Time Courses of Proprioceptive Recalibration and Reach Adaptation to a Visuomotor Distortion

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Statement of Contribution of Collaborators

I hereby declare that I am the sole author of this Master of Science thesis. My contributions included: a review of relevant literature in the area of interest, participant recruitment, participant testing, data collection and analysis, data compilation, statistical analyses, and the write-up of the thesis document. All of these duties were performed under the guidance and mentorship of my research supervisor, Dr. Erin K. Cressman.

The original conception of the experiment in this thesis was performed in collaboration with Dr. Erin K. Cressman (School of Human Kinetics, University of Ottawa) and Dr. Denise Y.P. Henriques (School of Kinesiology and Health Science, York University). They provided editorial corrections and feedback, and were co-authors in the article presented in this thesis.

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Abstract

When subjects are presented with distorted visual feedback of their hand during a goal-directed movement (i.e. subjects view a cursor representing their hand that is rotated from their hand's actual position while reaching in a virtual reality environment), they typically adapt their movements so that the cursor is brought to the target, thus reducing reaching errors. In addition to motor adaptation, it has recently been shown that reaching with distorted visual feedback of the hand results in sensory changes, such that proprioceptive estimates of hand position are shifted in the direction of the visual feedback (Cressman and Henriques 2009). The current study looked to establish how quickly these sensory changes arise while training to reach with distorted visual feedback of the hand. Additionally, by comparing sensory to motor changes across time, we looked to determine the relationship between their underlying processes. Subjects trained to reach to a single visual target while seeing a cursor that was aligned with their actual hand position (50 trials: aligned reach training), or rotated 30° clockwise (CW) relative to their actual hand position (150 trials: rotated reach training). Reach errors and proprioceptive estimates of felt hand position were assessed following the aligned reach training trials and at 7 different times during the rotated reach training trials by having subjects reach to the target without visual feedback, and provide estimates of the position of their hand relative to a visual reference marker respectively. Results revealed a slow change in proprioceptive estimates over the course of reach training with the rotated cursor relative to estimates after the aligned reach training, and in fact, significant sensory changes were not observed until after 70 trials. In contrast, reach adaptation showed a much steeper increase and significant adaptation after a limited number of reach training trials with a rotated cursor. These different time courses suggest that proprioceptive recalibration and reach adaptation arise due to separate neural processes.

Chapter I: Literature Review

1. General Introduction

It has been suggested that the human brain's most important job is to program goal-directed movements, as they are our primary means of interacting with one another and the environment (Wolpert et al. 2001). However, our body and environment are continuously changing, such that we may need to learn *new* movements, or adapt our *learned* movements in order to accommodate for changing intrinsic and extrinsic conditions. For example, the perceived spatial location of an object may be altered after putting on a new pair of prescription glasses. Motor learning can be defined as the process of improving performance (or returning to normal (baseline) levels of performance) when encountering novel task demands or a novel environment (Hallett et al. 1996; Wolpert et al. 2001). One method of studying the processes underlying motor learning is to present subjects with distorted visual feedback of their hand during a goal-directed movement in the form of a misaligned on-screen cursor (i.e. subjects view a cursor representing their hand that is shifted from their hands actual position while reaching in a virtual reality environment), and to monitor how they adapt their movements in response. Reaching with this distorted visual feedback typically results in rapid adjustments of one's movements (i.e. within 20 reaches; Krakauer et al. 2000; Rabe et al. 2009), in order to reduce reaching errors so that the cursor is brought to the target. Moreover, when subjects reach in the absence of visual feedback, they continue to produce movements in the direction opposite to the visual distortion. These persistent deviations in their movements reflect plastic changes in the motor system (i.e. reach adaptation), and are referred to as reach aftereffects (Martin et al. 1996; Krakauer et al. 1999 2000; Baraduc and Wolpert 2002; Buch et al. 2003).

In addition to reach adaptation, recent research has suggested that reaching with distorted visual feedback of the hand also results in sensory changes, such that proprioceptive estimates of hand position shift in the direction of the visual distortion (Efstathiou and Held 1964; Harris 1963, 1965; Craske and Gregg 1966; Hay and Pick 1966; Redding and Wallace 1988, 1996, 2002, 2003, 2006; Cressman and Henriques 2009). This is thought to involve a recalibration of subjects' sense of felt hand position (i.e. proprioceptive recalibration) to match the visual representation of the hand provided (Cressman and Henriques 2009, 2010; Cressman et al. 2010; Salomonczyk et al. 2011, 2012).

