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Single session motor learning demonstrated using a visuomotor task: Evidence from fMRI and behavioural analysis

Shaun G. Boe [a,b,c,d,*], Ryan J. Cassidy [e], William E. McIlroy [c,d,g], Simon J. Graham [c,e,f,h]

[a] Laboratory for Brain Recovery and Function, School of Physiotherapy and Department of Psychology, Dalhousie University, Halifax, NS, Canada
[b] School of Health and Human Performance, Dalhousie University, Halifax, NS, Canada
[c] Heart and Stroke Foundation Centre for Stroke Recovery, Sunnybrook Health Sciences Centre, Toronto, ON, Canada
[d] Mobility Team, University Centre, Toronto Rehabilitation Institute, Toronto, ON, Canada
[e] Rotman Research Institute, Baycrest Centre for Geriatric Care, 3560 Bathurst St., Toronto, ON, Canada M6A 2E1
[f] Imaging Research, Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, 2075 Bayview Ave., Toronto, ON, Canada M4N 3M5
[g] Department of Kinesiology, University of Waterloo, 200 University Ave. West, Waterloo, ON, Canada N2L 3G1
[h] Department of Medical Biophysics, University of Toronto, Ontario Cancer Institute, Princess Margaret Hospital, Toronto, ON, Canada

HIGHLIGHTS

- Application of a novel visuomotor task to permit within-session motor learning.
- Time course of learning extended over the entire fMRI scan session (~1 h).
- Behavioural results show a learning-related improvement in performance.
- fMRI data showing changes in brain activation support the behavioural findings.

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ABSTRACT

There is a continuing need to improve understanding of the central nervous system control of learning. Specifically, there is a need to examine the characteristics of cortical and sub-cortical activity linked to the stages of motor learning, including those occurring within a single-session. In this study we sought to design and investigate a visuomotor task to determine its ability to assess the component of motor learning occurring during a single session of fMRI (i.e., the 'online' improvement in motor performance). Fourteen healthy control subjects performed a visuomotor task requiring a combination of bilateral grip force to accurately move a cursor towards a target. We assessed online motor learning by comparing behavioural measures (accuracy and error magnitude) and the extent of spatial activation in specific brain regions of interest (ROIs) using fMRI pre- and post-training. Results showed a training-related improvement in performance based on increased accuracy ($p < 0.0125$) and decreased error magnitude ($p < 0.0125$) from pre- to post-training. Decreases in the extent of spatial activation from pre- to post-training in the majority of ROIs supported a training-related attenuation in brain activity associated with online motor learning. Importantly, decreases in error magnitude across conditions ($p < 0.05$) confirmed that improvements in performance continued over the entire course of the experiment. Establishing this task may permit more extensive study of the neural correlates of single-session, online learning in healthy individuals and those with motor control challenges. Information obtained from such studies may provide an opportunity to improve interventions in neurological rehabilitation.

1. Introduction

Motor learning can be considered a performance-related improvement in the execution of a given motor task that results from repetitive task practice during which execution (e.g., how the movement is performed) and outcome (e.g., accuracy) are emphasized. Performance-related improvements (e.g., increased accuracy) are facilitated by augmenting repetitive task practice with the provision of feedback to guide error correction (for in-depth reviews please see Salmoni et al., 1984; Winstein, 1991). Studies utilizing functional magnetic resonance imaging (fMRI) in motor learning have permitted the spatial (Doyon and Benali, 2005; Karni et al., 1995; Seidler, 2010; Seidler and Noll, 2008; Shadmehr and Holcomb, 1997) and temporal (Coynel et al., 2010; Floyer-Lea

* Corresponding author at: School of Physiotherapy, Dalhousie University, Rm 418, 4th Floor Forrest Building, 5869 University Avenue, PO Box 15000, Halifax, NS, Canada B3H 4R2. Tel.: +1 902 494 6360; fax: +1 902 494 1941.
E-mail address: s.boe@dal.ca (S.G. Boe).

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and Matthews, 2004, 2005; Toni et al., 1998) aspects of brain activation underlying motor task performance to be identified, and have characterized the respective activation changes related to performance improvements as learning evolves.

Many studies examining motor learning classically define it as a process where improvements in performance are seen over a series of discrete training sessions and, following a delay and subsequent consolidation of the skill, similar levels of performance are observed on a retention test (Salmoni et al., 1984; Savion-Lemieux and Penhune, 2010; Winstein, 1991). Within the motor learning literature however, it has been demonstrated that learning occurs in the absence of consolidation; this 'short-term' learning characterizes training-related improvements in performance occurring within minutes-hours (for example see Floyer-Lea and Matthews, 2004; Karni et al., 1998). In their 2009 study, Reis et al. (2009) identify both 'online' and 'offline' effects of motor skill learning, which relate to within-session performance improvements (short-term learning) and the consolidation of a motor skill occurring over multiple sessions (long-term learning), respectively.

To date, considerable research incorporating fMRI analyses of motor learning have utilized experimental paradigms that permit the examination of either online (fast; within minutes) or offline (long-term; over the course of days) learning (Coynel et al., 2010; Doyon and Benali, 2005; Floyer-Lea and Matthews, 2005; Karni et al., 1995, 1998; Penhune and Doyon, 2005). In contrast, few studies have examined the online, or short-term, learning that occurs over the duration of a typical fMRI scan session (approximately 1 h). Considering that contemporary evidence from motor learning studies suggests that distinct neural mechanisms are engaged during the different stages of learning (i.e., fast, short- or long-term learning, Doyon et al., 2003; Floyer-Lea and Matthews, 2005; Karni et al., 1995, 1998), coupled with the understanding that short-term learning is a fundamental component of robust, long-term skill acquisition, it is critical to have a means of examining the neural correlates of short-term learning that occurs within this approximately 1 h time frame.

Notably, two studies have developed and applied paradigms to investigate learning over such a time course. Tang et al. (2009) designed a vibrotactile discrimination task to explore the cortical mechanisms underlying short-term, single-session learning. Over a time course that paralleled a single fMRI scan session, behavioural results showed subjects improved their ability to discriminate between different vibrotactile stimuli (i.e., correctly identifying matching/non-matching pairs). This finding, which provides evidence of online learning, was based on significant reductions in both error rate and reaction time. In a single subject who performed the task during fMRI, execution of the vibrotactile task resulted in activation of brain regions within a frontoparietal network, including middle frontal gyrus (MFG), pre- and post-central gyri, inferior parietal lobule and anterior cingulate cortex. Owing to the preliminary nature of the fMRI portion of the study however, learning-related changes in activation were not quantified across the pool of subjects.

Insight into learning-related changes in brain activity that occur over the time course of a single fMRI session have been previously documented by Toni et al. (1998), who examined motor sequence learning in a small sample ($N = 3$). Over the course of a 40 min scan session, subjects learned an eight finger movement sequence by trial and error, a process that was augmented by the provision of feedback. Functional MRI analyses revealed increased activation in a number of cortical [dorsolateral prefrontal cortex, anterior cingulate cortex, supplementary motor area (SMA), sensorimotor cortex] and sub-cortical (cerebellar hemispheres, corpus striatum and thalamus) brain regions. The early increase in activation observed in the majority of regions examined was related to the initial or early stage of learning, during which subjects showed a rapid improvement in task performance (error rate reached zero by ~9 min after study onset). The later stages of learning (termed 'overlearning' by the study authors), was generally associated with decreased activation in cortical and sub-cortical brain regions, a finding most likely related to increased automaticity in task performance. Exceptions to this trend of decreased activation were the SMA and ventrolateral thalamus, where higher levels of activation were largely maintained throughout the course of the study.

