in the center of the screen to a target location (green). Lower right: the joystick manipulated by the participant is mounted to a rigid table attached to the scanner table at the level of the abdomen

shown during each inter-trial interval. The length of the inter-trial interval was randomly selected from the range of 0.5–1.5 s. Participants completed 16 blocks, each consisting of 12 trials for a total of 192 trials. 30 s of resting data were acquired after each block and before the first block, during which crosshairs were shown for 30 s and participants were instructed not to move the joystick. Each target location (left, right, above, below) appeared three times per block. The relative ordering of target locations within each of the

16 blocks was generated randomly at the beginning of the study, and this same random ordering was presented to each participant in the study.

Each participant was randomly assigned to train either the dominant (D) or the non-dominant (ND) hand. Participants were not informed of their group assignment prior to the MRI scan. Each block was executed using the trained or non-trained hand and represented one of two visual feedback conditions (Table 1). In the non-rotated (“Easy”) feedback condition, the direction of joystick deflection corresponded exactly to the direction of motion of the red cursor on the screen. In the rotated (“Hard”) feedback condition, there was a 90° difference between the direction of joystick deflection and the direction of motion of the red cursor on the screen. The first four blocks assessed pre-training baseline performance under all four combinations of hand use and feedback condition. Blocks 5–12 constituted task training, i.e., subjects completed the task using the trained hand and the rotated feedback condition. Blocks 13–16 assessed post-training performance under all four combinations of hand use and feedback condition.

Differences in task performance and fMRI signals between pairs of blocks were used to evaluate adaptation phenomena associated with the training of the visuo-motor task. Task acquisition, i.e., the degree to which performance on the trained task increased with repeated attempts, was assessed by comparing the first block using the trained hand in the rotated condition (block 4) to the last block using the trained hand in the rotated condition (block 12); all intervening blocks (blocks 5–11) used the trained hand in the rotated condition. Bilateral transfer of learning was assessed

Table 1 Top: experimental paradigm showing, for those randomized to task training with the non-dominant (ND, top row) and dominant (D, bottom row) hand, which hand the task is executed with during each block (D or ND) as well as whether that block is completed in the hard or easy visual feedback condition, bottom: differences in

fMRI signals and motor skill learning performance were assessed between pairs of blocks to quantify adaptation phenomena associated with the training of the visuo-motor task including skill acquisition, bilateral transfer, persistence of adaptation, and after-effects

	Pre-training blocks				Training blocks								Post-training blocks			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Difficulty	Easy	Easy	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Easy	Easy
Non-Dominant Hand Trained	D	ND	D	ND	ND	ND	ND	ND	ND	ND	ND	ND	D	ND	D	ND
Dominant Hand Trained	ND	D	ND	D	D	D	D	D	D	D	D	D	ND	D	ND	D

Contrast	Blocks compared	
Acquisition	4	12
Persistence of adaptation	12	14
Bilateral transfer	3	13
Aftereffects	2	16

by comparing the first block using the untrained hand in the rotated condition (block 3) to the last block using the untrained hand in the rotated condition (block 13). Persistence of learning was assessed by comparing the final acquisition block using the trained hand in the rotated condition (block 12) to the next block that used the trained hand in the rotated condition (block 14), which occurred after a break (block 13) during which the task was switched back to the untrained hand. After-effects were assessed by comparing the first block using the trained hand in the non-rotated condition (block 2, prior to training) to the final block using the trained hand in the non-rotated condition (block 16, after training).

fMRI data acquisition

We acquired functional magnetic resonance imaging (fMRI) scans on a 3T MRI scanner (General Electric, 750 W Discovery, 32ch quadrature head coil) using a blood oxygen level-dependent echo-planar imaging (BOLD-EPI) pulse sequence. Subjects wore a respiratory monitoring belt and pulse oxygenation sensor during scanning to correct for cardiac and respiratory influences on fMRI signals. Key acquisition parameters were: voxel size: $3.4 \times 3.4 \times 3.5 \text{ mm}^3$, TR: 3 s, number of slices: 52, flip angle: 90° , and TE: 30 ms. Structural images acquired for data analysis were obtained using a T1-weighted magnetization-prepared gradient echo pulse sequence with the following parameters: TR: 8.7 ms, TE: 3.8 ms, FA: 8° , number of slices: 176, and voxel size: $1 \times 1 \times 1 \text{ mm}^3$.

Behavioral data analysis

During task performance, the position of the cursor on the screen and corresponding time stamps were recorded at 35 Hz. The task was implemented using MATLAB R2016a with Psychophysics Toolbox (Brainard 1997; Kleiner et al. 2007; Pelli 1997) and the GStreamer multi-media framework. Joystick data were analyzed using in-house data analysis software. First, position data were filtered using a dual low-pass fourth-order Butterworth filter, with a cutoff frequency of 16 Hz. Velocity and acceleration were calculated by differentiation. Two measures were used to assess the accuracy of the cursor trajectory: initial direction error at 80 ms (IDE80) and straightness error (SErr). IDE80 was calculated as the angle between two vectors: one connecting start and target positions, the other connecting start position and the joystick position 80 ms after movement onset (Pan and van Gemmert 2013). SErr was the difference between the start-to-target distance and the total distance traveled in pixels, divided by the start-to-target distance (Romero et al. 2003a). Movement time (MT) was the time elapsed between onset and cessation of movement. Onset and cessation were

defined as the moment in time when velocity first rose to 5% of the peak velocity from the start of the trial, and the moment in time when velocity last fell to 5% of the peak velocity before the end of the trial. These moments were adjusted to the time point corresponding to the nearest zero crossing or local minimum of the acceleration profile for movement (Poston et al. 2009; Romero et al. 2003a, b). This method for calculating movement time was employed to eliminate movement artifacts due to the use of a digitalized pixel coordinate system, as well as allow for comparison to previous research. Reaction time (RT) was defined as the time elapsed between target presentation and movement onset. All trials that resulted in at least one pixel of overlap between the cursor and the target dot were rated as successes. The percentage of trials rated as successes (accuracy) was calculated as an additional behavioral measure.