It is well established that sensory changes arise after reaching with distorted visual feedback of the hand; however, it is currently unclear how quickly these changes arise and how quickly they arise relative to reach adaptation. Research investigating the time course of sensory changes and their relationship to motor changes will provide insight into the mechanisms underlying sensory and motor plasticity. Previous research using a velocity-dependent force-field paradigm, in which subjects learned to adapt their reaches in order to compensate for forces applied to the hand, has suggested a link between sensory and motor changes (Matter et al. 2013). Specifically, this research found that motor changes occurred much earlier than sensory changes, and thus suggested that reach adaptation may drive sensory changes when subjects reach within a velocity-dependent force-field. However, research from our lab has suggested that motor and sensory changes may be independent processes, as proprioceptive recalibration is not correlated with reach adaptation (Cressman and Henriques 2009, 2010; Henriques and Cressman 2012). Additionally, these two processes have shown different patterns of generalization across target distances and between limbs (Mostafa et al. 2014**a,** 2014**b**). It is therefore unclear whether reach adaptation and proprioceptive recalibration arise due to a single mechanism or separate, independent mechanisms occurring during reaches with distorted visual feedback.

The purpose of this research is to establish the time course of proprioceptive recalibration. After establishing the time course of proprioceptive recalibration, we will then compare it to the time course of reach adaptation in order to establish the relationship between these two processes. Thus, we performed a similar experiment to Mattar et al. (2013), except that we assessed the time course of sensory and motor changes in response to a visuomotor distortion, rather than a velocity-dependent force-field. Specifically, the current study looked to address the following question: *How long does it take for sensory changes (i.e. proprioceptive recalibration) to arise when reaching with distorted visual feedback of the hand? And, when do changes arise relative to reach adaptation?* Research in this area is critical to advance our current understanding of the processes that underlie proprioceptive recalibration and reach adaptation. Additionally, this research will be useful in improving rehabilitation programs for individuals with sensorimotor dysfunction (e.g. Parkinson’s disease, stroke, etc.), as results will provide insight into if it is possible to develop rehabilitation techniques that restore or improve motor function through sensory recalibration.

This literature review will provide background information which is relevant to the specific objectives of the current project. First, the production of goal-directed movement and its reliance on visual and proprioceptive information will be discussed. Next, the internal model, which is a theoretical framework put forth to understand the sensorimotor transformations involved in movement production and reach adaptation will be explained. This will be followed by a discussion of the paradigms which are used to assess motor plasticity, as well as the proposed processes which underlie motor changes and the time course of these processes. The paradigms, mechanisms, and time courses involved in sensory plasticity will also be discussed. Lastly, the proposed relationship between motor and sensory changes put forth in the literature will be outlined.

2. Goal-Directed Movements

We are constantly performing goal-directed reaches: movements performed by the body or parts of the body, in order to carry out a specific task or goal (Kroger et al. 2010). These movements enable us to interact with different objects and within a variety of different environments (Wolpert and Kawato 1998). In order to perform these movements, the central nervous system must transform sensory information about hand and target location into appropriate motor commands to move the hand to the desired location (Jeannerod 1988; Flanders et al. 1992; Desmurget et al. 1998). The primary sources of this sensory information (i.e. vision and proprioception) will now be briefly described.

2.1 Vision

Humans tend to rely more on visual cues than other sensory cues for information regarding the position of one's body and objects in one's environment (Cohen 1999; Bhatnagar 2002; Schmidt and Lee 2011). Visual receptors (i.e. photoreceptors) are located on the retina at the back of the eye. Photoreceptors are categorized as either rods or cones. Rods are situated on the outer edges of the retina and are used in peripheral vision. Rods are not able to distinguish colours; however, they are the primary photoreceptors involved in night vision (Curcio et al. 1990; Cohen 1999; Bhatnagar 2002). Cones, on the other hand, are present in the fovea and are sensitive under conditions of more intense light relative to rods.

Hence, they are responsible for distinguishing colours and details in our surroundings (Cohen 1999; Bhatnagar 2002).