Given the relative lack of studies examining learning over the time course outlined above, and the importance of online, short-term learning as the foundation for offline, long-term consolidation of motor skills, our objective in the current study was to develop and evaluate a visuomotor task that was challenging enough in healthy adults to permit a slow rate of learning over a single fMRI scan session to assess the changes in cortical activity that vary with short-term improvements in performance. Specifically, we sought to investigate the 'online' or within-session component of motor learning as defined above. Thus, for the purpose of this study, we define 'motor learning' as the training-related improvement in performance occurring within a single-session of training. Clearly identifying the component of motor learning being examined is critical when interpreting study results, particularly in light of previous findings indicating differences in brain activation patterns between learning that occurs in the short- (e.g., single-session) and long-term (Floyer-Lea and Matthews, 2005; Meehan et al., 2011). Although not addressed directly in the current study, our additional motivation was to design a task that would facilitate the future investigation of online, short-term motor learning in patients with neurologic control challenges. Considering that interventions aimed at improving function following neurologic injury are generally based on principles of motor skill acquisition or learning (Askim et al., 2009; Bastian, 2008; Classen et al., 1998; Krakauer, 2006; Newell and Ranganathan, 2009; Schmidt, 2003; Winstein, 1991), related fMRI analyses are potentially very informative. For instance, a better understanding of the brain regions involved as well as the time course of motor learning in individuals with neurologic control challenges can influence the parameters (e.g., dosing and intensity) of treatments used to promote recovery of function.

Given these objectives, the primary criteria for the task was to permit the investigation of online, short-term learning over the course of a typical fMRI examination period of approximately 1 h, a time period which also approximates the duration of a typical session of rehabilitation. Additional criteria were to develop a task that involved the scaling of forces with hand grip. Gripping was chosen over finer motor tasks that require use of the digits (e.g., compressing a force transducer between the thumb and first digit or performing a sequential finger tapping task) as sufficient control of the digits is less often observed in patients with neurologic injury compared to a gross motor action such as mass gripping. Bilateral control was used to obtain insight into activation linked to the control of both limbs simultaneously.

With regard to the development and testing of this new task, it was hypothesized that (1) task performance would result in activation of brain regions consistent with motor performance involving the upper extremities; and (2) as learning occurred (pre–post training), attenuation in regional activation (e.g., pre-motor, motor and cerebellar activation) would be observed consistent with prior motor learning studies of a similar duration. A secondary objective of the study was to examine the generalizability of the training condition. Specifically, we wished to investigate whether the training and learning-related changes in brain activity would transfer to a contextually identical motor task featuring reversed input requirements. Here we present group behavioural and fMRI data demonstrating an online, single-session learning effect using this new task.

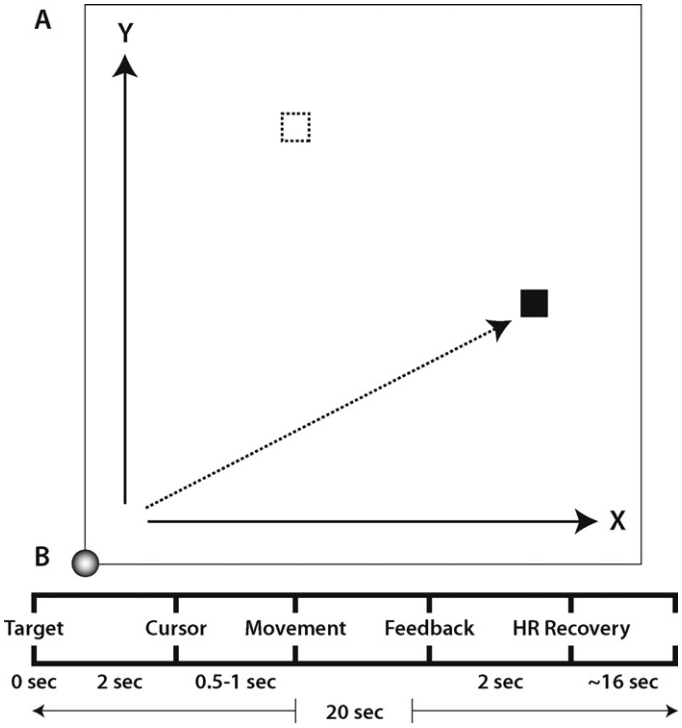

Fig. 1. (A) Visuomotor task: subjects move a cursor (grey circle, lower left) from its starting position to the target (black square) by gripping a set of pressure bulbs. The solid arrows (X and Y) represent cursor movement if the bulbs are gripped individually (left = Y, right = X), while the dashed arrow is representative of one possible combination of left and right inputs. The dashed square (upper left) represents the target position during the 'reverse' condition. (B) Timeline of the visuomotor task during fMRI (pre- and post-training conditions). HR = haemodynamic response.

2. Methods

2.1. Subjects

Fourteen right handed (Oldfield, 1971) subjects (8 male, 24.7 ± 3.4 years, 175.4 ± 9.0 cm, 68.6 ± 13.4 kg) agreed to participate in the study. All subjects were free of neurological disorder and each provided written, informed consent prior to the onset of the study. Prior to participation, subjects were screened for contraindications to MRI (e.g., implanted metal) according to institutional procedure. The study was conducted with approval from the Research Ethics Board at Baycrest according to the principles of the Declaration of Helsinki.

2.2. Visuomotor task

To address our study objective, we developed a visually cued bilateral gripping task with visual feedback. The goal of the visuomotor task was to move accurately a cursor towards a target located a fixed distance (18.5 'virtual cm') and angle (22°) from the initial cursor position (see Fig. 1A). Subjects held two rubber bulbs (inflation bulbs from a sphygmomanometer), one each in the left and right hand, which controlled vertical and horizontal movement of the cursor, respectively. Cursor movement was achieved by gripping the bulbs. The air pressure generated when a bulb was squeezed was transmitted through pneumatic tubing outside the magnet room, via a waveguide in the radiofrequency shield of the magnet room, to a corresponding pressure sensor (model ASCX15DN; Honeywell Sensing and Control, Golden Valley, MN) that converted air pressure to an output voltage. The output voltage was translated into cursor movement such that the angle of cursor movement, and the distance the cursor moved, were each proportional to the magnitude of the summed input of the left and right hand. For instance, too little or too much force applied to the bulbs resulted in under- or over-shoot of the target, respectively. Regarding cursor angle, gripping the bulbs individually resulted in an angle of either 90° (vertical movement only; left hand bulb; *Y* direction, Fig. 1A) or 0° (horizontal movement; right hand bulb; *X* direction, Fig. 1A) whereas gripping the bulbs simultaneously would generate an angle between 0° and 90° based on the magnitude of the input from the left and right hand (R > L input = 0–45°; L > R input = 45–90°; Fig. 1A).

Cursor movement was determined from a 300 ms synchronous sampling epoch of the output voltage from the left and right bulb (1000 Hz sampling frequency, USB 6251M-Series Multi-function DAQ; National Instruments, Austin, TX), 100 ms after the onset of the gripping action. Owing to the brief sampling duration, the task was discrete, not continuous: participants did not have the opportunity within a single trial to 'correct' their input. Rather, they had to wait until the next trial to make adjustments to improve performance. Considering the need to have the correct cursor angle and distance, successful completion of the task required a precise combination of input from both the left and right hand in terms of grip force and duration.

To aid in trial to trial learning, the task incorporated visual feedback relating to task performance. Behavioural measures were displayed trial-by-trial to participants, including accuracy [accurate ($\leq$1.5 'virtual cm' from the target) vs. inaccurate] and error magnitude [absolute distance (virtual cm) of the centre of the cursor from the centre of the target]. In addition to these primary measures of performance, response time and cursor angle were also obtained and recorded on a trial-by-trial basis for subsequent analysis to quantify performance pre- and post-training and to aid in the characterization of learning.

Each trial began with the presentation of the target (black square), followed 2 s later by the presentation of the cursor (grey circle lower left). Appearance of the cursor provided the cue for participants to perform gripping. Immediately after participant input, cursor movement was indicated and visual feedback regarding task performance was presented for 2 s, followed by an inter-trial interval to allow recovery of the fMRI haemodynamic response. The total duration of the interval was dependent on the participant's response time. A longer response time resulted in a shorter break such that the total time for a single trial did not exceed 20 s. Response time was measured as the time (ms) between the presentation of the cursor and the onset of participant input. It is important to note that although the response time for each trial was recorded, this was not a response time task per se; participants were informed that the goal was to be as accurate as possible, and that they should respond at their own pace. A single trial timeline is depicted in Fig. 1B.

