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A Role for the Somatosensory System in Motor Learning by Observing

Heather R. McGregor  
*The University of Western Ontario*

Supervisor  
Gribble, Paul L.  
*The University of Western Ontario*

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Abstract

An influential idea in neuroscience is that action observation activates an observer’s sensory-motor system. This idea has recently been extended to motor learning; observing another individual undergoing motor learning can promote sensory-motor plasticity as well as behavioural changes in both the motor and somatosensory domains. While previous research has suggested a role for the motor system in motor learning by observing, this thesis presents a series of experiments testing the hypothesis that the somatosensory system is also involved in motor learning by observing.

The experiments included in this thesis used force field (FF) adaptation as a model of motor learning, a task in which subjects adapt their reaches to a robot-imposed FF. Subjects observed a video showing another individual adapting his or her reaches to a FF, and motor learning by observing was assessed behaviourally following observation.

First, we used functional magnetic resonance imaging (fMRI) to assess changes in resting-state functional connectivity (FC) associated with motor learning by observing. We identified a functional network consisting of visual area V5/MT, cerebellum, primary motor cortex (M1), and primary somatosensory cortex (S1) in which post-observation FC changes were correlated with subsequent behavioural measures of motor learning achieved through observation.

We then investigated if pre-observation measures of brain function or structure could predict subsequent motor learning by observing. We found that individual differences in pre-observation resting-state FC predicted observation-related gains in motor learning. Subjects who exhibited greater FC between bilateral S1, M1, dorsal premotor cortex (PMd), and left superior parietal lobule (SPL) prior to observation achieved greater motor learning by observing on the following day.
In a subsequent experiment, we tested the involvement of the somatosensory system in motor learning by observing using median nerve stimulation and electroencephalography (EEG). In experiment 1, we showed that interfering with somatosensory cortical processing throughout observation (by delivering median nerve stimulation) can disrupt motor learning by observing. In a follow-up experiment, we assessed pre- to post-observation changes in S1 excitability by acquiring somatosensory evoked potentials (SEPs) using EEG. We showed that SEP amplitudes increased after observing motor learning. Post-observation SEP increases were correlated with subsequent behavioural measures of motor learning achieved through observation.

In a final experiment, we tested if improving subjects’ somatosensory function would enhance subsequent motor learning by observing. Subjects underwent perceptual training to improve their proprioceptive acuity prior to observation. We found that improving proprioceptive acuity prior to observation enhanced the extent to which subjects benefitted from observing motor learning (compared to subjects who had not undergone perceptual training). We further found that post-training increases in proprioceptive acuity were correlated with subsequent observation-related gains in motor performance.

Collectively, these studies suggest that motor learning by observing is supported by a fronto-parieto-occipital network in which the somatosensory system is an active element. We have shown that observing motor learning changes somatosensory activity in a behaviourally-relevant manner. Observing motor learning resulted in S1 plasticity that corresponded to the extent of learning achieved through observation. Moreover, manipulating somatosensory activity influenced motor learning by observing. Interfering with somatosensory processing throughout observation disrupted motor learning by observing whereas improving somatosensory function prior to observation enhanced motor learning by observing. These experiments therefore suggest that the somatosensory system is indeed involved in motor learning by observing.
Keywords

action observation, motor learning, sensory-motor adaptation, arm movements, robotic manipulandum, force field, resting-state fMRI, functional connectivity, somatosensory evoked potentials, perceptual learning, somatosensory system, proprioception
Co-authorship Statement


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JGAC assisted with designing the experiment presented in Chapter 5. PLG assisted with designing the experiment, interpreting the results, and revising the manuscript.
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Chapter 1

Introduction
1.1 Overview

The studies presented in this thesis tested the hypothesis that the somatosensory system is involved in motor learning by observing.

In the study presented in Chapter 2, we used a force field learning paradigm coupled with resting-state functional magnetic resonance imaging (fMRI) to investigate the neural basis of motor learning by observing. We examined resting-state functional connectivity (FC) before and after subjects observed a video showing a tutor adapting her reaches to a robot-imposed force field (FF). Following observation and fMRI scans, motor learning by observing was behaviourally assessed by instructing subjects to perform reaches in a force field. We performed whole-brain seed-based correlation analyses to examine pre- to post-observation changes in resting-state FC among visual, motor, and somatosensory brain areas. We revealed a functional network consisting of visual area V5/MT, cerebellum, primary motor cortex (M1), and primary somatosensory cortex (S1) in which FC changes were correlated with behavioural measures of motor learning achieved through observation. No such resting-state FC changes were found in a group of control subjects who observed a tutor performing reaches in an unlearnable FF. FC changes in this network are therefore not due to visual attention to motion or observation of movement errors, but rather are specifically linked to observing motor learning. These results support the idea that visual, motor, and somatosensory brain areas linking action observation and motor control facilitate
While action observation can facilitate the acquisition of novel motor skills, there is considerable individual variability in the extent to which observation promotes motor learning. In the experiment presented in Chapter 3, we reanalyzed the neuroimaging data from Chapter 1 to test if individual differences in brain function or structure can predict subsequent observation-related gains in motor learning. Subjects underwent an anatomical MRI scan and resting-state fMRI scans to assess pre-observation grey matter volume and pre-observation resting-state FC, respectively. On the following day, subjects observed a video showing a tutor adapting her reaches to a novel FF. After observation, we assessed motor learning by observing by instructing subjects to perform reaches in a FF. We performed whole-brain seed-based correlation analyses on the pre-observation resting-state fMRI data and performed voxel-based morphometry on the pre-observation T1 anatomical scans. We found that individual differences in pre-observation resting-state FC, but not grey matter volume, predicted observation-related gains in motor learning. Pre-observation resting-state FC between bilateral primary somatosensory cortices, dorsal premotor cortices, primary motor cortices, and left superior parietal lobule was positively correlated with behavioural measures of motor learning acquired on the following day. Sensory-motor resting-state FC can thus predict the extent to which observation will promote subsequent motor learning.

The experiments presented in Chapter 4 explored the involvement of the somatosen-
sory system in motor learning by observing. In experiment 1, we tested if the somatosensory system plays a necessary role in motor learning by observing. Here we asked if interfering with somatosensory cortical processing throughout observation would disrupt motor learning by observing. Subjects observed a video showing a tutor undergoing FF adaptation. During observation, median nerve stimulation was delivered to the subject’s right arm (the same arm being used by the tutor in the video), to the left arm, or to both arms simultaneously. All subjects then reached in a FF as a behavioural assessment of motor learning by observing. We found that applying median nerve stimulation during observation disrupted motor learning by observing in a limb-specific manner; stimulation delivered to the right arm (the same arm used by the tutor) disrupted learning whereas left arm stimulation did not. This result is consistent with the idea that a somatosensory representation of the observed effector plays an important role in motor learning by observing and must be available during observation for learning to occur. In a follow-up experiment, we tested a more specific hypothesis that primary somatosensory cortex (S1) is involved in motor learning by observing. Using median nerve stimulation and electroencephalography (EEG), we acquired somatosensory evoked potentials (SEPs) before and after observation. A learning group observed a video which showed a tutor adapting her reaches to a FF. A control group observed a video which showed a tutor performing reaches in an unlearnable, randomly-varying FF. Subjects then performed reaches in a FF as a behavioural assessment of motor learning by observing. We examined pre- to post-
observation changes in the amplitude of the N20-P25 component of the SEP, which has been linked to the earliest afferent processing in S1. We found that the amplitude of the N20-P25 component increased following observation only for those subjects who had observed the learning video. Moreover, across subjects in the learning group, the extent to which the N20-P25 component increased following observation corresponded to behavioural measures of motor learning by observing. This finding suggests that functional plasticity in S1 supports motor learning by observing. Taken together, these experiments suggest that the somatosensory system plays an important role in motor learning by observing.

If the somatosensory system is indeed involved in motor learning by observing, then improving subjects’ somatosensory function prior to observation should enhance subsequent motor learning by observing. In the experiment presented in Chapter 5, we used a perceptual learning protocol to improve subjects’ proprioceptive acuity (sensitivity to displacements in limb position) prior to observation. All subjects performed a proprioceptive discrimination task in the absence of visual feedback. During this task, a robotic manipulandum passively moved the subject’s hand and he or she made judgments about the position of the hand. All subjects performed 5 blocks of the proprioceptive discrimination task. During blocks 1 and 5, the experimenter did not provide trial-by-trial accuracy feedback to subjects. During blocks 2-4, subjects in a Trained Learning group received trial-by-trial accuracy feedback to improve their proprioceptive acuity. Subjects in an Untrained Learning group performed the task
without trial-by-trial accuracy feedback. All subjects then observed a learning video showing a tutor adapting her reaches to a FF. We found that subjects in the Trained Learning group, who had superior proprioceptive acuity prior to observation, benefited more from observing learning compared to subjects in the Untrained Learning group. Furthermore, across subjects in the Trained Learning group, post-training increases in proprioceptive acuity were correlated with subsequent behavioural measures of motor learning by observing. Improving somatosensory function (i.e., proprioceptive acuity) can therefore enhance subsequent observation-related gains in motor learning. This study provides further evidence that the somatosensory system supports motor learning by observing.

1.2 Literature Review

1.2.1 Motor Learning

Humans possess the ability to produce skilful movements in an ever-changing world. This ability relies on the brain’s capacity to modify our motor behaviour through motor learning. For example, consider the case of moving your arm while holding an object in your hand. The weight of the object alters the arm’s dynamic environment, changing the relationship between applied muscle forces and limb motion. Motor commands used to move the arm when the hand was empty will no longer result in the same movement. Nevertheless, the brain alters its motor commands to account
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for the dynamic properties of the hand-held object, thereby regaining accurate motor performance. This process, known as sensory-motor adaptation, occurs quickly and with apparent ease. However, the brain’s ability to perform sensory-motor adaptation remains a major topic of research in the field of motor control.

We often undergo sensory-motor adaptation through physical practice, a process referred to as active motor learning throughout this thesis. However, we can also learn about how to adapt our motor behaviour from observing the movements of others. We refer to this as motor learning by observing. This chapter will begin with a brief overview of active motor learning followed by a discussion of how these concepts apply to motor learning by observing.

1.2.2 Active Motor Learning

In studies of sensory-motor adaptation, perturbations are applied to well-learned movements such as reaching or object lifting. Subjects are provided with perturbed sensory inputs or motor outputs and they must modify their movements in order to regain a baseline level of performance.

Prior to executing a movement, the brain is thought to use a “forward model” to predict the sensory consequences of the planned movement (e.g., how the intended movement should look and feel). When sensory inputs or motors outputs are altered (as in an adaptation task), the actual sensory outcomes of a movement do not match
the brain's predictions. Visual and somatosensory feedback, in particular, inform the brain of how the executed movement differs from the intended movement. It is thought that sensory-motor adaptation is driven by sensory prediction errors, differences between the predicted and actual sensory outcomes of a movement. The brain uses systematic sensory prediction errors to guide the modification of subsequent motor commands in order to counteract a perturbation (e.g., Miall & Wolpert, 1996; Wolpert et al., 1998).

Commonly used sensory-motor adaptation tasks include visuomotor adaptation, fingertip force adaptation, and force field adaptation. Each of these paradigms is outlined briefly below.

**Visuomotor Adaptation**

In a visuomotor adaptation task, subjects are provided with altered visual feedback such that there is a discrepancy between the actual trajectory of the hand and the visual consequence of the movement. Visuomotor adaptation has been studied extensively using a range visual manipulations. For example, visual feedback can be shifted laterally using prism lenses (e.g., Martin et al., 1996), inverted using mirrors (e.g., Imamura et al., 1996), rotated in a virtual environment (e.g., Krakauer et al., 2005), etc. When subjects are first exposed to a novel visuomotor environment, executed movements do not result in the predicted visual outcome. The brain updates its motor commands to account for the visual perturbation based on sensory prediction errors.
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errors. Once fully adapted, subjects aim their movements in the opposite direction of the visual perturbation and successfully complete the task. Studies of visuomotor adaptation suggest that the brain predicts the visual outcome of movements, and if there is a consistent mismatch between the predicted and actual visual feedback of a movement, the brain will adapt its planning of movement direction in order to bring the predicted and actual visual outcomes back into alignment.

Fingertip Force Adaptation

In studies of fingertip force adaptation, subjects learn to adjust the force with which they grip and lift objects of varying weights. Before lifting an object for the first time, the brain makes a prediction about the object’s weight based on its visual characteristics, such as its size or material (Ellis & Lederman, 1999; Johansson & Westling, 1984, 1988). This prediction influences lifting behaviour in terms of the force applied by the fingertips (grip force) and the force with which subjects lift the object (load force) (Gordon et al., 1991).Immediately before lifting an object, studies have shown that subjects increase their grip force and load force in parallel according to the anticipated weight of the object. If the prediction is inaccurate, subjects will generate inappropriate forces and the object may slip, be lifted sooner than expected, or not at all. In such cases, grip forces and lift forces are quickly adjusted based on sensory feedback (Johansson & Westling, 1984). The brain’s sensory predictions are rapidly updated, fully adapting forces to the object’s actual weight in as little
as one trial (Johansson & Westling, 1988). Fingertip force adaptation studies have demonstrated that the brain predicts the force requirements for lifting objects and, if a prediction is inaccurate, motor commands for force production are rapidly modified such that the object can be lifted in the intended manner.

**Force Field Adaptation**

Another widely used task is force field adaptation in which subjects adapt their reaching movements to forces applied by a robotic manipulandum. The experiments presented in this thesis used force field adaptation as a model of motor learning. For this task, subjects grasp the handle at the end of a robotic manipulandum with their right hand and are instructed to move the handle in a straight line to an on-screen target. In the baseline condition, subjects perform reaches in the absence of applied forces (termed “null field” trials). In the learning phase, the robotic manipulandum applies velocity-dependent forces (“force field”, FF) at the hand. For example, in a left FF, the robot pushes the subject’s hand to the left during movements. Initial movements in this FF are highly curved to the left and, as such, there is a discrepancy between predicted and actual sensory feedback. Based on systematic sensory prediction errors, the motor system will update subsequent motor commands so as to generate (rightward) forces that will counteract the applied (leftward) FF. In doing so, movements become straighter, eventually returning to their baseline state.

A hallmark of force field adaptation is the presence of aftereffects when the FF is
unexpectedly removed. For example, if a subject had fully adapted to a left FF and then the FF was unexpectedly removed, aftereffects would be indicated by rightward curved movements in the null field that are mirror images of initial movements in the left FF. These aftereffects indicate that the subject had learned to generate a pattern of time-varying forces that would precisely counteract the applied left FF (Shadmehr & Mussa-Ivaldi [1994]).

1.2.3 Neural Basis of Active Motor Learning

The Motor System and Active Motor Learning

While primary motor cortex (M1) is perhaps most commonly associated with motor function, active motor learning involving physical practice has been shown to rely on a broad network of brain areas. Hardwick and colleagues (2013) conducted a meta-analysis of neuroimaging data from 70 motor learning studies which used sensory-motor tasks and serial reaction time tasks. A global analysis across all tasks revealed that active motor learning involves activation of left dorsal premotor cortex (PMd), supplementary motor area (SMA), primary motor cortex (M1), primary somatosensory cortex (S1), thalamus, bilateral putamen, and various regions of the cerebellum. A sub-analysis examining only the data from sensory-motor learning tasks (which included adaptation tasks) revealed reliable activation in left PMd and bilateral M1, putamen, and the cerebellum.
Dorsal premotor cortex is thought to play an important role in visuomotor control and motor learning with respect to its proposed role in selecting and updating movements in response to visual cues (e.g., Kalaska & Crammond 1995). Activation of SMA has been linked to self-initiation of voluntary movements and movement sequence coding (e.g., Hoffstaedter et al. 2012). M1 is predominantly associated with motor execution, but it has also been proposed that M1 plays a role in the retention of movements learned through repetitive performance (e.g., Galea et al. 2010). Somatosensory activation during active motor learning is thought to reflect tactile and proprioceptive reaference. It is hypothesized that somatosensory feedback plays a crucial role in motor learning with respect to its use in detecting sensory prediction errors which drive sensory-motor adaptation (Miall & Wolpert 1996, Wolpert et al. 1998). The cerebellum is proposed to be involved in state estimation, allowing the brain to form sensory predictions. It is further hypothesized that the cerebellum detects and corrects sensory prediction errors (e.g., Izawa et al. 2012, Miall & Wolpert 1996, Wolpert et al. 1998).

The results of the sub-analysis of sensory-motor task-based neuroimaging data reported by Hardwick and colleagues (2013) are consistent with the findings of resting-state fMRI studies examining the neural basis of sensory-motor adaptation. Albert and colleagues (2009) acquired resting-state fMRI data before and after subjects underwent a visuomotor adaptation through physical practice. One group of subjects adapted their movements to rotated visual feedback while subjects in a control group performed
similar movements using veridical visual feedback. Undergoing visuomotor adaptation was found to alter subsequent activity within fronto-parietal and cerebellar resting-state networks. Resting-state activity changes were observed only following visuomotor adaptation, not following motor performance using veridical visual feedback. This finding suggests that sensory-motor adaptation involves functional changes within frontal brain areas, parietal brain areas, and the cerebellum.

Vahdat and colleagues (2011) similarly assessed the neural basis of active motor learning using resting-state fMRI. Subjects underwent resting-state fMRI scans before and after adapting to a FF through physical practice. Following the final fMRI scan, subjects performed reaches in a FF to assess the degree of motor learning each subject had achieved. It was found that actively adapting to a FF resulted in resting-state FC changes involving M1, SMA, and cerebellum that were reliably correlated with behavioural scores of active motor learning.

The Somatosensory System and Active Motor Learning

The studies reviewed above have shown that active motor learning changes motor behaviour and results in functional changes within predominantly motor circuits. However, the effects of active motor learning are not restricted to the motor system. There is accumulating evidence that active motor learning also changes proprioception (the sense of limb position) and alters activity within the somatosensory system.
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Recent work has shown that undergoing active motor learning can improve proprioceptive acuity (Wong et al., 2011) and alter perceived limb position (Haith et al., 2009; Cressman & Henriques, 2009; Ostry et al., 2010; Vahdat et al., 2011). For example, Ostry and colleagues (2010) showed that undergoing FF adaptation results in systematic proprioceptive changes. Subjects’ proprioception was assessed before and after FF adaptation. Proprioception was assessed using a discrimination task in which a robotic manipulandum passively moved the subject’s hand and he or she judged whether it had been displaced to the left or to the right (in the absence of visual feedback). Following FF adaptation, subjects’ perceived boundary between left and right shifted in the direction opposite to the applied FF. That is, after adapting to a leftward FF, subjects’ proprioceptive judgments were biased to the left and their perceptual boundary therefore shifted to the right. Moreover, subjects’ adapted movements were aligned to the shifted perceptual boundary. Perceptual changes accompanying FF adaptation were found to persist for 24 hours after the training session (which lasted as little as 10 minutes). The authors then tested if the observed proprioceptive changes were brought about by motor learning or simply by the experience of repetitive movement. One group of subjects performed a passive movement task in place of FF adaptation. The robotic manipulandum passively moved the subject’s hand along the same kinematic trajectories as subjects who had actively adapted to the FF. No proprioceptive changes were observed following the passive movement task, even though subjects had experienced the same repetitive
movements as subjects who had undergone motor learning. This showed that the changes in proprioception following FF adaptation were specifically tied to motor learning. Overall, this study demonstrated that undergoing FF adaptation results in lasting, systematic changes in somatosensory perception.

Neuroimaging and EEG studies provide further evidence for the idea that the effects of active motor learning extend to the somatosensory system (Vahdat et al., 2011; Nasir et al., 2013). Using resting-state fMRI, Vahdat and colleagues (2011) showed that active motor learning alters FC involving somatosensory brain areas. Resting-state fMRI data were collected before and after subjects actively adapted to a FF and underwent proprioceptive discrimination tests. As found previously, FF adaptation altered both motor performance and somatosensory perception. The authors examined pre- to post-learning changes in resting-state FC, distinguishing those functional changes that could be attributed to motor learning from those that were associated with somatosensory perceptual changes. They reported FC changes between second somatosensory cortex, ventral premotor cortex, and supplementary motor area that were related to perceptual changes following learning. FC increases among these areas were correlated with behavioural measures of perceptual boundary shifts that accompanied motor learning. This study showed that active motor learning alters proprioceptive function as well as activity within a brain network involving second somatosensory cortex.
Nasir and colleagues (2013) similarly showed that active motor learning alters activity in somatosensory brain areas. Somatosensory evoked potentials (SEPs) were acquired before and after subjects adapted to a FF through physical practice. SEPs were recorded using EEG and elicited by passive movement of the subject’s arm. They found that SEP amplitudes decreased after motor learning, and that SEP amplitude decreases were reliably correlated with the extent to which subjects had adapted to the FF. As done by Ostry and colleagues (2010), one group of subjects passively experienced the kinematic trajectories associated with FF adaptation in place of FF adaptation. Passive movement alone did not bring about SEP changes. This study showed that FF adaptation involved functional changes within somatosensory cortex.

Further support for a link between the somatosensory system and active motor learning comes from recent demonstrations that somatosensory perceptual training can enhance subsequent motor learning (Rosenkranz & Rothwell, 2012, Wong et al., 2012, Darainy et al., 2013, Vahdat et al., 2014). Darainy and colleagues (2013) trained subjects on a proprioceptive discrimination task in which a robotic manipulandum passively moved the subject’s hand from a reference position along one of several fan-shaped trajectories and subjects made judgments regarding the displacement of the hand. When provided with reinforcement accuracy feedback during the proprioceptive task, subjects’ proprioceptive performance improved. Subjects showed post-training increases in perceptual acuity as well as decreases in perceptual bias. Perceptual training also resulted in improvements in subsequent FF adaptation. Trained subjects...
showed superior performance in terms of their rate of learning, extent of learning, and measures of predictive compensatory forces (assessed based on lateral forces subjects applied on the robot handle). Post-training increases in proprioceptive acuity were correlated with the extent of subsequent motor learning (Darainy et al., 2013). Improving somatosensory perception through perceptual training therefore enhanced active motor learning.

**Anatomical Basis for Sensory-Motor Link**

Neuroanatomical studies using non-human primates have provided insight into the anatomical basis of the functional link between motor and somatosensory brain regions in motor learning. Primary somatosensory cortex receives projections from primary motor cortex (Jones et al., 1978; Pons & Kaas, 1986; Darian-Smith et al., 1993; Burton & Fabri, 1995; Huffman & Krubitzer, 2001; Liao et al., 2013), supplementary motor area (Jones et al., 1978; Darian-Smith et al., 1993; Cipolloni & Pandya, 1999; Huffman & Krubitzer, 2001), as well as premotor cortex (Pons & Kaas, 1986; Cipolloni & Pandya, 1999). Motor regions (including primary motor cortex, premotor cortex, and supplementary motor area) receive projections from primary somatosensory cortex (Darian-Smith et al., 1993; Jones et al., 1978), second somatosensory cortex (Cipolloni & Pandya, 1999), and posterior parietal cortex (Petrides & Pandya, 1984). It is feasible that such reciprocal connections between somatosensory and motor brain regions also exist in the human brain and contribute to a functional link between
motor and somatosensory areas during active motor learning.

1.2.4 Motor Learning by Observing

Motor learning can be achieved not only through physical practice, but also by observing the movements of another individual (“a tutor”). Observation-related gains in motor performance have been reported using various experimental sensory-motor adaptation paradigms.

Visuomotor Adaptation

Observation has been shown to facilitate the learning of novel visuomotor environments. Subjects observed a tutor learning to reach to targets in a novel visuomotor environment in which an on-screen cursor was rotated 30° clockwise with respect to the tutor’s actual hand position. Upon subsequent exposure to that same rotated visual environment, observers’ movements were more accurate in guiding the cursor to the targets (by aiming counterclockwise) compared to subjects who had not previously observed a tutor. While subjects’ movements did not fully compensate for the visual rotation, their performance was facilitated from having had previously observed the tutor’s movements (Ong & Hodges 2010, Ong et al. 2012, Lim et al. 2014). This indicates that individuals can learn about how to adapt to a novel visuomotor environment, at least to some extent, through observation.
Fingertip Force Adaptation

Action observation can also facilitate the adaptation of fingertip forces when lifting objects. In a recent study, subjects repeatedly lifted an object in turn with a tutor such that the subjects observed the tutor lifting the object before lifting it themselves. During catch trials, the object’s weight was unexpectedly changed such that it was heavier or lighter than usual. If the object became lighter, the tutor overestimated the load force and overshot the target lift height. Subjects were able to acquire information about the object’s new weight by observing just one of the tutor’s lifts and they were able to use this information to adapt their own load force when subsequently lifting the object \cite{Reichelt2013}. Buckingham and colleagues \cite{Buckingham2014} examined the consequences of observing a tutor making load force errors when lifting small and large objects of identical weights. Subjects observed videos showing either a novice tutor making lifting errors (i.e., overestimating load forces for the large object and underestimating load forces for the small object) or an expert tutor who performed fully adapted, error-free lifts. After observation, the subjects lifted the objects shown in the videos. The subjects who had observed the novice tutor’s lifts outperformed those subjects who had observed the expert tutor’s lifts. Specifically, those subjects who had observed the novice tutor’s lifts were less likely to commit load force overestimations when lifting the larger object and, as a result, required smaller force adjustments. This suggests that observing the novice’s errors allowed subjects to gain information
about the forces required for lifting the objects, which they used to their benefit when lifting the objects themselves (Buckingham et al., 2014). Observers are therefore able to use visual information of others’ movement errors to adapt their own fingertip force output.