After visual cues are captured in the retina, visual information is passed to the primary visual cortex (V1), in the occipital lobe. From there, visual information is relayed along the dorsal and ventral visual pathways to the parietal and temporal cortex respectively. These two visual pathways have been proposed to be responsible for different functions (Ungerleider and Mishkin 1982; Goodale and Milner 1992; Schmidt and Lee 2011). In particular, processing in the dorsal stream is associated with the ability to localize objects specifically for the visual control of movement (i.e. action), while processing in the ventral stream is associated with object recognition (i.e. perception). In the current work, we are primarily interested in the role of vision for action and hence processes occurring in the dorsal visual stream. Early work by Woodworth (1899) demonstrated the importance of vision in movement execution, as movements made to targets in the absence of vision were found to be much less accurate than movements made with vision. More recent studies have assessed the role of vision in movement planning and execution by having subjects reach with distorted visual feedback of their limb (Krakauer et al. 1999 2000; Simani et al. 2007). These studies typically show that subjects make large, initial errors, but quickly learn to adjust their movements so that the visual estimate of the limb moves to the target.

2.2 Proprioception

Humans also rely on their sense of proprioception when planning a reaching movement. In particular, proprioceptive information is relayed from receptors located in the muscles, joints, tendons and skin to the parietal cortex and provides information on the orientation/position of one’s arm and body. Muscle spindles are the primary proprioceptor that gives rise to one’s sense of arm position. They are located within the body of a muscle and run parallel with the muscle fibers. These sensors detect changes in the length of a muscle, as their length changes relative to the length of the muscle (Gordon and Ghez 1991; Pearson and Gordon 2000). Golgi tendon organs are a second type of proprioceptor located within tendons and detect changes in muscle tension, corresponding to force-production (Gordon and Ghez 1991; Pearson and Gordon 2000). Additionally, sensors located in the skin, called mechanoreceptors, are activated by mechanical stimulation such as touch, pressure, vibration and movement (Cohen 1999). These different proprioceptors work together to provide important information with regards to the orientation and movement of one’s body in space.

Proprioception has been shown to have a very important role in movement planning and execution. For example, individuals with no proprioceptive input (i.e. deafferented patients) are much less accurate than healthy control subjects in producing movements to a visual target in the absence of visual feedback of their hand (Ghez et al. 1995). Additionally, similar results were found when healthy (control) subjects had their proprioceptive sense disrupted using tendon-vibration, such that their reaches were significantly more deviated than without the vibration (Larish et al. 1984).

2.3 Internal Model

In order to perform a goal-directed movement, a series of sensorimotor processes occur. Sensory information from the seen (i.e. visual) and felt (i.e. proprioceptive) position of the limb is optimally combined in order to form a coherent estimate of the limb’s position in space (Ernst and Banks 2002). This sensory information regarding the position of the limb is then combined with sensory information regarding the target position and transformed into an appropriate set of motor commands to move the limb to the desired location (Jeannerod 1988; Flanders et al. 1992; Desmurget et al. 1998; Wolpert and Kawato 1998).

The internal model is a theoretical framework which provides insight into how these sensorimotor transformations occur, and ultimately, how movements are performed. An internal model is comprised of two components: (1) an inverse model, which determines the motor commands that will produce the desired limb movement, and (2) a forward model, which utilizes the current motor commands to predict the next state of the limb (i.e. its position and velocity) (Wolpert and Kawato 1998). In other words, the inverse model determines the necessary motor commands required to perform a specific movement, while the forward model predicts the sensory consequences of the movement, including changes in the effector that will result from these motor commands, given the limb's current position.

Forward models have an important role in motor control and motor learning. Forward models can be used to anticipate the sensory outcome of an action using the efference copy (i.e. an internal "copy" of the motor command, Jeannerod 2003), which can then be compared to the actual sensory consequences of the action (Wolpert et al. 1995**a**). This comparison between predicted and actual sensory feedback regarding limb position can occur both during and following a movement. If the forward model detects a difference between the limb's predicted and actual position (i.e. error), this information can be used by the inverse model to update the motor command. For example, if the seen position of the reaching hand does not achieve the target or differs from the predicted visual outcome, the motor system will use this error signal to update its internal model and change one's motor performance on subsequent movements. This learning process has been mathematically modeled as an iterative updating of the internal model in order to provide an appropriate mapping between motor commands and predicted motor and sensory consequences (Huang et al. 2011).

3. Motor Plasticity

Motor learning can be defined as the acquisition of skilled movements that arises from interacting with the environment (Wolpert et al. 2001). One common form of motor learning is motor adaptation. If an environmental perturbation is presented during a well-learned movement, the motor plan that was used to perform the movement is no longer appropriate. The internal model that represents the movement must therefore change in order to accommodate for this perturbation. This process is known as motor adaptation, which can be defined as a reduction in systematic errors of a movement in order to return to a desired level of performance (Krakauer 2009). Motor adaptation provides insight into the plasticity of the motor system, specifically its ability to modify its structure and function in response to sudden or gradual changes in environmental conditions (Ungerleider et al. 2002).