2.3. Visuomotor task conditions

Four task conditions were used in the present study. The first three conditions shared the same target location (black square; Fig. 1A) and included: (1) pre-training ('pre') – 20 trials to characterize the "unlearned" state; (2) training (no fMRI) – 600 trials split by two short rest intervals; and (3) post-training ('post') – 20 trials to characterize the "learned" state. To examine the generalizability of training, a second post-training condition ('reverse') consisted of 20 trials in which the target was moved to a different location such that the input required from the left and right hands was swapped (dashed square; Fig. 1A). Pilot testing of the visuomotor task confirmed that 20 trials were sufficient for the non-training conditions to generate activation maps that were suitably robust for use in a group fMRI study. All pre- and post-training trials proceeded according to the timeline described above (Fig. 1B).

To decrease the overall duration of the experiment, the timing of the individual training trials was reduced to approximately 2.5 s, which included a 1 s period between presentation of the target and the cursor; a period representing participant response time (between cursor presentation and participant input) which varied from trial to trial; and a 1 s period for the presentation of visual feedback. In contrast to the pre- and post-training conditions, a break between trials to allow recovery of the haemodynamic response was not needed in the training condition, as fMRI was not performed. The visuomotor task software was custom-programmed in the LabVIEW environment (v7.1; National Instruments, Austin, TX).

2.4. MRI acquisition

Imaging data were collected using a 3.0 T whole-body MRI system (MAGNETOM Tim Trio, VB15A software; Siemens AG, Erlangen, Germany) using a standard 12 channel phased head array coil. Anatomical images were acquired with a T_1-weighted high resolution oblique-axial 3D magnetization prepared rapid gradient echo (MPRAGE) sequence with parameters: TI/TR/TE/FA = 1100 ms/2000 ms/2.63 ms/9°, 256 mm × 192 mm FOV, 256 × 192 matrix, 1.0 mm thickness, 160 slices, where TI is the inversion time, TR is the repetition time, TE is the echo time, FA is the flip angle, and FOV is the field of view. Functional MRI was acquired using T_2*-weighted oblique-axial 2D gradient echo planar imaging (EPI) with parameters: TR/TE/FA = 2000 ms/30 ms/70°, 200 mm × 200 mm FOV, 64 × 64 matrix, 5.0 mm thickness, 30 slices and 208 measurements per run. Pulse and respiration rate were collected throughout fMRI using the photoplethysmograph and respiratory cushion available on the MRI system, respectively, for physiological motion correction in data pre-processing.

2.5. Experimental protocol

The visuomotor task was presented to participants on a rear projection screen viewed through a mirror mounted on the head coil. Prior to the onset of each experiment, the visuomotor task was described to participants and each was provided an opportunity to clarify any questions regarding the task or the protocol in general. All experiments proceeded in the same temporal sequence: (1) pre-training fMRI (pre); (2) training condition (no fMRI); and (3) post-training fMRI (post and reverse, performed in two separate fMRI runs). To enable steady-state magnetization to be achieved prior to visuomotor task performance, each fMRI run included an initial 16 s period during which participants fixated on a filled circle centred on the projection screen. Including this period, each fMRI run lasted 416 s (6:56 min). The training condition was performed in 3 blocks of 200 trials (T_{200}, T_{400} and T_{600}), with a 5 min break provided after each block. Considering the timing described above, each block of training trials lasted approximately 500 s (8:20 min). For time efficiency, anatomical images were acquired during the first block of training. Total time in the scanner was approximately 60 min, with 20:48 min of fMRI.

2.6. Visuomotor task analysis

Behavioural measures (accuracy, error magnitude, cursor angle and response time) were compared pre- and post-training to characterize training-related improvements and to assess the generalizability of training. To facilitate comparison across the three fMRI conditions (pre-, post- and reverse) and across the three training blocks (T_{200}, T_{400} and T_{600}), a mean value for each of the behavioural measures was determined per subject for each condition/block. Prior to statistical analysis, data were examined for normality using the D'Agostino and Pearson omnibus normality test (D'Agostino, 1986). Although the majority of the data demonstrated a normal distribution ($p > 0.05$), results of the normality test revealed a degree of variability about the normal distribution, including data from two conditions [pre (error) and post (accuracy)] that were slightly non-Gaussian ($p < 0.05$). Given that the deviation from the normal distribution was sufficiently negligible, and considering the robustness of parametric statistics to violations of their underlying assumptions (Glass et al., 1972; Zimmerman, 1998), it was determined that parametric statistics could be appropriately applied to assess training-related changes in performance.

Accordingly, the within-subject effect of training on behavioural performance was assessed in two ways. First, pre- and post-training behavioural measures were compared using paired *t*-tests (pre vs. post). Second, behavioural measures were compared across the three blocks of training (T_{200}, T_{400} and T_{600}) using a one-way repeated measures analysis of variance (ANOVA). If a significant main effect was detected amongst the three training blocks, post hoc analysis was performed to determine the significant interactions using the Tukey test. Generalizability of training was determined by comparing post-training behavioural measures using paired *t*-tests (post vs. reverse). All statistical analyses were performed using GraphPad Prism 4 (GraphPad Software v. 4.02, San Diego, CA). To account for multiple comparisons across the four dependent measures (*t*-tests), a Bonferroni correction was applied and as a result significance for these tests is denoted by an a priori alpha level of $p < 0.0125$. Unless noted otherwise, in-text data are presented as mean values ± standard deviation. For illustrative purposes, graphical data are presented as mean values ± standard error.

2.7. fMRI analysis

Preprocessing of functional image data was performed using Analysis of Functional Neuroimages (AFNI) software (Cox, 1996; Cox and Hyde, 1997). Corrections for physiologic artefact (cardiac pulsatility and respiration) were made using the *3dretroicor* algorithm (Glover et al., 2000), followed by the application of image slice timing and head motion correction (via *3dTshift* and *3dvolreg* respectively) with the latter assuming rigid body motion. Spatial smoothing was performed using a 5 mm FWHM Gaussian kernel.

Preprocessed functional data for each subject were analysed using the General Linear Model (GLM) (Friston et al., 1995) focused on the 4 s interval between the cue for movement (cursor appearance) and the appearance of feedback for each of the pre- and post-training conditions (Fig. 1B). Contrast maps of differential brain activity were computed based on the trials for each of the pre- and post-training conditions (pre, post and reverse) and compared with baseline functional activity assessed during the rest period (i.e., the entire interval between the end of feedback on a given trial and the beginning of the cue for the subsequent trial). Haemodynamic response functions were determined in a data-driven manner over a duration of 6 TR (12 s) for each condition, and 3rd order Legendre polynomial detrending was incorporated into the GLM analysis (via the *3dDeconvolve* algorithm). The contrast maps were derived based on results of the individual GLM using Student's *t*-tests such that a map was created for each subject in each condition (pre, post and reverse). The maps were then corrected for multiple comparisons using a false-discovery rate (FDR; *3dFDR*) method, and thresholded at a FDR of 0.05 (Genovese et al., 2002).

To facilitate group analysis ($N = 14$) of task-related brain activity, the contrast maps calculated for each subject were transformed into Talairach–Tournoux coordinates using *auto_tlrc* (Talairach and Tournoux, 1988). Group contrast maps were then computed using Student's *t*-tests for the pre, post, and reverse conditions. The resulting maps were corrected for multiple comparisons using

Table 1
Behavioural measures across conditions (parentheses indicate standard deviation).

	Pre (20 trials)	Post (20 trials)	Reverse (20 trials)	T_{200} (1–200)	T_{400} (201–400)	T_{600} (401–600)
Accuracy	1.6 (2.0)	5.4 (3.6)	3.5 (2.7)	35.9 (27.8)	46.4 (34.4)	58.5 (32.1)
Error (cm)	5.4 (2.1)	2.7 (0.8)	3.6 (1.4)	3.8 (1.2)	3.2 (1.1)	2.6 (0.9)
CA_{diff}[a] (°)	10.6 (6.4)	5.0 (3.2)	10.2 (2.7)	7.5 (2.9)	6.2 (2.9)	5.1 (2.4)
Response time (ms)	1094.2 (196.4)	1071.9 (198.8)	1125.6 (207.8)	853.5 (149.6)	797.7 (174.8)	841.6 (167.5)

[a] CA_{diff}: absolute difference in cursor angle between the actual and required angle of cursor trajectory.

a family-wise error correction technique (Monte Carlo simulation utility *AlphaSim*; Forman et al., 1995). Correction for multiple comparisons in this manner resulted in the removal of activation clusters smaller than 11 voxels, producing a corrected significance level of $p < 0.05$ (uncorrected threshold $p < 0.001$). To examine task-related brain activity in individual subject and group contrast maps, regions of interest (ROIs) known to be involved in motor execution, control and learning were determined using standard atlases available in AFNI including the cerebellum (CB), thalamus, MFG, SMA, and primary motor cortex (M1) (Eickhoff et al., 2005; Lancaster et al., 2000).