**Force Field Adaptation**

Individuals can also learn about how to move in novel force environments by observing a tutor’s movements (Mattar & Gribble, 2005). Subjects observed a video showing a tutor adapting his reaching movements to a force field (FF) applied by a robotic manipulandum. Subjects who later performed reaches in the same FF as they had observed in the video showed a benefit, performing straighter movements in the FF compared to non-observing control subjects. Conversely, subjects who later performed reaches in the opposite FF to what they had observed showed a detriment, performing more curved movements in the FF compared to non-observing control subjects. This study suggested that subjects were able to learn about how to reach in novel FF environments through observing the tutors’ movements. Mattar and Gribble (2005) found that the beneficial effect of observing motor learning persisted even if subjects performed a cognitive distractor task while watching the video, indicating that observational motor learning does not depend on the use of explicit cognitive strategies. However, observational learning was reduced if the motor system was engaged during the video by the performance of an unrelated movement task. This
demonstrated that the observer’s motor system plays an important role in motor learning by observing. Taken together, these results suggest that learning about novel force environments through observation occurs through implicit engagement of the observer’s motor system.

Mattar and Gribble (2005) indirectly assessed the extent to which subjects had learned about generating compensatory forces on the basis of their kinematic performance (i.e., movement straightness) following observation. However, their findings were later confirmed by a study in which Wanda and colleagues (2013) directly measured subjects’ applied forces during post-observation reaches. Subjects observed a video showing a tutor undergoing FF adaptation. After observation, subjects performed reaches in a “force channel” in which the robotic arm constrained subjects’ movements to a narrow channel connecting the start position and target, enforcing a straight movement trajectory. A force transducer in the handle of the robot recorded the lateral forces subjects applied against the channel walls. They found that, during post-observation reaches, subjects generated forces that mirrored the FF that had been observed. This is the same pattern of compensatory forces that subjects exhibit in a force channel after they have adapted to a FF through physical practice. This demonstrated that subjects had learned about the time-varying pattern of muscle forces required for moving in the observed FF.

The ability to learn about forces through observation is an interesting phenomenon
since the observer cannot see the FF environment, but only its consequences on the tutor’s movements. Therefore, the observer can only learn about the FF dynamics using visual information about the tutor’s movement kinematics.

Observing the tutor making kinematic errors is critical for learning about FFs through observation. Brown and colleagues (2010) showed subjects videos of a tutor reaching in a FF and making either high error movements, low error movements, or a mixture of high and low error movements. Observing high error movements led to the greatest observation-gains in motor performance. Subjects also benefitted, although to a lesser extent, from observing both high and low errors. These results demonstrate the importance of observing a tutor’s kinematic errors.

Not all observed kinematic errors will promote motor learning. In their study, Mattar and Gribble (2005) presented one group of subjects with a video showing a tutor performing reaches in a FF in which the direction of the applied force varied randomly from trial to trial. The tutor was unable to predict which force direction would be encountered on a given trial and therefore unable to correct for the perturbation. This video showed the tutor making high and low error movements, but lacked the gradual progression from curved to straight movements that is indicative of motor learning. A post-observation behavioural assessment showed that subjects who had viewed the randomly-varying FF video performed comparably to non-observing control subjects. Subjects were therefore unable to learn from observing the tutor’s movements in the
randomly-varying FF. In order for motor learning by observing to occur, subjects must observe the tutor making (and correcting for) systematic errors.

### 1.2.5 Action Observation

A potential neural basis for the link between action and observation has emerged from the discovery of so-called mirror neurons in the ventral premotor cortex (area F5) of the macaque brain using single-cell recordings (di Pellegrino et al., 1992). These cells discharge while a monkey performs goal-directed actions and also while the animal observes an experimenter performing similar actions (di Pellegrino et al., 1992; Gallese et al., 1996; Rizzolatti et al., 1996). Subsequent studies have reported the existence of mirror neurons in the macaque inferior parietal lobule (e.g., Fogassi et al., 2005; Rozzi et al., 2008; Bonini et al., 2009), primary motor cortex (e.g., Tkach et al., 2007; Dushanova & Donoghue, 2010; Vigneswaran et al., 2013), and dorsal premotor cortex (Tkach et al., 2007).

Since direct evidence of mirror neurons in humans is scarce (e.g., Mukamel et al., 2010), many neuroimaging studies have examined the neural basis of action observation in humans in terms of a broader functional network known as the action observation network (AON). The AON is a network of sensory-motor brain regions that are activated when observing the actions of others (e.g., Calvo-Merino et al., 2004; Buccino et al., 2004; Vogt et al., 2007; Cross et al., 2009; Caspers et al., 2010).
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(Gardner et al., 2015). The AON primarily consists of dorsal and ventral premotor cortices, supplementary motor area, primary somatosensory cortex, superior and inferior parietal lobules, intraparietal sulcus, and middle temporal gyrus extending into visual area V5/MT (Caspers et al., 2010). Although some of the brain areas of the AON are involved in the visual processing of actions (such as V5/MT), many of the brain areas are also known to be involved in movement production.

Action Observation and the Somatosensory System

Of particular relevance to this thesis is the involvement of primary somatosensory cortex (S1) in action observation. Primary somatosensory cortex (most often Brodmann areas 1 and 2) is consistently activated by the observation of hand actions, particularly those involving object manipulation (Avikainen et al., 2002; Hasson et al., 2004; Cross et al., 2006; Pierno et al., 2008; Gazzola & Keysers, 2008; Caspers et al., 2010).

It has been suggested that S1 activity during the observation of object manipulation contributes to our ability to infer the weight of the object based on an actor’s kinematics. Valchev and colleagues (2017) applied continuous theta-burst stimulation (cTBS) to S1 before subjects viewed videos showing an actor lifting objects of different weights. Applying cTBS to S1 decreased the accuracy of subjects’ weight estimations based on observed lifting movements (relative to sham cTBS). The authors reported that cTBS-induced weight judgment errors were specific to trials in which subjects observed human interactions with objects. Applying cTBS to S1 did not affect subjects’ weight
estimations based on videos of a bouncing ball. Moreover, the detrimental effect of cTBS on observation-based weight estimations was specific to S1; applying cTBS to M1 or SPL prior to observation did not affect judgment accuracy. This study suggests that S1 plays a role in extracting information about weight and forces from observing the movement kinematics of others.

1.2.6 Neural Basis of Motor Learning by Observing

A great deal of the research on the AON has focused on its potential role in higher cognitive functions such as understanding and inferring the intentions of others’ actions (Rizzolatti et al., 1996; Rizzolatti & Fadiga, 1998; Gallese & Goldman, 1998; Rizzolatti et al., 2001; Gallese et al., 2004). However, recent work suggests that some of the brain areas within the AON also play a role in motor learning by observing.

The Motor System and Motor Learning by Observing

Evidence from neuroimaging, neurophysiological, and behavioural studies suggest a role for the motor system in motor learning by observing. Brown and colleagues (2009) investigated the role of M1 in motor learning by observing using repetitive transcranial magnetic stimulation (rTMS). In their study, subjects observed a video of a tutor adapting to a FF then received rTMS to left M1 in order to reduce M1 excitability. The idea was that applying rTMS following observation would interfere with learning mechanisms in M1. After receiving rTMS to M1, subjects who were
tested in the observed FF did not show behavioural gains associated with observation. Subjects who received rTMS to M1 and were then tested in the opposite FF to what was observed did not show interference in the behavioural assessment. Therefore, reducing M1 excitability following observation disrupted motor learning by observing. In contrast, applying rTMS to a control brain area not involved in motor control did not disrupt motor learning by observing. These findings suggest that observing motor learning engages learning mechanisms within the observer’s M1.

Recently, we further tested the role of primary M1 in motor learning by observing using single-pulse TMS. Here we assessed changes in offline corticospinal excitability associated with observing motor learning. Before and after observation, we acquired motor evoked potentials (MEPs) from muscles in the right hand while subjects rested and fixated a crosshair. Subjects assigned to a learning group observed a video depicting a tutor undergoing FF adaptation. Subjects in a control group observed a video showing a tutor performing reaches in an unlearnable, randomly-varying FF. We found that observing FF learning increased MEP amplitudes. No changes in MEP were found for subjects who had observed the tutor performing reaches in the unlearnable FF. These results suggest that motor learning by observing involves functional changes within M1, corticospinal networks, or both (McGregor & Gribble, submitted).

Malfait and colleagues (2010) showed that observing a tutor committing movement
errors during FF adaptation engages a network that is involved in processing our own movement errors. Subjects underwent a fMRI scan while they observed videos of a tutor adapting her reaches to a FF, gradually progressing from curved to straight movements. During observation, activity in dorsal premotor cortex, intraparietal sulcus, and the cerebellum was modulated by the magnitude of the tutor’s reach errors. Interestingly, this network showed considerable overlap with a network engaged in processing one’s own movement errors during physical practice. This study provided evidence that the observer’s motor system is activated when processing visual information about others’ movement errors, particularly when large kinematic errors are made.

The Somatosensory System and Motor Learning by Observing

One behavioural study has investigated the possibility that the somatosensory system is involved in learning about FFs through observation, as seems to be the case for active motor learning. Bernardi and colleagues (2013) examined somatosensory function before and after subjects observed a video depicting a tutor undergoing FF adaptation. Somatosensory function was assessed using a proprioceptive discrimination task in which subjects made judgments about the position of their hand in the absence of visual feedback. Consistent with previous findings (e.g., Mattar & Gribble 2005), observing motor learning facilitated subjects’ motor performance when they later encountered the observed FF environment. As had been demonstrated in the active motor learning literature (Ostry et al. 2010, Darainy et al. 2013, Vahdat et al. 2013).
observing motor learning resulted in systematic changes in proprioception depending on the FF that had been observed. Subjects who had observed a video showing right FF adaptation subsequently perceived their arm to be positioned more rightward than it actually was. In contrast, subjects who observed a video showing left FF adaptation subsequently perceived their arm to be positioned more leftward than it actually was. Bernardi and colleagues (2013) reasoned that post-observation perceptual changes indicated that observing motor learning had altered activity within the somatosensory system. The results of this study raised the possibility that, as in active motor learning, motor learning by observing promotes plasticity not only within the motor system, but also within the somatosensory system. However, it was unknown whether such observation-related changes in somatosensory activity support motor learning by observing or whether they are epiphenomenal.

Anatomical Basis for Visual and Sensory-Motor Link

Non-human primate studies have provided insight into an underlying anatomical basis by which visual information could influence activity within the sensory-motor system. For example, middle temporal visual area V5/MT is often activated during action observation (Caspers et al., 2010). This area has been implicated in visual motion processing in both humans (e.g., Zeki et al., 1991) and non-human primates (e.g., Zeki, 1974). Non-human primate neuroanatomical studies have shown that V5/MT receives direct projections from primary visual cortex (Movshon & Newsome, 1996) and indirect
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projections via secondary visual cortex (Ponce et al., 2008). Visual information is then relayed from V5/MT to the cerebellum via the pontine nuclei (Ungerleider et al., 1984). V5/MT also sends inputs to the posterior parietal cortex, an area in which multi-sensory integration is thought to occur. Visual, somatosensory, and auditory inputs are integrated in the ventral intraparietal area and the inferior parietal lobule (Maunsell & van Essen, 1983; Lewis & Van Essen, 2000) then relayed to the cerebellum (Glickstein et al., 1980; Langer et al., 1985) or to somatosensory, motor, and premotor brain areas (Vogt & Pandya, 1978; Tanné-Gariépy et al., 2002; Keysers & Perrett, 2004). There is evidence that these pathways are also reciprocally connected, with the cerebellum both projecting to and receiving input from the posterior parietal cortex and M1 via the thalamus (Dum & Strick, 2003; Thach et al., 1992). The human brain may rely on similar structural connectivity in order for visual information about the movements of others to be propagated to the sensory-motor system.

1.3 Summary

While it is well established that the motor system supports active motor learning, recent evidence has suggested that the somatosensory system also plays a role in motor learning through physical practice. The nature of the relationship between the somatosensory and motor systems in active motor learning is reciprocal: motor learning changes somatosensory brain activity and somatosensory performance, and somatosensory perceptual learning can in turn affect activity within motor circuits.
and enhance subsequent motor learning.

As has been reported in the active motor learning literature, there is evidence that the motor system is involved in motor learning by observing. Furthermore, the findings of one behavioural study have shown that observing FF learning results in somatosensory perceptual changes (Bernardi et al., 2013). The findings of this study suggest that observing motor learning brings about functional changes within the somatosensory system. However, it is unknown whether such observation-related changes in somatosensory activity constitute part of processes underlying motor learning by observing (as appears to be the case in active motor learning) or whether they are a side effect of motor learning by observing.

The aim of this thesis was to test the idea that, much like in active motor learning, the somatosensory system is involved in motor learning by observing.


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Chapter 2

Functional Connectivity Changes

and Observational Learning

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Chapter 2. Functional Connectivity Changes and Observational Learning

2.1 Introduction

Our capacity for interacting with the world depends on our facility for dexterous movement and the expansion of our motor repertoire through learning. How the brain achieves motor learning remains an important unresolved question and a problem of significant clinical importance, as many neurological conditions affect movement. Here we examine how action observation facilitates motor learning through functional plasticity in sensory and motor brain areas.

Motor learning is commonly studied with laboratory tasks in which subjects learn to adapt movements to counteract experimentally imposed changes in sensory feedback (Ghahramani et al., 1996) or mechanical perturbations (Shadmehr & Mussa-Ivaldi, 1994). However, outside the laboratory, motor learning typically begins quite differently, often by observing a tutor. In human development, infant speech perception and speech motor learning are guided by visual and auditory observation of a caregiver’s speech (Goldstein et al., 2003; Kuhl, 2004; Stevens & Lindblom, 1987). Observation also facilitates motor learning in adults. Mattar and Gribble (2005) showed that complex muscle force patterns can be learned by observing a tutor learning to reach in a novel force field (FF) environment. Subjects observed a tutor learning to perform straight reaches in a novel FF environment. Those subjects who were subsequently exposed to the same FF environment they had observed showed a performance benefit, executing straighter movements compared with non-observing control subjects. Conversely, those
subjects who were subsequently exposed to a different (opposite) FF environment than they had observed showed a significant disadvantage, performing more curved movements compared with the non-observing control subjects (Mattar & Gribble, 2005). These findings demonstrated that subjects had acquired representations of the observed dynamical environment.

The ability to learn about forces through observation is very interesting, since the observer cannot see the FF environment directly but only its consequences on the tutor’s movements. Therefore, the observer only has access to visual information about the tutor’s movement kinematics. To achieve motor learning, the brain must transform the visual information about the tutor’s movements into the motor domain so as to allow the motor system to acquire a representation of the novel environment and the required changes to subsequent muscle force patterns.

A potential neural basis for the link between action and observation has emerged from the discovery of so-called mirror neurons in the premotor and parietal cortices of the macaque. These cells discharge while a monkey performs specific goal-directed actions and also while the animal observes another individual performing the same actions (di Pellegrino et al., 1992; Gallese et al., 1996; Rizzolatti et al., 1996). Neuroimaging studies support the idea that a similar system exists in the human brain (Buccino et al., 2001; Frey & Gerry, 2006; Gallese et al., 2004). This putative human mirror neuron system is part of a broader action observation network (AON) including supplementary
motor area (SMA), premotor, primary motor (M1) and primary somatosensory (S1) cortices, superior parietal lobule (SPL), and middle temporal visual area (V5/MT) (Caspers et al. 2010).

The functional role of the AON has been examined in prediction (Prinz 1997, 2006), action understanding (Rizzolatti et al. 1996; Rizzolatti & Fadiga 1998), and inferring action intentions (Gallese et al. 2004; Gallese & Goldman 1998), but surprisingly little work has addressed its potential role in motor learning (Buccino et al. 2004; Cross et al. 2009; Higuchi et al. 2012; Stefan et al. 2005).

Here we tested the hypothesis that brain areas linking observation and action are also involved in motor learning through observation. We used resting-state fMRI to examine functional connectivity (FC) before and after subjects observed a tutor learning to reach in a novel FF imposed by a robot arm. We describe a network involving visual area V5/MT, cerebellum, M1, and S1 in which changes in FC were correlated with subsequent behavioural measures of motor learning achieved through observation. Importantly, in a follow-up experiment we show that these FC changes are not explained by visual attention to motion or observation of movement errors but rather are specifically related to motor learning by observing. This network thus provides a neural basis by which visual information about the actions of others is propagated to sensory-motor circuits for learning.
2.2 Materials and Methods

2.2.1 Subjects

Thirty healthy subjects participated in this study: 15 in the learning group in experiment 1 (6 males, 9 females; mean age 22.87 years ± 1.02 SE) and 15 in the control group in experiment 2 (6 males, 9 females; mean age 22.53 years ± 0.86 SE). All subjects were right handed and naïve to FFs, had normal or corrected-to-normal vision, and reported no neurological or musculoskeletal disorders. Informed consent was obtained from all subjects before participation in procedures approved by the University of Western Ontario’s Research Ethics Board.

2.2.2 Apparatus

Subjects sat at a custom tabletop and grasped the handle of a two-degree of freedom robotic arm (IMT2, Interactive Motion Technologies) with their right hand (see Figure 2.1A). An air sled was placed under the right arm to support the arm against gravity and reduce friction with the tabletop surface during the performance of reaching movements. The height of the chair was adjusted such that the subject’s right arm (secured on the air sled) was abducted approximately 90 from the sagittal plane. The reaching task involved guiding the robot handle in a reaching movement to a visual target in the horizontal plane. A semi-silvered mirror was mounted horizontally just
above the robotic handle. An LCD monitor projected visual feedback onto the semi-
silvered mirror, including the start position (20-mm blue circle), the target (20-mm
white circle), and a cursor representing hand position (12-mm pink circle) during the
reaching task (Figure 2.1B). Vision of the robotic arm and the subject’s arm was
occluded below the semi-silvered mirror.

Subjects were instructed to perform reaching movements toward a single visual target
while holding the handle of the robot arm. The target was located 15 cm in front of
the start position along the sagittal plane. We instructed subjects to move directly to
the target in a straight line without corrective movements. Upon the completion of
each reach, the target changed colour to provide visual feedback regarding movement
duration. The target disappeared if the movement was within the desired time (500
± 50 ms), turned red if the movement was too fast, or turned green if the movement
was too slow. These criteria were used to keep movement speed consistent and were
not used to exclude trials. After feedback, the robot returned the subject’s hand to
the start position along a straight trajectory.

The robot was programmed to alter limb dynamics through the application of force on
the subject’s hand during movements. The robot applied a clockwise FF to deflect the
hand rightward (right FF; Figure 2.1C) or a counterclockwise FF to deflect the limb
leftward (left FF). Velocity-dependent FFs were applied according to the following
equation:
Figure 2.1: A, Subjects grasped the handle of a robotic arm with the right hand. An LCD TV (not shown) projected visual feedback onto a semi-silvered mirror surface mounted just above the robotic arm. B, Subjects performed straight reaches in the horizontal plane from the start position (blue circle) to a target (white circle). C, Sample hand trajectory of a reach in a right force field (FF). The curvature of each movement was assessed in terms of the maximum perpendicular deviation (PD) of the hand path relative to a straight line connecting the home and target.
where x and y are lateral and sagittal directions, Fx and Fy are the applied robot forces, vx and vy are hand velocities, k = 14 Ns/m, and d = +1 (right FF), -1 (left FF) or 0 (null field).

Video stimuli showed a top-down view of a tutor reaching to a single target while holding the robotic arm with the right hand. Two video recordings were made, one in which a tutor learned to reach in a left FF and a second in which a different tutor reached in a random FF. Neither tutor had any previous experience reaching in a FF. A recording of the start position, target, and cursor was superimposed onto each video of the tutors’ arm movements with Final Cut Pro 10 (Apple). A learning video was created that depicted the tutor performing 200 reaches as the robot applied a left FF (duration: 15 minutes). This video was made with three 30-s video clips from the left FF recording, each showing the typical progression from curved to straight movements during FF learning. The control video showed the tutor performing 200 reaches as the robot applied a FF that varied pseudorandomly from trial to trial between a left, right, or null FF (duration: 15 minutes). The three 30-s clips used in this video thus showed movements that varied in their curvature but lacked the orderly progression from
curved to straight movements depicted in the learning video. Maximum movement curvature was comparable between the learning and control videos. However, while the tutor in the learning video clips showed progressively decreasing movement curvature, the tutor in the control video clips showed consistently curved movements. A random force environment cannot be learned [Takahashi et al., 2001], and so the control video was used to test for changes in FC that may arise because of nonlearning factors such as visual attention to motion or observation of movement errors. Video clips were randomly ordered to create each video.

### 2.2.3 Experiment 1 Protocol

Subjects (n = 15) participated in three sessions, each held on one of three consecutive days (Figure 2.2A). On day 0, subjects were familiarized with the robotic arm and performed 50 practice reaching trials in a null field, in which the robot did not apply force to the hand. The day 1 and day 2 sessions were held at the same time on each day. On day 1, we acquired baseline measures. First, subjects performed 200 reaching trials in a null field to allow us to assess baseline movement curvature. Next, subjects walked to the imaging facility and underwent a baseline fMRI scan session. During the day 1 fMRI scan session (detailed description below), we measured baseline resting-state FC. The scan session began approximately 20 minutes after completion of the reaching task and lasted 60 minutes. On day 2, subjects watched the video of the tutor learning to reach in a left FF in the laboratory (Figure 2.2B). Subjects
were seated in front of the robotic arm, and the LCD monitor projected the video onto the semi-silvered mirror. While watching the video, subjects sat still with both arms resting on the tabletop (not holding the handle of the robot arm). We instructed subjects to count the total number of times the tutor in the video performed a reach at the desired speed (indicated by the target disappearing). Subjects reported the final tally to the experimenter at the end of the video. This was done to assess whether subjects were paying attention to the video. Tallies from subjects in the learning group are reported below in terms of accuracy. These data were not incorporated into behavioural or neuroimaging analyses. Next, subjects walked to the imaging facility and underwent a second fMRI scan session, which used the same protocol as on day 1. During the day 2 fMRI scan session, we again measured resting-state FC. This allowed us to assess how resting-state FC changed from baseline (day 1) to after observation (day 2). Finally, subjects walked back to the laboratory for a behavioural motor learning test. For the motor learning test, subjects performed 100 reaching movements while the robotic arm applied a rightward FF (test FF). This allowed us to assess the extent to which the learning and retention of the observed (left) FF interfered with performance in the opposite (right) test FF.

As has been used previously (Vahdat et al., 2011; Cothros et al., 2006; Mattar & Gribble, 2005), the direction of the test FF (right) was chosen to be opposite to the direction of the FF that acted on the tutor in the learning video (left). A hallmark of motor adaptation is the presence of aftereffects, that is, the continued use of a
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Figure 2.2: A, On day 1, subjects grasped the handle of a robotic arm and performed 200 reaches in a null field (no force applied). Subjects then underwent resting-state fMRI scans. On day 2, subjects in a learning group (n=15) observed a video showing a tutor learning to perform straight reaches in a left force field (FF). Subjects in a control group (n = 15) observed a video showing a tutor performing reaches in an unlearnable, randomly-varying FF. Subjects then underwent post-observation resting-state fMRI scans. Finally, as a behavioural motor learning test, subjects performed 100 reaches in a right FF. B, A screenshot of the learning video (top) showing the tutor’s progressive decrease in movement curvature as the left FF is learned. A screenshot of the control video (bottom) showing the tutor’s high- and low-curvature movements in the unlearnable, randomly-varying FF. Superimposed trajectories are for demonstrative purposes and were not shown in the videos.
learned behaviour when the environment is unexpectedly changed. For example, subjects who have learned to reach in a left FF have acquired a representation of the novel environment and the muscle force pattern required to counteract the applied leftward force by compensating rightward. Subjects continue to use the learned muscle force pattern even when the force environment is changed. For example, if the force environment was removed (null field), subjects’ movements would initially be curved to the right (Shadmehr & Mussa-Ivaldi, 1994). Aftereffects are particularly pronounced if the force environment changes such that it is the opposite of the learned (left) FF. When exposed to the right FF, the subject would compensate rightward (persistence of the learned muscle force pattern) in addition to being pushed rightward by the robotic arm. Thus, those subjects who better learned the muscle force pattern required to perform straight reaches in the left FF would execute worse, more curved movements in the opposite (right) FF. In the present study, greater learning and retention of the observed left FF would bring about greater movement curvature when exposed to the right FF during the motor learning test (Brown et al., 2009; Cothros et al., 2006).