Behavioral data analysis

We used repeated-measures ANOVA models to identify differences in the behavioral measures between D and ND groups and to identify differences between pairs of trial blocks. Group (D vs ND), block number, and the interaction between group and block number were the predictors in all models. Separate ANOVA models were conducted for each outcome measure: IDE80, SErr, RT, MT, and accuracy. A *p* value less than 0.05 was considered statistically significant. Effect size was quantified using Cohen's *d*.

fMRI data processing

Functional MRI data were analyzed using MATLAB R2016a and the Statistical Parametric Mapping 12 (SPM12) toolbox. Preprocessing steps included realignment to correct for head motion, co-registration to the T1-weighted structural scan, slice timing correction, smoothing using a 6 mm full width at half maximum Gaussian kernel, and warping to the Montreal Neurological Institute (MNI) template. Cardiac and respiratory components of each time series were removed using the RETROICOR algorithm (Gary et al. 2000). Time points representing volumes with excessive head motion (defined as greater than 1.5° of rotation or 1.5 mm of translation from the previous time point) and activation spike artifact (defined as global mean brain activation greater than 2.3 standard deviations above the mean across all time points) were removed from analysis.

fMRI statistical analysis

The data for each subject were entered into a first-level voxel-wise analysis using the general linear model. Each trial was modeled as a boxcar function convolved with the canonical hemodynamic response function that began at the

onset of the stimulus presentation. First-level beta maps, performed at the single-subject level, quantified differences in BOLD signal within an individual between pairs of blocks; all such block pairs, corresponding to our contrasts of interest, are shown in Table 1. Second-level analyses identified voxels at which block pair differences in fMRI signals were significantly different from zero at the group level at the $p < 0.005$ confidence level. Finally, second-level analysis tested whether block pair differences in fMRI signals differed significantly between D and ND groups. The REST AlphaSim Toolbox (Xiao-Wei et al. 2011) was used to correct each second-level analysis for multiple comparisons via clustering generated by Monte Carlo simulations, with a cluster-level p value threshold of $p < 0.05$. To improve visualization of the differences between groups, mean differences in fMRI signals between individual task blocks and rest blocks were calculated within regions of interest, and these mean values were plotted visually.

Results

Participants consisted of 11 females and 16 males with an overall mean age of 23.8 ± 3.2 years and an age range of 18–35 years. Group D consisted of 5 women and 8 men with a mean age of 23.6 years. Group ND consisted of 6 women and 8 men with a mean age of 24.0. The percentage of trials accurately completed (success rate) was uniformly high (mean $87.0\% \pm 1.6\%$ across all trials), did not differ significantly between any pair of blocks, and did not differ significantly between D and ND (data not shown). All fMRI results, including mean values, standard deviations, and approximate effect sizes, are included in the supplementary material (Table 2, supplementary material).

Behavioral differences by hand of training

Movement time (Fig. 2) did not differ significantly between D and ND groups within any of the 16 completed blocks. Reaction time was significantly faster within the D group in blocks 5, 6, and 11 (Fig. 2 and Supplemental Table 1). SErr was significantly lower in the D group in block 2 (Fig. 3). IDE80 was significantly greater in the D group compared to the ND group during block 4 (Fig. 4). No other differences within individual blocks between D and ND groups were statistically significant.

Acquisition

Figure 5 shows representative trials in the beginning (block 4) and end (block 12) of task acquisition, completed using the dominant hand in the rotated feedback condition. Though the joystick was prone to move in cardinal directions due to

the preferred strafing movements, most participants chose to move only in those directions because of the location of the target relative to the starting point. Another possible cause for this movement pattern was that the participants were lying supine, so normal movements in the transverse plane correspond to movements in the frontal plane. The locations of the targets together with the setup of the joystick may have led to a preference in moving in cardinal directions; however, many trials showed curved trajectories.

The latter trajectory clearly shows greater spatial efficiency. Correspondingly, movement time (Fig. 2), straightness error (Fig. 3), and IDE80 (Fig. 4) improved significantly between blocks 4 and 12 ($p < 0.05$). These data confirm that training was adequate to induce acquisition of the task. Figure 6 shows brain regions where brain activation differed significantly between blocks 4 and 12. In the overall sample, brain activation in a cluster of voxels in the left middle occipital gyrus increased significantly over the course of acquisition (cluster size = 50, p value = 0.001, effect size = 1.15). Changes in brain activation over the course of acquisition differed significantly between the D and ND groups in two clusters covering the left middle occipital gyrus and left precentral gyrus. In these two clusters, activation decreased over the course of acquisition in the D group and increased over the course of acquisition in the ND group (first cluster size = 151, p value = 0.012, effect size = 1.93; second cluster size = 349, p value < 0.001, effect size = 0.75).

Bilateral transfer

Performance of the trained and untrained hands increased by approximately the same amount over the course of training in both D and ND groups, suggesting that acquisition-related gains in performance transferred from the trained to untrained limb (Figs. 2, 3, 4). Specifically, average movement time, straightness error, and IDE80 all decreased significantly between the first block using the untrained hand in the rotated condition (block 3), and the last block using the untrained hand in the rotated condition (block 13) in both D and ND groups (all $p < 0.05$). Changes in brain activation between blocks 3 and 13 differed significantly between the D and ND groups in a cluster of voxels that covered the left precuneus and Brodmann area 7 (cluster size = 56, p value < 0.001, effect size = -1.82). In the D group, activation in this cluster increased from block 3 to block 13, while in the ND group, activation in this cluster decreased (Fig. 7).

After-effects

None of the behavioral measures differed significantly between the first and last blocks completed in the non-rotated condition with the trained hand (i.e., between blocks 2 and 16). Changes in brain activation between