In the context of goal-directed movements, the plasticity of the motor system can be examined by introducing distorted visual feedback of the hand using (1) (laterally-displacing) prism goggles or (2) a virtual-reality setting (i.e. aiming while seeing a cursor on the screen that represents the hand). As well, researchers have manipulated the dynamics of a movement by having subjects reach within a velocity-dependent force-field (i.e. where velocity-dependent loads are applied to the reaching limb during the movement, pushing the hand off its initial course). These specific perturbations will be described in more detail below. However, in general, experiments examining reach adaptation using these perturbations typically have subjects reach to visual targets while seeing their hand or a visual representation of their hand (Cressman and Henriques 2009, 2010; Redding and

Wallace 1993 1996; Simani et al. 2007; Ostry et al. 2010). The reaching movements are first performed in the absence of an external perturbation, in order to acquire "baseline" characteristics of the movement. The perturbation is then applied and subjects tend to make large initial reaching errors in these reaching trials. However, subjects quickly adapt their movements to compensate for the perturbation such that they begin to perform movements that are similar to their baseline reaches. In addition to observing changes in reaches while the perturbation is applied, subjects are often required to reach to (visual) targets in the absence of visual feedback following reach training trials. Subjects tend to make reaching errors on these trials, such that they continue to reach as if they were still influenced by the perturbation. These reach-errors are referred to as reach aftereffects, and they indicate that a persistent change in the motor system (i.e. reach adaptation) has occurred (Martin et al. 1996; Krakauer et al. 1999, 2000; Baraduc and Wolpert 2002; Buch et al. 2003).

3.1 Prism Adaptation

Motor plasticity or adaptation was originally studied using a prism-reaching paradigm, such that subjects reached to visual targets while wearing laterally displacing prism goggles that shifted visual cues in the direction of the apex of the prism (Von Helmholtz 1909/1962; Held 1965; Harris 1963, 1965; Redding and Wallace 1993, 2002, 2003). Von Helmholtz (1909/1962) was one of the first to use this paradigm and found that reach errors caused by a prism-induced shift in the visual field progressively decreased during repeated reaches. Furthermore, after removal of the prism, subjects experienced reach errors in the opposite direction. Following the work by Von Helmholtz, Harris (1963) had subjects point for three minutes at visual targets while wearing prism goggles that displaced the targets about 12 cm to the right or left. The prism goggles were then removed, and subjects were told to point either to visual targets, or to a “straight ahead” (i.e. proprioceptive) target. Harris (1963) found that there were significant initial reach errors (i.e. aftereffects), such that subjects reached about 6 cm from the target (or about 50% of the magnitude of the distortion) for both visual and proprioceptive targets, in the opposite direction of the visual shift, even after only 3 minutes of reach training with the prism goggles. Based on these shifts in reaches to visual and proprioceptive targets, it has been suggested that one’s sense of proprioception is recalibrated following reaches with prism goggles (Redding and Wallace 1993, 2002, 2003)

3.2 Virtual-reality Adaptation

A more recent method of displaying altered visual feedback of the hand is to have subjects reach to targets within a virtual-reality environment. In this environment, the subject’s hand is hidden from view, and an on-screen cursor represents the location of the hand as being shifted from its actual position. This cursor can be translated (left or right) or rotated (clockwise or counter clockwise) relative to the actual location of the reaching hand. Similar to the prism studies discussed above, this method has also been shown to result in significant aftereffects in the opposite direction of the shift of the visual representation of the reaching hand (Wolpert et al. 1995**b**; Vetter et al. 1999; Sainburg and Wang 2002; Cressman and Henriques 2009; Krakauer 2009). For example, Cressman and Henriques (2009) found that subjects produced reach aftereffects that were about 3.4 cm to the left of the target after training with a 4 cm rightward translation, and about 18° counter clockwise after training with a 30° clockwise rotation (or about 60-70% of the distortion introduced). Simani et al. (2007) also found that reaching-training with a distorted visual cursor led to comparable shifts in subsequent aftereffect trials to both visual and proprioceptive targets (i.e. the untrained hand).