2.2.4 Experiment 2 Protocol

We conducted a follow-up experiment to assess the extent to which the functional changes in the network identified in experiment 1 were specifically related to observational motor learning as opposed to other factors unrelated to learning, specifically visual attention to motion or observation of movement errors. A different group of
subjects (n = 15) participated in experiment 2. As shown in Figure 2.2A, the day 1 protocol was identical for both experiments 1 and 2. On day 2, control subjects watched the control video showing the tutor performing reaches in an unlearnable FF that randomly varied from trial to trial between a left, right, or null FF (Figure 2.2B). Therefore, similar to the learning group, the control subjects observed movement errors and attended to visual motion while watching the video of the tutor. The critical difference was that the control subjects did not observe the tutor learning. As with the learning group, the control subjects observed the video of the tutor’s movements in the laboratory while sitting in front of the robotic arm. Similarly, control subjects were instructed to count the number of times the tutor in the control video performed a reach at the correct speed (indicated by the white target disappearing) and to report the final tally to the experimenter. This was done as a check to verify that control subjects also paid attention to the video of the tutor’s movements. Tallies from the control subjects are also reported below in terms of accuracy. These data were not incorporated into behavioural or neuroimaging analyses. As in experiment 1, control subjects underwent a second resting-state fMRI scan and a motor learning test (reaches in a right FF) after observation of the video of the tutor’s movement. In summary, the control experiment used the same experimental design as experiment 1, with the only exception that control subjects observed a tutor performing reaching movements with similar amounts of curvature as depicted in the learning video but not motor learning.
2.2.5 Behavioural Data Analysis

The robot handle position, velocity, and applied force were sampled at 600 Hz. The position data were low-pass filtered at 40 Hz. The start and end of each trial were defined as the position at which the hand’s velocity increased above and decreased below 5% of the peak velocity, respectively. Movement curvature was calculated for each trial as the maximum perpendicular deviation of the hand (PD) relative to a straight line connecting the start position and reaching target (Mattar & Gribble, 2005). Motor learning was assessed after the day 2 fMRI scan session, 80 minutes after subjects watched the reaching video. A motor learning by observing score was calculated for each subject as the mean PD of the first 3 trials in the test FF relative to the mean PD of the last 50 trials in the null FF. In this way, we were able to quantify the extent to which the learning and retention of the observed FF interfered with each subject’s subsequent performance in the (right) test FF. We also assessed movement curvature throughout the entire motor learning test. Individual PD scores were averaged over 10-trial blocks, and group means were compared with analysis of variance and Bonferroni-corrected post hoc tests.

2.2.6 fMRI Image Acquisition

During each hour-long fMRI scan session, subjects underwent two 8-minutes resting-state scans under the instruction to remain awake with their eyes closed. The two
resting-state runs were separated by a 5-minutes-long anatomical scan. During the anatomical scan, subjects were instructed to remain awake with their eyes open and fixate on a cross hair. Subjects then performed two 6-minutes functional localizer tasks. The localizer tasks were designed to allow us to determine the coordinates of 10 a priori-selected regions of interest (ROIs; see below) for use in the FC analyses described below.

The AON localizer task consisted of interleaved blocks of viewing intact and scrambled video clips of a tutor performing reaches while holding the robotic arm (ten 36-s blocks). Intact video clips showed a top-down view of a tutor performing straight reaching movements in a null FF. For the baseline condition the video clips were scrambled, with only the start position and target remaining in their original locations. This approach preserved the low-level motion-related features of the visual image such as movement direction and velocity while disrupting the details of the movement such as shoulder and elbow joint rotations and hand path curvature \cite{Malfait2010}. During observation of the AON localizer video, all subjects were instructed to count the total number of times the target disappeared and report it to the experimenter at the end of the video. This was done as a check to make sure each subject paid attention to the AON localizer video. Subjects’ reported tallies were not incorporated into the behavioural or neuroimaging analyses.

The motor localizer task consisted of interleaved blocks of arm movement and rest
(ten 36-s blocks). During movement blocks, subjects slowly moved their right forearm along the frontal plane in a cyclic manner (90° elbow flexion). Movements were paced at a frequency of 0.1 Hz with colour-coded visual cues.

Neuroimaging data were acquired with a 3-T Siemens Magnetom Tim Trio imaging system with a 32-channel head coil. Whole-brain functional data were acquired with a T2*-weighted EPI sequence (TR = 3,000 ms, TE = 30 ms, flip angle = 90°, 3-mm isotropic voxels, 80 x 80 x 50 matrix, iPAT acceleration factor = 2). The T1-weighted anatomical images were collected with a MPRAGE sequence (TR = 2,300 ms, TE = 2.98 ms, flip angle = 9°, 1-mm isotropic voxels, 192 x 240 = 256 matrix). For each scanning session a field map was acquired with a gradient echo sequence (TR = 531 ms, TE = 4.92 ms/7.38 ms, flip angle = 60°, 3-mm isotropic voxels, 80 x 80 x 50 matrix).

2.2.7 fMRI Image Preprocessing

Neuroimaging data analyses were performed with FSL version 5.0.4 (FMRIB’s Software Library, www.fmrib.ox.ac.uk/fsl). Image preprocessing consisted of the removal of the first 2 volumes in each functional run, slice-timing correction, motion correction, nonbrain tissue removal, spatial smoothing using a 6-mm FWHM Gaussian kernel, and high-pass temporal filtering (100 s). Field map distortion correction and linear coregistration of functional and anatomical images were performed with boundary-
based registration (BBR) in FLIRT. Images were transformed into standard space (MNI’s 152-brain T1 template, 2-mm isotropic voxel size) with a 12-DOF linear registration.

2.2.8 Regions of Interest

We selected 10 a priori ROIs involved in action observation and/or motor learning (see Table 2.1). These regions included left SMA, dorsal premotor cortex (PMd), ventral premotor cortex (PMv), M1, S1, V5/MT, SPL, inferior parietal lobule (IPL), putamen (BG), and right cerebellum (CB). ROI coordinates were determined with the data acquired during the independent functional localizer tasks. While the localizer tasks were performed after the resting-state scans on both days, the seed region coordinates were defined with only the data collected from the localizer tasks performed during the day 1 (baseline) scan session. This was done to ensure that the data used to define seed regions were based on scans following identical experiences of the two groups. If we had also included day 2 scans to define seed regions, the BOLD response evoked by the localizer tasks might have differed across groups due to each group having observed a different video at the beginning of day 2 (learning vs. control).

The task-induced response for each localizer was assessed with a per-subject GLM. All 30 subjects were then included in a mixed-effects analysis of the localizer tasks (cluster threshold of Z > 2.3, p < 0.05). The 10 brain regions listed above were identified
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In the resulting Z map with the Julich histological (cyto- and myelo-architectonic) atlas (Eickhoff et al., 2005), the Harvard-Oxford subcortical structural atlas (Desikan et al., 2006), or the probabilistic cerebellar atlas (Diedrichsen et al., 2009). Within each of the 10 brain regions, the ROI coordinate was chosen as the peak voxel (Table 2.1). ROIs included all voxels within a 6-mm-radius sphere centered on the activation peaks. The same standard (MNI) space seed coordinates were used for both groups.

2.2.9 Functional Connectivity Analysis

The FC analysis was performed on both resting-state runs acquired on day 1 and both resting-state runs acquired on day 2. The ultimate goal of the analysis was to estimate how FC on day 2, after observation of learning, differs from baseline FC on day 1. Each preprocessed resting-state run was band-pass filtered, preserving frequencies between 0.01 and 0.1 Hz, within which resting-state activity is observed (Biswal et al., 1995; Damoiseaux et al., 2006). Intensity normalization was performed by scaling the mean value of each run to 10,000 to factor out global intensity differences between resting-state runs. Seed-based correlation analyses were then carried out for each subject to assess FC between each seed ROI and the rest of the brain. The mean time series from each ROI was used as a predictor in a whole-brain regression analysis implemented in FILM (FMRIB’s Improved General Linear Model). The following signals were included in the model as nuisance regressors: the temporal derivative of the ROI signal, six rigid body motion parameters obtained from motion correction,
### Table 2.1: Seed regions and coordinates used for resting-state functional connectivity analyses.

<table>
<thead>
<tr>
<th>ROI</th>
<th>MNI Coordinates</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMA</td>
<td>-4 -10 56</td>
<td>5.93</td>
</tr>
<tr>
<td>PMd</td>
<td>-24 -22 66</td>
<td>6.02</td>
</tr>
<tr>
<td>PMv</td>
<td>-42 -6 56</td>
<td>5.16</td>
</tr>
<tr>
<td>M1</td>
<td>-26 -30 64</td>
<td>6.41</td>
</tr>
<tr>
<td>S1</td>
<td>-30 -36 62</td>
<td>6.32</td>
</tr>
<tr>
<td>V5/MT</td>
<td>-42 -76 2</td>
<td>5.70</td>
</tr>
<tr>
<td>SPL</td>
<td>-22 -48 68</td>
<td>5.87</td>
</tr>
<tr>
<td>IPL</td>
<td>-60 -44 22</td>
<td>4.01</td>
</tr>
<tr>
<td>BG</td>
<td>-28 -14 8</td>
<td>4.52</td>
</tr>
<tr>
<td>CB</td>
<td>26 -44 -26</td>
<td>5.22</td>
</tr>
</tbody>
</table>

ROI, region of interest; SMA, supplementary motor area; PMd, dorsal premotor cortex; PMv, ventral premotor cortex; M1, primary motor cortex; S1, primary somatosensory cortex; V5/MT, middle temporal visual area; SPL, superior parietal lobule; IPL, inferior parietal lobule; BG, putamen; CB, cerebellum.
mean global signal, mean white matter signal, and mean CSF signal. All signals were
band-pass filtered (0.01-0.1 Hz) prior to nuisance regression.

The resulting contrast images were entered into a mixed-effects model (FLAME) for
each group. In this analysis, the binary GLM predictor modeling the change in FC
from day 1 to day 2 was weighted by each subject’s respective motor learning by
observing score (Vahdat et al., 2011). In this way, the resulting change in FC can
be linked to the behavioural measure of motor learning. The predictor of interest
reflecting subject behaviour was orthogonalized with respect to regressors modeling
each subject’s overall mean. Corrections for multiple comparisons were carried out
at the cluster level (Z > 2.6, cluster significance: p < 0.05, corrected for familywise
error with Gaussian random field theory). We further applied a Bonferroni correction
for the number of ROIs examined; thus reported clusters are those that survived a
size threshold of p < 0.005 (i.e., p < 0.05/10 ROIs). These analyses yielded Z score
maps reflecting networks whose changes in FC from day 1 to day 2 were related to
our behavioural measure of motor learning achieved. FC was defined as the temporal
correlation (Fisher Z-transformed correlation coefficients) between the seed region
time course and the average time course of target clusters.
2.3 Results

2.3.1 Behavioural Results

Observing the tutor learning a left FF affected subjects’ subsequent motor behaviour in the final test FF. Subjects who observed left FF learning performed significantly worse (i.e., more curved) movements when they later encountered the test (right) FF compared with control subjects who observed similar curved movements in an unlearnable random FF (experiment 2). The learning group’s poorer performance in the test FF is indicative of proactive interference due to learning of the observed left FF (Brown et al., 2009; Cothros et al., 2006). Figure 2.3A shows mean movement curvature (PD) over the entire motor learning test, averaged over 10 trial blocks. Movements in the test FF were initially highly curved to the right but subsequently decreased in curvature over the course of trial blocks. While both groups reduced trajectory curvature in the test FF as a function of trial block, the pattern of the decrease depended on the FF that was previously observed (F(9,154) = 2.39, p < 0.05, Greenhouse-Geisser corrected). The behavioural difference between groups is indicated by reliably higher motor learning by observing scores for the learning group (Figure 2.3B; t(28) = 2.58, p < 0.01). This behavioural difference was seen in the first block of the test FF movements, during which subjects who had observed left FF learning exhibited 40% greater trajectory curvature than control subjects (t(28) = 2.99, p <
This result is consistent with previous observational learning studies (Bernardi et al., 2013; Brown et al., 2009; Mattar & Gribble, 2005; Williams & Gribble, 2012).

2.3.2 Experiment 1 Neuroimaging Results

To investigate brain areas involved in motor learning by observing, we examined post-observation changes in FC (day 2 vs. day 1) involving our functionally defined ROIs (Table 2.1) that were related to subjects’ respective motor learning by observing scores (as assessed after the final resting-state scan on day 2). In this way, we sought to identify functional networks associated with the amount of motor learning achieved through observation.

These analyses yielded statistically reliable results only for our ROI in left V5/MT. Left V5/MT, an area involved in visual motion perception (Watson et al., 1993; Zeki et al., 1991), was the most highly activated region during our AON localizer task. Figure 2.4 shows target clusters that exhibited FC changes with left V5/MT that were related to motor learning by observing scores. The top panel of Figure 2.4 shows that left V5/MT exhibited decreased FC with a cluster in left cerebellar cortex (lobule VI and Crus I) after observation of left FF learning; as shown on the bar graph, the negative correlation between V5/MT and cerebellum on day 1 approached zero on day 2 after observation of FF learning. At the top right of Figure 2.4 we have presented the relationship between al motor learning by observing scores, used as regressors of
Figure 2.3: Motor learning by observing behavioural results. A, Maximum perpendicular deviation (PD) for movements in the right FF. The first 10 movements are shown as averages of 5-trial blocks. Subsequent movements are shown as averages of 10-trial blocks. Greater perpendicular deviation (PD) for initial movements in the right FF indicates greater interference due to the learning of the observed left FF. Subjects who observed the (left FF) learning video showed greater movement curvature when first exposed to the right (test) FF compared to control subjects (blue). B, Motor learning by observing scores as a function of video observed. * indicates p < 0.01. Error bars represent SE.
interest in our FC analysis, and the changes in FC to further illustrate how subjects with higher motor learning by observing scores exhibited greater decreases in FC between V5/MT and cerebellum. The nonindependence of this particular correlation may inflate the effect size; thus we have presented this analysis as a sanity check for illustrative purposes, not as the basis for inference [Poldrack & Mumford, 2009].

It is worth noting that while the FC between V5/MT and cerebellum decreased from day 1 to day 2, the scatterplot shows a positive correlation. This is due to the subtraction of negative (day 1) FC values from near-zero (day 2) FC values, yielding positive FC changes (day 1 and day 2 FC values are shown in detail in Figure 2.5 below). The bottom panel of Figure 2.4 shows that left V5/MT also exhibited decreased FC with a cluster spanning left M1 and left S1; the bar graph shows that the positive correlation between V5/MT, M1 and S1 on day 1 approached zero on day 2 after observation. The scatterplot at the far right presents the relationship between behavioural motor learning by observing scores and decreases in FC between V5/MT, M1 and S1, again illustrating that those subjects who achieved greater motor learning through observation exhibited greater FC decreases. Subjectwise FC values on day 1 (baseline) and day 2 (after observation) are shown in Figure 2.5. Anatomical labels and local Z value maxima for each cluster are reported in Table 2.2.
Figure 2.4: Changes in resting-state functional connectivity (FC) from day 1 (baseline) to day 2 (after observation) related to motor learning by observing scores. In the learning group, the region of interest (ROI) in V5/MT (inset at left) exhibited decreased FC with the cerebellum (top) and also primary motor (M1) and primary somatosensory (S1) cortices following observation of the learning video (bottom). Z score maps are thresholded at $Z > 2.6$ and corrected for familywise error with Gaussian random field theory ($p < 0.005$). Scatterplots further illustrate that the observed functional changes are indeed related to our behavioural measure of motor learning, as assessed during the motor learning test after the day 2 fMRI scan. Bar graphs on the far right show that FC between left V5/MT and each cluster decreased from day 1 to day 2 such that FC approached zero after the observation of left FF learning.
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<table>
<thead>
<tr>
<th>ROI</th>
<th>Cluster P Values</th>
<th>Z Score Maximum</th>
<th>MNI Coordinates</th>
<th>Anatomical label</th>
</tr>
</thead>
<tbody>
<tr>
<td>L V5/MT</td>
<td>0.001</td>
<td>4.89</td>
<td>-44 -76 -32</td>
<td>L cerebellum (Crus I)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.27</td>
<td>-38 -66 -22</td>
<td>L cerebellum (lobule VI)</td>
</tr>
<tr>
<td></td>
<td>0.004</td>
<td>4.00</td>
<td>-30 -32 46</td>
<td>L S1 (BA3a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.60</td>
<td>-30 -40 50</td>
<td>L S1 (BA2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.37</td>
<td>-32 -28 50</td>
<td>L M1 (BA4p)</td>
</tr>
</tbody>
</table>

**Table 2.2:** Clusters in which post-observation changes in FC correlated with motor learning by observing scores. Functional connectivity (FC) data corresponding to the cerebellar clusters are shown in the top two rows and data corresponding to the sensory-motor cluster are shown in the bottom three rows. L, left.
Figure 2.5: Subjectwise resting-state functional connectivity (FC) values on day 1 (baseline, blue circles) and day 2 (after observation, green squares) for the learning group. Subjects are rank ordered along the x-axis according to increasing motor learning by observing scores (indicated below in brackets). A, FC between V5/MT and cerebellum (CB) decreased from day 1 to day 2 such that subjects with higher motor learning by observing scores showed greater decreases in FC (i.e., correlations approach zero). B, FC between V5/MT and M1 and S1 also decreased from day 1 to day 2 such that those subjects with higher motor learning by observing scores exhibited greater decreases in FC (i.e., correlations approach zero).
2.3.3 Experiment 2 Neuroimaging Results

To examine the extent to which the changes in the identified functional network are specifically related to motor learning by observing, we conducted a follow-up experiment in which subjects observed a tutor reaching in an unlearnable random FF.

During the motor learning test, control subjects’ movements were significantly less curved upon initial exposure to the (right) test FF compared with those subjects who observed FF learning (Figure 2.3A), indicating less learning and retention of the observed random FF. Similarly, their motor learning by observing scores were reliably lower than subjects who observed left FF learning (Figure 2.3B).

The FC analyses described above were also carried out for the control group. The same parameters were used for these analyses, including the same ROI coordinates. FC analyses for the control group yielded no statistically reliable clusters for the V5/MT seed region. To further explore these data, we repeated the group-level analysis using lower Z thresholds. No significant target clusters appeared for the V5/MT ROI until the threshold was lowered to $Z > 2.2$. Even at lower threshold levels, the clusters bear no resemblance to the learning group result (see Figure 2.6). In sum, this indicates that the FC changes within the functional network observed in the learning group are not simply due to observing movement error or attending to visual motion but rather are specifically linked to motor learning.
Figure 2.6: Changes in resting-state functional connectivity (FC) from day 1 (baseline) to day 2 (after observation) for the control group with respect to the ROI in left V5/MT. As shown in the top panel, no significant clusters appeared when the group-level analysis was thresholded at $Z > 2.6$ and corrected for familywise error with Gaussian random field theory ($p < 0.005$). Clusters appeared only when the threshold was lowered to $Z > 2.2$ (middle). Even at lower threshold levels ($Z > 1.8$, bottom), the clusters that survive bear no resemblance to those clusters observed in the learning group.
2.3.4 Control Analysis Results

To ensure that subjects paid attention to the videos, we instructed them to count the total number of trials in which the tutor performed a reaching movement at the desired speed (indicated by the target disappearing). Reported values were highly accurate for both the learning and control groups, with mean accuracy scores of 95% and 98%, respectively.

During the motor learning test, the robotic arm applied the FF in a velocity-dependent manner. To ensure that the curvature differences of movements performed in the test FF were due to learning and not to differences in applied force to the hand, we compared movement time and peak tangential velocity (and hence peak force applied by the robot) for each movement block between the groups. No significant differences were observed ($p > 0.05$); thus applied forces to the hand did not differ between the groups during the motor learning test.

The motor learning by observing scores were based on the maximum curvature (PD) of the first three test FF trials relative to (i.e., minus) baseline curvature in the null FF. To assess the robustness of our learning group result, we computed three additional motor learning by observing scores: 1) PD of the first test FF trial relative to baseline curvature, 2) mean PD of the first two test FF trials relative to baseline curvature, and 3) mean PD of the first four test FF trials relative to baseline curvature. We
repeated our group-level analysis for the V5/MT seed region, using each of these motor learning by observing scores as the regressor of interest. Each of these analyses yielded clusters very similar to the learning group result presented in Figure 2.4.

We further explored the robustness of our learning group result across various parameters used in the neuroimaging preprocessing stage. We ran additional analyses using spatial smoothing kernels of 4 mm and 5 mm as well as seed region radii of 4 mm and 5 mm. Again, these analyses yielded results qualitatively similar to the learning group result presented in Figure 2.4.

2.4 Discussion

Here we assessed changes in resting-state FC after subjects observed a tutor learning to reach in a novel FF. We revealed a novel functional network in which changes in FC were correlated with the amount of observational motor learning achieved, as assessed behaviourally after resting-state fMRI scans. We found that left V5/MT showed decreased FC with left cerebellum such that those subjects who learned more through observation exhibited greater decreases in FC. Left V5/MT also showed decreased FC with left M1 and left S1 such that those subjects who learned more through observation exhibited greater decreases in FC. Furthermore, in experiment 2, we showed that functional changes in the identified network are not seen in subjects who observed a tutor performing curved movements but not learning. Thus, the patterns observed in
the identified functional network are not the result of observing movement errors or attending to visual motion, but rather these FC changes are specifically related to motor learning through observation.

FC changes in the identified network may reflect a decoupling between visual and sensory-motor systems, as the visual information about the tutor’s movements is transferred to the sensory-motor system for use in motor learning. Subjects who learned more from observation, as assessed by their subsequent motor performance, showed a greater disengagement between V5/MT and cerebellum and between V5/MT and M1 and S1. This visuo-motor decoupling may represent the transference of learning-related activity into motor regions such as cerebellum and sensory-motor cortex for the establishment of internal models of the observed FF (Diedrichsen et al., 2005; Imamizu et al., 2000; Nezafat et al., 2001; Vahdat et al., 2011). Differences in the degree of visual and sensory-motor decoupling may thus reflect differences in the extent to which visual information about the tutor’s movements is propagated into the motor domain and mapped onto the observer’s own sensory-motor system.

Decreases in FC from day 1 to day 2 were correlated with subsequent behavioural measures of motor learning achieved through observation. While decreases in FC are not as commonly reported in the literature as increases, they are not without precedent (e.g., Vahdat et al., 2014). It is commonplace for resting-state fMRI studies to perform seed-based correlation analyses and report changes in FC after an
experimental manipulation. However, if one does not examine the pre- and post-FC values, it cannot be ruled out that reported increases in FC may, in fact, be decreases in FC. As seen here, the subtraction of negative (day 1) FC values from near-zero (day 2) FC values yielded arithmetically positive FC changes. However, upon inspection of the day 1 and day 2 FC values, it is clear that the changes in FC actually correspond to decreases in FC (negative correlations approaching zero). One possible interpretation for this is that on day 1 sensory-motor brain regions and visual motion areas such as V5/MT were coactivated during the baseline null field movements and residual components of this activity were present during the subsequent (day 1) resting-state scan. On day 2, no active movements were completed prior to the resting-state scan; subjects had only watched a tutor learning to reach in a FF prior to the day 2 fMRI scan session. Therefore, during the day 2 resting-state scan sensory-motor regions were not primed as strongly as on day 1, and so perhaps this is why correlations between visual and sensory-motor regions were weaker. However, the observed changes in FC reported here from day 1 to day 2 were reliably related to the degree of learning each subject achieved through observation, and this cannot be explained by differences in sensory-motor priming on day 1 vs. day 2. Furthermore, we did not detect such FC changes in the control group, and this group difference cannot be explained by differences in visual or sensory-motor priming on day 1 vs. day 2. The findings reported here represent a potential neural basis that specifically links observation of learning with sensory-motor plasticity and associated performance changes in motor
Resting-state fMRI is a powerful technique for studying motor learning. Motor learning does not occur in isolation but rather is accompanied by changes in task performance such as changes in reaction time and decreased attentional demand (Poldrack 2000). This poses a challenge for traditional task-based fMRI studies of motor learning, which examine activation changes from pre-learning to post-learning performance, because they are unable to distinguish those changes in activation that are due to learning from those changes due to differences in performance. Since resting-state fMRI is task free, it is exempt from such performance confounds and observed changes in activation can be directly attributed to learning.

The topographies of resting-state networks closely correspond to those functional networks activated during behavioural tasks (e.g., Fox et al. 2005). Moreover, the coactivation of brain areas during active behaviour can modulate subsequent resting-state activity. Task-induced changes in resting-state activity have been demonstrated between visual and fronto-parietal attention areas after visual perceptual learning (Lewis et al. 2009), among fronto-parietal and cerebellar networks after visuomotor adaptation (Albert et al. 2009), and among premotor, motor, and cerebellar circuits after FF learning (Vahdat et al. 2011).