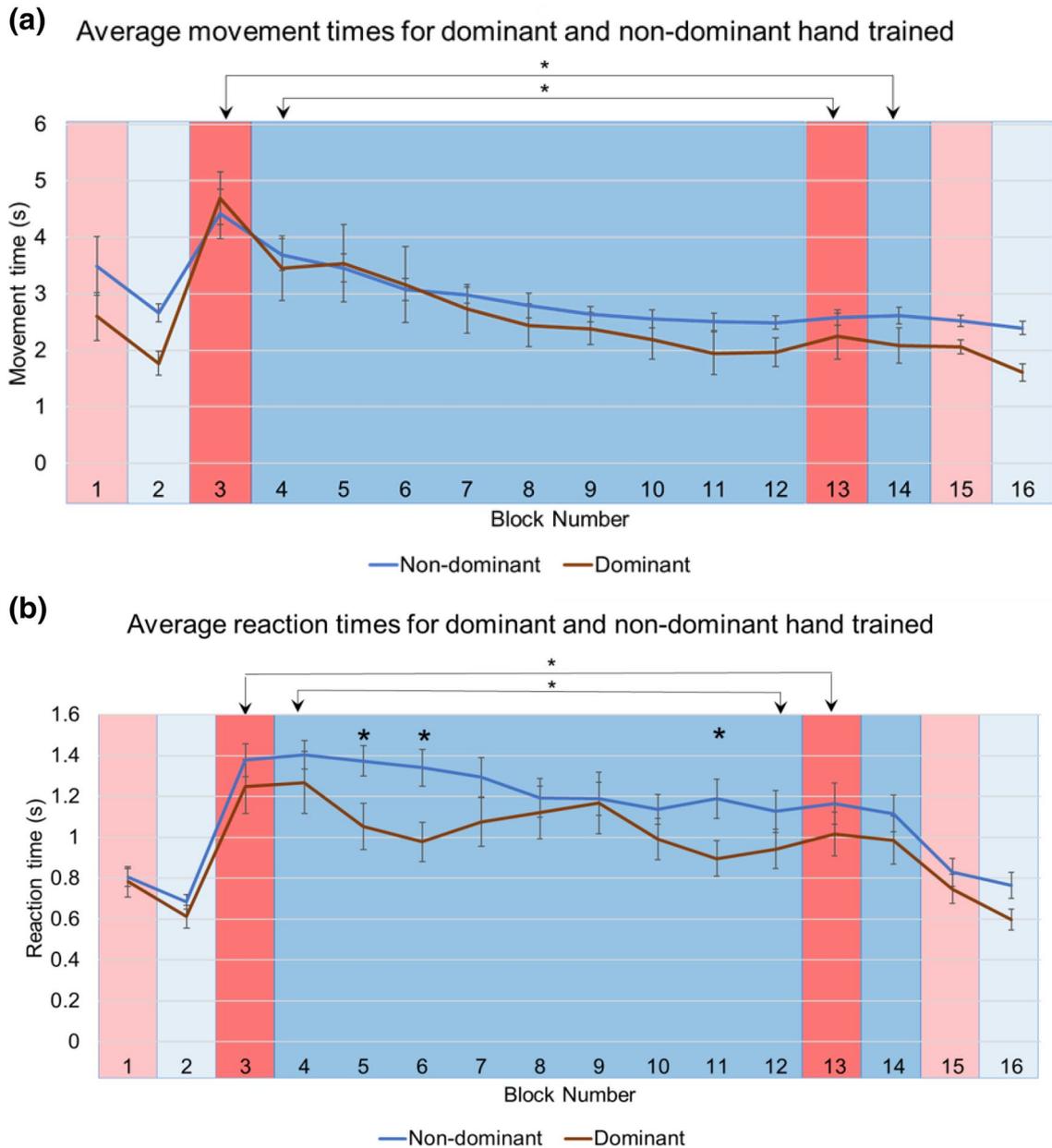


Fig. 2 Average movement times **(a)** and reaction times **(b)** within each block over the course of the experiment. Diacritic marks (*) indicate significant differences ($p < 0.05$) between blocks within both

D and ND groups. Significant differences were seen for reaction time in blocks 5, 6, and 11, and none were seen for movement time

blocks 2 and 16 differed significantly between the D and ND groups in a cluster of voxels that covered the left precuneus (cluster size = 154, p value = 0.008, effect size = -1.60). In the D group, activation in this cluster increased from block 2 to block 16, while in the ND group, activation in the same area decreased (Fig. 8).

Persistence

We found no significant differences in any behavioral measure (average movement time, straightness error, or IDE80) between blocks 12 and 14, confirming that the motor skill acquired between blocks 4 and 12 persisted to

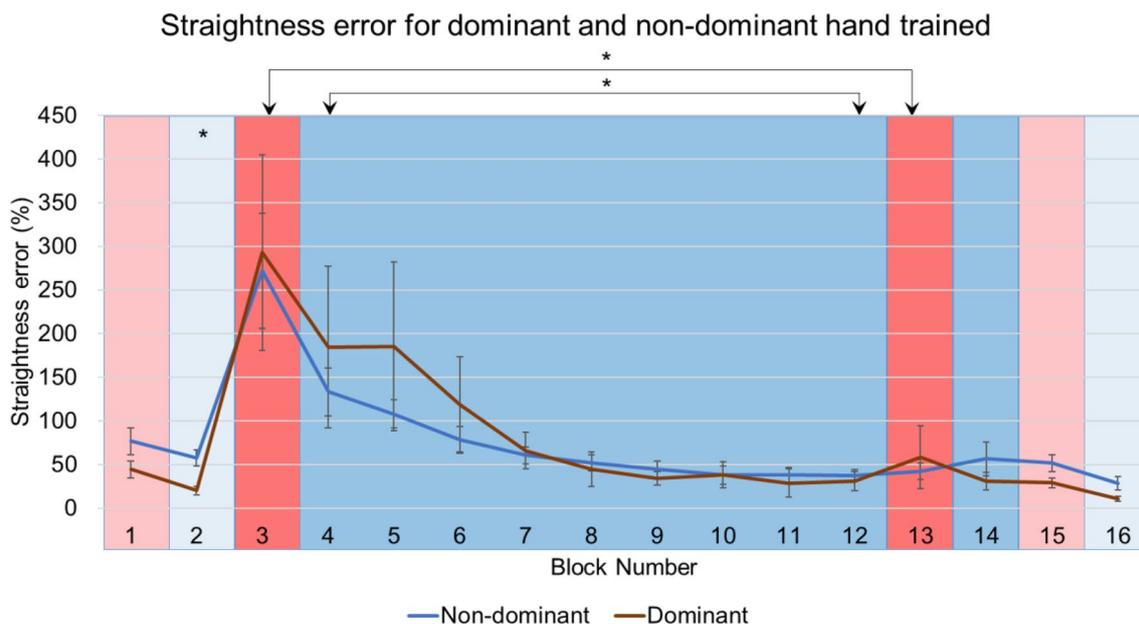


Fig. 3 Average straightness error, converted to percentage, within each block of the task. Diacritic marks (*) represent the same as in Fig. 2. Significant differences between D and ND groups are shown as well, occurring in block 2