For individual subjects, differences in brain activity between the pre, post and reverse conditions were investigated by comparing counts of voxels that exceeded the FDR-corrected level of 0.05 over (1) the whole brain; and (2) the specified ROIs. Thus, for each subject, 3 voxel counts were available for each ROI and the whole brain, corresponding to the pre, post and reverse conditions. The spatial extent of task-related brain activation for the whole brain and the ROIs were then examined using a one-way, repeated measures ANOVA to analyse the effect of training over the three pre- and post-training conditions (pre, post and reverse). If a significant main effect was detected among the pre, post and reverse conditions, post hoc analysis was performed to determine the significant interactions using the Tukey test. An a priori alpha level of $p < 0.05$ was used to denote significance for these analyses.

3. Results

3.1. Visuomotor task

Analysis of the behavioural measures for the pre and post condition showed a significant training-related improvement in performance. Specifically, participants achieved greater accuracy following training [$t(13) = 4.222$, $p < 0.0125$], demonstrating an increase in the number of accurate trials in the post-training condition (post: 5.4 ± 3.6) compared to the pre-training condition (pre: 1.6 ± 2.0; Table 1 and Fig. 2A). In agreement with the finding of increased accuracy post-training, we observed a decrease in error magnitude [$t(13) = 4.917$, $p < 0.0125$] from pre- (5.4 ± 2.1 cm) to post-training (2.7 ± 0.8 cm; Table 1 and Fig. 2A). To further capture training-related improvements in performance, we calculated the absolute difference in cursor angle (CA_{diff}) by subtracting the actual angle of cursor trajectory (i.e., the angle that resulted from participant input) from the required angle of cursor trajectory (i.e., the angle required for accurate performance). Similar to our finding of decreased error, CA_{diff} decreased after training [$t(13) = 3.585$, $p < 0.0125$], from $10.6 \pm 6.1°$ to $5.0 \pm 3.2°$ (pre and post, respectively; Table 1).

To demonstrate the progression of learning throughout the training period, we compared performance on the visuomotor task across the three blocks of training. As training progressed, an increase in accuracy was shown as a main effect of training block

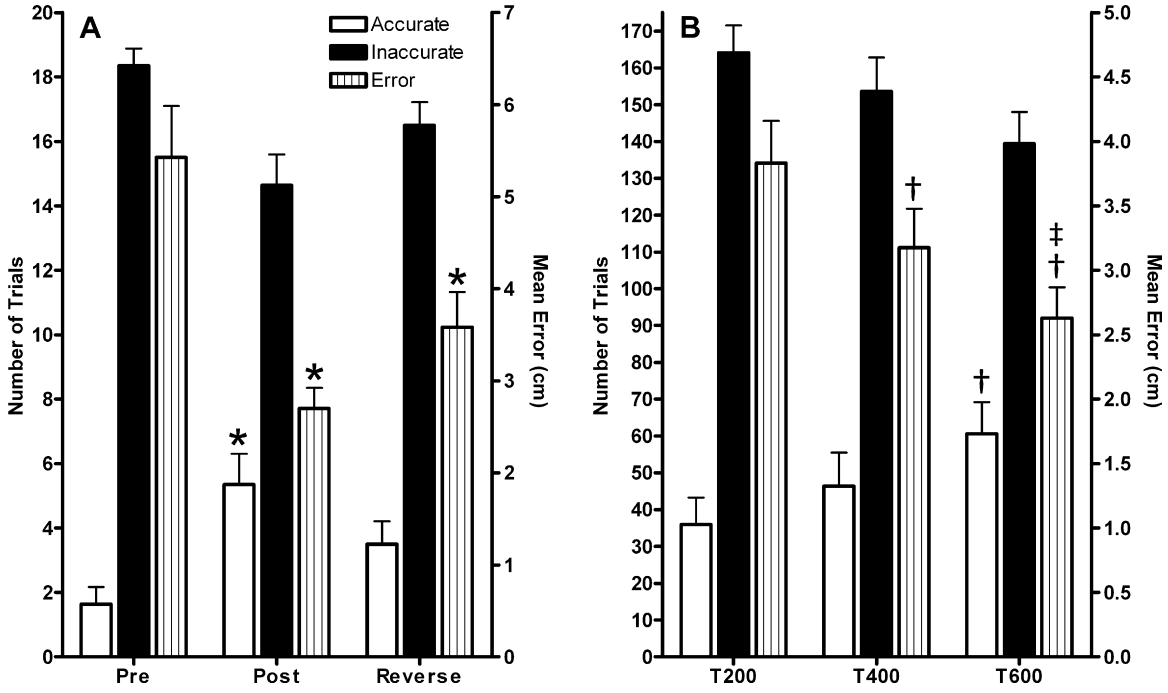

Fig. 2. Behavioural data ($N = 14$) for the pre- and post-training (A) and training (B) conditions. (A) In support of a training-related increase in performance, a significant increase in the number of accurate trials (unfilled bars, left *y*-axis) was observed pre-post training. In parallel with this increase in accuracy, a significant decrease was observed for error magnitude (striped bars, right *y*-axis) in the post- compared to the pre-training condition. (B) A progressive improvement in performance was also observed across the three blocks of training, with significantly improved accuracy (unfilled bars, left *y*-axis) and a significant decrease in error magnitude (striped bars, right *y*-axis). *Significant difference from pre-training; †Significant difference from T_{200}; ‡Significant difference from T_{400}. Bars represent standard error.

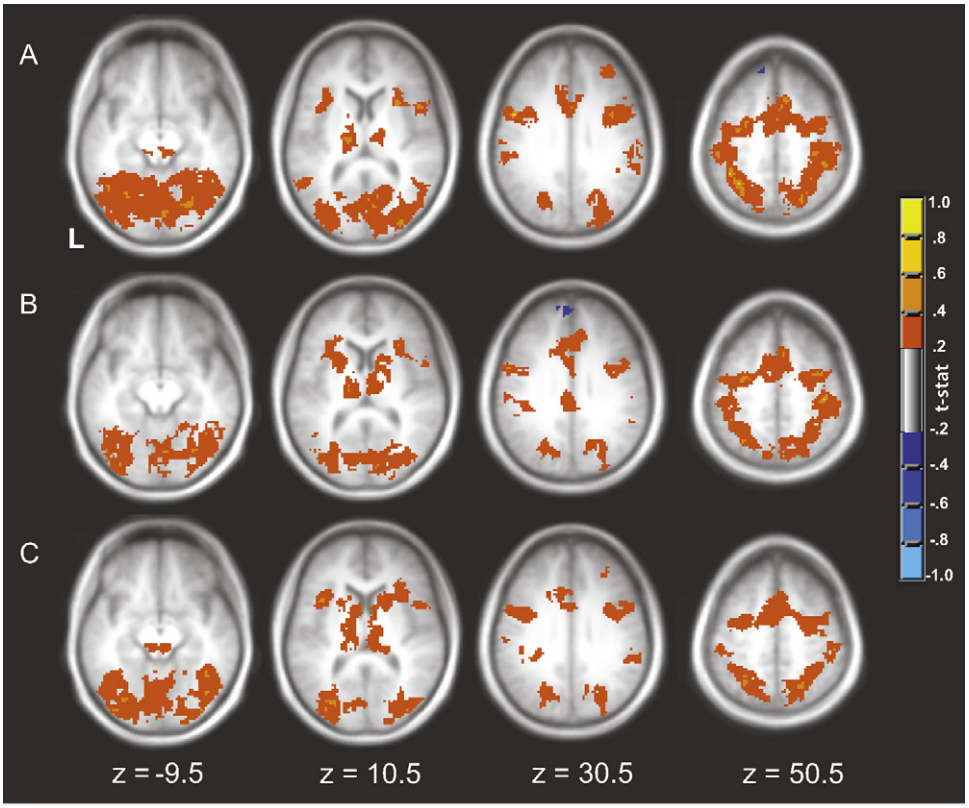

Fig. 3. Group ($N = 14$) statistical parametric maps (t-scored) contrasting the pre (A), post (B) and reverse (C) conditions relative to baseline activity. Brain regions shown include the cerebellum (CB; $z = -9.5$), thalamus ($z = 10.5$), middle frontal gyrus (MFG; $z = 30.5$), supplementary motor area (SMA) and primary motor cortex (M1; $z = 50.5$). In general, the spatial extent of activations decreased from pre- (A) to post- (B) training with an intermediate level of activation (relative to pre and post) observed for the reverse (C) condition.