There is considerable overlap between the functional network identified in the present study and brain areas involved in motor learning, namely, M1 (Grafton et al. 1992).
Steele & Penhune (2010) and cerebellum (Flament et al., 1996; Imamizu et al., 2000; Vahdat et al., 2011). Vahdat and colleagues (2011) have previously examined changes in resting-state FC following FF learning achieved through physical practice using a very similar experimental design (though without a control group). Vahdat and colleagues (2011) reported post-learning changes in resting-state FC involving M1, SMA, and cerebellum that were reliably correlated with behavioural scores of active motor learning. Here we observed resting-state FC changes involving visual motion perception area V5/MT, M1, S1, and cerebellum that were related to behavioural scores of motor learning achieved through observation. The present study and that of Vahdat and colleagues both indicate the involvement of M1 and cerebellum in motor learning achieved through either observation or physical practice, respectively. Engagement of these areas during motor learning has been interpreted as reflecting error detection and the execution of corrective movements (e.g., Steele & Penhune, 2010). In addition (and in contrast with the study by Vahdat and colleagues), the present study indicates that visual area V5/MT and somatosensory cortex are also engaged when motor learning occurs through observation.

A subset of the brain regions in the identified functional network is also common to the AON, namely, visual area V5/MT, S1, and M1 (Caspers et al., 2010). Moreover, some recent studies also suggest a role for the cerebellum in action observation (e.g., Calvo-Merino et al., 2006; Gazzola & Keysers, 2008).
Resting-state networks strongly coincide with underlying structural connectivity. However, some brain regions can exhibit resting-state FC via indirect structural connections (Vincent et al., 2007). Many of the functional links between V5/MT, cerebellum, M1, and S1 identified in the present study likely arise from such indirect anatomical connections. Neuroanatomical studies have shown that middle temporal area V5/MT projects directly to the cerebellum via the pontine nuclei in the macaque (Ungerleider et al., 1984). V5/MT also projects to the posterior parietal cortex, which in turn relays input to the cerebellum via the pontine nuclei (Glickstein et al., 1980; Langer et al., 1985). The posterior parietal cortex also sends input from V5/MT to S1 and indirectly to M1 (Tanné-Gariépy et al., 2002; Vogt & Pandya, 1978). These pathways are also reciprocally connected, with the cerebellum both projecting to and receiving input from the posterior parietal cortex and M1 via the thalamus (Dum & Strick, 2003; Thach et al., 1992). Consistent with previous anatomical studies, we observed that the cluster spanning M1 and S1 in the learning group indeed extended into the left posterior parietal cortex (SPL area 5L) when the Z threshold was lowered to 2.2 (Figure 2.7).

Neuroimaging studies of action observation and motor learning consistently report ipsilateral or bilateral patterns of cerebellar activity (Calvo-Merino et al., 2006; Flament et al., 1996; Gazzola & Keysers, 2008; Vahdat et al., 2011). In this context, it is perhaps surprising that we observed activation in the contralateral (i.e., left) cerebellar hemisphere in the present study. To further explore the changes in cerebellar
Figure 2.7: Changes in resting-state functional connectivity (FC) from day 1 (baseline) to day 2 (after observation) with respect to the ROI in left V5/MT for the learning group. When thresholded at $Z > 2.5$, the cluster in left cerebellar hemisphere extends to right cerebellar hemisphere (top). When thresholded at $Z > 2.2$, the primary sensory-motor cortical cluster extends into left posterior parietal cortex (bottom). Analyses are corrected for familywise error with Gaussian random field theory ($p < 0.005$).
activation in our learning group, we tested the sensitivity of the observed pattern of cerebellar FC changes to the chosen statistical threshold. When the Z threshold was lowered to $Z > 2.5$, we observed a target cluster in Crus I of the right medial cerebellar hemisphere that showed reliable changes in FC with the V5/MT seed region (Figure 2.7).

A functional link between V5/MT and cerebellum has been previously implicated in visual attention to motion. Kellermann and colleagues (2012) showed that effective connectivity between cerebellum (Crus I) and V5/MT was enhanced while subjects attended to moving bars compared with passive fixation. It may be argued that the FC changes between V5/MT and cerebellum observed in the present study may be driven by visual attention to motion. However, the control group showed no FC changes between V5/MT and cerebellum after their observation of the tutor’s movement. It is unlikely that visual attention to the tutor’s movement, a feature common to both groups, would be the cause of FC changes between V5/MT and cerebellum in the learning group only.

The identified network consisting of V5/MT, cerebellum, M1, and S1 represents a link between visual systems for motion perception and sensory-motor circuits for motor learning. This network may form the basis by which visual information about the movements of others influences sensory-motor circuits for learning to form new motor representations of novel motor skills.
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Chapter 3

Functional Connectivity Predicts

Observational Learning

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3.1 Introduction

Recent work has shown that action observation can promote motor learning. For example, individuals can learn how to reach in novel robot-imposed force field (FF) environments by observing the movements of a tutor (Mattar & Gribble 2005). Subjects observed a video of a tutor adapting his reaches to a novel robot-imposed FF. Subjects who later performed reaches in the same FF showed a benefit, performing better (straighter) reaches compared with control subjects who did not observe a tutor. Subjects who later performed reaches in the opposite FF performed worse (more curved) reaches than subjects who did not observe. While these results demonstrate that FFs can be partially learned from observation, there is considerable inter-individual variability in the extent to which observation promotes motor learning. Little is known about why this may be. Some individuals may be more predisposed to learning from observation than others, whether from birth, from experience-dependent plasticity, or a combination of these or other individual differences. Here we test the idea that individual differences in brain function or structure underlie the extent to which observation promotes subsequent motor learning.

In a recent review article, Zatorre (2013) discussed findings showing how structural and functional neural connectivity patterns predict individual differences in musical training and speech learning. Other studies have shown similar predictability for a wide array of cognitive abilities including executive function (Barnes et al. 2014).
Reineberg et al. (2015), reading (Koyama et al., 2011), second language acquisition (Chai et al., 2016), visual perceptual discrimination (Baldassarre et al., 2012), and memory recall (King et al., 2015). In the motor domain, Tomassini and colleagues (2011) demonstrated that individual differences in both functional and structural magnetic resonance imaging (MRI) measures correlate with the acquisition of a novel visuomotor tracking skill through active movement training. Task-based functional activation levels in a network involving prefrontal, premotor, and parietal cortices, as well as basal ganglia and the cerebellum, were associated with behavioural measures of active motor learning. Structural differences within the premotor cortex, higher-order visual areas, and the cerebellum were also positively correlated with learning abilities (Tomassini et al., 2011). Similarly, using dense-array electroencephalography (EEG), Wu and colleagues (2014) showed that resting-state functional connectivity (FC) between premotor, primary motor, and parietal cortices predicts individual differences in the subsequent learning of a visuomotor tracking task. Together, these studies suggest that functional and structural variations in motor learning-related brain networks can, in part, explain individual differences in the ability to learn novel motor tasks through active movement practice. The results of these studies raise the possibility that individual differences in brain structure or function may also be predictive of motor learning by observing.

Here we tested the hypothesis that individual differences in brain function or structure can predict the extent to which individuals will learn to perform a novel sensory-motor task.
task (FF reaching) from observation. On the basis of our previous work (McGregor & Gribble, 2015; McGregor et al., 2016), we expected that individual differences in brain function and structure within visual and sensory-motor brain networks would be predictive of motor learning by observing. On day 1, subjects performed baseline (no FF) reaches using a robotic arm and then underwent pre-observation anatomical and resting-state functional MRI (fMRI) scans. Twenty-four hours later, subjects in a learning group observed a video of a tutor learning to reach in a novel FF. Subjects in a control group observed a video of a tutor performing reaches in an unlearnable FF. After observation, all subjects performed reaches in a FF as a behavioural assessment of motor learning by observing. We found that, for the learning group, pre-observation (day 1) resting-state FC between bilateral dorsal premotor cortex (PMd), primary motor cortex (M1), and primary somatosensory cortex (S1) and left superior parietal lobule (SPL) was reliably correlated with behavioural scores of motor learning by observing acquired on day 2. No such correlation between pre-observation FC and motor learning by observing scores was found for the control group. Moreover, we found that individual differences in gray matter volume could not predict subsequent motor learning by observing. Pre-observation sensory-motor resting-state FC can thus explain part of the between-subject variation in motor learning by observing.
3.2 Materials and Methods

3.2.1 Subjects

Thirty healthy subjects participated in this study. Fifteen subjects were assigned to a learning group (6 men, 9 women; mean age 22.87 years ± 1.02 SE), and fifteen were assigned to a control group (6 men, 9 women; mean age 22.53 years ± 0.86 SE). All subjects were right handed, had normal or corrected-to-normal vision, were naïve to FFs, and reported no neurological or musculoskeletal disorders. Subjects provided written informed consent before participating. All experimental procedures were approved by the Research Ethics Board at The University of Western Ontario.

3.2.2 Apparatus

Subjects were seated in front of a custom tabletop and grasped the handle of a two-degree of freedom robotic arm (IMT2, Interactive Motion Technologies) with the right hand. The chair height was adjusted such that the subject’s upper arm was abducted approximately 90° from the trunk. An air sled was secured beneath the subject’s right arm to support the arm against gravity. A semi-silvered mirror, mounted horizontally just above the robotic arm, occluded the subject’s vision of his or her own arm and the robotic arm. During the reaching task, a liquid crystal display television (LCD TV) projected visual feedback onto the semi-silvered mirror. Visual feedback included
a start position (20-mm blue circle), a single target (20-mm white circle), and a cursor representing hand position (12-mm pink circle).

The reaching task involved guiding the handle of the robotic arm from the start position to the target, which was located 15 cm in front of the start position. Subjects were instructed to move as straight as possible. At the end of each reach, the target changed colour to provide feedback about movement time: the target disappeared if the movement time was within the desired time range (450 to 550 ms duration), turned red if the movement was too fast (< 450 ms), or turned green if the movement was too slow (> 550 ms). After each reach, the robotic arm returned the subject’s hand to the start position.

The robot applied a velocity-dependent FF during the reaching task according to Equation 1:

\[
\begin{bmatrix}
F_x \\
F_y
\end{bmatrix}
= \begin{bmatrix}
0 & dk \\
-dk & 0
\end{bmatrix}
\begin{bmatrix}
v_x \\
v_y
\end{bmatrix}
\]

where \(x\) and \(y\) are lateral and sagittal directions, \(F_x\) and \(F_y\) are the applied robot forces, \(v_x\) and \(v_y\) are hand velocities, \(k = 14 \text{ Ns/m}\), and \(d = +1\) (right FF), -1 (left FF) or 0 (null field).

Each video showed a top-down view of a tutor performing the reaching task described
above with her right arm. The tutors in the videos were naïve to FFs. The learning video consisted of a series of 30-s clips showing a tutor adapting her reaches to a leftward FF (left FF). These clips showed the gradual progression from curved to straight movements that is indicative of motor learning. The control video consisted of a series of 30-s clips showing a tutor performing reaches in an unlearnable FF in which the direction of the FF varied randomly from trial to trial (left FF, right FF, or null field). These clips showed the tutor performing both high- and low-curvature movements but lacked the progressive decrease in movement curvature depicted in the learning video. Therefore, the control video included movements similar to those shown in the learning video but did not depict learning. The videos showed 200 reaches each and were 15 min in duration (including regular breaks). Video screenshots are shown in Figure 3.1B. Note that the dashed trajectories and superimposed labels have been included for demonstrative purposes here and were not shown to subjects in the experiment.

3.2.3 Experimental Protocol

The experimental design is shown in Figure 3.1A. All subjects (n = 30) participated in three sessions. For each subject, the sessions were held at the same time on three consecutive days. On day 0, subjects were familiarized with the reaching task by performing 50 practice movements in a null field (no force applied by the robot). On day 1, subjects performed 200 baseline reaches in the null field and then walked to the
imaging facility for a fMRI scan session. The scan session, described in detail below, began approximately 20 minutes after the completion of the reaching task and lasted 1 h. Data collected during the day 1 scan session were used to estimate pre-observation resting-state FC involving 10 visual and sensory-motor brain areas [see regions of interest (ROIs) below] and to estimate whole brain gray matter volume. On day 2, subjects performed the observational motor learning task. Subjects watched either the learning video or the control video while seated in front of the robotic arm. The video was played on the LCD TV positioned above the robotic arm and was projected onto the semi-silvered mirror surface. To ensure that subjects paid attention during the video, we instructed them to count the number of correctly timed reaches in the video (indicated by the target disappearing upon the completion of a reach) and to report the final tally to the experimenter after the video. Reported tallies were analyzed to verify that subjects attended to the video, but these data were not incorporated into the behavioural or neuroimaging analyses. Note that subjects were not told to pay attention to any particular part of the movement trajectory or arm, nor were they told that the robot would be applying forces to the arm. Approximately 80 minutes after video observation, we assessed motor learning by observing by having subjects perform 100 reaches while the robotic arm applied a rightward FF (right FF).

During the 80 minutes between video observation and the motor learning test on day 2, both groups underwent a second fMRI scan session identical to the day 1 fMRI scan session. Data from the second fMRI scan session were not used in any of the
Figure 3.1: A, On day 1, subjects grasped the handle of a robotic arm with their right hand and performed 200 reaches in a null field (no force applied). Subjects then underwent resting-state fMRI scans. On day 2, subjects in the learning group (n=15) observed a tutor learning to perform straight reaches in a left force field (FF). Subjects in a control group (n = 15) observed a video of a tutor performing reaches in an unlearnable, randomly-varying FF. Finally, as a behavioural motor learning test, subjects performed 100 reaches in a right FF. B, A screenshot of the learning video (top) showing the tutor’s progressive decrease in movement curvature as the left FF is learned. A screenshot of the control video (bottom) showing the tutor’s high- and low-curvature movements in the unlearnable, randomly-varying FF. Superimposed trajectories are for demonstrative purposes and were not shown in the videos.
analyses presented here since the main objective of the present study was prediction of motor learning by observing based on pre-observation (day 1) neuroimaging data. Using this same data set, we have previously examined changes in resting-state FC from pre-observation (day 1 scan) to post-observation (day 2 scan). See McGregor and Gribble (2015) for details of FC changes from day 1 to day 2 and how they relate to observation-related gains in motor learning.

We assessed motor learning behaviourally by having subjects perform reaches in a right FF, which was the opposite FF to what was depicted in the learning video. The more subjects learned about the observed left FF, the worse their performance would be in the right FF. The idea is that during observation subjects learn about the compensatory pattern of muscle forces (i.e., rightward compensation) that is required to counteract the left FF. Subjects use this learned pattern of muscle forces when they subsequently perform reaches, resulting in aftereffects (e.g., Shadmehr & Mussa-Ivaldi, 1994). As is the case in this study, aftereffects are especially large if the FF is changed such that it is the opposite of the learned environment. This is because the subject compensates rightward (persistence of the learned pattern of muscle forces) and the robotic arm also pushes the hand to the right. Therefore, we expected that those subjects who better learned about the observed left FF would perform more highly curved reaches when first exposed to the right FF (Cothros et al., 2006; Brown et al., 2010; McGregor & Gribble, 2015; McGregor et al., 2016). We chose to use this interference paradigm to assess motor learning by observing because it tends to be
a more sensitive measure compared with testing subjects in the same FF that they observed.

### 3.2.4 Behavioural Data Analysis

During the reaching task, the position and velocity of the robotic handle were sampled at 600 Hz and stored for offline analysis. Positional data were low-pass filtered offline at 40 Hz. The start and end of each trial were defined with a threshold of 5% of the peak tangential velocity of the hand. Movement curvature was quantified for each trial as the maximum perpendicular deviation (PD) of the hand from a straight line connecting the start and target locations (Mattar & Gribble, 2005).

We calculated a behavioural motor learning by observing score for each subject. The motor learning by observing scores were calculated as the mean PD of the first 3 reaches in the right FF minus the mean PD of the last 50 reaches in the baseline null field. This approach allowed us to examine the extent to which observing the left FF interfered with subjects’ initial performance in the right FF compared with control subjects who did not observe the tutor undergoing learning. As in our previous work (Cothros et al., 2006; Brown et al., 2010; McGregor et al., 2016), we expected that motor learning by observing would primarily affect initial performance in the right FF, after which motor learning through active movement in the right FF would occur for both groups.
3.2.5 fMRI Image Acquisition

Neuroimaging data were acquired by a 3-T Siemens Magnetom Tim Trio imaging system using a 32-channel head coil. Whole brain functional data were acquired with a T2-weighted EPI sequence (TR = 3,000 ms, TE = 30 ms, 90° flip angle, 3-mm isotropic voxels, 80 x 80 x 50 matrix, iPAT acceleration factor = 2). T1-weighted anatomical images were collected with a MPRAGE sequence (TR = 2,300 ms, TE = 2.98 ms, 9° flip angle, 1-mm isotropic voxels, 192 x 240 x 256 matrix). For each subject, a field map was acquired at the beginning of the scan session with a gradient echo sequence (TR = 531 ms, TE = 4.92 ms/7.38 ms, 60° flip angle, 3-mm isotropic voxels, 80 x 80 x 50 matrix).

The fMRI scan session lasted 1 h. The scan session began with two 8-minute resting-state runs during which subjects were instructed to relax with their eyes closed. The resting-state runs were separated by a 5-minute anatomical scan during which subjects were instructed to fixate their gaze on a cross hair projected onto a screen. Subjects then performed two 6-minute functional localizer tasks: an action observation network localizer task and a motor localizer task. We selected 10 a priori ROIs known to be involved in action observation and/or motor learning (see below). The two localizer tasks allowed us to determine the coordinates of each ROI for use in the functional connectivity analysis described below.
For the action observation network localizer task, subjects viewed intact and scrambled video clips of a tutor performing reaches while holding the robotic arm (ten 36-s interleaved blocks in total). Intact video clips showed a top-down view of a tutor performing straight reaching movements in a null field (no forces applied by the robot). For the baseline condition, subjects viewed scrambled versions of these video clips in which only the start and target positions remained in their original locations. Scrambling the videos allowed us to preserve the low-level motion features such as movement direction and velocity while removing such movement features as shoulder and elbow joint rotations and the hand path \cite{Malfait et al., 2010}. During the action observation network localizer task, subjects were instructed to count the number of correctly timed movements the tutor performed and to report the final tally to the experimenter at the end of the video. This was done to verify that subjects attended to the video. Reported tallies were not incorporated into the behavioural or neuroimaging analyses.

For the motor localizer task, subjects performed interleaved blocks of arm movement and rest (ten 36-s blocks in total). During movement blocks, subjects slowly moved their right forearm along the frontal plane in a cyclic manner (90° elbow flexion). Colour-coded visual cues were used to pace movements at a frequency of 0.1 Hz.
3.2.6 fMRI Image Preprocessing

We carried out a whole brain seed-based correlation analysis to examine whether intersubject differences in resting-state FC on day 1 could predict the amount of motor learning by observing that subjects would achieve on the following day. Neuroimaging data analyses were performed with FSL version 5.04 (FMRIB’s Software Library, https://fsl.fmrib.ox.ac.uk/fsl/). Image preprocessing steps for the functional connectivity analysis included the removal of the first two volumes in each functional run, slice-timing correction, motion correction, spatial smoothing using a 6-mm kernel, and high-pass temporal filtering (100 s). Field map distortion correction and affine coregistration of functional and anatomical images were performed with boundary-based registration (BBR) in FLIRT. Subjects’ images were registered to Montreal Neurological Institute (MNI) standard space (MNI’s 152-brain T1 template, 2-mm isotropic voxel size) with a 12-degrees of freedom affine registration.

After preprocessing, each resting-state run was band-pass filtered between 0.01 Hz and 0.1 Hz (Biswal et al., 1995; Damoiseaux et al., 2006). Mean-based intensity normalization was performed (mean value of 10,000) to remove global intensity differences between runs (Damoiseaux et al., 2006). We then carried out our seed-based correlation analysis with FILM (FMRIB’s Improved General Linear Model).
3.2.7 Regions of Interest

We selected 10 a priori ROIs known to be involved in action observation and/or motor learning. These ROIs were used only for the functional connectivity analysis. ROIs included left supplementary motor area (SMA), PMd, ventral premotor cortex (PMv), M1, S1, visual area V5/MT, SPL, inferior parietal lobule (IPL), putamen, and right cerebellum. We determined the coordinates of each ROI based on the results of the block-design analyses of the action observation network localizer task and the motor localizer task. For each localizer, the task-induced response was assessed with a per-subject general linear model (GLM). Data from all 30 subjects were then included in a mixed-effects analysis (Z > 2.3, p < 0.05, cluster-based thresholding) for each localizer. These analyses yielded Z-score maps showing areas of the brain that were activated (on average across all 30 subjects) during arm movement or action observation, which we used to determine the coordinates of our ROIs. For each of our 10 ROIs, we found the peak activated voxel within that brain area and centered the ROI on that voxel. Each ROI consisted of all voxels within a 6-mm radius of the activation peak. Table 3.1 shows the coordinates of the activation peaks on which each ROI was centered.
### Table 3.1: Seed regions and coordinates used for resting-state functional connectivity analyses.

<table>
<thead>
<tr>
<th>ROI</th>
<th>MNI Coordinates</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMA</td>
<td>-4 -10 56</td>
<td>5.93</td>
</tr>
<tr>
<td>PMd</td>
<td>-24 -22 66</td>
<td>6.02</td>
</tr>
<tr>
<td>PMv</td>
<td>-42 -6 56</td>
<td>5.16</td>
</tr>
<tr>
<td>M1</td>
<td>-26 -30 64</td>
<td>6.41</td>
</tr>
<tr>
<td>S1</td>
<td>-30 -36 62</td>
<td>6.32</td>
</tr>
<tr>
<td>V5/MT</td>
<td>-42 -76 2</td>
<td>5.70</td>
</tr>
<tr>
<td>SPL</td>
<td>-22 -48 68</td>
<td>5.87</td>
</tr>
<tr>
<td>IPL</td>
<td>-60 -44 22</td>
<td>4.01</td>
</tr>
<tr>
<td>BG</td>
<td>-28 -14 8</td>
<td>4.52</td>
</tr>
<tr>
<td>CB</td>
<td>26 -44 -26</td>
<td>5.22</td>
</tr>
</tbody>
</table>

ROI, region of interest; SMA, supplementary motor area; PMd, dorsal premotor cortex; PMv, ventral premotor cortex; M1, primary motor cortex; S1, primary somatosensory cortex; V5/MT, middle temporal visual area; SPL, superior parietal lobule; IPL, inferior parietal lobule; BG, putamen; CB, cerebellum.
resting-state runs together as well as separately (see Results).

Group-level analysis results were thresholded based on Gaussian random field theory using a maximum height thresholding ($Z > 5.3$) with a corrected significance level of $p = 0.005$ (voxelwise thresholding, corrected for familywise error). We applied a Bonferroni correction for the number of ROIs used; therefore, our corrected significance threshold of $p = 0.005$ reflects $p = 0.05/10$ ROIs. These analyses resulted in 10 Z-score maps per group (1 per ROI) showing areas that, on average, exhibited FC with the seed region across subjects.

For each of the 10 resulting Z-score maps, FC was computed for each subject in the group as the temporal correlation (Fisher Z-transformed correlation coefficient) between the ROI time series and the average time series across all clusters in the identified network. This allowed us to estimate each subject's day 1 FC between the ROI and all of the clusters in each of the identified networks. At the group level, we computed the correlation (across subjects) between day 1 FC values and day 2 motor learning by observing scores for each of the identified networks. This was done to assess whether individual differences in day 1 FC among brain areas in any of the identified networks were related to performance during the behavioural test of motor learning by observing on day 2. We again applied a Bonferroni correction for the number of ROIs used; therefore, we considered statistically significant only those correlations between day 1 FC and motor learning by observing scores for which $p <$
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0.005 (i.e., p = 0.05/10 ROIs).