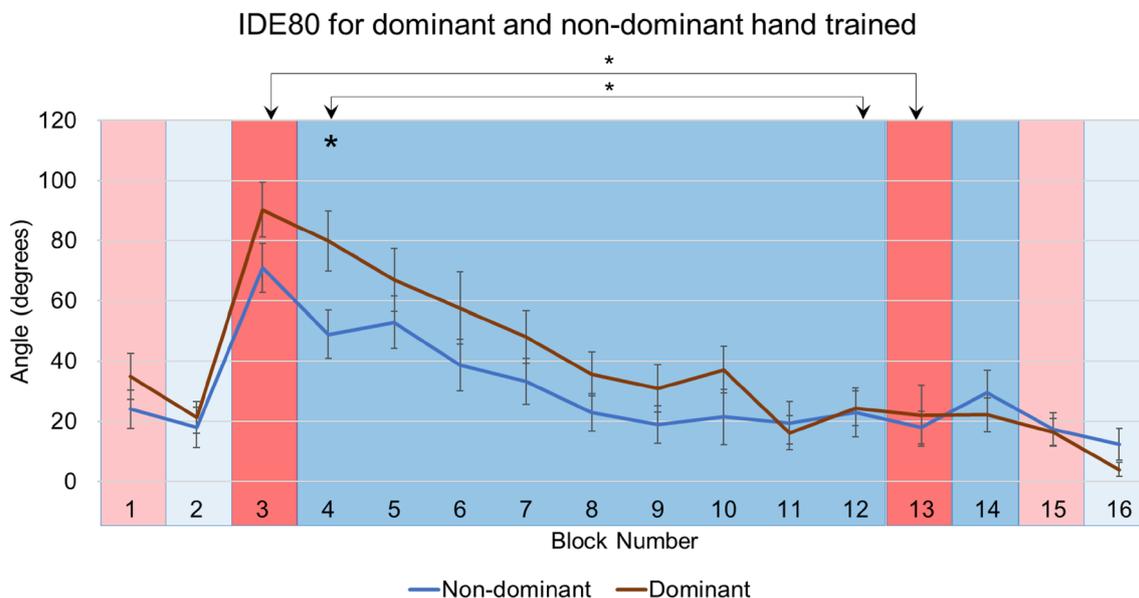


Fig. 4 Average IDE80 within each block over the course of the experiment. Diacritic marks (*) have the same meaning as in Fig. 2. Significant differences between D and ND groups are shown as well, occurring in block 4

block 14 despite a switch to the contralateral hand in block 13. Changes in brain activation between blocks 12 and 14 differed significantly between the D and ND groups in a cluster of voxels located in the sensorimotor cortex, specifically the right precentral gyrus and right postcentral gyrus (Fig. 9). Between blocks 12 and 14 in this cluster, activation increased in the D group and decreased in the ND group (cluster size = 229, *p* value = 0.002, effect size = -1.71).

Discussion

In this study, 27 healthy young adults were trained to complete a joystick-aiming task with rotated visual feedback during collection of fMRI data. There were two key findings. First, the task recapitulated several expected motor skill adaptation phenomena: participants performed better

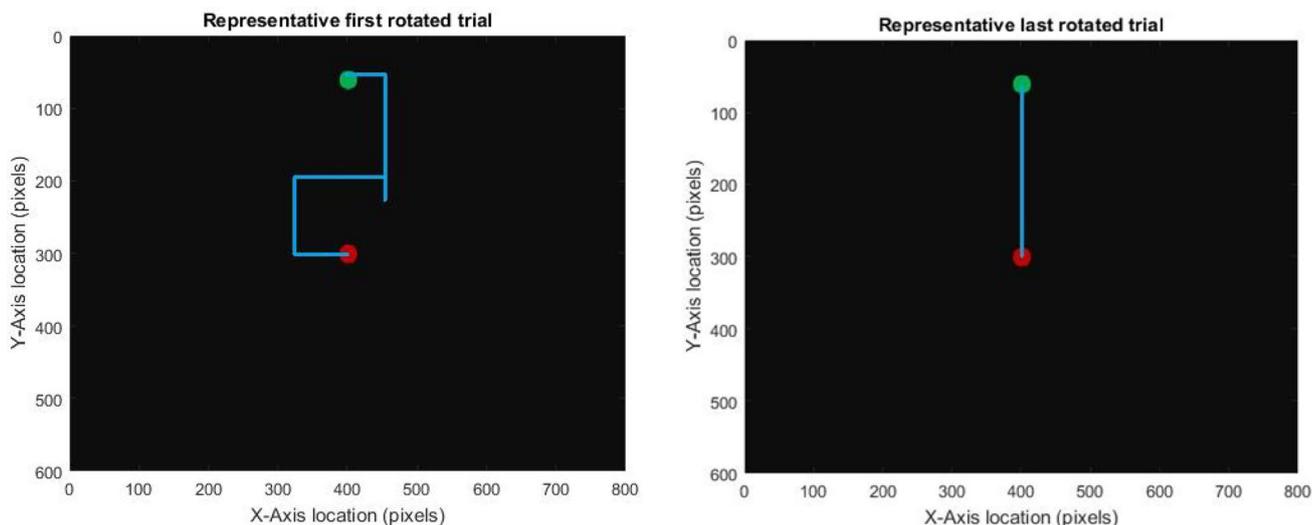
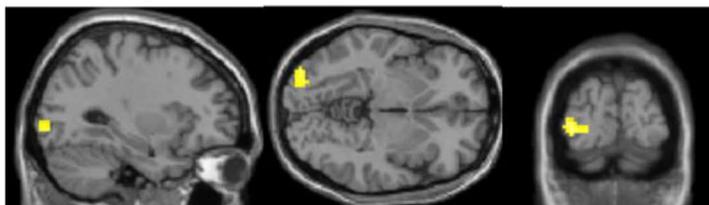


Fig. 5 Representative trials from the first (left) and last (right) block completed with the dominant hand in the rotated (“hard”) condition. The blue curves represent the trajectories followed by the cursor as it was steered toward the green dot by the participant

	Pre-training blocks				Training blocks								Post-training blocks			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Difficulty	Easy	Easy	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Easy	Easy
Non-Dominant Hand Trained	D	ND	D	ND	ND	ND	ND	ND	ND	ND	ND	ND	D	ND	D	ND
Dominant Hand Trained	ND	D	ND	D	D	D	D	D	D	D	D	D	ND	D	ND	D

All participants (4 < 12)



D vs. ND trained (D < ND)

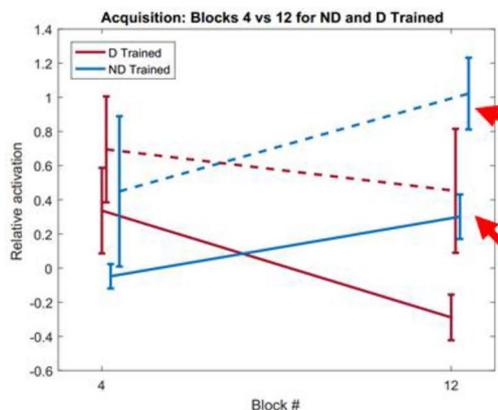
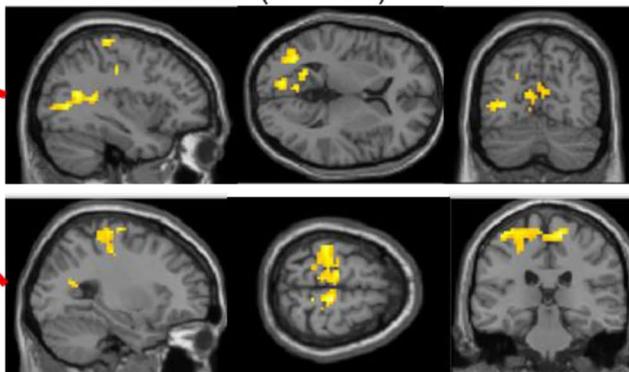