3.3 Force-field Adaptation

Whereas the previous two paradigms looked at reach adaptation in response to altered visual feedback of the hand, velocity-dependent force-field paradigms require subjects to reach to targets while externally imposed forces are applied to the reaching limb (Shadmehr and Mussa-Ivaldi 1994; Scheidt et al. 2001; Mattar et al. 2011, 2013). Therefore instead of adapting the kinematics of their movements in response to distorted visual feedback of the hand, subjects are required to change the dynamics (i.e. force-production) of their movements in order to counteract the external forces and achieve the target. Shadmehr and Mussa-Ivaldi (1994) were among the first investigators to use this paradigm to study reach adaptation. Subjects were told to make sequential reaching movements to randomized targets while a velocity-dependent force was applied to their reaching hands. At first, subjects made movements that were severely distorted such that their trajectories curved away from the direction of the target. Subjects would then stop, before making a second movement to the target. However, with practice, subjects began to produce hand trajectories that were very similar to those that they made when the distortion was not present, such that they moved directly to the target without using a second, corrective movement (Shadmehr and Mussa-Ivaldi 1994). After the reach training phase, subjects experienced a sudden removal of the force-field, and produced trajectories that were *mirror images* (i.e. curved in the opposite direction to the velocity-dependent force-field) of the initial reaching-training trials when the distortion was introduced (Shadmehr and Mussa-Ivaldi 1994). These aftereffects demonstrated that motor learning had occurred. The experimenters suggested that the subjects had incorporated the force field into their internal models, so that their movements would compensate for the expected forces (Shadmehr and Mussa-Ivaldi 1994).

Taken together results from these paradigms demonstrate that the motor system adapts in response to a perturbation. The internal model framework suggests that this adaptation arises due to differences in predicted and actual sensory feedback (i.e. error). The discrepancy between desired and actual sensory feedback is reduced through adaptation of the inverse (i.e. motor command) and forward (i.e. expected sensory feedback) models, such that the models are updated to accommodate for the environmental perturbations (Krakauer 2009).

3.4 Motor Adaptation via Use-dependent and Operant Learning

Motor adaptation as outlined above, has been proposed to arise due to the updating of an internal model, or in other words is primarily due to “error-based” learning (Tseng et al. 2007; Berniker and Kording 2008; Wei and Kording 2009; Shadmehr et al. 2010; Miall and Wolpert 1996). In addition to error-based learning, it has been suggested that learning can arise due to other mechanisms that are independent of an internal model (i.e. model-free learning). For example, Diedrichsen et al. (2010) suggested that “use-dependent plasticity” is important in motor learning, such that subsequent movements adapt to become more similar to previous movements. In their task, subjects reached to a visually elongated target that could be hit anywhere along its horizontal extent. In order to test for use-dependent learning, the reaching limb was first passively guided by a robot on a trajectory angled 8° rightward or leftward from the midline, which alternated between blocks of trials (Diedrichsen et al. 2010). After the passive trials, subjects were required to actively move to the elongated target, and the researchers found that there was a change in the angle of the active movement that was in the same direction as the preceding block of passive trials (Diedrichsen et al. 2010). From these results, they concluded that use-dependent and error-based learning can both contribute simultaneously to reach adaptation in response to an external perturbation.

Furthermore, Huang et al. (2011) have suggested that an operant process is also involved in motor learning, such that adaptation is reinforced when it is associated with repeated successful attainment of the target in the presence of an external perturbation. They claim that this operant process accounts for a phenomenon in motor adaptation known as "savings," which reflects faster relearning of a given perturbation that has been learned in the past (Huang et al. 2011).

Motor learning may involve a combination of error-based, use-dependent and operant processes. For example, motor learning in response to external perturbations may first occur due to processes associated with fast error-based adaptation, followed by a slower improvement through model-free learning. In other words, the motor system initially updates an internal model fairly quickly based on its judgement of performance errors. Adaptation of the motor command is subsequently reinforced through repetition and practice according to use-dependent and operant mechanisms. Although the contribution of these different processes to motor adaptation is outside of the scope of the present investigation, they are important to keep in mind for future research, as they may play a role in the time course of motor changes.