3.2.9 Voxel Based Morphometry Analysis

We carried out a whole brain voxel-based morphometry (VBM) analysis to test for intersubject differences in gray matter volume across the whole brain (measured on day 1) that could predict motor learning by observing scores on day 2. This analysis was carried out on the T1-weighted images with FSL-VBM v1.1. First, each subject’s anatomical image was brain extracted, gray matter segmented, and transformed to MNI space using a nonlinear registration. The resulting anatomical images were then averaged and flipped along the x-axis to generate a left-right symmetrical, study-specific template. Each subject’s gray matter-segmented anatomical image was registered to the study-specific template and smoothed with a 3-mm Gaussian kernel. The VBM analysis was carried out with a voxelwise GLM. The predictor of interest modelled the subjects’ motor learning by observing scores (demeaned). Two nuisance regressors were also included in the GLM; one modelled the gray matter grand mean across all subjects, and the second modelled each subject’s unnormalized total brain volume. Each subject’s total brain volume was estimated before standard space normalization using FSL’s SIENAX tool. The voxelwise GLM was applied using nonparametric permutation (50,000 iterations) to correct for multiple comparisons with a significance threshold of p = 0.05.
3.3 Results

3.3.1 Behavioural Results

Figure 3.2 shows the behavioural data from the learning and control groups. It can be seen that on day 1 reaches are straight in the baseline null field condition for both groups. After video observation on day 2, we assessed motor learning by observing by instructing subjects to perform straight reaches while the robotic arm applied a right FF (the opposite FF to what had been observed in the learning video). The more subjects learned about the observed left FF, the worse their performance would be during their initial performance in the right FF. Indeed, we found that subjects who observed the tutor adapting to a left FF in the learning video exhibited greater PD during initial reaches in the right FF compared with control subjects who observed the tutor performing curved reaches in an unlearnable FF. As in previous work (Mattar & Gribble, 2005; Cothros et al., 2006; Brown et al., 2009, 2010; Bernardi et al., 2013; McGregor et al., 2016; Williams & Gribble, 2012), the effects of observation are most apparent early in the motor learning test (i.e., the first 10 reaches shown as blocks 1 and 2 in Figure 3.2A) and diminish as subjects in both the learning and control groups adapt to the right FF. Average motor learning by observing scores are shown in Figure 3.2B. Motor learning by observing scores reflect the PD of the first three reaches in the right FF relative to the subject’s baseline PD in the null field. Subjects
who observed the tutor undergoing left FF learning exhibited significantly higher
motor learning by observing scores compared with control subjects who observed the
tutor performing reaches in an unlearnable FF ($t(28) = 2.58, p < 0.01$).

### 3.3.2 Functional Connectivity Results

We performed a functional connectivity analysis using the resting-state fMRI data
acquired on day 1 to test whether individual differences in pre-observation FC could
predict motor learning by observing scores on the following day. Of the 10 ROIs used,
only the analysis using the left S1 ROI revealed a network in which pre-observation
FC was reliably correlated with day 2 motor learning by observing scores for the
learning group. As can be seen in Figure 3.3, day 1 FC between the left S1 ROI and
the average FC across clusters in bilateral PMd, bilateral M1, bilateral S1, and left
SPL was positively correlated with day 2 motor learning by observing scores ($r = 0.76,
p = 0.001$) for the learning group. Subjects with greater pre-observation FC among
these areas on day 1 went on to achieve higher motor learning by observing scores
on the following day. Table 3.2 shows cluster activation peaks and statistics for the
learning group. For the control group, the analysis using the left S1 ROI revealed a
qualitatively similar network consisting of bilateral PMd, bilateral M1, bilateral S1,
and left SPL. This is expected because subjects in the learning and control groups
have had identical experiences as of the day 1 resting-state scan session. However, for
the control group, day 1 FC within the identified network was not reliably correlated

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Figure 3.2: Motor learning by observing behavioural results. **A**, Maximum perpendicular deviation (PD) for movements in the right force field (FF). The first 10 movements are shown as averages of 5-trial blocks. Subsequent movements are shown as averages of 10-trial blocks. Greater perpendicular deviation (PD) for initial movements in the right FF indicates greater interference due to the learning of the observed left FF. Subjects who observed the (left FF) learning video showed greater movement curvature when first exposed to the right (test) FF compared to control subjects (blue). **B**, Motor learning by observing scores as a function of video observed. * indicates p < 0.01. Error bars represent SE.
with day 2 behavioural motor learning by observing scores ($r = -0.43, p = 0.67$; Figure 3.4A).

Our computed motor learning by observing score took into account the average PD of a subject’s first three reaches in the right FF relative to his or her baseline PD in the null field. To assess the sensitivity of the learning group’s correlation between pre-observation FC and motor learning by observing scores, we computed additional motor learning by observing scores to use in our analysis. The additional motor learning by observing scores reflected the average PD of the first 4, 5, 6, 7, 8, 9, or 10 reaches in the right FF minus the average PD of the last 50 reaches in the null field. The learning group’s correlation between day 1 FC and motor learning by observing scores remained statistically significant for all of the additional measures.

The GLMs used for the group-level functional connectivity analyses included a nuisance regressor modeling each subject’s baseline PD in the null field during the last 50 trials. This nuisance regressor was included to account for variability in pre-observation resting-state FC that could be explained by intersubject differences in movement curvature at baseline. Our results were consistent whether the null field nuisance regressor reflected the average PD of the last 3, 5, 10, or 50 null field reaches or the average PD of the first 3, 5, 10, or 50 null field reaches.

It is possible that the correlation between pre-observation FC and the day 2 motor learning by observing scores is due to random chance (e.g., spurious correlations in
Figure 3.3: This figure shows neuroimaging data from the learning group only. Pre-observation (day 1) resting-state functional connectivity (FC) between the left S1 ROI (inset at left) and clusters in bilateral PMd, bilateral M1, bilateral S1, and left SPL are shown. Across subjects in the learning group, the average day 1 resting-state FC within this network was positively correlated with day 2 motor learning by observing scores. As shown in the scatterplot on the far right, subjects who exhibited stronger resting-state FC within this network on day 1 achieved greater motor learning by observing scores on the following day \((r = 0.76, p = 0.001)\). FC values reflect the Fisher Z-transformed temporal correlation between the ROI time series and the average time series of all clusters in the identified network for each subject.
Table 3.2: The functional connectivity analysis using the ROI in left S1 (see Table 3.1) revealed a sensory-motor functional network in which pre-observation (day 1) FC predicted day 2 motor learning by observing scores for the learning group. Z score activation peaks, MNI coordinates and anatomical labels of the sensory-motor clusters in the identified functional network are shown here. ROI, region of interest; L, left; R, right; SMA, supplementary motor area; PMd, dorsal premotor cortex; M1, primary motor cortex; S1, primary somatosensory cortex; SPL, superior parietal lobule; FC, functional connectivity.
Figure 3.4: Pre-observation resting-state functional connectivity (FC) did not predict motor learning by observing scores for the control group. As was the case with the learning group, subjects in the control group exhibited pre-observation (day 1) FC between the ROI in left S1 and clusters in bilateral PMd, M1, and S1 and left SPL (not shown). However, across subjects in the control group, there was no correlation between day 1 resting-state FC within this network and day 2 motor learning by observing scores. This was the case when both runs were analyzed together (r = -0.38, p = 0.15; shown in scatterplot on left) as well as when the runs were analyzed separately (r = -0.03, p = 0.91; shown in scatterplot on right). FC values reflect the Fisher Z-transformed temporal correlation between the ROI time series and the average time series of all clusters in the identified network.
the BOLD time series) and not due to stable individual differences in functional connectivity. To assess this, we repeated the functional connectivity analysis on each of the two resting-state runs separately. The resting-state runs were independent, separated in time by a 5-minute anatomical scan. Again using the ROI in left S1, we found consistent spatial patterns of pre-observation (day 1) FC between left S1, bilateral PMd, M1, and S1, and left SPL for both individual runs (see Figure 3.5). Moreover, for the learning group, the correlation between pre-observation (day 1) FC and day 2 motor learning by observing scores was statistically significant for both resting-state run 1 \( (r = 0.75, p = 0.001) \) and run 2 \( (r = 0.63, p = 0.01) \). Therefore, when performed on the each of the two independent resting-state runs, our analysis yielded similar results in terms of both the spatial extent of the clusters and the correlations with day 2 motor learning by observing scores. It is therefore unlikely that our main result arises from a spurious correlation. For the control group, there was no statistically significant correlation between pre-observation FC during either run 1 or run 2 and motor learning by observing scores \( (r = -0.38, p = 0.15 \) and \( r = -0.03, p = 0.91 \), respectively; Figure 3.4B).

### 3.3.3 Voxel Based Morphometry Results

We carried out a whole brain VBM analysis on the T1-weighted anatomical images. This was done to test whether individual differences in gray matter volume could predict subsequent motor learning by observing scores. This analysis yielded no significant
**Figure 3.5:** Pre-observation resting-state functional connectivity (FC) in run 1 and run 2 both predicted motor learning by observing scores for the learning group. This figure shows neuroimaging data from the learning group only. Data from resting-state run 1 and run 2 were analyzed separately. For each run, the ROI in left S1 (inset at left) exhibited resting-state FC with clusters in bilateral PMd, bilateral M1, bilateral S1, and left SPL. For each of the runs, pre-observation (day 1) resting-state FC between bilateral PMd, M1, and S1 and left SPL was reliably correlated with day 2 motor learning by observing scores across subjects in the learning group. As shown in the scatterplot on right, subjects who exhibited stronger FC within the network identified in each run on day 1 achieved greater motor learning by observing scores on day 2. FC values reflect the Fisher Z-transformed temporal correlation between the ROI time series and the average time series of all clusters in the identified network.
results. We tested the sensitivity of this null result to the chosen statistical threshold. For the learning group, no significant clusters survived statistical thresholding at the group level until the p-value threshold was raised to 0.27, at which level clusters survived in left frontal lobe (-32, 54, 12) and Broca’s area (-50, 20, 12). When the p value threshold was raised further to 0.37, a cluster survived that spanned right premotor cortex (54, -8, 52), M1 (54, -10, 46), S1 (56, -14, 44), and IPL (64, -20, 40). However, since none of these clusters survived an appropriate statistical threshold, these results are not interpretable. In the context of the data set here, individual differences in gray matter volume could not account for variability in the extent to which observation promotes motor learning.

3.4 Discussion

Here we examined whether pre-observation measures of brain function or structure could account for individual differences in the extent to which observation facilitates motor learning. We acquired measures of resting-state FC and gray matter volume with MRI before an observational learning task on the following day. We found that, for the learning group, pre-observation (day 1) resting-state FC between bilateral PMd, bilateral M1, bilateral S1, and left SPL was reliably correlated with behavioural scores of motor learning by observing acquired on day 2. Those subjects in the learning group who exhibited greater resting-state FC on day 1 achieved greater motor learning by observing scores on day 2. No such correlation between pre-observation FC and
motor learning by observing scores was found for the control group who observed a tutor performing reaches but not learning. Individual differences in gray matter volume could not predict subsequent motor learning by observing behavioural scores. Although the analyses presented here are correlational, the temporal order of events in the experimental design, namely the resting-state scans preceding the observational motor learning task by 24 hours, supports the idea that greater FC in a network linking S1, PMd, M1, and SPL predisposes individuals to learn more about a novel motor skill through visual observation.

The finding that pre-observation resting-state FC between S1 and PMd, M1, and SPL predicts subsequent motor learning by observing is consistent with previous work demonstrating that M1 and the somatosensory system play necessary roles in motor learning by observing. Brown and colleagues (2010) used repetitive transcranial magnetic stimulation (rTMS) to reduce cortical excitability in M1 immediately after subjects observed a FF learning video. A subsequent behavioural assessment showed that reducing M1 excitability after observation disrupted motor learning by observing. rTMS applied to M1 after observation of FF learning reduced the beneficial effect of observing congruent forces and eliminated the detrimental effect of observing incongruent forces. These results suggest that M1 plays a key role in motor learning by observing.

We have also recently demonstrated that the somatosensory system plays a necessary
role in motor learning by observing (McGregor et al., 2016). We used median nerve stimulation to occupy the somatosensory system with unrelated afferent inputs while subjects observed a video of a tutor undergoing FF learning. During observation, subjects received median nerve stimulation either to the right arm (the same arm used by the tutor in the video) or to the left arm (opposite the arm used by the tutor) or no stimulation. Stimulation disrupted motor learning by observing in a limb-specific manner, such that stimulation of the right arm (observed effector) interfered with learning whereas stimulation applied to the opposite arm did not. This result demonstrated that the somatosensory representation of the observed effector is necessary and therefore must be unoccupied during observation for motor learning by observing to occur. In a follow-up EEG experiment, we showed that S1 cortical activity, as assessed using somatosensory evoked potentials, increased for subjects who observed learning by an amount that positively correlated with subsequent behavioural motor learning by observing scores. These results suggest that observation-induced functional changes in S1 support motor learning by observing (McGregor et al., 2016).

The network identified in the present study overlaps with those identified in neuroimaging studies showing that sensory-motor networks support observational learning. We have previously shown that observing motor learning results in changes in resting-state FC between M1, S1, visual area V5/MT, and the cerebellum. Functional connectivity changes within this network were correlated with behavioural measures of motor learning, assessed after the fMRI sessions (McGregor & Gribble, 2015). Cross and colleagues
(2009) showed that observation of learned dance movement sequences recruits brain areas including premotor and parietal cortices. The authors reported greater activation in premotor and parietal regions when subjects observed movement sequences on which they had been trained (by observation) over the previous 5 days, compared with untrained movement sequences. These studies suggest that the neural substrates of motor learning by observing include premotor cortex, M1, S1, and parietal cortex. This is consistent with the results of the present study in which subjects who exhibited greater pre-observation resting-state FC between S1 and PMd, M1, and SPL later showed the greatest observation-related facilitation of motor learning.

More generally, the present study provides insight into the neural basis of motor learning. The network identified here closely corresponds to functional networks involved in active motor learning. For example, resting-state fMRI studies of active motor learning have found FC changes between M1, PMd, and the cerebellum following FF adaptation (Vahdat et al., 2011) and FC changes within the fronto-parietal resting-state network following visuomotor adaptation (Albert et al., 2009). Several task-based neuroimaging studies have similarly suggested a role for PMd (e.g., Steele & Penhune, 2010), M1 (e.g., Grafton et al., 1992; Steele & Penhune, 2010), S1, and SPL in motor learning through active movement (e.g., Hardwick et al., 2013).

There are commonalities between the functional network identified in the present study and those functional networks that have been previously reported to predict
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aspects of motor learning through active movement training. Tomassini and colleagues (2011) showed that the task-based activation of premotor and parietal cortices (along with prefrontal cortex, basal ganglia, and the cerebellum) is associated with higher behavioural measures of motor learning. Wu and colleagues (2014) have similarly shown that resting-state FC (as measured by high-density EEG) between M1, premotor cortex, and parietal cortex can predict skill acquisition. The consistency between predictive functional networks for learning through active movement training and observational motor learning provides evidence in favor of similar neural substrates for these two forms of motor learning.

There is evidence from the motor learning literature that individual differences in brain structure can predict learning through active practice. Tomassini and colleagues (2011) demonstrated that individual differences in gray matter volume within the cerebellum and higher-order visual areas (V2, V3, V5/MT) can also predict behavioural measures of motor learning during a visuomotor tracking task. While there is evidence for structure-based predictability of active motor learning, in the present study we found that this was not the case for motor learning by observing; individual differences in gray matter volume could not account for variability in behavioural scores of motor learning by observing. The discrepancy between the results of the present study and that of Tomassini and colleagues (2011) may be due to methodological differences in terms of the T1-image acquisition parameters and VBM analysis procedures used, and/or the present study may have had insufficient statistical power. Future studies
investigating gray matter volume correlates of motor learning by observing should have a larger sample size to increase statistical power.

Here we tested whether pre-observation measures of brain function or structure could predict subsequent motor learning by observing. We found that pre-observation resting-state FC between bilateral S1, PMd, M1 and left SPL predicted the extent to which observation would promote motor learning on the following day. Individual differences in gray matter volume could not predict behavioural scores of learning following observation. These results demonstrate that individual differences in resting-state FC among sensory-motor cortical brain areas can explain part of the individual variability in the extent to which observation facilitates motor learning. This finding is consistent with the idea that those individuals who have more “primed” sensory-motor circuits are more predisposed to motor learning through observation. pre-observation FC within the identified sensory-motor network may be used as a biomarker of the extent to which observation will promote motor learning. Predicting an individual’s predisposition for motor learning by observing could be valuable in a clinical context for planning individualized rehabilitation strategies and improving prognostic accuracy ([Stinear 2010]).

The origin of individual variability in pre-observation sensory-motor FC is still unclear. In one scenario, it is possible that the observed individual differences in FC are a reflection of functional variability and not anatomical variability within this network.
However, given the close correspondence between anatomical and functional connectivity (see, e.g., Fox et al., 2005), another scenario is that the observed differences in FC arise from individual differences in anatomical connectivity. For example, it could be the case that greater structural connectivity between these sensory-motor brain areas results in higher pre-observation sensory-motor FC that, in turn, promotes greater motor learning by observing. Since we did not acquire images for performing structural connectivity-based analyses (such as diffusion tensor images) in the present study, we cannot rule out the possibility that individual differences in structural connectivity among sensory-motor brain areas underlie the effect seen here, whereby pre-observation FC predicts motor learning by observing.

However, resting-state FC does not only reflect anatomical connectivity. Indeed, much work has shown that resting-state FC can be shaped by recent experiences. Such “stimulus-rest interactions” have been demonstrated across several domains. For example, exposure to visual stimuli (Lewis et al., 2009) or undergoing active motor learning (Albert et al., 2009) can change resting-state FC. Since resting-state FC is affected by both structure and function, it is likely the case that both of these factors contribute to individual differences in pre-observation sensory-motor FC. While we cannot pursue this question further with the present data set, this would be an interesting avenue for future research. Since previous experiences can alter resting-state FC, it is likely that performance of null field reaches in the baseline condition primed sensory-motor networks before the day 1 resting-state scans and perhaps increased the
sensitivity of the present study. It would be of interest to examine whether baseline measures (i.e., without prior null field reaches) of resting-state FC within the identified network could also predict motor learning by observing. Another outstanding issue is the stability of these individual differences in pre-observation FC over time. Future research should examine the test-retest reliability of pre-observation FC over longer time periods (e.g., several days or weeks apart) to establish the long-term stability of the FC patterns within the network presented here. This would allow one to better distinguish within-session patterns from those more permanent structural or functional patterns.
References


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Chapter 4

Somatosensory Plasticity and Observational Learning

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4.1 Introduction

An influential idea in neuroscience is that the sensory-motor system is activated when observing the actions of others (Gazzola & Keysers, 2008; Caspers et al., 2010). This idea has recently been extended to motor learning, in which observation results in sensory-motor plasticity and behavioural changes in both motor and somatosensory domains (Mattar & Gribble, 2005; Williams & Gribble, 2012; Brown et al., 2009; Cothros et al., 2006; McGregor & Gribble, 2015; Bernardi et al., 2013; Wanda et al., 2013). However, it is unclear how the brain maps visual information onto motor circuits for learning. Here we test the idea that the somatosensory system, and specifically primary somatosensory cortex (S1), plays a role in motor learning by observing. In experiment 1, we applied stimulation to the median nerve to occupy the somatosensory system with unrelated inputs while subjects observed a tutor learning to reach in a force field. Stimulation disrupted motor learning by observing in a limb-specific manner. Stimulation delivered to the right arm (the same arm used by the tutor) disrupted learning, whereas left arm stimulation did not. This is consistent with the idea that a somatosensory representation of the observed effector must be available during observation for learning to occur. In experiment 2, we assessed S1 cortical processing before and after observation by measuring somatosensory evoked potentials (SEPs) associated with median nerve stimulation. SEP amplitudes increased only for subjects who observed learning. Moreover, SEPs increased more for subjects who
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exhibited greater motor learning following observation. Taken together, these findings support the idea that motor learning by observing relies on functional plasticity in S1. We propose that visual signals about the movements of others are mapped onto motor circuits for learning via the somatosensory system.

Although many of our motor skills are acquired through physical practice, we can also learn how to make movements by observing others. For instance, individuals can learn how to reach in novel dynamical environments (“force fields”) by observing the movements of a tutor. Action observation promotes sensory-motor plasticity and behavioural changes in both the motor and sensory domains (Mattar & Gribble, 2005; Williams & Gribble, 2012; Brown et al., 2009; Cothros et al., 2006; McGregor & Gribble, 2015; Bernardi et al., 2013; Wanda et al., 2013). However, it remains unclear how the brain maps visual information about the movements of others onto motor circuits for learning. One possibility is the involvement of the somatosensory system. Somatosensory cortical regions have substantial anatomical connections with visual and motor areas of the brain, and so it is feasible that the somatosensory system may link visual and motor areas for motor learning by observing (Maunsell & van Essen, 1983; Lewis & Van Essen, 2000; Colby & Duhamel, 1991; Jones & Friedman, 1982; Rossini et al., 1987, 1989). Here we present two experiments demonstrating that the somatosensory system, and more specifically primary somatosensory cortex (S1), is indeed involved in motor learning by observing.
4.2 Results

4.2.1 Experiment 1

In experiment 1, we tested the hypothesis that the involvement of the somatosensory system is necessary for motor learning by observing. We used a learning task that involved holding the handle of a robotic arm with the right hand and performing straight reaches to a visual target. Participants first observed a learning video depicting a tutor adapting her reaches to a robot-imposed leftward force field (left FF). To test the role of the somatosensory system in motor learning by observing, we used median nerve stimulation to deliver afferent inputs to the somatosensory system that were unrelated to the observed learning task. Median nerve stimulation reliably activates S1, second somatosensory cortex, and posterior parietal cortex (Backes et al., 2000; Del Gratta et al., 2000, 2002; Allison et al., 1991; Balzamo et al., 2004). During observation, subjects either received median nerve stimulation to both arms simultaneously, to the right arm only, or to the left arm only or received no stimulation. If the involvement of the somatosensory system is necessary for motor learning by observing, then we expected that occupying somatosensory cortical processing with unrelated afferent inputs during observation would disrupt learning. A control group observed, without stimulation, a control video depicting a tutor performing curved reaches in a randomly varying (and thus unlearnable) FF. All subjects then performed
a motor learning test in which they reached to a visual target in a right FF (Figure 4.1). No nerve stimulation was applied during the motor learning test. The more subjects learned about the left FF through observation, the worse (more curved) their movements would be in the right FF (Mattar & Gribble, 2005; Williams & Gribble, 2012; Brown et al., 2009; Cothros et al., 2006; McGregor & Gribble, 2015; Bernardi et al., 2013). Therefore, motor learning by observing scores reflect interference (greater movement curvature) caused by learning to counteract the observed FF.

We chose to use an interference paradigm in experiment 1 (i.e., testing for learning in an opposite FF) because it provides a built-in control for potential non-learning-related effects of stimulation. If we had used an experimental design in which subjects observed a left FF and were later tested in the same left FF, the prediction would be that right arm stimulation during observation would diminish the benefit of observation on learning, and hence subsequent movements in the left FF would be more curved. However, in this case, it would be unclear why subjects performed more poorly in the left FF. One explanation (our main hypothesis of interest) would be that the somatosensory representation of the right arm (the observed effector) was occupied during observation and was therefore unavailable for motor learning by observing. However, another possibility is that median nerve stimulation during observation impaired subsequent movements, for example by disrupting the basic ability to control movements of the right arm. The use of an interference paradigm allows us to rule out the latter scenario. If the somatosensory representation of the right arm (the observed
Figure 4.1: Subjects held onto the handle of a robotic arm with the right hand. In the baseline condition, all subjects performed straight reaches to a visual target in the null field in which the robot did not apply force. No nerve stimulation was applied during baseline reaches. Subjects then observed either the learning video or the control video. The learning video showed a tutor learning to reach in a leftward force field (left FF). The control video showed a tutor performing curved reaches in a randomly varying (and thus unlearnable) FF. During observation, subjects received median nerve stimulation to both arms simultaneously, to the right arm only (the same arm used by the tutor), to the left arm only (opposite the arm used by the tutor), or no stimulation. Finally, as a motor learning test, all subjects performed the reaching task while the robotic arm applied a rightward force field (right FF). No nerve stimulation was applied during reaches in the right FF.
effector) plays a necessary role in motor learning by observing, we expected that subjects who received median nerve stimulation during observation would perform better, straighter movements in the (opposite) right FF. An interference paradigm allows us to attribute this change in motor performance to learning resulting from observation.

Participants who observed the (left FF) learning video without nerve stimulation exhibited greater movement curvature in the right FF, and hence exhibited higher motor learning by observing scores, compared to subjects who observed the control video without nerve stimulation ($t(30) = 1.85, p = 0.037$; Figure 4.2). This is consistent with previous demonstrations that observing FF learning interferes with subsequent performance in an opposite FF (Mattar & Gribble, 2005; Williams & Gribble, 2012; Brown et al., 2009; Cothros et al., 2006; McGregor & Gribble, 2015; Bernardi et al., 2013). The effects of observation seen here are unlikely to be due to changes in limb stiffness, but rather are a result of subjects learning an internal model of the FF experienced by the tutor. In previous studies involving the same paradigm used here it has been shown that changes in movement curvature following observation are modulated in opposite directions based on the direction of the observed FF (Mattar & Gribble, 2005; Brown et al., 2009, 2010). In another recent study it was shown that following observation, movements in force-channel trials exhibited systematic changes in the magnitude and direction of the force applied by subjects changes that mirrored the direction of the observed FF (Wanda et al., 2013).
Figure 4.2: A, Group average learning curves for reaches performed in the right (test) FF. The first ten movements are plotted individually and five-trial blocked averages are plotted thereafter. Greater perpendicular deviation for initial movements in the right FF indicates greater interference due to the learning of the observed left FF. The grey shaded region of the plot indicates the first 3 trials in the right FF, which were used to calculate motor learning by observing scores (relative to baseline PD in the null field). B, Motor learning by observing scores reflecting initial interference in the right FF. Subjects who observed the learning video without stimulation (purple) exhibited higher motor learning by observing scores compared to subjects who observed the control video without stimulation (blue). Nerve stimulation applied to both arms simultaneously (green) and to the right arm only (the same arm used by the tutor; yellow) during observation resulted in lower motor learning by observing scores. In contrast, subjects who received nerve stimulation to the left arm only (opposite the arm used by the tutor; orange) exhibited higher motor learning by observing scores. Error bars represent SEM. * indicates p < 0.05.
Median nerve stimulation applied to both arms during observation eliminated the effect of observing left FF learning. Bilateral median nerve stimulation resulted in straighter movements in the right FF compared to the group that had observed learning without nerve stimulation ($t(30) = 1.88$, $p = 0.035$). The bilateral arm stimulation group performed comparably to the control group that did not observe learning. One potential account of this result is that occupying the somatosensory cortical representation of the arms with unrelated afferent inputs during observation disrupted motor learning by observing.