Fig. 6 Brain activation changes over the course of acquisition. Top right: a cluster of voxels in the left middle occipital gyrus (MNI coordinates $-30, -94, -4$, see yellow highlight) showed significantly greater activation in block 12, compared to block 4, in the overall cohort. Bottom right: clusters in the left middle occipital gyrus ($-36, -70, 5$, dotted line) and left precentral gyrus ($-27, -28, 65$, solid

line) showed significantly greater activation increases between blocks 4 and 12 in the ND group, compared to the D group. Bottom left: mean relative fMRI activation in blocks 4 and 12, relative to rest blocks, within the two clusters showing significant D vs ND activation differences. Activation in these clusters increased among ND-trained participants and decreased among D-trained participants

with repeated attempts, transferred adaptation-related performance gains from trained to untrained limbs, and maintained persistent adaptation-related performance gains after a break in which they switched to the other hand.

The second key finding is that changes in brain activation over the course of task acquisition, bilateral transfer, persistence, and after-effects depended on whether the dominant or non-dominant limb was trained to do the task. It is

	Pre-training blocks				Training blocks								Post-training blocks			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Difficulty	Easy	Easy	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Easy	Easy
Non-Dominant Hand Trained	D	ND	D	ND	ND	ND	ND	ND	ND	ND	ND	ND	D	ND	D	ND
Dominant Hand Trained	ND	D	ND	D	D	D	D	D	D	D	D	D	ND	D	ND	D

D vs. ND trained (D > ND)

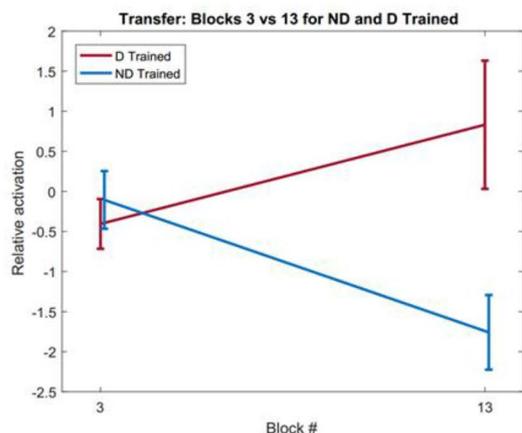
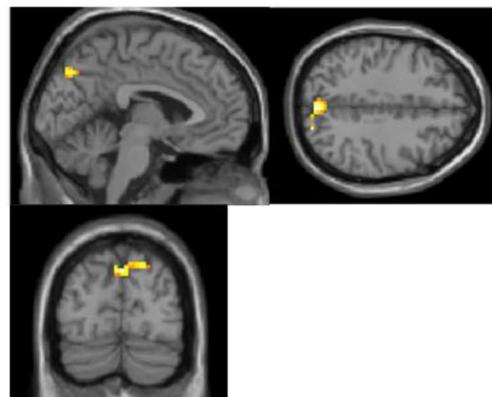


Fig. 7 Right: over the course of training, a cluster of voxels in the left precuneus and Brodmann area 7 showed activation increases in the D group, and decreases in the ND group, in blocks performed with the untrained hand (see yellow highlight, MNI coordinates of peak activation: $-3, -79, -41$). Lower left: mean relative fMRI activation in blocks 3 and 13, relative to periods of rest, within the region showing D vs ND activation change differences

variation: $-3, -79, -41$). Lower left: mean relative fMRI activation in blocks 3 and 13, relative to periods of rest, within the region showing D vs ND activation change differences

	Pre-training blocks				Training blocks								Post-training blocks			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Difficulty	Easy	Easy	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Hard	Easy	Easy
Non-Dominant Hand Trained	D	ND	D	ND	ND	ND	ND	ND	ND	ND	ND	ND	D	ND	D	ND
Dominant Hand Trained	ND	D	ND	D	D	D	D	D	D	D	D	D	ND	D	ND	D

D vs. ND trained (D > ND)

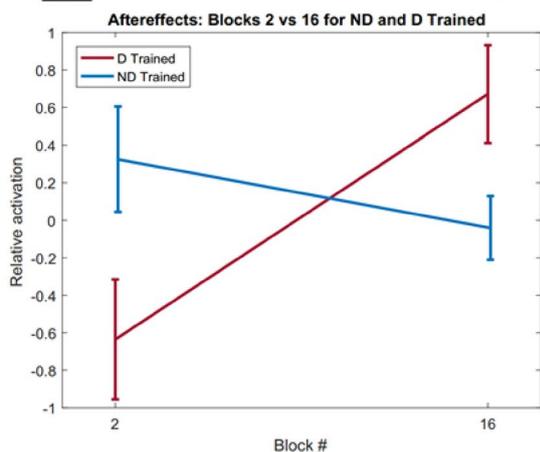
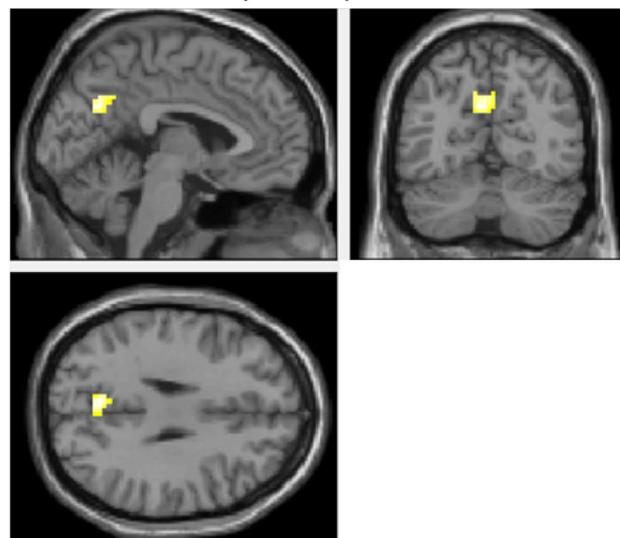
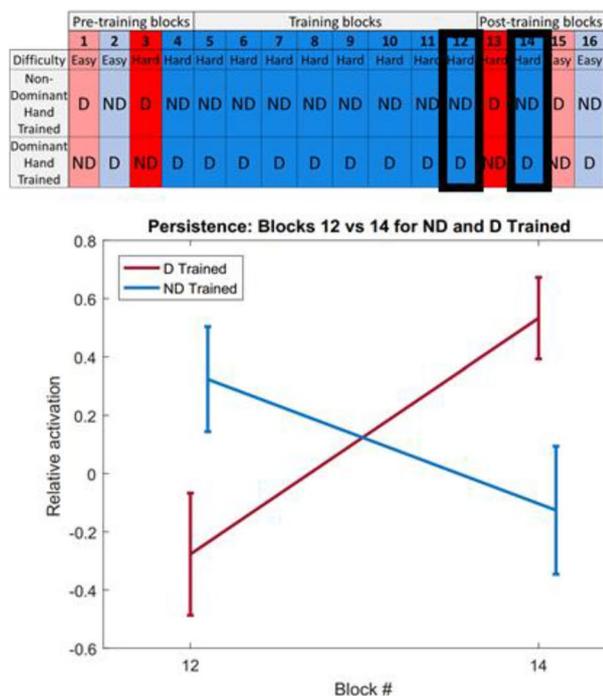