3.5 Time Course of Motor Adaptation

Large changes in the motor system have been shown to arise quickly. For example, in prism adaptation paradigms, reaching performance returns to near-baseline levels within as few as 15 reach training trials, such that subjects begin to point to the actual, rather than the visually-shifted target (Rossetti et al. 1993; Redding and Wallace 1993, 2000). In virtual-reality paradigms, reach performance returns to near baseline levels within as little as 20 training trials to a single target with a 30° cursor rotation (Krakauer et al. 2000; Neva and Henriques 2013) and within 30 training trials with a 40° cursor rotation (Yamamoto et al. 2006). Adaptation to velocity-dependent force fields has also been shown to occur within approximately 20 reach training trials (Malfait and Ostry 2004; Ostry et al. 2010; Mattar et al. 2011, 2013). However, for the most part, these studies have assessed motor adaptation by measuring changes in performance during training trials in which the perturbation (e.g. visual distortion, velocity-dependent force-field) was still present. Training trials may not be the best measure of motor adaptation, as they may involve strategic processes which lead to quick reductions in error, rather than adaptive processes (Weiner et al. 1983; Pisella et al. 2004). Thus, it is unclear if motor adaptation follows a similar time course when assessed through reach aftereffects, which provide a measure of "true" motor adaptation (Weiner et al. 1983; Pisella et al. 2004; Redding et al. 2005).

According to a number of individuals, motor learning involves two processes. Specifically, Redding and Wallace (1996, 2002, 2003, 2006) have suggested that motor adaptation results from: (1) strategic control and (2) spatial realignment based on results using a prism adaptation paradigm. Strategic control involves a strategic reduction of movement errors in order to quickly improve performance, while spatial realignment involves a more implicit visuomotor remapping which persists into aftereffect trials when the prisms are removed. Along the same line, visuomotor adaptation in a virtual-reality cursor adaptation paradigm has been suggested to involve an explicit component, such that subjects consciously correct their movements to quickly bring the cursor to the target, and an implicit component which involves an error-based updating of an internal forward model (Taylor and Ivry 2011; Taylor et al. 2014). Finally, Smith et al. (2006), using a force-field adaptation paradigm, have also suggested that motor adaptation involves two separate adaptive processes (Shadmehr et al. 2010; Smith et al. 2006). Specifically, one process leads to a rapid reduction in errors in order to quickly improve performance. This process has a very poor rate of retention. On the other hand, a second process responds slowly to errors but retains information well from one trial to the next. The latter slow learning process is associated with long-term motor changes in the effector. This dual process model is able to explain such phenomena in motor learning as savings (i.e. faster relearning of previously learned movements which have been extinguished), anterograde interference (i.e. learning one adaptation adversely affects the learning of an opposite adaptation), and rapid unlearning/de-adaptation (Smith et al. 2006).

While these models differ with respect to their terminology, there appears to be a general consensus within a number of motor learning paradigms that there are two processes involved in motor learning: one fast process which may involve explicit or strategic mechanisms and one slower process which gives rise to implicit adaptation in the motor system. It is unclear what the subtle differences are between these process, and what specific roles they play during adaptation to a visuomotor distortion.

4. Sensory Plasticity

Reach adaptation has been shown to be accompanied by changes in the sensory system. Moreover, it has been suggested that, changes in reaching performance may also be partially due to a recalibration in the proprioceptive sense of hand position, in order to align it with the seen hand position (Craske and Gregg 1966; Cressman and Henriques 2010;

Efstathiou and Held 1964; Harris 1963, 1965; Hay and Pick 1966; Redding and Wallace 1988, 2002, 2003, 2006).

4.1 Sensory Plasticity in Alignment Tasks

Changes in the sensory system were first proposed based on findings using a prism adaptation paradigm. Harris (1963) blindfolded subjects after they adapted their reaches to a distortion introduced through prism goggles. He then had subjects move their unexposed (i.e. un-adapted) hand different distances from their exposed hand. He found that subjects felt that their hands were farther apart than they actually were compared to when they had not undergone prism-induced reach adaptation (Harris 1963). Based on these results, Harris (1963, 1965) argued that the discrepancy between the felt location of the hand and the visual perception of the hand position during prism reaching was resolved through a recalibration of the sense of hand position. Efstathiou and Held, (1964) also tested for a change in position sense following reaches made while wearing prisms by having subjects point to their adapted limb with their unexposed limb (i.e. proprioceptively-guided reaching), and found significantly larger reach errors than control subjects who had not worn prisms. More recently, Simani et al. (2007) used “alignment tasks” to measure sensory recalibration after subjects reached with distorted visual feedback of the hand within a virtual-reality environment. Subjects first reached to visual targets with visual feedback of the hand that was translated relative to actual hand location. Subjects were then asked to actively align the fingertip of their unseen hand either with a visual target or with the other unseen hand before and after reach training trials (Simani et al. 2007). Results indicated that sensory recalibration followed a form of “additivity,” in which the shift in alignment between vision and the exposed hand (reaching with their exposed hand to a visual target) was equal to the vector sum of the shifts between vision and the unexposed hand (reaching with the unexposed hand to a visual target) and the right and left hands (reaching to the unexposed hand with the exposed hand). Taken together, these findings have been suggested to indicate that reach adaptation is partly mediated by a change in the felt position of the hand (i.e. proprioceptive recalibration) (Harris 1963, 1965; Hay and Pick 1966; Redding and Wallace 1988, 1993, 1996**,** 2002; Simani et al. 2007).