It is possible that the cause of this effect is more cognitive in nature, namely that median nerve stimulation disrupted motor learning by observing because subjects were distracted by the cutaneous sensation of nerve stimulation. However, additional tests allowed us to rule this out. We tested subjects who received stimulation to the right arm only or to the left arm only while observing the learning video. If this effect is driven by the somatosensory system, we predicted that stimulation would disrupt learning in a limb-specific manner. That is, stimulation delivered to the right arm (the same arm used by the tutor) during observation would disrupt learning but stimulation delivered to the left arm (opposite that used by the tutor) would not. Indeed, as shown in Figure 4.2, right (same) arm stimulation resulted in lower motor learning by observing scores compared to the learning group that did not receive stimulation ($t(30) = 2.01$, $p = 0.027$). In contrast, the left (opposite) arm stimulation group performed comparably to the learning group that did not receive stimulation.
Moreover, the left arm stimulation group exhibited higher motor learning by observing scores than the right arm stimulation group ($t(30) = 2.15, p = 0.02$) and the both arm stimulation group ($t(30) = 2.01, p = 0.027$). This establishes that this effect is not driven by distraction, which would have had similar effects for both the left and right arm stimulation groups. There were no differences in stimulation intensities ($t(30) = -0.74, p = 0.47$) or stimulus pain ratings ($t(30) = -0.53, p = 0.60$) between the right and left arm stimulation groups, further supporting the idea that this effect is not due to distraction. The results of experiment 1 are consistent with the idea that a somatosensory representation of the observed effector is necessary, and therefore must be available, for motor learning by observing to occur.

### 4.2.2 Experiment 2

The findings above suggest that the somatosensory system plays a role in motor learning by observing. In experiment 2, we tested a more specific hypothesis that S1 is involved in motor learning by observing. We assessed changes in S1 cortical processing from before to after observation by measuring somatosensory evoked potentials (SEPs; Figure 4.3A). SEPs were elicited by applying median nerve stimulation at the right wrist and were recorded using an EEG electrode over left S1 (Figure 4.3B). SEPs were acquired before and after subjects observed the learning video or the control video. No stimulation was applied during observation. Finally, subjects performed reaches to a visual target in a right FF as a motor learning test.
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Somatosensory Evoked Potentials (SEPs)

N20-P25

-1.5

-1.0

-0.5

0

0.5

1.0

1.5

Amplitude (μV)

Time (ms)

-10 10 20 30 40 50 60 70

Perform

Baseline
50 null field reaches

[No nerve stimulation]

Observe

Learning Video

OR

Control Video

[No nerve stimulation]

Perform

Test
50 right FF reaches

[No nerve stimulation]

A

B

C

Somatosensory Evoked Potentials (SEPs)

Figure 4.3: A, Subjects held onto the handle of a robotic arm with the right hand. In the baseline condition, all subjects performed straight reaches to a visual target in the null field in which the robot did not apply force. No nerve stimulation was applied during baseline reaches. To assess changes in S1 excitability, we acquired somatosensory evoked potentials (SEPs) immediately before and after subjects observed either the learning video (purple) or the control video (blue). Finally, all subjects performed a motor learning test to behaviourally assess motor learning by observing. No nerve stimulation was applied reaches in the right FF. B, SEP acquisition. A stimulating electrode was placed on the subject’s right wrist and delivered 3-Hz electrical stimulation to the median nerve (shown at left). SEPs were recorded using an EEG electrode over left (contralateral) S1 while subjects rested. The inset on the far right shows an SEP from a representative subject. The SEP trace is the average of approximately 500 stimulations, where stimulation was delivered at 0 ms (orange dashed line). The amplitude of the N20-P25 component of the SEP (indicated by the gray dashed arrow) reflects the earliest afferent processing in S1.
As in experiment 1, subjects who observed the tutor undergoing left FF learning performed more curved movements in the right FF (Figure 4.4A), exhibiting higher motor learning by observing scores compared to control subjects who did not observe learning ($t(30) = 1.75, p < 0.05$; Figure 4.4B).

We assessed pre- to post-observation changes in the N20-P25 component of the SEP, occurring approximately 20-25 ms following median nerve stimulation. The N20-P25 component is a reflection of the earliest cortical processing of afferent signals by S1 (Allison et al., 1991, 1992; Balzamo et al., 2004). In addition, the N20-P25 component is highly reproducible and largely unaffected by one’s cognitive state (Arthurs et al., 2004). Subjects who observed the tutor undergoing left FF learning exhibited reliable increases in the N20-P25 component amplitude measured over left S1 ($t(30) = 2.72, p < 0.02$; Figures 4.5A and 4.5B) compared to the control group that observed curved movements in an unlearnable FF. Moreover, across subjects in the learning group, increases in the N20-P25 component amplitude were reliably correlated with their subsequent motor learning by observing scores ($r = 0.55, p < 0.03$; Figure 4.5C).

These results are consistent with the idea that motor learning by observing involves functional plasticity in S1.

It is possible that SEP changes could have been caused by changes in applied stimulation from pre- to post-observation due to skin conductance changes or electrode slippage. To control for this possibility, we also recorded sensory nerve action potentials.
Figure 4.4: A, Group average learning curves for reaches performed in the right (test) FF. The first ten movements are plotted individually and five-trial blocked averages are plotted thereafter. Greater perpendicular deviation for initial movements in the right FF indicates greater interference due to the learning of the observed left FF. Participants who observed the (left FF) learning video showed greater movement curvature when first exposed to the right (test) FF compared to control subjects (blue). The grey shaded region of the plot indicates the first 3 trials in the right FF, which were used to calculate motor learning by observing scores (relative to baseline PD in the null field). B, Average motor learning by observing scores for the learning group (purple) and control group (blue). Motor learning by observing scores reflect interference (greater movement curvature) in the right FF caused by learning of the observed left FF. Error bars represent SEM. * indicates $p < 0.05$. 

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Figure 4.5: A, Average time-varying difference in SEP amplitudes from before to after observation for the learning group. Positive values indicate an increase in SEP amplitude following observation. Stimulation was delivered at 0 ms (orange vertical dashed line at left). It can be seen that the N20-P25 component amplitude (beginning at the black vertical dashed line on the right) increased after observing learning. Shaded region represents SEM.

B, Mean change in N20-P25 amplitude after subjects observed the tutor learning a left FF (purple) or observed the tutor reaching in an unlearnable FF (blue). Error bars represent SEM. * indicates $p < 0.05$.

C, Across subjects in the learning group, increases in the N20-P25 amplitude correlated with subsequent behavioural motor learning by observing scores.

$r = 0.54$

$p < 0.05$
(SNAPs) during SEP recordings. SNAPs were recorded from the median nerve just above the right elbow (Figure 4.6A). This allowed us to confirm stimulus consistency between recordings. SNAP amplitude changes from the pre- to post-observation did not differ between the learning and control groups (t(28) = 0.19, p = 0.85; Figures 4.6B and 4.6C). Thus, the group differences seen in SEP changes can be attributed to changes in S1 processing, and not to changes in stimulation applied to the median nerve.

### 4.3 Discussion

In experiment 1, we showed that the application of median nerve stimulation during observation disrupts motor learning by observing in a limb-specific manner. This is consistent with the idea that a somatosensory representation of the observed effector is necessary and therefore must be available during observation for motor learning by observing to occur. In experiment 2 we showed that S1, in particular, is involved in motor learning by observing. SEPs recorded over S1 increased in amplitude only for those subjects who observed learning. Moreover, across subjects in the learning group, increases in S1 functional plasticity were positively correlated with subsequent behavioural measures of motor learning.

Much of the work on the activation of the motor system through observation has focused on so-called mirror neurons in the premotor cortex, which are activated both
Figure 4.6: Sensory nerve action potentials (SNAPs). A, SNAPs were acquired during SEP recordings in order to ensure consistent stimulation was applied to the median nerve across recordings. Stimulation was applied to the right wrist. SNAPs were recorded using a pair of recording electrodes on the anterior surface of the right arm just above the right elbow. B, Representative SNAPs acquired from a single subject during pre-observation (black) SEP recordings and during post-observation SEP recordings (green). Each trace is the average of approximately 1500 stimulations, each delivered at 0 ms. Shaded regions represent SEM. C, Mean change in SNAP amplitude from pre- to post-observation for the learning group (purple) and the control group (blue). Error bars represent SEM.
when observing an action and when performing the same action (di Pellegrino et al., 1992). However, a great deal of this work has focused on cognitive and social effects of action observation such as action understanding, empathy, and theory of mind (Iacoboni, 2009). Here we tested a different idea, namely that visual signals about the actions of others are mapped onto somatosensory and motor circuits to facilitate motor learning. Together, the results from the experiments presented here support the idea that the somatosensory system is involved in this mapping.

This idea is also supported by the existence of reciprocal anatomical connections between visual, somatosensory, and motor areas of the brain. Afferent inputs are projected from primary and secondary somatosensory cortices to posterior parietal cortex (e.g., ventral intraparietal area), where they are integrated with visual inputs (Lewis & Van Essen, 2000; Maunsell & van Essen, 1983; Colby & Duhamel, 1991). Parietal areas then project the integrated information to motor and premotor areas via S1 (Jones & Friedman, 1982) and/or thalamic relays (Rossini et al., 1987, 1989).

Recent work has shown that active motor learning involving physical practice results in functional changes in somatosensory brain areas. This has been demonstrated in neuroimaging (Vahdat et al., 2011) and in SEP studies using EEG (Bernier et al., 2009; Nasir et al., 2013; Andrew et al., 2015). Similarly, behavioural studies have shown systematic changes in sensed limb position (Cressman & Henriques, 2009; Ostry et al., 2010; Haith et al., 2009) and increased perceptual acuity (Wong et
Chapter 4. Somatosensory Plasticity and Observational Learning

al., 2011) following active motor learning. If motor learning by observing involves similar neural circuitry as active motor learning, we should also see somatosensory functional plasticity and behavioural changes with observation. Although previous work has shown that observing FF learning involves concurrent changes in sensory-motor resting-state functional connectivity (McGregor & Gribble, 2015) and sensed limb position (Bernardi et al., 2013), these studies did not directly test the role of the somatosensory system.

There is behavioural evidence that during observation, subjects use a feedforward process to predict the sensory consequences of the tutor’s movement (e.g., how the movement should look) (Flanagan & Johansson, 2003). When the tutor’s hand is displaced by a FF, visual feedback of kinematic errors could drive the updating of the subject’s forward model (Shadmehr et al., 2010). It is currently unclear how motor learning by observing might differentially influence or involve feedforward versus feedback control. This is a potentially interesting avenue for future work.

Median nerve stimulation undoubtedly activates the somatosensory system (Backes et al., 2000; Del Gratta et al., 2000, 2002; Allison et al., 1991; Balzamo et al., 2004); however, it may also affect primary motor cortex excitability (Chen et al., 1999). Although it is possible that changes in primary motor cortex (M1) may have contributed to the results of experiment 1, the primary effect of continuous stimulation to the median nerve is the activation of the somatosensory system (Backes et al., 2000).
Moreover, in experiment 2, we showed that observing a tutor learning to reach in a FF is associated with S1 functional plasticity that predicts, across subjects, behavioural measures of learning following observation. Taken together, the results of the two experiments presented here support the idea that motor learning by observing is driven not only by activation of the motor system but also by plasticity in the somatosensory system and, in particular, S1. In future studies it would be interesting to investigate potential interactions between M1 and S1 during observation to gain a better understanding of how both sensory and motor plasticity contribute to motor learning by observing.

In conclusion, the results of experiment 1 are consistent with the idea that a somatosensory representation of the observed effector plays a necessary and limb-specific role in motor learning by observing. Experiment 2 demonstrated that functional plasticity in S1, in particular, supports motor learning by observing. Collectively, these results support the hypothesis that visual signals about the movements of others are mapped onto motor circuits via the somatosensory system to aid in motor learning.
4.4 Experimental Procedures

4.4.1 Participants

Eighty healthy subjects participated in experiment 1 (20.5 years ± 0.28 SE, 28 males, 16 subjects per group). Thirty-two participated in experiment 2 (21.3 years ± 0.53 SE, 12 males, 16 subjects per group). Both experiments utilized a between-subjects design. Participants were right handed, had normal or corrected-to-normal vision, had no neurological or musculoskeletal disorders, and were naïve to FFs. Participants provided written informed consent to experimental procedures approved by the Research Ethics Board at The University of Western Ontario.

4.4.2 Apparatus

Participants grasped the handle of an InMotion2 robotic arm (Interactive Motion Technologies) with the right hand and performed straight reaches to a visual target in the horizontal plane. An air sled positioned under the elbow supported the right arm against gravity. An LCD television projected visual feedback onto a horizontal semi-silvered mirror mounted above the robot handle. Visual feedback consisted of a start position (20-mm blue circle), target (20-mm white circle), and cursor (12-mm pink circle) indicating hand position.
Participants were instructed to perform straight reaches from the start position to the target located 15 cm in front. Colour-coded visual feedback was provided to keep movement speed consistent between trials. The target disappeared if the movement was correctly timed (450-550 ms), and turned red or green if the movement was too fast or too slow, respectively. The robot handle position and velocity were sampled at 600 Hz.

The robotic arm altered limb dynamics by applying velocity-dependent FFs. FFs were applied according to the following equation:

\[
\begin{bmatrix}
F_x \\
F_y
\end{bmatrix} = \begin{bmatrix}
0 & dk \\
-dk & 0
\end{bmatrix} \begin{bmatrix}
v_x \\
v_y
\end{bmatrix}
\]

where \(x\) and \(y\) are lateral and sagittal directions, \(F_x\) and \(F_y\) are the applied robot forces, \(v_x\) and \(v_y\) are hand velocities, \(k = 14 \text{ Ns/m}\), and \(d = +1\) (right FF), -1 (left FF) or 0 (null field).

### 4.4.3 Videos

The videos have been described in detail elsewhere (McGregor & Gribble, 2015). Briefly, the videos showed a top-down view of a tutor performing the reaching task using the right arm. The learning video showed clips of a tutor adapting her reaches...
to a left FF, gradually progressing from curved to straight movements. The control video showed clips of a tutor performing curved reaches in an unlearnable FF, which varied randomly from trial to trial between a left FF, right FF, and null field (no force applied; Figure S2B).

4.4.4 Experimental 1 Protocol

Participants first performed 50 baseline reaches in a null field (no applied forces). For the stimulation groups, we applied median nerve stimulation during observation to both arms simultaneously, to the right arm only, or to the left arm only. Because stimulation was applied throughout the 15-min video, we stimulated the upper arm to reduce subjects’ discomfort. If applicable, a bipolar bar stimulation electrode was placed (cathode proximal) over the median nerve on the anterior surface of the arm(s) 3 cm proximal to the elbow. An isolated square wave stimulator delivered 0.2-ms pulses at a rate of 3 Hz. Stimulation intensity was set to 2.5 times the subject’s sensory threshold. To verify that perceived stimulation was similar across groups, subjects rated the perceived stimulus pain from 0 to 10, where 0 indicated that they could not feel the stimulation and 10 corresponded to the worst pain they had ever experienced. Participants then observed either the learning video or the control video and, if applicable, stimulation was applied. Participants were not informed about FFs in the video. Participants were instructed to sit still, count the number of correctly timed reaches (indicated by the target disappearing), and report the final tally. This
was done to verify that subjects attended to the videos. The stimulation electrodes were then removed. Finally, as a behavioural motor learning test, subjects performed 50 reaches in a right FF. The better that subjects learned the muscle force pattern required for counteracting the left FF from observing the tutor, the more curved their movements would be in the (opposite) right FF. Thus, greater rightward curvature in the motor learning test indicates greater motor learning by observing (\cite{Mattar2005,Williams2012,Brown2009,Cothros2006,McGregor2015,Bernardi2013}).

### 4.4.5 Experimental 2 Protocol

Participants first performed 50 baseline reaches in the null field. The bipolar stimulation electrode was then placed on the right median nerve at the wrist, and the EEG cap and SNAP electrodes were applied. We then acquired three 3-min-long SEP recordings while the subject rested with their eyes closed. As in experiment 1, stimulation consisted of 0.2-ms pulses at a rate of 3 Hz. Stimulation intensity was adjusted to elicit involuntary thumb oppositions. To ensure stimulation was consistent across SEP recordings, we also recorded SNAPs. SNAPs were recorded using two electrodes placed 2 cm apart along the median nerve on the anterior surface of the arm, just above the right elbow (Figure 4.6). The proximal electrode served as the reference, and a ground electrode was placed on the right olecranon. SNAPs were recorded in the same location where stimulation was applied in experiment 1. During
median nerve stimulation, we acquired EEG and SNAP data using an active electrode system (g.Gamma; g.tec Medical Engineering) and amplifier (g.USBamp; g.tec Medical Engineering). Our cap-mounted montage consisted of an electrode over left S1 (site CP3) and a ground electrode on the forehead (site FPz). A reference electrode was clipped to the left earlobe. Impedances were maintained below 5 kΩ. Data were sampled at 4,800 Hz and filtered online with band-pass (0.1-1,000 Hz) and notch (60 Hz) filters. Following SEP recordings, subjects observed either the learning video or the control video. No stimulation was applied during observation. As in experiment 1, subjects were not informed about FFs in the video and were instructed to sit still and counted correctly timed reaches. We then acquired three 3-min-long SEP recordings while subjects rested with their eyes closed. The stimulation electrode, EEG cap, and SNAP electrodes were then removed. Finally, subjects performed 50 reaches in a right FF as a motor learning test.

4.4.6 Behavioural Data Analysis

Positional data were low-pass filtered at 40 Hz. We computed the curvature of each movement as the maximum perpendicular deviation (PD) relative to a straight line connecting the start position and target. Motor learning by observing scores were computed as the mean PD of the first 3 right FF trials minus the mean PD of the last 25 null field trials. Motor learning by observing scores indicated the extent to which observing the left FF interfered with subsequent motor performance, in terms
of movement curvature, in the right FF (Mattar & Gribble, 2005; Williams & Gribble, 2012; Brown et al., 2009; Cothros et al., 2006; McGregor & Gribble, 2015; Bernardi et al., 2013). Our results for experiments 1 and 2 were consistent whether or not our motor learning by observing scores took into account the average PD of the first two through the first five right FF trials (relative to baseline).

### 4.4.7 SEP and SNAP Data Analysis

The EEG and SNAP data were band-pass filtered (between 20-100 Hz and 20-300 Hz, respectively) using second-order Butterworth filters. All signals were segmented into 80-ms epochs time locked to stimulation onset (-10 to 70 ms). We subtracted pre-stimulus baseline from each epoch and excluded epochs in which signal voltages exceeded ±50 mV from baseline. We obtained SEPs and SNAPs by averaging the remaining artifact-free epochs. SEP amplitudes were quantified as the peak-to-peak amplitude between the N20 and P25 components. SNAP amplitudes were quantified as the amplitude between the peak occurring 5 ms post-stimulation and the following peak of opposite deflection.
References


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Chapter 5

Somatosensory Perceptual Training

and Observational Learning
5.1 Introduction

Neuroimaging, neurophysiological, and behavioural studies provide evidence for a link between action observation and motor control in humans (e.g., Fadiga et al., 1995; Strafella & Paus, 2000; Buccino et al., 2001; Flanagan & Johansson, 2003; Watkins et al., 2003). A great deal of this work has focused on the potential role of an action-observation link in higher cognitive functions such as understanding and inferring the intentions of others’ actions (e.g., Gallese & Goldman, 1998; Rizzolatti et al., 2001). However, a growing body of work has also suggested a role for observation-related sensory-motor activity in motor learning (Heyes & Foster, 2002; Mattar & Gribble, 2005; Cross et al., 2006; Alaerts et al., 2010; Buckingham et al., 2014).

A series of studies has demonstrated that action observation can facilitate force field adaptation (Mattar & Gribble, 2005; Cross et al., 2006; Brown et al., 2009; Wanda et al., 2013; Bernardi et al., 2013; McGregor & Gribble, 2015; McGregor et al., 2016; McGregor & Gribble, 2017). For this task, subjects grasp the handle of a robotic manipulandum and adapt their reaching movements to forces (“force field”, FF) applied by the robot (Shadmehr & Mussa-Ivaldi, 1994). In a previous study, Mattar and Gribble (2005) presented subjects with a video showing another individual (“a tutor”) adapting his reaches to a robot-applied FF. Subjects who later performed reaches in the same FF as they had observed showed a benefit, performing straighter movements in the FF compared to non-observing subjects. Conversely, subjects who
later performed reaches in the opposite FF to what they had observed showed a
detriment, performing more curved movements in the FF compared to non-observing
subjects. This study showed that subjects are able to learn about how to reach in
novel FF environments through observing a tutor’s movements (Mattar & Gribble,
2005).

Motor learning by observing brings about changes in motor performance and functional
changes in motor areas of the brain (Mattar & Gribble, 2005; Cross et al., 2006; Brown
et al., 2009; Williams & Gribble, 2012; Wanda et al., 2013; McGregor & Gribble
2015). However, the effects of observing motor learning are not restricted to the motor
domain; there is accumulating evidence of observation-related neural and behavioural
changes within the somatosensory domain as well (Bernardi et al., 2013; McGregor &
Gribble, 2015; McGregor et al., 2016; McGregor & Gribble, 2017).

Our recent work has suggested that the somatosensory system plays a role in motor
learning by observing. Using EEG, we measured changes in S1 excitability associated
with motor learning by observing. We found that somatosensory evoked potentials
increased from pre- to post-observation and did so only for those subjects who
had observed a tutor adapting to a FF. Furthermore, post-observation increases in
S1 excitability corresponded to subsequent behavioural measures of motor learning
by observing. These results are consistent with the idea that observation-induced
functional changes in S1 are involved in motor learning by observing (McGregor et al.,
2015).
In a follow-up experiment, we showed that interfering with somatosensory cortical activity throughout observation can disrupt motor learning by observing. We applied electrical stimulation to the median nerve while subjects observed a video showing a tutor undergoing FF learning. The idea was to occupy the somatosensory system with afferent inputs that were unrelated to the observed learning task. During observation, subjects received median nerve stimulation to either the right arm (the same arm used by the tutor in the video), to the left arm, or no stimulation. Nerve stimulation disrupted motor learning by observing in a limb-specific manner. Stimulation of the right arm (the observed effector) interfered with learning whereas stimulation applied to the left arm did not [McGregor et al. 2016]. These findings are consistent with the idea that a somatosensory representation of the observed effector plays a role in motor learning by observing.

If the somatosensory system is indeed involved in motor learning by observing, as the studies above suggest, then we predicted that improving subjects’ somatosensory function prior to observation should enhance subsequent motor learning by observing. We tested this idea in the current study by using a perceptual training paradigm to improve subjects’ proprioception before observation. Subjects performed a proprioceptive discrimination task in which a robotic arm displaced the hand and subjects made judgments about the relative location of their hand in the absence of visual
feedback. Subjects in a Trained group received trial-by-trial reinforcement feedback during the proprioceptive task. Trial-by-trial feedback was withheld from subjects in an Untrained group. Subjects then observed a video showing a tutor adapting to a FF. Finally, subjects performed reaches in a FF as a behavioural assessment of motor learning by observing. We found that providing trial-by-trial accuracy feedback during the proprioceptive discrimination task increased subjects’ proprioceptive acuity. The post-observation behavioural assessment revealed that Trained subjects, who had superior proprioceptive acuity prior to observation, benefited more from observing motor learning compared to Untrained subjects. Moreover, across subjects in the Trained group, post-training changes in proprioceptive acuity were reliably correlated with subsequent observation-related gains in motor performance. This finding is consistent with the idea that somatosensory perceptual training improves proprioceptive function which in turn enhances motor learning by observing.