on the number of accurate trials [$F(2, 13) = 10.93$, $p < 0.05$]. Post hoc analysis revealed a significant difference in the number of accurate trials between the first (T_{200}) and last (T_{600}) block of training [$q(13) = 5.559$, $p < 0.05$; Table 1 and Fig. 2B]. A main effect of training block was also observed for error magnitude [$F(2, 13) = 15.21$, $p < 0.05$], with post hoc analysis revealing differences between each of the training blocks, such that error magnitude decreased significantly between T_{200}, T_{400}, and T_{600} [$q(13) = 4.243$, 7.791 and 3.548 (T_{200}, T_{400}, and T_{600} respectively), $p < 0.05$; Table 1 and Fig. 2B]. Training results for CA_{diff} were similar to those observed for accuracy, with a main effect of training block representing a decrease in CA_{diff} as training progressed. Post hoc analysis revealed a significant difference between T_{200} and T_{600} [$q(13) = 6.159$, $p < 0.05$; Table 1].

Comparison of behavioural measures between the post-training conditions (post vs. reverse) revealed evidence supporting the generalizability of the training condition. Specifically, our primary measures of behavioural performance, accuracy and error magnitude, were not statistically different between the post and reverse conditions [$t(13) = 1.632$, $p > 0.0125$ and $t(13) = 1.874$, $p > 0.0125$, accuracy and error respectively; Table 1 and Fig. 2A], confirming that training would transfer to a contextually identical task with reversed input requirements. Conversely, a lack of transfer would have resulted in performance in the reverse condition returning to levels observed in the pre condition, resulting in a significant difference between the post and reverse conditions. Although accuracy and error were not found to differ significantly between the two post-training conditions, we sought further evidence to confirm the generalizability of the training condition owing to the difference in mean values between post and reverse for both accuracy (-1.9 trials) and error (+0.9 cm; Table 1). To further test the generalizability of training, we compared accuracy and error values from the reverse condition to those obtained pre-training using paired t-tests as described previously. If the training resulted in generalization or skill transfer, then we would expect behavioural measures from the reverse condition to differ from the pre-training values. Despite a greater than doubling of the number of accurate trials (Table 1), accuracy values did not differ significantly between the pre- and reverse conditions [$t(13) = 1.970$, $p > 0.0125$]. Unlike accuracy, error magnitude differed significantly between the pre and reverse conditions [$t(13) = 3.190$, $p < 0.0125$, Fig. 2A], with a decrease of 1.8 cm (5.4 ± 2.1 to 3.6 ± 1.4 cm, pre and reverse respectively).

Interestingly, our findings with regard to CA_{diff} did not support the generalizability of the training condition, as CA_{diff} from the reverse condition was found to differ significantly from post CA_{diff} [$t(13) = 4.599$, $p > 0.0125$] but not from pre CA_{diff} [$t(13) = 0.2343$, $p < 0.0125$; Table 1]. Lastly, participant response times did not differ across any of the test conditions ($p > 0.0125$ for all contrasts; Table 1). Participant response times were lower during the training conditions relative to the test conditions, an observation we attribute to the self-paced nature of the training trials. Similar to the test conditions, response times did not differ across the three blocks of training [$F(2, 13) = 1.752$, $p > 0.05$; Table 1].

3.2. Brain activity

Brain activation revealed by group functional maps for each of the three conditions is shown in Fig. 3. Regions of interest reflecting bilateral activation for all conditions included the CB ($z = -9.5$), thalamus ($z = 10.5$), SMA ($z = 50.5$) and M1 ($z = 50.5$). For the CB, the volume of activation was greatest during pre-training trials, and lowest in the post-training trials (Fig. 3A and B respectively), with

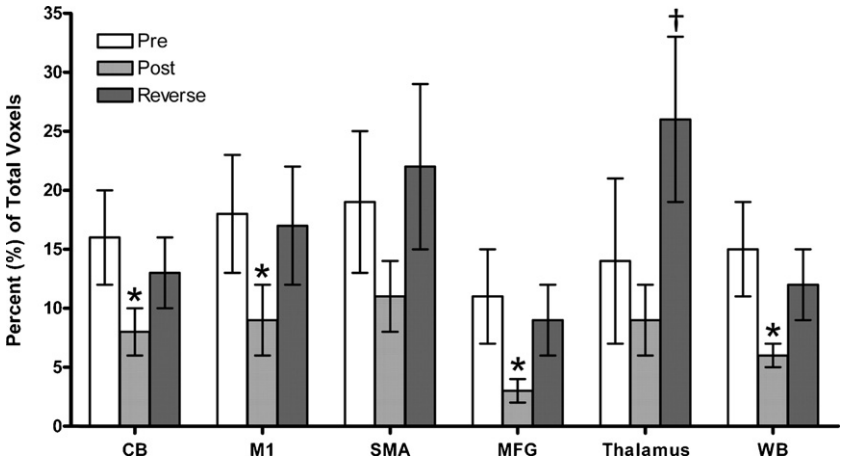

Fig. 4. Spatial extent of activation (amount of active voxels in a given region depicted as a percentage of total voxels in each region) across the pre (unfilled bars), post (light grey bars) and reverse (dark grey bars) conditions. Analysis revealed a trend towards a reduced extent of spatial activation from the pre to post condition in support of a training-related reduction in brain activation. In general, an intermediate level of activation (relative to pre and post) was observed for the reverse condition suggesting generalizability of the training. *Significant difference from 'pre'; †Significant difference from 'post'. CB, cerebellum; M1, primary motor cortex; SMA, supplementary motor area; MFG, middle frontal gyrus; WB, whole brain.

corresponding voxel counts of 7466 (pre) and 4861 (post). Relative to the pre and post conditions, an intermediate level of activation was observed for the reverse condition (Fig. 3C), with a voxel count of 5498. In contrast to the CB, the volume of activation decreased progressively from pre- to post-training for the SMA and M1 bilaterally (Fig. 3) with voxel counts of 1276, 1114, and 943 (SMA) and 2177, 1693, and 1578 (M1) for the pre, post and reverse conditions, respectively. Regardless of the trend in activation extent across task conditions, activations were symmetric bilaterally for the majority of brain regions, consistent with the bimanual nature of the task.

Statistical analysis of the extent of activation based on individual subject voxel counts demonstrated a significantly reduced extent of brain activation from pre- to post-training (see Fig. 4 and Table 2). A significant main effect of condition on the extent of spatial activation for the whole brain, CB, MFG, and M1 [$F(2, 13) = 5.362$, 3.884, 4.610, and 4.462, respectively; $p < 0.05$] was observed, with post hoc analyses revealing a significantly reduced number of active voxels in the post-compared to the pre-training condition for the whole brain [$q(13) = 4.496$, $p < 0.05$], CB [$q(13) = 3.927$, $p < 0.05$], M1 [$q(13) = 3.937$, $p < 0.05$] and MFG [$q(13) = 4.058$, $p < 0.05$]. Although not statistically significant, the number of activated voxels for the thalamus and SMA followed a similar trend, with a decreased number of voxels observed pre- to post-training (Fig. 4).