Fig. 8 Right: a cluster of voxels in the left precuneus ($-3, -64, 29$) showed activation increases between blocks 2 and 16 in the D group, and corresponding decreases in the ND group (see yellow highlight, MNI coordinates of peak difference: $-3, -64, 29$). Bottom left:

mean relative fMRI activation in blocks 2 and 16, relative to periods of rest, within the region showing D vs ND activation change differences



D vs. ND trained (D > ND)

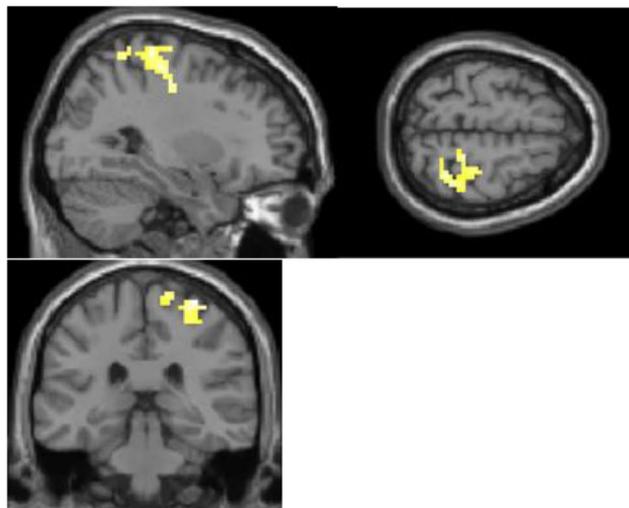


Fig. 9 Right: a cluster of voxels in the right precentral and post-central gyri showed activation increases between blocks 12 and 14 in the D group, while the same region showed decreases in the ND group (cluster shown in yellow, MNI coordinates of peak difference:

30, -31, 62). Bottom left: mean relative fMRI activation in blocks 12 and 14, relative to periods of rest, within the sensorimotor region showing D vs ND differences

possible that we started with between-group differences, which were not accounted for since the groups differed as to which hand was trained and thus tested. However, even though the between-group differences do seem to be minimal, we cannot exclude this possibility. The key implication of the brain activation findings is that the pattern of brain activity enabling adaption to the visuo-motor task may differ significantly depending on which side of the body is trained to perform the skill. This outcome, if confirmed, has implications for training one side of the body to perform motor tasks, as is common, for example, after single-hemisphere stroke (see also Dobkin 2004). For example, dose–response relationships, as well as expected rate and ceiling of function recovery, can be based on the hand that is performing the skill.

Acquisition

Overall, brain activation increased in the left middle occipital gyrus (extending into Brodmann area 18) during the acquisition phase between blocks 4 and 12. These areas are responsible for visual monitoring (Antal et al. 2004), indicating that acquisition may be accompanied by greater recruitment of brain resources used to provide visual feedback during execution. The middle occipital gyrus and left precentral gyrus showed greater brain activation increases

over the course of acquisition in the ND group compared to the D group. The left precentral gyrus has been suggested (Seidler et al. 2006) as one among several key loci of support for the sensorimotor process of adaptation to novel motor task demands. The other loci identified in that study were not significant in our study, possibly due to a variety of methodological differences between the two, as well as different statistical tests and corrections. Successful acquisition of the task with the non-dominant hand may require greater recruitment of resources to accomplish these aspects of the task, while acquiring the task with the dominant hand requires so few resources that recruitment of brain resources reduces slightly during the acquisition period. Possibly, the calibration process in which visual information is attuned with perceived action outcomes was still ongoing during acquisition, and thus, even though behavioral data suggested that a plateau was reached in adaptation to the demands of the visuo-motor task, the calibration process was still ongoing. The latter suggests that the task performance did reach its optimum before the visual system was fully calibrated, thus suggesting that the motor task is not challenging enough to find small improvements at the end of a training cycle. Another option is that it may suggest that the motor task still improved but that it was not possible to measure the improvements due to the resolution of the performance measures. The difference between the ND and D group

offers some support, assuming that the calibration process of the non-dominant limb is less efficient and possibly relies heavily on mental rotation. A prior meta-analysis on mental rotation indicates both the left middle occipital gyrus and left precentral gyrus as loci of mental rotation tasks (Barbara and Michele 2016).

Bilateral transfer

Behavioral data suggested that bilateral transfer of the trained motor task did occur; i.e., performance of one limb increased simply because the other one adapted to the task requirements. The performance increase in the untrained limb was accompanied by brain activation changes that differed between D and ND groups. Specifically, in the D group, a cluster of voxels in the left precuneus showed greater activation when the non-dominant hand performed the task after training, compared to before training. Conversely, among non-dominant-hand-trained individuals, this cluster of voxels showed less activation when the dominant hand performed the task after training, compared to before training. Previously (Seidler and Noll 2008), the left precuneus was shown to be involved in acquisition of a visuo-motor aiming task similar to ours. The precuneus is believed to be responsible for proprioception during spatially demanding tasks that require coordination between two limbs (Wenderoth et al. 2005), and precuneus engagement has specifically been reported in tasks requiring mental rotation (Hugdahl et al. 2006). Our finding may suggest that transferring a spatially demanding skill from the dominant to non-dominant hand requires relatively greater neural recruitment to reach the same level of performance. To our knowledge, this is the first report of asymmetry in bilateral transfer-related brain recruitment between dominant and non-dominant hand training. If confirmed, the key implication of this finding is that bilateral transfer to a non-dominant hand might require additional brain activity to be successful.