However, Cressman and Henriques (2009) have put forth that the reaching tasks used to assess proprioceptive recalibration in both prism and visuomotor distortion paradigms discussed above have not truly isolated and hence, measured changes in “proprioceptive sense” following reach adaptation. Firstly, prisms cause a visual shift of the entire workspace, and therefore adaptation of the motor and sensory systems could be due to a spatial realignment of the workspace rather than recalibration of the sensory system (Henriques and Cressman 2012). Moreover, Hatada et al. (2006) have found that the straight-ahead reaching tasks typically used to assess proprioceptive recalibration involve more than just a shift in the proprioceptive sense. Specifically, they claim that these active tasks use adapted motor commands (i.e. an adapted inverse model), and therefore these tasks do not truly provide a measure of proprioceptive recalibration (Hatada et al. 2006). The alignment tasks used by Simani et al. (2007) are also problematic because they involve active reaching tasks to measure proprioceptive recalibration, potentially allowing subjects to use adapted motor commands. Thus, these studies cannot be used to determine the role of proprioceptive recalibration in in reach adaptation.

4.2 Current Method for Measuring Proprioceptive Recalibration

Cressman and Henriques (2009) recently developed a new, innovative method of measuring hand proprioception (i.e. sense of felt hand position) in order to assess proprioceptive recalibration following visuomotor adaptation within a virtual-reality setting. Their technique avoids the issue of a shift in the visual workspace associated with prism-exposure, and eliminates subjects having to make active reaching movements to proprioceptive targets (Cressman and Henriques 2009, 2010; Cressman et al. 2010; Jones et al. 2010; Salomonczyk et al. 2011).

To measure proprioceptive sense of hand position, Cressman and Henriques (2009) used a two-joint robot manipulandum to place or guide the subject's hand to different places in the workspace (i.e. movements were not "actively" guided by the subject). Once the hand was positioned, subjects were asked whether their unseen hand was left or right of either a visual or proprioceptive reference marker (i.e. body midline). Subjects were not shown the visual reference marker until after the movement was completed, which prevented the subject from using it as a "reaching" target. The position that the hand was placed relative to the reference marker was adjusted over trials using an adaptive staircase algorithm, according to a subject's responses (see FIG. 1A; Kesten 1958; Treutwein 1995). Subjects completed fifty trials in total for each reference marker, with one staircase starting at positions to the left of the reference marker and one staircase starting at positions to the right of the reference marker. A logistic function was then fitted to each subject's responses for a particular reference marker to determine the subject's bias (i.e. proprioceptive estimate of hand position at which the subject thought their hand was aligned with the reference marker), and uncertainty range (the difference between the values at which the probability of the subject responding "left" was 25% and 75%, which provides insight into subjects' precision, see FIG. 1B).