4. Discussion

The objective of the present study was to develop and investigate a visuomotor task that was challenging enough to require learning to occur over the duration of a typical fMRI scan session (approximately 1 h). The design and use of such a task would provide an opportunity to explore changes in nervous system activity concurrent with online, short-term motor skill acquisition. To address these objectives, we developed a visuomotor task that featured a bilateral gripping action requiring a precise combination of grip force and timing to achieve successful task performance. Subsequent to application of the task, learning was confirmed based on the finding of training-related improvements in performance and attenuation in the extent of spatial activation in brain regions concurrent with motor learning and performance. Collectively these findings provide evidence to support the use of this visuomotor task in examining the neural correlates of online motor learning occurring over the course of a single fMRI scan session.

4.1. Evidence to support learning

4.1.1. Behavioural performance

As highlighted previously, to demonstrate the utility of the visuomotor task for the assessment of online, single-session motor learning, it was necessary to establish evidence showing a learning-related effect behaviourally and from a brain activation perspective. With regard to behavioural performance, we observed significant differences from pre-post training for both of our primary measures, accuracy and error magnitude. Although direct comparison to other studies of motor learning is complicated by methodological differences (notably the task employed and duration of the learning paradigm), the increase observed in the number of accurate trials from pre-post training (Table 1 and Fig. 2A) parallels performance improvements observed in other studies (Anguera et al., 2007; Floyer-Lea and Matthews, 2004; Karni et al., 1998; Penhune and Doyon, 2005; Rémy et al., 2008; Staines et al., 2002). Interestingly, the number of accurate trials observed across subjects in each of the four conditions (pre, training, post, and reverse) was low relative to our expectation of performance; for instance, subjects managed to complete only 8% of the trials in the pre-training condition accurately. The low number of accurate trials may partly be attributable to the criteria applied to discern an accurate vs. inaccurate trial. The software utilized in the present study identified a trial as accurate when the centre of the cursor stopped within 1.5 'virtual cm' of the target centre. The application of less stringent criteria would have increased the number of accurate trials in all conditions. For example, applying a more liberal criterion of 2.5 'virtual cm' would result in an average increase in the number of accurate trials of $40.6 \pm 3.9\%$. Importantly, this increase would be nearly uniform across conditions, indicating that the training-related improvement in performance was not merely a by-product of the criteria used to classify an accurate trial.

Although the finding of a significant increase in the number of accurate trials after training is evidence that online learning occurred, this is a coarse, discrete measure of change in behaviour. Consequently, learning was further characterized based on the error magnitude recorded for each trial, a continuous variable that resolves behavioural performance more finely. A significant decrease in error magnitude (approximately 50%) was observed pre-post training, indicating improved ability to produce the necessary grip force while coordinating the appropriate balance of left and right hand input. This latter point is confirmed by the

Table 2
Individual subjects FDR-corrected voxel count data across selected ROIs and the whole brain. SD, standard deviation; SE, standard error.

Subject	CB			M1			SMA			MFG			Thalamus			Whole brain		
	Pre	Post	Reverse	Pre	Post	Reverse	Pre	Post	Reverse	Pre	Post	Reverse	Pre	Post	Reverse	Pre	Post	Reverse
1	3247	1	112	1433	2	195	171	3	0	568	30	77	4	0	0	18,772	383	2111
2	383	173	2611	554	170	378	445	392	375	357	240	283	0	113	822	7226	3579	13,880
3	1917	579	193	100	8	10	72	32	9	53	18	8	1	0	0	9755	4425	857
4	592	2252	2140	197	129	143	4	11	5	60	92	175	0	44	221	4200	6609	10,938
5	5536	3297	3360	813	846	548	646	457	558	724	256	384	9	34	195	26,174	13,624	18,275
6	4039	3819	3853	1134	1060	1081	560	196	229	298	182	286	179	147	145	26,637	22,702	26,606
7	3979	147	4637	603	71	829	4	0	142	260	7	574	0	14	461	17,896	1086	21,150
8	11,441	850	2388	4313	196	2593	2153	362	1446	3642	227	1158	1408	32	611	87,901	13,591	37,784
9	10,787	2279	4519	5565	2548	4163	2136	1117	1555	3066	715	2224	1212	545	1009	91,965	26,868	49,472
10	1331	904	5237	1049	264	2422	174	323	1517	320	23	1640	2	69	962	13,687	4739	40,447
11	2518	2736	1158	999	409	69	67	166	22	1243	305	197	12	2	0	19,333	10,992	7109
12	5580	5302	6207	2393	2821	4305	791	1177	1651	1275	774	2337	522	675	1133	34,906	31,366	50,887
13	6600	4249	8649	2997	1823	4138	1317	832	2334	820	530	1061	359	552	1486	44,141	26,743	60,290
14	558	300	7	166	244	0	15	19	0	45	29	8	7	164	0	5454	4714	577
Mean	4179	1921	3219	1594	757	1491	611	363	703	909	245	744	265	171	503	29,146	12,244	24,313
SD	3545	1749	2515	1654	960	1683	751	406	813	1115	258	810	472	235	501	28,122	10,563	20,224
Mean[a]	0.16	0.08	0.13	0.18	0.09	0.17	0.19	0.11	0.22	0.11	0.03	0.09	0.14	0.09	0.26	0.15	0.06	0.12
SD[a]	0.14	0.07	0.10	0.19	0.11	0.19	0.23	0.12	0.25	0.14	0.03	0.10	0.25	0.12	0.26	0.14	0.05	0.10
SE[a]	0.04	0.02	0.03	0.05	0.03	0.05	0.06	0.03	0.07	0.04	0.01	0.03	0.07	0.03	0.07	0.04	0.01	0.03

CB, cerebellum; M1, primary motor cortex; SMA, supplementary motor area; MFG, medial frontal gyrus.
[a] Indicates mean, SD and SE for a given ROI expressed as the amount of active voxels depicted as a percentage of total voxels in each region.

significant decrease in CA_{diff} after training which shows participants produced a cursor trajectory closer to the target. Error magnitude also showed decreased variability post- relative to pre-training (standard deviation of 0.8 vs. 2.1 'virtual cm') indicating participants were consistently closer to the target after training, albeit not close enough to achieve a higher accuracy rate according to the chosen accuracy threshold.

4.1.2. Brain activity

Consistent with prior studies, execution of the visuomotor task resulted in robust activation of brain regions that underlie motor execution and performance including M1, SMA and MFG (Doyon et al., 1996; Eliassen et al., 2003; Floyer-Lea and Matthews, 2005; Karni et al., 1995; Müller et al., 2002). Moreover, performance of the task in the pre-training condition produced considerable activation bilaterally in the CB (Fig. 3A), a region implicated in error detection/correction, and more generally in the evolution of learning (Doyon et al., 2002, 2003; Flament et al., 1996; Matsumura et al., 2004; Penhune and Doyon, 2005; Seidler and Noll, 2008). In accordance with our hypotheses and in concert with the aforementioned behavioural measures, we observed changes in the extent of spatial activation in these regions from pre- to post-training, indicating reorganization in the brain resulting from online, short-term learning.

Throughout the whole brain, we observed a significant decrease in the extent of spatial activation indicative of a reduced demand on neural resources as participants learned to execute the task. Examination of specific ROIs revealed a similar trend, with significantly reduced numbers of activated voxels in CB, M1 and MFG. Although not significantly different from pre-training, the extent of activation in the thalamus and SMA followed the general trend of reduced activity post-training, consistent with prior studies of short-term motor learning (Floyer-Lea and Matthews, 2004). The reduction observed in the CB is consistent with results observed in the vast majority of motor learning studies, which suggest cerebellar activity decreases owing to a diminished need to evaluate and subsequently modify movement execution as performance improves. The decreased activity in the CB is also consistent with motor learning theory proposed by Doyon and Benali (2005) and Doyon et al. (2002, 2003), who suggest that as performance improves and learning progresses, there is a shift from a cerebellar-cortical to a striatal-cortical network (Doyon and Benali, 2005; Doyon et al., 2002, 2003).