After-effects

In this study, there were no notable behavioral after-effects on task performance in the non-rotated condition. We suggest that the process of adapting to the non-rotated condition after training was so fast that it transpired over only the first few trials of the first non-rotated block, thus making accurate detection of after-effects difficult. This agrees with previous research (Kagerer et al. 1997) showing more pronounced after-effects when the onset of practice is gradual (during acquisition trial-to-trial changes are gradual until the maximum change is reached), rather than sudden (during acquisition all trials trained with the maximum change). In addition, because the rotation was very obvious to the participant, this pattern of results may suggest that performing the task

with the contralateral hand in block 15 allowed participants to develop a high-level cognitive strategy governing performance with both trained and untrained limbs, resulting in fast adaptation in block 16 and the absence of observed after-effects. Another related explanation would suggest that a slow rate of adaptation during training in the unusual (hard) condition occurs because this condition requires both cognition and calibration. When the condition reverted back to the non-rotated condition (block 16), after-effects may have disappeared quickly if the individual was able to revert back to its pre-existing, non-rotated calibration. Although behavioral after-effects were not evident, there were notable brain activation after-effects. Those trained with the dominant hand showed greater activation of the left precuneus during execution in the non-rotated condition after training compared to before; while those trained with the non-dominant hand showed less activation in this same region after training compared to before. A possible reason for this finding is that the dominant hand may be so efficient at optimizing itself for the rotated task over the course of acquisition, that a large amount of brain activation is needed to inhibit this optimization and force the system to behave differently when presented with the non-rotated task. There are several reports of fMRI activation differences occurring in a visuo-motor task without behavioral changes (Clements et al. 2006; Hugdahl et al. 2006; Levin et al. 2005). A previous study (Van Gemmert and Van Galen 1997) showed in a series of experiments that increases in task demands do not necessarily lead to notable changes in behavior, even though assumed expenditures of resources increase. Our results show that current motor control theories need to be expanded. Effort seems to play a crucial role. When effort can reduce the behavioral effects, differential activation in the brain can still occur, indicating that resources are expended to counteract the behavioral changes.

Persistence

Persistence refers to maintenance of practice-related improvements in performance after a period without practice on the specific task (Schmidt and Lee 2014). In this study, task performance remained stable after acquisition, despite a break during which the task was perturbed by switching the hand of performance. In addition, there were no overall differences in brain activation between pre- and post-break task performance. However, there were differences in pre- to post-break brain activation changes between those who were trained with the dominant vs non-dominant hand. Specifically, in a cluster of voxels covering parts of the right precentral and postcentral gyri, activation was relatively greater after the break among those trained with the dominant hand, and relatively less after the break among those trained with the non-dominant hand. These brain regions are

responsible for primary somatosensory and motor function on the left-hand side of the body, i.e., the non-dominant side (Kandel et al. 2013). Thus, for individuals trained with the dominant hand, a break to perform the task with the non-dominant hand resulted in persistent brain activation in a region that was presumably required to perform the task during the break. However, we did not observe a similar cluster of lingering brain activation after the break among non-dominant-hand-trained individuals in the corresponding left sensorimotor cortex—i.e., the region presumably required to perform the task with the dominant hand during the break. This could indicate that brain regions controlling task execution may be able to adapt faster to changes in motor conditions, for example cessation of task execution with the dominant hand.

This study is not without limitations. As a study of healthy young adults, we were unable to investigate many of the populations relevant to physical rehabilitation, such as those in stroke recovery. We investigated adaptation to visuo-motor skill over a single training session, and thus were not able to investigate adaptation- and/or learning-related brain changes over longer term periods. We only enrolled right-hand-dominant individuals and thus we are unable to determine if our findings carry over to left-hand-dominant individuals, even though a previous study (Uggetti et al. 2016) suggests that it might carry over to left handers. Future work should seek to explore whether the current findings extend to these relevant problem domains.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

References

- Antal A, Nitsche MA, Kincses TZ, Kruse W, Hoffmann K-P, Paulus W (2004) Facilitation of visuo-motor learning by transcranial direct current stimulation of the motor and extrastriate visual areas in humans. *Eur J Neurosci* 19(10):2888–2892. <https://doi.org/10.1111/j.1460-9568.2004.03367.x>
- Barbara E, Michele E (2016) Effects of stimulus type and strategy on mental rotation network: an activation likelihood estimation meta-analysis. *Front Hum Neurosci*. <https://doi.org/10.3389/fnhum.2015.00693>
- Brainard DH (1997) The psychophysics toolbox. *Spat Vis* 10(4):433–436
- Canizares M, MacKay C, Davis AM, Mahomed N, Badley EM (2009) A population-based study of ambulatory and surgical services provided by orthopaedic surgeons for musculoskeletal conditions. *BMC Health Serv Res* 9(1):56. <https://doi.org/10.1186/1472-6963-9-56>
- Catalan MJ, Honda M, Weeks RA, Cohen LG, Hallett M (1998) The functional neuroanatomy of simple and complex sequential finger movements: a PET study. *Brain* 121(2):253–264
- Clements AM, Rimrodt SL, Abel JR, Blankner JG, Mostofsky SH, Pekar JJ, Cutting LE (2006) Sex differences in cerebral laterality of language and visuospatial processing. *Brain Lang* 98(2):150–158. <https://doi.org/10.1016/j.bandl.2006.04.007>
- Gary HG, Tie-Qiang L, David R (2000) Image-based method for retrospective correction of physiological motion effects in fMRI: RETROICOR. *Magn Reson Med* 44(1):162
- Gerloff C, Corwell B, Chen R, Hallett M, Cohen LG (1998) The role of the human motor cortex in the control of complex and simple finger movement sequences. *Brain* 121(9):1695–1709
- Guralnik JM, Alecxih L, Branch LG, Wiener JM (2002) Medical and long-term care costs when older persons become more dependent. *Am J Public Health* 92(8):1244–1245. <https://doi.org/10.2105/AJPH.92.8.1244>
- Harrington DL, Rao SM, Haaland KY, Bobholz JA, Mayer AR, Binder JR, Cox RW (2000) Specialized neural systems underlying representations of sequential movements. *J Cogn Neurosci* 12(1):56–77. <https://doi.org/10.1162/08989290051137602>
- Hikosaka O, Nakamura K, Sakai K, Nakahara H (2002) Central mechanisms of motor skill learning. *Curr Opin Neurobiol* 12(2):217–222. [https://doi.org/10.1016/S0959-4388\(02\)00307-0](https://doi.org/10.1016/S0959-4388(02)00307-0)
- Hlustik P, Solodkin A, Gullapalli RP, Noll DC, Small SL (2002) Functional lateralization of the human premotor cortex during sequential movements. *Brain Cognit* 49:54–62
- Hugdahl K, Thomsen T, Erslund L (2006) Sex differences in visuospatial processing: an fMRI study of mental rotation. *Neuropsychologia* 44(9):1575–1583. <https://doi.org/10.1016/j.neuropsychologia.2006.01.026>
- Jansson K-Å, Granath F (2011) Health-related quality of life (EQ-5D) before and after orthopedic surgery. *Acta Orthop* 82(1):82–89
- Kagerer FA, Contreras-Vidal JL, Stelmach GE (1997) Adaptation to gradual as compared with sudden visuo-motor distortions. *Exp Brain Res* 115(3):557–561
- Kami A, Meyer G, Jezzard P, Adams MM, Turner R, Ungerleider LG (1995) Functional MRI evidence for adult motor cortex plasticity during motor skill learning. *Nature* 377(6545):155–158. <https://doi.org/10.1038/377155a0>
- Kandel ER, Schwartz JH, Jessell TM, Siegelbaum SA, Hudson AJ (2013) Principles of neural science, 5th edn. McGraw-Hill, New York
- Kelly AMC, Garavan H (2005) Human functional neuroimaging of brain changes associated with practice. *Cereb Cortex* 15:1089–1102
- Kleiner M, Brainard DH, Pelli D, Ingling A, Murray R, Broussard C (2007) What's new in Psychtoolbox-3. *Perception* 36:1–16. <https://doi.org/10.1068/v070821>
- Kosse NM, Dutmer AL, Dasenbrock L, Bauer JM, Lamoth CJC (2013) Effectiveness and feasibility of early physical rehabilitation programs for geriatric hospitalized patients: a systematic review. *BMC Geriatr* 13(1):107
- Kremers HM, Larson DR, Crowson CS, Kremers WK, Washington RE, Steiner CA, Berry DJ (2015) Prevalence of total hip and knee replacement in the United States. *J Bone Jt Surg* 97A:1386–1397
- Kumar S, Mandal M (2005) Bilateral transfer of skill in left- and right-handers. *Laterality* 10(4):337–344
- Levin SL, Feroze BM, Steven MP (2005) Common ground for spatial cognition? A behavioral and fMRI study of sex differences in mental rotation and spatial working memory. *Evol Psychol*. <https://doi.org/10.1177/147470490500300116>
- Lisberger SG (1988) The neural basis for learning of simple motor skills. *Science* 242(4879):728
- Luppa M, Luck T, Weyerer S, König H-H, Brähler E, Riedel-Heller SG (2010) Prediction of institutionalization in the elderly.