5.2 Materials and Methods

5.2.1 Subjects

Seventy-eight subjects participated in this experiment. Subjects were assigned to one of three groups: a Trained Learning group (n = 26, 8 males, mean age = 21.6 years ± 0.65 years SEM), an Untrained Learning group (n = 26, 9 males, mean age = 21.4 ± 0.58 years SEM) or a Trained Control group (n = 26, 8 males, mean
age = 20.8 years ± 0.44 years SEM). All subjects were right handed, had normal or corrected-to-normal vision, and were naïve to force fields. Subjects reported no neurological or musculoskeletal disorders. Subjects provided written informed consent to experimental procedures approved by the Research Ethics Board at the University of Western Ontario.

5.2.2 Apparatus

Subjects were seated in front of a custom tabletop and grasped the handle of a two degree-of-freedom robotic arm (InMotion2, Interactive Motion Technologies) with their right hand. The right arm was abducted approximately 80° from the trunk and was secured atop an air sled, which supported the arm against gravity. A liquid crystal display (LCD) TV projected visual feedback onto a semi-silvered mirror mounted horizontally above the robotic arm during the reaching task.

5.2.3 Reaching Task

During the reaching task, subjects were instructed to guide the robot handle in a straight line from a home position (20-mm blue circle) to a single visual target (20-mm white circle). The position of the robot handle was represented by a 5-mm pink circular cursor. Upon the completion of each reach, the target changed colour to provide subjects with feedback about movement timing. The target disappeared if the
movement was completed within the desired time range (375 ± 100 ms). The target
turned red or green to indicate that a movement duration was too slow or too long,
respectively. Following movement timing feedback, the robot moved the subject’s arm
back to the home position to begin the next trial.

The robotic arm applied a velocity-dependent force field (FF) during the reaching
task according to the following equation:

\[
\begin{bmatrix}
F_x \\
F_y
\end{bmatrix} =
\begin{bmatrix}
0 & dk \\
-dk & 0
\end{bmatrix}
\begin{bmatrix}
v_x \\
v_y
\end{bmatrix}
\]

in which x and y are lateral and sagittal directions, Fx and Fy are the robot forces
applied at the hand, v_x and v_y are hand velocities, k = 14 Ns/m, and d = +1 (right
FF), -1 (left FF) or 0 (null field).

5.2.4 Reaching Video Stimuli

Two videos were used in the study, each showing a tutor performing the reaching task
described above from a top-down perspective (e.g., McGregor & Gribble, 2015). A
learning video consisted of a series of 30-s clips showing a tutor adapting her reaches
to a left FF. This video depicted highly curved movements that gradually straightened
as the tutor adapted to the FF. A control video consisted of a series of 30-s clips
showing a tutor performing reaches in an unlearnable randomly-varying FF. The direction of the force field in this video varied randomly from trial-to-trial between a left FF, right FF or a null field. The control video therefore showed both high and low curvature movements, but lacked the progressive decrease in movement curvature that was depicted in the learning video. Each video showed a total of 200 reaches and was 15 minutes in duration (including regular breaks).

5.2.5 Proprioceptive Discrimination Task

Here we used a proprioceptive discrimination task to assess subjects’ proprioceptive acuity (sensitivity to displacements in limb position). This was a two-alternative forced choice task in which subjects made judgments about the relative position of their hand (e.g., Ostry et al. 2010; Wong et al. 2011). Subjects held onto the handle of the robotic arm with their right hand, closed their eyes and relaxed their right arm, which was supported by an air sled. Each trial consisted of a reference phase, a passive movement phase, and a judgment phase.

A trial started with the reference phase, during which the robot held the subject’s hand at the central reference position for 2 s. Next, in the passive movement phase, the robot moved the subject’s hand away from the reference and back (along a left-right axis), stopping at a test location near the reference. Subjects were instructed not to resist movement by the robot. The aim of the passive movement phase was to bring
the subject’s hand from the reference position to the test location without providing cues that could be used in aiding subject’s subsequent judgments. Features of the passive movement were randomized from trial to trial including: movement direction (left or right), total path length (14 \pm 2 cm SD), and movement duration (1-1.6 s). Passive movements followed a minimum jerk trajectory (Flash & Hogan, 1985).

During the judgment phase, the robot held the subject’s hand at the test location and the subject reported whether his or her hand had been displaced to the left or to the right of the reference position. Following the subject’s response, the robot moved the hand to the reference position via an indirect path (along a left-right axis). The direction, path length, and duration were randomized for passive movements back to the reference position such that subjects were not provided with cues about the accuracy of their judgment on the previous trial.

Each block of the proprioceptive discrimination task consisted of 74 trials. We presented test locations at 7 distances from the reference (0 \pm 0.67, 1.33, and 3.0 cm). Test locations were presented using the method of constant stimuli with the following frequencies: 0 cm (14 trials), \pm 0.67 cm (12 trials each), \pm 1.33 cm (12 trials each), and \pm 3 cm (6 trials each). The \pm 3 cm test locations were presented less frequently because subjects typically respond with a 100% judgment accuracy at these test locations.

All subjects performed 5 blocks of the proprioceptive discrimination task (370 pro-
prioceptive judgment trials in total). Subjects were given breaks halfway through
each block and between blocks (i.e., every 37 trials). During each break, all subjects
were told their percent accuracy over the previous 37 trials. To motivate subjects
throughout the proprioceptive task blocks, we offered a performance-based monetary
bonus of up to $10 CAD in addition to the hourly base rate of compensation.

5.2.6 Experimental Design

Each subject participated in one 2-hour session (see Figure 5.1). The experimental
session began with subjects performing 30 practice reaches in a null field (no force
applied, data not shown). Subjects then performed 50 reaches to the visual target in
the null field. This allowed us to assess subjects’ baseline movement curvature.

Subjects were then assigned to one of three groups, two of which received perceptual
training ("Trained" groups) and one of which did not ("Untrained" group). All subjects
performed 5 blocks of the proprioceptive discrimination task described above. During
blocks 1 and 5, trial-by-trial accuracy feedback was withheld from all subjects. During
blocks 2-4, Trained subjects received trial-by-trial accuracy feedback. Immediately
after making a verbal response ("left" or "right"), the experimenter informed the
subject if the judgment was correct or if it was incorrect and informed him or her of
the correct response. During blocks 2-4, subjects in an Untrained group continued
performing the proprioceptive task without trial-by-trial accuracy feedback. The idea
was to improve proprioceptive acuity of subjects in both of the Trained groups, but not for subjects in the Untrained group. Regardless of their training condition, all subjects were told their percent accuracy during each break (i.e., every 37 trials).

Following the proprioceptive discrimination task, all subjects performed a second set of 50 reaches in the null field. This allowed us to test whether the perceptual training itself resulted in changes in movement curvature.

Next, the Untrained group and one group of Trained subjects observed the learning video (Untrained Learning group and Trained Learning group, respectively) which showed a tutor adapting her reaches to a left FF. The remaining group of Trained subjects observed the control video (“Trained Control” group) which showed a tutor performing reaches in an unlearnable randomly-varying FF. During observation, all subjects remained still with their arms rested on the tabletop beneath the robot arm. In order to ensure that subjects paid attention to the video, they were instructed to count the number of times the tutor in the video performed a reach within the desired time range (indicated by the target disappearing). Subjects reported their tallies during video breaks. Reported tallies were not incorporated into data analyses. Reported tallies were over 95% accurate on average for all groups, and subjects were not excluded based on their reported tallies.

Finally, we assessed motor learning by observing by having all subjects perform reaches in a left FF. The more subjects learned about the left FF from observing the learning
video, the better, straighter reaches they would perform when they later encounter that same left FF. Therefore, lower movement curvature in the left FF would indicate greater motor learning by observing.

5.2.7 Proprioceptive Data Analysis

Here we assessed if improving proprioceptive function prior to observation could enhance motor learning by observing. We estimated each subject’s proprioceptive acuity on the basis of his or her binary judgment data from blocks 1 and 5 of the proprioceptive discrimination task, during which trial-by-trial feedback was withheld from all subjects. For each of these blocks, we estimated a sigmoidal psychometric function based on the subject’s binary judgment data. Proprioceptive acuity was quantified as the interquartile range (IQR) of the psychometric function, a measure also known as uncertainty range (Henriques & Soechting, 2003). This measure is inversely related to acuity such that a smaller IQR value indicates that the slope of the psychometric function is steep and therefore the subject is sensitive to small displacements in limb position. We predicted that providing trial-by-trial feedback during blocks 2-4 of the proprioceptive discrimination task would increase perceptual acuity (and hence decrease IQR values) from block 1 to 5 for the Trained Learning and Trained Control groups.

Changes in proprioceptive acuity were analyzed using a split-plot analysis of variance
Figure 5.1: Subjects held onto the handle of the robotic arm with their right hand. Subject performed 50 reaches in a null field (no force applied by the robot). Next, all subjects performed the proprioceptive discrimination task in which the robot passively moved the right hand and subjects judged whether the hand was displaced to the left or to the right of a central reference position. During blocks 1 and 5, subjects did not receive accuracy feedback following each judgment. During blocks 2, 3 and 4, subjects in the Trained Learning group and the Trained Control group received trial-by-trial feedback regarding their judgment accuracy. For the Trained groups, the experimenter provided verbal accuracy feedback immediately following each reported judgment, informing the subject if the judgment was correct or incorrect (and what the correct answer was). The Untrained Learning group did not receive trial-by-trial feedback during any of the blocks. All subjects then performed 50 null field reaches. Subjects in the Trained Learning and Untrained Learning groups observed the video showing a tutor adapting her reaches to a left FF. Subjects in the Trained Control group observed the video showing a tutor performing reaches in an unlearnable, randomly-varying FF. Finally, all subjects performed reaches in a left FF as a behavioural assessment of motor learning by observing.
(ANOVA) followed by planned pairwise comparisons. The dependent measure for the ANOVA was the IQR of the psychometric function. The ANOVA used group (Trained Learning, Untrained Learning, Trained Control) as the between-subjects factor and proprioceptive task block (1, 5) as the within-subject factor. We also examined changes in subjects’ judgment accuracy from block 1 and block 5. For this analysis, we performed a split-plot ANOVA using group (Trained Learning, Untrained Learning, Trained Control) as the between-subjects factor and proprioceptive task block (1, 5) as the within-subject factor. The dependent measure was the percent correct judgments within each of the blocks.

5.2.8 Motor Behaviour Analysis

Robot handle positions were sampled at 600 Hz. Velocities were computed using a central difference algorithm. Positions and velocities were low-pass filtered offline using a Butterworth filter implemented in MATLAB (Mathworks, Inc.) with a cutoff frequency of 40 Hz. For each trial, we computed the maximum point of lateral deviation of the hand path relative to a straight line connecting the home and target. This measure is known as the maximum perpendicular deviation (PD). We then computed a motor learning by observing score for each subject. This measure was computed as the average PD of the subject’s first 3 reaches in the left FF minus the average PD of the last 25 reaches in the baseline null field condition. This measure therefore reflects the extent to which the subject’s performance in the left FF benefitted from observation.
relative to his or her baseline PD in the null field. As we have demonstrated previously (Mattar & Gribble, 2005; Brown et al., 2009; Bernardi et al., 2013), learning about a FF from observation results in better, straighter movements when subjects later perform reaches in the same FF. As such, we predicted that greater motor learning by observing would result in straighter movements in the left FF and therefore higher (i.e., less negative/closer to zero) motor learning by observing scores. Group differences in motor learning by observing scores were assessed using a one-way between-subjects ANOVA.

5.3 Results

5.3.1 Proprioceptive Training Results

We tested for changes in IQR using a split-plot ANOVA, which revealed a group x proprioceptive test block interaction ($F(2,75) = 3.72, p < 0.03$; Figure 5.2A). Subjects in the Trained Learning group and the Trained Control group had identical experiences by the end of the proprioceptive discrimination task. The only difference between the protocol used for these two groups was the video that was observed following proprioceptive training. Therefore, the observed IQR changes depended on whether or not reinforcement feedback had been provided during blocks 2 through 4. The Trained Learning group exhibited greater IQR decreases compared to subjects in the Untrained Learning group ($t(50) = -2.47, p < 0.01$). Similarly, the Trained Control
group exhibited greater IQR decreases compared to subjects in the Untrained Learning group \( t(50) = -2.25, p < 0.02 \). No reliable differences in post-training IQR decreases were observed between the Trained Learning and Trained Control groups \( t(50) = 0.06, p = 0.95 \). Changes in IQR are further illustrated in Figure 5.2B which shows the average psychometric fit for each group during blocks 1 and 5. The IQR of a psychometric function is inversely related to perceptual acuity, with smaller IQR values indicating greater sensitivity to displacements in limb position. Subjects in both of the Trained groups therefore exhibited superior proprioceptive acuity prior compared to subjects in the Untrained group prior to observation.

5.3.2 Motor Behaviour Results

Training subjects on the proprioceptive discrimination task resulted in improvements to perceptual acuity. We tested if those trained subjects with superior somatosensory performance prior to observation go on to achieve greater motor learning by observing. Following the proprioceptive task, subjects observed either a learning video showing a tutor adapting to a left FF or a control video showing a tutor reaching in an unlearnable FF. Following observation, we assessed the extent to which subjects learned from observation by instructing them perform reaches in a left FF (the same FF that was shown in the learning video). As in previous work [Mattar & Gribble, 2005; Brown et al., 2009; Bernardi et al., 2013], we expected that motor learning by observing would primarily affect initial performance in the left FF, after which all
Figure 5.2: Proprioceptive training increased proprioceptive acuity. A, Perceptual acuity assessed during block 1 and block 5 of the proprioceptive discrimination task, both during which trial-by-trial accuracy feedback was withheld. Perceptual acuity was estimated based on the interquartile range (IQR) of the subject’s psychometric fit. During block 1, the three groups have comparable IQR values. In block 5, only the Trained Learning group (purple) and the Trained Control group (green) exhibited decreases in IQR values. Error bars represent SE. * indicates $p < 0.05$. B, Average psychometric fits to subjects’ binary judgment data during blocks 1 and 5 for each group. The IQR of each fit is indicated by the shaded areas. IQR values decreased from block 1 to block 5 only for the Trained Learning group (left, purple) and the Trained Control group (right, green).
groups would adapt to the left FF through physical practice.

Figure 5.3A shows average learning curves in the left FF for each group. It can be seen that the Trained Learning group, who had superior proprioceptive acuity prior to observation, performed straighter movements when first exposed to the left FF compared to subjects in the Untrained Learning group. This is consistent with the idea that superior proprioceptive acuity prior to observation enhanced the extent to which subjects in the Trained Learning group benefited from observing learning. However, it is possible that the Trained Learning groups straighter movements in the left FF were due to general increases in movement straightness following perceptual training (and not to motor learning by observing). Superior proprioceptive acuity may have made subjects in the Trained Learning group more sensitive to felt displacements in limb position during left FF reaches and allowed for faster movement corrections. Therefore, it is feasible that increased perceptual acuity alone could account for the observed group differences in left FF performance. If this were the case, then we would predict that increasing proprioceptive acuity would result in similar movement curvature in the left FF as that of the Trained Learning group regardless of the video that was observed. We tested this idea by running a Trained Control group. Subjects in the Trained Control group showed similar post-training increases in proprioceptive acuity as the Trained Learning group following the proprioceptive discrimination task. However, after observing the control video, subjects in the Trained Control group
performed movements in the left FF that were more curved than either the Trained Learning group or Untrained Learning group (Figure 5.3A).

We quantified subjects’ performance in the left FF by computing motor learning by observing scores (Figure 5.3B). A one-way between-subjects ANOVA revealed reliable group differences in motor learning by observing scores ($F(2,75) = 8.39, p = 0.01$). The Trained Learning group exhibited higher motor learning by observing scores compared to the Untrained Learning group ($t(50) = 1.94, p < 0.03$), even though both groups had observed the same learning video. Moreover, the movements of the Trained Control group were more curved in the left FF compared to those of either the Trained Learning group ($t(50) = 3.87, p < 0.001$) or the Untrained Learning group ($t(50) = 2.24, p < 0.02$).

We further examined the relationship between the extent to which proprioceptive acuity changed following the proprioceptive task and motor learning by observing. As shown in Figure 5.3C, across subjects in the Trained Learning group, there was a statistically reliable correlation between post-training decreases in the IQR of the psychometric fit and subsequent behavioural measures of motor learning by observing ($r = -0.41, p < 0.04$). That is, those subjects who showed the greatest improvements in perceptual acuity following perceptual training were those who went on to benefit more from observing motor learning. No reliable relationship between perceptual acuity change and observation-related changes in movement was seen for subjects in
the Untrained Learning group ($r = 0.004$, $p = 0.98$) and the Trained Control group ($r = 0.25$, $p = 0.22$; Figure 5.3D).

### 5.4 Discussion

Here we tested the idea that somatosensory perceptual training will improve somatosensory function and this will in turn enhance subsequent motor learning by observing. Subjects underwent perceptual training on a proprioceptive discrimination task to improve their proprioceptive acuity. They then observed a video of a tutor undergoing FF adaptation. A final behavioural assessment showed that subjects in a Trained Learning group who had underwent somatosensory perceptual training prior to observation benefited more from observing learning compared to subjects in an Untrained Learning group. For subjects in the Trained Learning group, post-training increases in proprioceptive acuity were reliably correlated with subsequent behavioural measures of motor learning by observing.

The Trained Learning group’s superior performance (i.e., straighter movements) in the left FF was not due to observing motor learning or perceptual training alone. If that were the case, we would have found comparable motor performance in the left FF across all three groups. Rather, our results show that their superior performance was due to the combination of perceptual training and observing motor learning. This suggests that improving proprioceptive acuity prior to observation can enhance
Figure 5.3: Proprioceptive training enhanced subsequent motor learning by observing. A, Evolution of perpendicular deviation (PD). The first 10 data points correspond to individual trial group averages. Data points thereafter correspond to the group averages of 5-trial blocks. The grey shaded region of the plot indicates the first 3 trials in the left FF, which were used to calculate motor learning by observing scores. Those subjects who observed the learning video (i.e., Trained Learning and Untrained Learning groups) showed a benefit, performing straighter reaches in the same (left) FF. B, Motor learning by observing scores as a function of video observed. Motor learning by observing scores reflect perpendicular deviation of initial movements in the left FF. Subjects in the Trained Learning and Untrained Learning groups therefore exhibited higher motor learning by observing scores (i.e., performed straighter movements in the left FF) compared to the Trained Control group. Moreover, subjects in the Trained Learning group exhibited higher motor learning by observing scores than the Untrained Learning group. * indicates $p < 0.05$. Error bars represent SE. C, Across subjects in the Trained Learning group, post-training decreases in the IQR of subjects’ psychometric fit correlated with subsequent behavioural measures of motor learning by observing. Post-training increases in perceptual acuity corresponded to the extent to which subjects subsequently benefitted from observing the left FF. D, There was no correlation between changes in perceptual acuity following the performance of the proprioceptive task and motor learning scores for either Untrained Learning group (blue) or the Trained Control group (green).
subsequent observation-related gains in motor learning.

The idea that the somatosensory system is involved in motor learning by observing is supported by previous behavioural work demonstrating that observing motor learning alters somatosensory perception. Bernardi and colleagues (2013) examined proprioceptive function before and after participants observed a video of a tutor learning to reach in a FF. Proprioceptive function was assessed using a discrimination task in which a robot manipulandum moved the hand away from the body along one of several trajectories and the subject judged whether the hand had been displaced to the left or the right (in the absence of visual feedback). Bernardi and colleagues (2013) reported that observing motor learning not only facilitated subjects’ motor performance in the observed FF, but it also altered subjects’ proprioceptive judgments. Observing motor learning resulted in systematic changes in subjects’ somatosensory perception depending on the FF that had been observed. Observing a video depicting right FF learning changed subjects’ proprioceptive perception such that judgments were biased toward the right. Conversely, observing a video depicting left FF resulted in proprioceptive judgments being biased toward the left. These results suggested that observing motor learning affects not only the motor system, but also the somatosensory system.

Using resting-state fMRI, we have shown that observing FF learning indeed results in functional changes to the somatosensory brain areas in addition to visual and
motor areas of the brain (McGregor & Gribble, 2015). We assessed changes in resting-state functional connectivity from pre- to post- observation that were related to behavioural measures of motor learning by observing. Observing motor learning changed functional connectivity between primary somatosensory cortex, visual area V5/MT, the cerebellum, and primary motor cortex. Observation-induced functional connectivity changes within this network were correlated with subsequent behavioural measures of motor learning by observing. That is, those subjects who showed greater functional connectivity changes after observing learning were those who achieved greater motor learning from observation (McGregor & Gribble, 2015).

In the current study, we used perceptual training to improve subjects’ somatosensory performance prior to observation. Our finding that subjects who possess superior pre-observation proprioceptive acuity benefit more from observing motor learning is consistent with our previous fMRI work, in which we showed that pre-observation measures of resting-state functional connectivity involving somatosensory areas of the brain can predict subsequent motor learning by observing. Subjects who exhibited greater resting-state functional connectivity between bilateral S1, M1, dorsal premotor cortex, and left superior parietal lobule prior to observation were those who gained more more observing motor learning on the following day, as assessed behaviourally (McGregor & Gribble, 2017).

Vahdat and colleagues (2014) have recently showed that a perceptual training pro-
tocol similar to the task used in the current study increases resting-state functional connectivity among somatosensory and motor brain areas. In their variation of the perceptual training task, a robotic manipulandum moved the subject’s hand away from the body along one of several fan-shaped trajectories and the subject judged whether the hand was displaced to the left or to the right of the midline. As in the current study, providing reinforcement feedback during this task resulted in improvements to acuity of sensed limb position. Resting-state fMRI data acquired before and after perceptual training showed increases in functional connectivity between bilateral primary S1, left M1, dorsal premotor cortex, and the superior parietal lobule (Vahdat et al., 2014). This network bears a strong resemblance to the network we reported in which pre-observation functional connectivity predicts subsequent motor learning by observing (McGregor & Gribble, 2017). Given the similarity between the perceptual training protocol used by Vahdat and colleagues (2014) and the protocol used the current study, it is likely that perceptual training in the current study induced functional changes in a similar network of sensory-motor brain areas.

More generally, the results of the current study complement the findings of studies of active motor learning, in which subjects learn by performing a task through physical practice. There is accumulating evidence that active motor learning involving physical practice results in changes to somatosensory perception. Motor learning can result in perceptual acuity improvements (Wong et al., 2011) as well as changes in sensed limb position (Haith et al., 2009; Cressman & Henriques, 2009; Ostry et al., 2010). For
example, FF adaptation has been shown to change sensed limb position, shifting it left or right depending on the direction of the learned FF (Ostry et al., 2010).

Neuroimaging and EEG studies further complement the evidence that functional changes in somatosensory brain areas occur with motor learning (Nasir et al., 2013; Vahdat et al., 2011). Using resting-state fMRI, Vahdat and colleagues (2011) showed that active motor learning alters functional connectivity involving somatosensory brain areas. Undergoing FF learning increased functional connectivity between second somatosensory cortex, ventral premotor cortex, and supplementary motor area. Moreover, the degree to which functional connectivity increased was correlated with behavioural measures of learning-related changes to sensed limb position.

Somatosensory perceptual training has also been shown to enhance subsequent motor learning through physical practice (Rosenkranz & Rothwell, 2012; Wong et al., 2012; Darainy et al., 2013; Vahdat et al., 2014). Darainy and colleagues (2013) trained subjects on a proprioceptive task similar to the one used in the present study, in which a robotic manipulandum moved the hand from a reference along one of several fan-shaped trajectories and subjects made judgments regarding the displacement of the hand. When provided with reinforcement accuracy feedback during the proprioceptive task, subjects showed increased perceptual acuity as well as decreases in perceptual bias such that they were more accurate in perceiving the boundary between left and right. They also found that perceptual training resulted in improvements in
subsequent FF adaptation, improving the rate of learning, the extent of learning, and measures of predictive compensatory forces (assessed based on subject’s applied forces during error clamp trials). As we found in the current study, post-training increases in proprioceptive acuity were correlated with improvements in motor learning (Darainy et al., 2013).

Here we showed that improving subjects’ proprioceptive acuity through perceptual training prior to observation increased observation-related gains in motor learning. Moreover, post-training increases in proprioceptive acuity were correlated with subsequent behavioural measures of motor learning. Improving somatosensory function (i.e., proprioceptive acuity) can therefore enhance motor learning through observation.

The findings of this study further support the idea that the somatosensory system plays a role in motor learning by observing.
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Chapter 6

General Discussion
Chapter 6. General Discussion

6.1 Summary of Findings

This thesis has presented a series of studies in which we tested the hypothesis that the somatosensory system is involved in motor learning by observing.

In the study presented in Chapter 2, we used functional magnetic resonance imaging (fMRI) to assess changes in resting-state functional connectivity (FC) associated with motor learning by observing. We showed that observing a tutor undergoing force field (FF) adaptation changed resting-state FC between visual area V5/MT, cerebellum, primary motor cortex (M1), and primary somatosensory cortex (S1). Post-observation FC changes within this network were correlated with subsequent behavioural measures of motor learning achieved through observation. No such FC changes were found in a group of control subjects who observed a tutor performing reaches in an unlearnable FF. The FC changes revealed in the learning group are therefore not due to visual attention to motion or observation of movement errors, but rather are specifically linked to observing motor learning. These results support the idea that brain networks linking action observation and motor control facilitate observational motor learning.