Conversely, our finding of decreased activation in the cortical ROI's examined, including M1, seems to oppose this theory. In the context of the study design and relative to other studies which show variable changes in cortical activity with motor learning, however, these findings are reasonable. A number of studies examining 'slow' or offline learning (i.e., over multiple sessions or days) have shown decreased CB and increased M1 activation as performance improved, consistent with the theorized shift from a cerebellar-cortical to a striatal-cortical network (Coynel et al., 2010; Doyon and Benali, 2005; Doyon et al., 2003; Penhune and Doyon, 2005). Importantly, studies examining the 'fast' or online, early components of learning (i.e., within minutes) have shown increased activation in both CB and M1, with the level of activation decreasing as subjects 'overlearned' the task (Floyer-Lea and Matthews, 2005; Karni et al., 1995, 1998; Toni et al., 1998). The discrepancy noted for changes in activation has been attributed in part to the duration of time over which learning was examined and the corresponding role of M1 in the execution of tasks in the early, intermediate (overlearned) and late (consolidation) phases of learning (Muellbacher et al., 2002; Smyth et al., 2010). For example, Toni et al. (1998) among others observed increased M1 activation early in learning (within minutes), followed by a decrease in activation in the later phases of their study (which

corresponded to the intermediate or 'overlearned' state) when pre-post imaging was performed within a single session (over 40 min). Conversely, imaging performed hours-days after training shows decreased activity in the CB and increased activity in M1 relative to pre-training levels (Doyon et al., 2002; Penhune and Doyon, 2005). The results of Reis et al. (2009) also support the changing role of M1 relative to the stage of motor learning; with the exception of the initial training session, no significant online (within-session) effects were observed between groups receiving either electrical or sham stimulation of M1 during practice of a novel motor skill. Examination of offline (across session) effects however revealed a significant difference between groups, supporting the role of M1 in the consolidation of motor skills, corroborating the findings of the above-noted offline, long-term studies of motor learning. Although the duration of learning in the present study exceeded that of previous 'fast' or online learning studies, the pre-post-training activation pattern observed in M1 suggests that subjects may have overlearned the task similar to the findings of Toni et al. (1998). This conclusion is based on our observation of decreased M1 activity post-training that is most likely related to increased automaticity in task performance related to online learning over a single-session (Floyer-Lea and Matthews, 2004; Toni et al., 1998). Lastly, given the duration of each fMRI session and the absence of an increase in M1 activity after training, it is clear the subjects had not yet experienced long-term consolidation of the learned movement pattern observed hours-days after training.

In determining the underlying factor leading to a reduction in brain activity, we considered the finding of significantly improved task performance that was concurrent with decreased intensity and spatial activation across the whole brain and specific ROIs to be evidence of a learning-related effect. Moreover, interpretation of this finding in the context of the motor learning literature (as noted above) reinforces that the observed reduction in brain activity is linked to increased automaticity in task performance. It is important however to consider the possibility that the changes observed in brain activation did not result from learning but rather from the level of effort required for task performance. Previous studies have shown that there is a relationship between the level of effort required for task performance and the level of cortical activation observed, with decreased levels of activation observed with tasks requiring less effort (Mochizuki et al., 2009; Remy et al., 1994; Wexler et al., 1997). For example, Mochizuki et al. (2009) contrasted two tasks requiring either easy (concurrent abduction of all digits) or hard (paired abduction of digits 2 and 3, and 4 and 5 simultaneously) finger movements. Based on level of perceived exertion (Borg scale) or a physiological index of effort (electrodermal response), brain activation assessed using fMRI revealed an increase in both the intensity and spatial extent of activation in the hard compared to the easy task. Although the study by Mochizuki et al. and others (Remy et al., 1994; Wexler et al., 1997) show that there is a link between task effort and the level of brain activation observed, several key points indicate the attenuation in brain activity in the current study resulted from learning, not an alteration in the level of effort required for task performance per se. While we state that the attenuation in brain activity is not due to an alteration in the level of effort required for task performance per se, we acknowledge that performance of the motor task may be less 'effortful' *after* compared to *before* training because of the increased automaticity associated with learning the task. Comparing the 'effort' associated with performance of the same task before and after training differs from comparing performance of two different, albeit related tasks, one of which is considered 'easy' while the other 'hard'. It is anticipated that learning-related changes may be associated with changes in the neural network underlying performance (i.e., a shift from a cerebellar-cortical to a striatal-cortical network; Coynel et al., 2010; Doyon and Benali, 2005; Doyon et al., 2003). The potential influence of 'effort' related differences upon such learning-related changes in activation remain to be determined.

Related to this previous point, participants in the current study performed the same task using the same technique throughout the pre, training and post conditions. Although we did not formally document the technique used by each participant, we provided consistent instructions to participants on how to hold and grip the bulbs, highlighting that the same position and grip technique be utilized throughout the study. Compliance with these instructions was high based on qualitative monitoring performed throughout each scan session using cameras mounted on the bore of the magnet and observed on a monitor in the control room. The consistency in the technique used in executing the visuomotor task suggests that activation changes did not result from participants making the task easier by modifying the technique utilized (for instance, use of a precision grip vs. a mass or 'power' grip as they were instructed could have potentially allowed participants to produce the requisite level of grip force more easily while also resulting in a different pattern of brain activation; Ehrsson et al., 2000). Moreover, while we did not normalize force input to each participant's maximal grip force, the level of force input required remained consistent for each participant, and thus differences across conditions cannot be attributed to changes in force output. This latter characteristic is important as several studies have shown that the level of force produced alters the extent and intensity of cortical activations (Dai et al., 2001; Thickbroom et al., 1998).

4.2. Generalizability of training

Based on the behavioural responses and extent of spatial activation observed for the reverse relative to the post-training condition, it was concluded that there was transfer in the training-related improvements in performance (i.e., learning) to performance of the contextually identical task with reversed input requirements. Our primary measures of performance showed an improvement from pre-training levels and in general were closer to the values seen in the post condition (Table 1). Interestingly, CA_{diff} did not follow this pattern as the value in the reverse condition (10.2°) was similar to that of the pre condition (10.6°). In light of the improvements in performance based on accuracy and error magnitude, which are partly based on the absolute force input from both hands, the CA_{diff} finding suggests participants had difficultly transitioning to the L > R hand input required in the reverse condition as opposed to the R > L hand input required in the other conditions (pre, post and training). Closer examination of the CA_{diff} values in the reverse condition, however, showed that participants were correcting performance throughout the 20 trials. Across participants, there was a trend in the first 10 trials of the reverse condition to produce a cursor angle closer to that required in the pre, post and training conditions (e.g., an angle $\leq$45°, indicating greater right hand input) vs. a trend to producing an angle $\geq$45° (indicating greater left hand input, as required in the reverse condition) resulting in a higher CA_{diff} value. In the latter 10 trials of the reverse condition however, CA_{diff} decreased as participants produced a cursor angle closer to that required in the reverse condition (e.g., >45°). The level of performance observed in the reverse compared to the pre condition suggests that transfer of learning resulted in a savings in the rate of improved performance, documented frequently in previous studies (Krakauer et al., 2005; Rémy et al., 2008; Seidler, 2010; Seidler and Noll, 2008).

The savings documented for behavioural performance was also seen in the extent of spatial activation observed in the reverse condition: throughout the whole brain and in the majority of ROIs examined, an 'intermediate' level of activation was seen relative to the pre and post conditions (Fig. 4), suggesting that transfer of learning resulted in a decreased demand on the neural resources

required for successful task performance. The degree to which activation decreased in the reverse condition in CB, M1, MFG and across the whole brain appears to be less than that observed in other studies examining transfer of learning (Seidler, 2010). This finding may be the result of methodological differences (e.g., the task utilized), but is more likely due to the fact that participants in the current study had not yet consolidated the newly acquired motor task. Additionally, the intermediate effect observed in the reverse relative to the pre and post conditions coupled with the inter-subject variability makes it challenging to observe results with statistical significance.