- A systematic review. *Age Ageing* 39(1):31–38. <https://doi.org/10.1093/ageing/afp202>
- Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, Das SR, de Ferranti S, Després JP, Fullerton HJ, Howard VJ, Huffman MD, Isasi CR, Jiménez MC, Judd SE, Kissela BM, Lichtman JH, Lisabeth LD, Liu S, Mackey RH, Magid DJ, McGuire DK, Mohler ER 3rd, Moy CS, Muntner P, Mussolino ME, Nasir K, Neumar RW, Nichol G, Palaniappan L, Pandey DK, Reeves MJ, Rodriguez CJ, Rosamond W, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Woo D, Yeh RW, Turner MB; American Heart Association Statistics Committee; Stroke Statistics Subcommittee (2016). Heart disease and stroke statistics-2016 update: a report from the American Heart Association. *Circulation* 133(4):e38–e360.
- Oldfield RC (1971) The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9(1):97–113
- Opara JA, Jaracz K, Broła W (2010) Quality of life in multiple sclerosis. *J Med Life* 3(4):352
- Pan Z, van Gemmert AWA (2013) The direction of bilateral transfer depends on the performance parameter. *Hum Mov Sci* 32(5):1070–1081. <https://doi.org/10.1016/j.humov.2012.02.013>
- Pelli DG (1997) The VideoToolbox software for visual psychophysics: transforming numbers into movies. *Spat Vis* 10(4):437–442
- Poston B, Van Gemmert AWA, Barduson B, Stelmach GE (2009) Movement structure in young and elderly adults during goal-directed movements of the left and right arm. *Brain Cogn* 69:30–38. <https://doi.org/10.1016/j.bandc.2008.05.002>
- Romero DH, Van Gemmert AWA, Adler CH, Bekkering H, Stelmach GE (2003a) Altered aiming movements in Parkinson's disease patients and elderly adults as a function of delays in movement onset. *Exp Brain Res* 151(2):249–261
- Romero DH, Van Gemmert AWA, Adler CH, Bekkering H, Stelmach GE (2003b) Time delays prior to movement alter the drawing kinematics of elderly adults. *Hum Mov Sci* 22:207–220. [https://doi.org/10.1016/S0167-9457\(02\)00160-4](https://doi.org/10.1016/S0167-9457(02)00160-4)
- Sainburg RL (2014) Convergent models of handedness and brain lateralization. *Front Psychol* 5:1092
- Sainburg RL, Wang J (2002) Interlimb transfer of visuomotor rotations: independence of direction and final position information. *Exp Brain Res* 145(4):437–447
- Schmidt RA, Lee TD (2014) Motor learning and performance: from principles to application, 5th edn. Human Kinetics, Champaign
- Seidler RD, Noll DC (2008) Neuroanatomical correlates of motor acquisition and motor transfer. *J Neurophysiol* 99(4):1836–1845. <https://doi.org/10.1152/jn.01187.2007>
- Seidler RD, Noll DC, Chintalapati P (2006) Bilateral basal ganglia activation associated with sensorimotor adaptation. *Exp Brain Res* 175(3):544–555
- Stevens JA, Burns E (eds) (2015) A CDC compendium of effective fall interventions: what works for community-dwelling older adults, 3rd edn
- Teixeira LA (2000) Timing and force components in bilateral transfer of learning. *Brain Cognit* 44:455–469
- Uggetti C, Ausenda CD, Squarza S, Cadioli M, Grimoldi L, Cerri C, Cariatì M (2016) Bilateral transfer phenomenon: a functional magnetic resonance imaging pilot study of healthy subjects. *Neuroradiol J* 29(4):250–253. <https://doi.org/10.1177/1971400916631992>
- Van Gemmert AW, Van Galen GP (1997) Stress, neuromotor noise, and human performance: a theoretical perspective. *J Exp Psychol Hum Percept Perform* 23(5):1299–1313
- Wenderoth N, Debaere F, Sanaert S, Swinnen SP (2005) The role of anterior cingulate cortex and precuneus in the coordination of motor behaviour. *Eur J Neurosci* 22(1):235–246
- Willingham DB (1999) The neural basis of motor-skill learning. *Curr Dir Psychol Sci* 8(6):178. <https://doi.org/10.1111/1467-8721.00042>
- Xiao-Wei S, Zhang-Ye D, Xiang-Yu L, Su-Fang L, Xi-Nian Z, Chao-Zhe Z, Yu-Feng Z (2011) REST: a toolkit for resting-state functional magnetic resonance imaging data processing. *PLoS One* 6(9):1–12. <https://doi.org/10.1371/journal.pone.0025031>

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