In Chapter 3, we investigated if pre-observation measures of brain function or structure could predict subsequent motor learning by observing. We found that individual differences in pre-observation resting-state FC, but not grey matter volume, predicted observation-related gains in motor learning. Subjects who exhibited greater
resting-state FC between bilateral S1, PMd, M1, and left SPL prior to observation (on day 1) were those who went on to show greater observation-related gains in motor performance during the day 2 behavioural assessment. No such correlation between pre-observation FC and motor learning by observing scores was found for a control group who observed a tutor performing reaches in an unlearnable FF. Individual differences in sensory-motor resting-state FC can therefore explain part of the individual variability in the extent to which observation facilitates motor learning.

In the experiments presented in Chapter 4, we tested the involvement of the somatosensory system in motor learning by observing using electroencephalography (EEG) and median nerve stimulation. We electrically stimulated the median nerve and used EEG to estimate S1 excitability before and after subjects observed motor learning. We found that observing motor learning increased the amplitude of the N20-P25 component of the somatosensory evoked potential (SEP), which has been linked to the earliest afferent processing in S1. Post-observation SEP changes were specifically linked to observing motor learning; no SEP changes were found in a group of control subjects who observed similar movements but not learning. Moreover, across those subjects who observed motor learning, the extent to which S1 excitability increased following observation corresponded to behavioural measures of motor learning by observing. This finding is consistent with the idea that observing motor learning results in functional plasticity in S1. In experiment 2, we used median nerve stimulation to test if the somatosensory system plays a necessary role in motor
learning by observing. Throughout observation, we applied median nerve stimulation to the subject’s right arm (the same arm being used by the tutor in the video), to the left arm, or to both arms simultaneously. Applying median nerve stimulation disrupted motor learning by observing in a limb-specific manner; stimulation delivered to the right arm (the same arm used by the tutor) disrupted learning whereas left arm stimulation did not. This result is consistent with the idea that a somatosensory representation of the observed effector plays an important role in motor learning by observing, and therefore must be available and unoccupied during observation for learning to occur.

Finally, in the experiment presented in Chapter 5, we tested if improving subjects’ somatosensory function prior to observation could enhance motor learning by observing. We trained subjects on a somatosensory discrimination task to improve their proprioceptive acuity prior to observing motor learning. Perceptual training indeed resulted in increased proprioceptive acuity. A post-observation behavioural assessment showed that trained subjects, who possessed superior proprioceptive acuity prior to observation, benefitted more from observing motor learning compared to subjects who had not received perceptual training. Across trained subjects, post-training increases in proprioceptive acuity were correlated with subsequent behavioural measures of motor learning by observing. These findings show that improving somatosensory function (i.e., proprioceptive acuity) can enhance subsequent observation-related gains in motor learning. This study provides further evidence that the somatosensory system
is involved in motor learning by observing.

6.2 Limitations

6.2.1 Chapter 2 Limitations

In the study presented in Chapter 2, we assessed changes in resting-state FC associated with observing motor learning. We revealed a visual-sensory-motor functional network in which post-observation FC changes correlated with behavioural measures of motor learning by observing. Since we acquired resting-state fMRI data at two time points only (i.e., before and after observation), the data from this experiment cannot provide information regarding the time course of FC changes throughout observation. It would be interesting to present the learning video in the MRI scanner and assess resting-state FC at regular breaks during the video. This would allow us to assess how FC within the identified network evolves during the observation of learning. Another limitation of all the studies included in this thesis is that we assessed motor learning by observing in terms of perpendicular deviation of the hand path during FF reaches. A more direct estimate of learned muscle force patterns would have been obtained by having subjects perform reaches in a force channel following observation. This would have allowed us to directly measure the time-varying pattern of forces that subjects applied at the robot handle after observing motor learning.
6.2.2 Chapter 3 Limitations

In the experiment presented in Chapter 3, we assessed if individual differences in grey matter volume or resting-state FC could predict subsequent motor learning by observing. We found that pre-observation resting-state FC between sensory-motor brain areas, but not grey matter volume, was correlated with behavioural measures of motor learning by observing as assessed on the following day. However, this study is subject to the following caveats and limitations:

First, our measures of resting-state FC and grey matter volume were not collected at baseline. Participants in both groups had performed practice reaches in a null field on day 0 as well as 100 null field reaches on day 1 prior to the fMRI scan session. Since recent experiences can alter resting-state FC (e.g., Albert et al., 2009; Lewis et al., 2009), it is likely that performing null field reaches altered sensory-motor FC prior to the fMRI scan session for both groups. It would be interesting to assess baseline resting-state FC before subjects have had any experience with the robotic manipulandum, and test if FC within the identified network still predicts subsequent observation-related gains in motor performance.

Second, we cannot rule out the possibility that the observed individual differences in pre-observation resting-state FC actually reflect variability in structural connectivity. There is a close correspondence between resting-state functional connectivity and
anatomical connectivity (e.g., Fox et al., 2005). As such, a subject could exhibit
greater resting-state FC among sensory-motor regions by virtue of having greater
anatomical connections among those regions. We cannot rule out this scenario since
we did not acquire structural images beyond T1-weighted anatomical scans.

6.2.3 Chapter 4 Limitations

In the first experiment of the study in Chapter 4, we applied electrical stimulation to
the median nerve in the arm to interfere with somatosensory processing throughout
observation. We found that applying median nerve stimulation to the right arm (the
same arm used by the tutor for the observed learning task) disrupted motor learning by
observing. Since median nerve stimulation broadly activates the somatosensory system
(Backes et al., 2000; Del Gratta et al., 2000, 2002; Allison et al., 1991; Balzamo et
al., 2004), we cannot determine which areas of the somatosensory system (or beyond)
were activated by our stimulation protocol.

In the second experiment, we showed that observing motor learning increases the
amplitude of the N20-P25 component of the somatosensory evoked potential (SEP), and
that post-observation SEP increases correspond to subsequent behavioural measures
of motor learning by observing. However, since we only acquired SEPs at two time
points (i.e., before and after observation), this experiment cannot provide information
regarding the time course of S1 functional changes during observation. Moreover, we
cannot determine which brain areas drove the observed changes in somatosensory activity. It is feasible that observing motor learning changes activity in brain areas beyond the somatosensory system (such as motor or premotor regions) which in turn drive changes in S1 excitability.

### 6.2.4 Chapter 5 Limitations

In the study presented in Chapter 5, subjects underwent somatosensory perceptual training to improve their proprioceptive acuity prior to observation. We found that improving subjects’ proprioceptive acuity prior to observation enhanced the extent to which they benefitted from observing motor learning. Subjects were instructed to relax their right arm throughout the proprioceptive task. This was done to prevent active motor outflow during the task so that changes in perceptual behaviour could be attributed to perceptual learning. However, without measures of active motor outflow (e.g., electromyographic activity), we cannot conclusively rule out the presence of active motor outflow during perceptual training.

### 6.3 Role of the Somatosensory System

While these studies suggest that the somatosensory system plays a role in motor learning by observing, a key question remains: what is the nature of the somatosensory system’s involvement in motor learning by observing?
6.3.1 A Proposed Role for S1 in Action Observation

The direct matching hypothesis posits that sensory-motor activity during action observation reflects the observer’s brain “covertly simulating” the observed action. The idea is that the observer’s brain maps a visual representation of the observed action onto the sensory-motor system, and activates (at a sub-threshold level) many of the same somatosensory and motor brain regions that would be used in performing the observed movement. In doing so, the observer’s sensory-motor system gains information about the observed movement. It has been proposed that sensory-motor knowledge gained from this covert simulation mechanism allows the observer to understand motor aspects of an observed action, to infer the intention of a movement, to allow for action prediction, etc. (e.g., Rizzolatti et al., 2001).

The ability to accurately predict the sensory outcomes of one’s movements is an important aspect of motor control and motor learning. It is thought that the brain uses a forward model to predict the sensory outcomes of a planned movement. Sensory prediction errors, differences between the predicted and actual sensory outcomes, are used to update an internal model and modify subsequent motor behaviour. It has been suggested that S1 activation during action observation reflects the observer’s brain simulating how it would feel to perform the observed movement (e.g., Caspers et al., 2010; Keysers et al., 2010; Bolognini et al., 2011). In the context of motor learning by observing, it is possible that observation-related S1 activity reflects the
observer’s sensory-motor system simulating the tutor’s upcoming movement and forming predictions about the tactile and/or proprioceptive outcomes (e.g., Caspers et al., 2010; Keysers et al., 2010; Bolognini et al., 2011).

6.3.2 A Proposed Role for S1 in Motor Learning

Much of the work on sensory-motor adaptation has focused on the roles of primary motor cortex and the cerebellum in generating sensory predictions and modifying subsequent motor commands based on sensory prediction errors (e.g., Miall & Wolpert, 1996; Wolpert et al., 1998; Tseng et al., 2007). A recent optogenetic study using a mouse model of FF adaptation has suggested a causal role for S1 in sensory-motor adaptation. Mathis and colleagues (2017) used a modified version of a FF reaching task in which mice grasped a joystick and performed pulling movements in the absence of visual feedback. Mice were able to adapt to a FF as evidenced by their gradual reduction in movement perpendicular deviation across trials in the FF and by the presence of aftereffects when the FF was unexpectedly removed. To test the role of S1 in FF adaptation, the authors photoinhibited the forelimb area of contralateral S1 during a subsequent block of FF adaptation phase of the task. Photoinhibition of S1 abolished motor adaptation; mice no longer reduced the perpendicular deviation of their movements in the FF and showed no aftereffects when the FF was removed. The detrimental effects of S1 photoinhibition were specific to motor adaptation. During photoinhibition sessions, mice were still able to perform reaching tasks with baseline
levels of accuracy and were still able to learn a reinforcement-based task in which they were rewarded for moving the joystick to a new target location. The finding that the mice were able to undergo reinforcement learning but not FF adaptation during S1 photoinhibition suggested that S1 photoinhibition impaired error-based adaptation processes. The authors then tested the nature of S1’s involvement in motor adaptation by inhibiting S1 partway through an adaptation block. S1 inhibition had no effect on previously adapted movements, but prevented mice from adapting further. Since S1 inhibition did not immediately abolish all adaptation, the authors reasoned that S1 is not the site of an internal model. Instead, these findings suggest that S1 plays a critical role in updating an internal model which is located in another brain region. While the optogenetics approach used in this study provides support for a causal role of S1 in FF adaptation, the nature of S1’s involvement remains unclear and warrants further study. For example, it is feasible that S1 participates in the formation of sensory predictions by simulating the somatosensory consequences of movements. It is also possible that S1 is involved in computing sensory prediction errors or it could relay somatosensory feedback to other brains areas, such as the cerebellum, which then compute sensory prediction errors (e.g., Miall & Wolpert, 1996; Wolpert et al., 1998; Tseng et al., 2007).

The results of Mathis and colleagues (2017) are consistent with the results of the study presented Chapter 4 in which we found that interfering with somatosensory processing during observation disrupted motor learning by observing McGregor et al.
It is possible that applying median nerve stimulation during the observation of motor learning disrupted the somatosensory system’s role in updating a forward model. For example, delivering nerve stimulation during observation may have added noise within the somatosensory system which could have corrupted the observer’s sensory predictions and/or interfered with sensory prediction error computations.

### 6.4 Contribution to the Field of Motor Control

Collectively, the studies presented in this thesis suggest that motor learning by observing is supported by a fronto-parieto-occipital network in which the somatosensory system is an active element.

A prevalent idea in psychology has been that the brain is organized in a modular fashion such that there are distinct systems, each with a different function. This idea has played a significant role in shaping our current textbook account of brain functional organization. It is often taught that action and perception engage separable systems - the visual system processes visual stimuli, the somatosensory system processes afferent stimuli, and the motor system is responsible for motor function. On the contrary, recent research (including the studies presented in this thesis) has demonstrated that sensory and motor processes often involve multiple systems. For example, functional neuroimaging studies in humans show that action observation engages visual, premotor, motor, and somatosensory brain areas - a broad network encompassing brain regions
well beyond visual areas within the occipital lobe (Calvo-Merino et al., 2004; Buccino et al., 2004; Vogt et al., 2007; Cross et al., 2009; Malfait et al., 2010; Caspers et al., 2010; Gardner et al., 2015). As a further example, perception can influence movement, and movement can in turn influence perception. Somatosensory experience alters motor performance and activity within the motor system (Rosenkranz & Rothwell, 2012; Wong et al., 2012; Darainy et al., 2013; Vahdat et al., 2014). Conversely, the effects of motor learning extend to the somatosensory system, resulting in both somatosensory functional plasticity and perceptual changes (Haff et al., 2009; Cressman & Henriques, 2009; Ostry et al., 2010; Wong et al., 2011; Vahdat et al., 2011; Nasir et al., 2013). The studies in this thesis provide further evidence of the interplay between perceptual and motor processes. Here we have shown that purely visual input of another’s movements can alter activity in both motor and somatosensory brain areas, and facilitate motor learning. Furthermore, we found that improving somatosensory perception influences the extent to which visual input can facilitate motor skill learning. These findings further cement the idea that perceptual and motor processes rely on multiple systems acting together.

This work also contributes to the growing literature suggesting that brain networks supporting motor learning by observing overlap with those involved in active motor learning (e.g., Calvo-Merino et al., 2004, 2006; Cross et al., 2006, 2009; Gardner et al., 2015). Here we have demonstrated that observing FF adaptation involves premotor cortex, primary motor cortex, primary somatosensory cortex, and the cerebellum.
Therefore, observing the tutor undergoing motor learning activates many areas of the observer’s brain that would be used if he or she ever performs the observed learning task.

Most importantly, this series of studies suggests a role for the somatosensory system in motor learning by observing. Bernardi and colleagues (2013) previously reported that observing motor learning changes somatosensory perception. The authors reasoned that the perceptual changes indicated that observing motor learning had altered activity within the somatosensory system. However, it was unknown whether such observation-related changes in somatosensory activity constitute part of processes underlying motor learning by observing (as appears to be the case in active motor learning) or whether they are a by-product of motor learning by observing. Here we have shown that observing motor learning changes somatosensory activity in a manner that is behaviourally-relevant. Observing motor learning results in S1 excitability increases which correspond to the extent to which motor learning by observing was achieved. Moreover, manipulating somatosensory activity can influence motor learning by observing. Interfering with somatosensory processing throughout observation can disrupt motor learning by observing whereas improving somatosensory function prior to observation can enhance motor learning by observing. The finding that manipulating somatosensory activity can enhance or disrupt motor learning by observing suggests that observation-related somatosensory changes are not epiphenomenal in nature, but rather are part of processes underlying motor learning by observing.
6.5 Future Directions

6.5.1 Time Course of Sensory-motor Changes

The studies included in this thesis assessed functional changes in sensory-motor brain areas at two points in time: before and after observation. We have reported that observing motor learning increases motor evoked potentials (MEPs) (McGregor & Gribble, submitted) as well as somatosensory evoked potentials (SEPs) (McGregor et al., 2016). While these findings suggest that observing motor learning changes M1 and S1 excitability, they do not provide insight into the time courses of the functional changes during observation.

A future study could probe M1 and S1 excitability during the regular breaks throughout the video (while subjects rest). Stimulation could be applied to the median nerve and SEPs could be recorded using EEG. Single-pulse transcranial magnetic stimulation (TMS) could be applied over the arm area within M1 and motor evoked potentials (MEPs) could be recorded. Acquiring these data at regular intervals would allow one to track changes in M1 and S1 excitability and compare their time courses. If observation-related changes in M1 activity drive changes in S1 activity, one would predict that MEP changes would occur earlier in the video compared to SEP increases. In contrast, if observation-related changes in S1 activity drive changes in M1 activity, one would expect the opposite pattern.
6.5.2 Gaze Behaviour

In each of the experiments presented in this thesis, subjects were instructed to watch a video and count the number of correctly-timed reaches the tutor performed. Subjects were not told about FFs prior to observation and they were not instructed to pay attention to any particular part of the video. Yet subjects who observed videos depicting a tutor undergoing FF adaptation were able to gain information about how to move in the FF environment. The question arises: which visual signals in the video did subjects use?

Eye tracking experiments have shown that humans implement proactive saccades while performing skilled goal-directed actions (e.g., Flanagan & Johansson, 2003). It is theorized that proactive saccades are made possible through the use of a forward model. Sensory predictions about the visual outcomes of a movement guide our saccades to locations in space where we expect our hand to be located as the movement unfolds (Miall & Wolpert, 1996; Ariff et al., 2002; Sailer et al., 2005).

Flanagan and Johansson (2003) have shown that subjects exhibit proactive gaze behaviour during the observation of skilled goal-directed actions. Subjects’ eye movements were tracked while they performed a block-stacking task and while observing an actor performing the same task. It was found that subjects used proactive saccades both while performing the block-stacking task and while they observed an actor
performing the task. The similarity in gaze behaviour suggests that observers used their own sensory-motor system to generate motor predictions of the future state of the actor’s hand.

Limited work has examined the evolution of gaze behaviour over the course of active motor learning. In one study, Sailer and colleagues (2005) tracked subjects’ gaze behaviour during an active motor learning task which involved turning and pulling dials to guide an on-screen cursor to targets. In early learning, subjects’ performance was poor and their gaze pursued the on-screen cursor. With practice, subjects’ performance improved rapidly and their gaze began to predict the cursor’s upcoming location. In the final stage of learning, subjects’ performance was further refined and they showed proactive saccades directly to the target (Sailer et al., 2005). This increase in the use of proactive saccades over the course of motor learning is thought to reflect the updating of an internal model (Miall & Wolpert, 1996; Flanagan & Johansson, 2003).

If the observer’s sensory-motor system is indeed simulating the tutor’s upcoming movements and predicting their sensory outcomes, the direct matching hypothesis would predict that subjects observing motor learning would exhibit a similar evolution of gaze behaviour during observation as subjects who actively learn through physical practice. Neuroimaging and neurophysiological techniques could be used to record and/or disrupt sensory-motor activity during observation sessions to gain further insight into the role of the sensory-motor system in motor learning by observing.


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Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., &


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Journal of Neurophysiology, 98(1), 54-62.


Chapter 7

Ethics Approval
Chapter 7. Ethics Approval

Use of Human Participants - Ethics Approval Notice

Principal Investigator: Dr. Paul Grabbio
Review Number: 18935
Review Level: Full Board
Approved Local Adult Participants: 120
Approved Local Minor Participants: 0
Protocol Title: Synapticity: Plasticity and Motor Learning
Department & Institution: Psychology, University of Western Ontario
Sponsor: Canadian Institutes of Health Research

Ethics Approval Date: July 22, 2011
Expiry Date: July 31, 2016

Documents Reviewed & Approved & Documents Received for Information:

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<tr>
<td>UWO Protocol</td>
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This is to notify you that the University of Western Ontario Health Sciences Research Ethics Board (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced study on the approval date noted above. The membership of this HSREB also complies with the membership requirements for REBs as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request form.

Member of the HSREB that are named as investigators in research studies, or declare a conflict of interest, do not participate in discussions related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The UWO HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Signature

Ethics Officer to Contact for Further Information

[Signature]
Grace Kelly
Shanice Walcott

This is an official document. Please retain the original in your files.

The University of Western Ontario
Office of Research Ethics
Support Services Building Room 5150 • London, Ontario • CANADA • N6A 3K7
PH: 519-661-3036 • F: 519-850-2466 • www.uwo.ca/research/ethics
Chapter 7. Ethics Approval

Research Ethics

Use of Human Participants - Revision Ethics Approval Notice

Principal Investigator: Dr. Paul Grizzle
File Number: 100859
Review Level: Delegated
Protocol Title: Somatosensory Plasticity and Motor Learning (REB #18106)
Department & Institution: Social Science/Psychology, Western University
Sponsor: Canadian Institutes of Health Research

Ethics Approval Date: Expiry Date: July 31, 2017
Documents Reviewed & Approved & Documents Received for Information:

<table>
<thead>
<tr>
<th>Document Name</th>
<th>Version Date</th>
<th>Comments</th>
</tr>
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<tbody>
<tr>
<td>Revised Western University Protocol</td>
<td></td>
<td>incl. EEG measurements of SEPs; revise study end date and increase in sample size to 20 participants</td>
</tr>
<tr>
<td>Revised Letter of Information &amp; Consent</td>
<td></td>
<td>version Oct 2013</td>
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This is to notify you that the University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Guidelines, and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above. The membership of this REB also complies with the membership requirements for REBs as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB’s periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the University of Western Ontario Updated Approval Request Form.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Ethics Office in Contact for Further Information

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anna Bloor</td>
<td>Chair</td>
</tr>
<tr>
<td>James Kelly</td>
<td></td>
</tr>
<tr>
<td>Wade Train</td>
<td></td>
</tr>
</tbody>
</table>

This is an official document. Please retain the original in your files.

Western University, Research, Support Services Bldg., Rm. 5150
London, ON, Canada N6A 3K7 t. 519.661.3036 t. 519.850.2466 www.uwo.ca/research/services/ethics
Chapter 7. Ethics Approval

Western University Non-Medical Research Ethics Board
NMREB Delegated Initial Approval Notice

Principal Investigator: Dr. Paul Gribble
Department & Institution: Social Science/Psychology, Western University

NMREB File Number: 108371
Study Title: Sensory Training and Observational Motor Learning

NMREB Initial Approval Date: August 30, 2016
NMREB Expiry Date: August 30, 2017

Documents Approved and/or Received for Information:

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<th>Comments</th>
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<tr>
<td>Western University Protocol</td>
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<td>August 20, 2016</td>
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<td>Letter of Information &amp; Consent</td>
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<td>2016/08/29</td>
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<td>2016/08/19</td>
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<td>Instruments</td>
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<tr>
<td>Other</td>
<td>Debriefing</td>
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The Western University Non-Medical Research Ethics Board (NMREB) has reviewed and approved the above named study, as of the NMREB Initial Approval Date noted above.

NMREB approval for this study remains valid until the NMREB Expiry Date noted above, conditional to timely submission and acceptance of NMREB Continuing Ethics Review.

The Western University NMREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the Ontario Personal Health Information Protection Act (PHIPA, 2004), and the applicable laws and regulations of Ontario.

Members of the NMREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

The NMREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000941.

Ethics Officer: on behalf of Dr. Rob Hinson, NMREB Chair or delegated board member

Ethics Officer: Erika Baule Nicole Kantki Grace Kelly Katelyn Harris Vikki Tom Karen Gopal

Western University, Research, Support Services Bldg., Rm. 5150
London, ON, Canada N6G 1C9  t. 519.661.3036  f. 519.850.2466  www.uwo.ca/research/ethics

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Chapter 8

Curriculum Vitae
Heather McGregor

Post-Secondary Education and Degrees

2018  Ph.D. (expected)  The University of Western Ontario  Neuroscience  
2011  Honours B.Sc.  McMaster University  Psychology  

Honours and Awards

2017  Australian Endeavour Research Fellowship  
11  NSERC Michael Smith Foreign Study Supplement  
11  Edmond & Lily Safra Center for Brain Sciences Israel Travel Grant  
2014  NSERC Canada Graduate Scholarship - Doctoral Level, 3 years  
11  Ontario Graduate Scholarship (declined)  
2013  Organization for Human Brain Mapping Trainee Abstract Award  
2012  Ontario Graduate Scholarship  
2011  NSERC Canada Graduate Scholarship - Master’s Level, 1 year  
11  Ontario Graduate Scholarship (declined)  

Publications

- McGregor HR, Cashaback JGA, & Gribble PL (submitted). Somatosensory perceptual training enhances motor learning by observing.  
- Cashaback JGA, McGregor HR, Mohatarem A, & Gribble PL (2017). Disassociating error-based and reinforcement-based loss functions during sensorimotor
Chapter 8. Curriculum Vitae


· Cashaback JGA, McGregor HR, Pun HCH, Buckingham G, & Gribble PL (2017). Does the sensorimotor system minimize prediction error or select the most likely prediction during object lifting? Journal of Neurophysiology, 117(1), 260-274.


Invited Talks


· Invited talk at the Progress in Motor Control meeting, Miami, FL: “A role for the somatosensory system in motor learning by observing”, July 22, 2017.

· Invited talk at the Centre for Vision Research Speaker Series, York University, Toronto, Canada: “Role of the somatosensory system in motor learning by observing”, Mar 31, 2017.


· Invited talk at the Brain and Mind Institute Symposium, The University of Western Ontario, London, Canada: “The somatosensory system supports motor


Poster Presentations


· McGregor HR, Cashaback JGA, & Gribble PL (2016). Functional plasticity in primary somatosensory cortex supports motor learning by observing. Poster
presented at the Canadian Association for Neuroscience meeting, Toronto, ON, May 29-31.