Exceptions to the pattern of decreased activation in the reverse relative to the pre-training condition included the SMA and thalamus. Increased activation in the SMA has been observed in previous studies of motor learning and is attributed to the role of the SMA in the implementation of the newly acquired motor sequence (Bischoff-Grethe et al., 2004; Doyon et al., 2002; Orban et al., 2010; Toni et al., 1998). Activation changes observed in the thalamus are most likely attributable to the role of thalamic nuclei (specifically the lateral nuclear group) in motor performance. For instance, the onset of a shift to a striatal-cortical network in the latter stages of learning may produce greater activity in the ventral anterior and lateral nuclei which have afferent connections with the striatum and reciprocal connections with motor regions in the frontal lobe, including SMA. As the intent of this study was not to investigate the neural correlates of online, single-session learning, the analyses utilized precluded the ability to identify the activity of specific thalamic nuclei. However, considering the nature of the task demands in the reverse condition, the above rationale for increased activation in the thalamus is reasonable.

4.3. Visuomotor task timing

Prior studies have contributed extensive information with regard to the neural correlates and evolution of online (fast; within minutes) and offline (slow; hours-days) components of motor learning. Here we sought to develop a task that would allow online motor learning to be studied over a duration that extends beyond minutes but that is still amenable to examination in a single fMRI session. The time course of learning in the present study extends beyond that typically observed in studies of 'fast' learning (for example see Floyer-Lea and Matthews, 2004). Across the pre, post and training conditions, participants were engaged in task performance for approximately 39 min. Importantly, analysis of our primary measures of performance for the training blocks showed participants improved significantly not just in contrasting pre- to post-training values, but also when values across each of the training blocks were compared (Fig. 2B). This finding coupled with the pre-post improvement in performance suggests learning evolved over the entire course of the experiment. This finding also differentiates the motor task utilized in the current study from others in which learning appeared to plateau after the initial 'fast' learning (on the order of minutes only; Floyer-Lea and Matthews, 2004; Ikegami and Taga, 2008; Karni et al., 1998). To further demonstrate the progression of learning across all trials, error magnitude was plotted trial-by-trial and fit with simple linear regression. Fig. 5C shows that across all participants, error magnitude progressively decreased as indicated by a regression line whose slope deviated significantly from zero ($p < 0.0001$).

4.4. Future directions and conclusion

As outlined above, examination of data across this sample of participants shows behavioural and fMRI evidence that learning occurred progressively over the course of the single scan session. Although this finding is clear when the data are examined collectively, it is evident from preliminary analysis of individual participant data that substantial inter-subject variability exists with regard to behavioural results and the extent of spatial activations. For instance, examining individual subject data by fitting error magnitude plotted trial-by-trial with simple linear regression revealed that two out of the fourteen participants did not necessarily experience learning, as shown by a flat regression line (e.g., a slope that did not deviate significantly from 0; Fig. 5, plots D and E). This finding opposed that of the other participants, whose plots were best fit by regression lines with slopes deviating significantly from 0 (Fig. 5, plots A and B; $p < 0.0001$). Variability was also evident in the extent of spatial activation across participants (Table 2). Data from all participants, regardless of the degree to which online learning was demonstrated, was included in the study as this is important to consider in light of our study objective to examine the ability of the visuomotor task to assess the online component of motor learning. Although investigation into the possible factors that contribute to this variability, as well as the relationship between behavioural and fMRI results is of interest, such analyses are beyond the scope of the current work. Considering the intended purpose of the study, we employed commonly used fMRI analyses that would provide an indication of training-related plasticity in key ROIs across our group of participants. Future work examining this inter-subject variability includes the possibility of using behavioural partial-least squares (PLS) analysis to stratify brain regions according to learning and subject-specific task performance (Krishnan et al., 2011).

To address our long-term goal of examining the neural correlates of online, short-term learning in individuals with motor control challenges, we considered two factors in the design of the current task. First, the task is amenable to modifications that would allow for online adjustment of the level of task difficulty to accommodate participants with varying skill level. For instance, it is possible to manipulate the output signal such that participants would be required to apply a different pattern of input (e.g., utilizing a derivative of the input signal to produce the output). Alternatively, a simple alteration in the gain of the input device would alter the level of task difficulty. Second, to accommodate individuals with motor control challenges it is possible to perform the task using alternate input devices. For instance, participants with limited hand function but who retain flexion or extension at the wrist could be accommodated using MR-compatible accelerometers; bilateral flexion or extension at the wrist would produce an output from the accelerometer that could be converted to a voltage that would drive the cursor. One caveat to the application of this task in individuals with motor control challenges may well be the need for bilateral input; independent control of the hands is often challenging in this patient population, which would increase task difficulty. Moreover, bilateral input would increase the complexity of neuroimaging analysis required to examine the brain activity associated with task performance. While recognizing the potential impact of these considerations, it is important to probe and understand brain activation linked to the control of both limbs simultaneously. With evidence now established to support the use of the current task to examine online, single-session motor learning in healthy controls, future work will be directed towards examining task modifications and their application in individuals with motor control challenges.

Results from both behavioural and fMRI data obtained in the current study were consistent with prior studies of online, short-term motor learning, supporting the conclusion that learning occurred in response to the current paradigm. Notably, the behavioural results from the three training blocks strengthen the case suggesting that learning occurred over the entire course of the scan session as participants improved performance progressively across the training blocks. Although the development of a task that allows learning

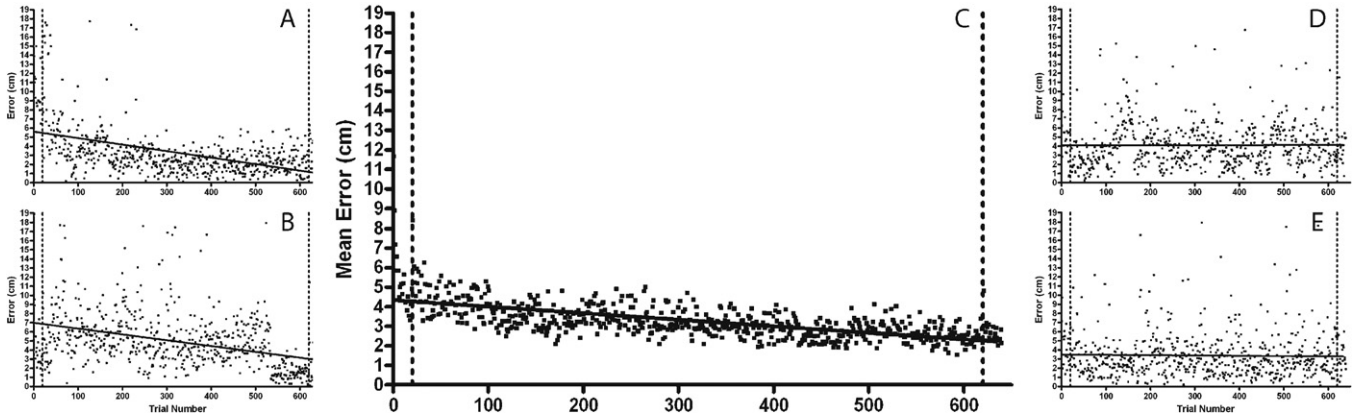

Fig. 5. Individual subjects learning 'profile' across pre-, post- and training conditions based on magnitude of error (cm). Smaller plots (A, B, D and E) represent single subjects while the large plot (C) represents the group average ($N = 14$). Dashed vertical lines on each plot represent the end of the pre-training condition (trials 0–20) and the start of the post-training condition (trials 620–640) from left to right respectively. Training trials (trials 20–620) are between the vertical dashed lines. All plots were fitted with a simple linear regression to characterize the progression of learning across trials. Plots A and B show data for two representative subjects who demonstrated training-related improvements in performance (slope value different than 0, $p < 0.05$), while plots D and E show data for the two subjects who did not demonstrate a training-related effect (slope value not different than 0, $p > 0.05$). Plot C (group average) is shown for comparative purposes.

to be examined over the duration of a single scan session is not entirely novel (for example see Tang et al., 2009; Toni et al., 1998), featuring a motor action such as gripping and incorporating the potential for task modification may permit more extensive study of the neural correlates of online, single-session learning in individuals with motor control challenges. A better understanding of the neural correlates of learning in individuals with neurological disorders has the potential to inform rehabilitative interventions, including modifying the dose, timing and intensity of the intervention to better match the 'learning profile' of the individual, in-turn optimizing the potential for recovery.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jneumeth.2012.06.016.

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