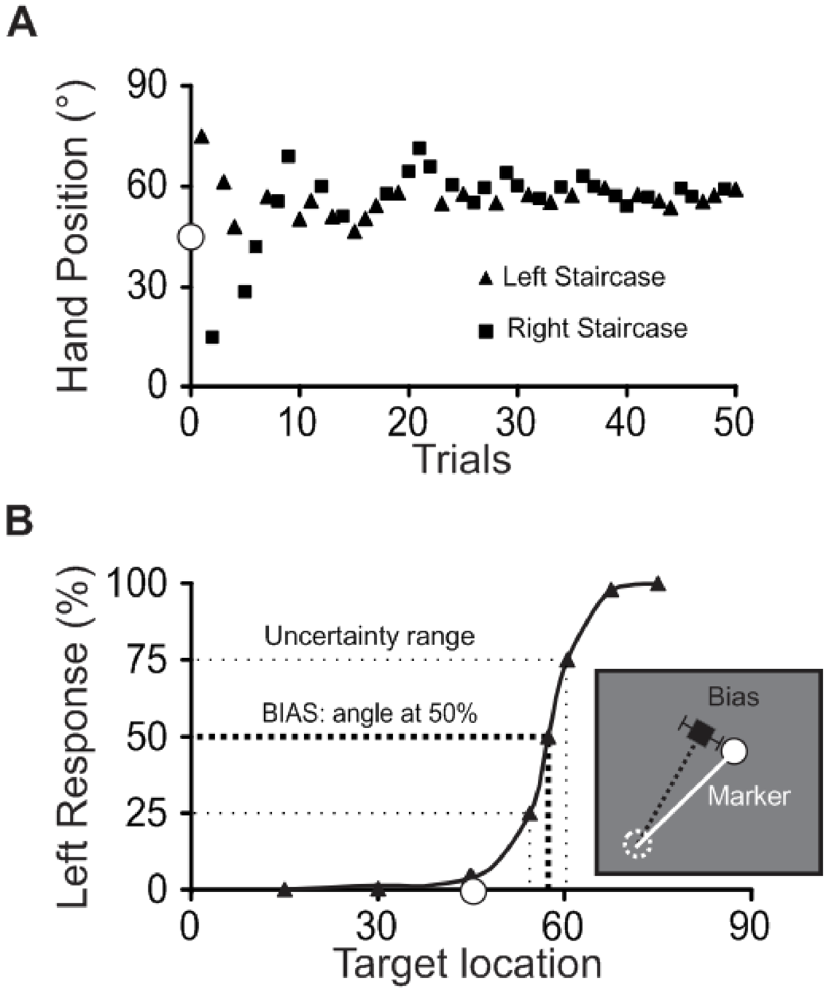

FIG. 1. Proprioceptive estimation task.

An example of the positions to which a subject's hand was moved during the proprioceptive estimate task. The reference marker was located at 45º (shown as an open white circle in (**A**) and (**B**)). (**A**) Hand position was adjusted according to the subject's responses to the question "Is your hand to the right or left of the reference marker?" using an adaptive staircase algorithm. One staircase started 20º to the left of the target (triangles) and one staircase started 20º to the right of the target (squares). **(B)**. A logistic curve was fitted to the subject's responses in order to determine the subject's bias (thick dotted line) and uncertainty range (difference between the thin dotted lines). The inset illustrates the position of the reference marker, the subject's bias (square) located to the left of the reference marker and the uncertainty range (thin lines).

Using the aforementioned technique, Cressman and Henriques (2009) looked at the effect of reaching with a visuomotor distortion on the sense of felt hand-position. Subjects trained to reach to visual targets while seeing a visual cursor that was either rotated or translated to the right of the actual hand position. After reaching with distorted visual feedback of the hand, subjects' estimates of hand position were biased towards the left, which was in the same direction and one third of the magnitude of their adapted movements. Specifically, Cressman and Henriques (2009) found that there was a 6° change in proprioceptive estimates following reach training with a 30° visuomotor rotation, and a 0.8 cm shift following reach training with a 4 cm visuomotor translation. The relative magnitude of changes in proprioceptive estimates was the same across both distortions (about 20% of the reach aftereffects) (Cressman and Henriques, 2009).

In additional work by Henriques and colleagues, proprioceptive recalibration has typically been assessed following reach training with a gradually-introduced visuomotor distortion (Cressman and Henriques 2009; Cressman et al. 2010; Salomonczyk et al. 2011). However, Salomonczyk et al. (2012) tested if abruptly introducing a 30° visuomotor distortion would alter sense of felt hand position. Similar to previous studies, they found that there was about an 8° shift in proprioceptive estimates of hand position following reach training trials. Based on these results, they suggested that proprioceptive recalibration can arise following visuomotor adaptation regardless of the initial magnitude of the error signal (i.e. it is not necessary to gradually introduce a distortion in order for proprioceptive recalibration to occur) (Salomonczyk et al. 2012).

Salomonczyk et al. (2011) have also looked into the effect of prolonged reach training on reach adaptation and proprioceptive recalibration. Specifically, subjects completed three reach training blocks while seeing a cursor that was rotated 30° clockwise from their actual hand position. Each block consisted of 99 reach training trials followed by reach aftereffect and proprioceptive estimate trials in order to assess reach adaptation and proprioceptive recalibration, respectively. While there was evidence of reach adaptation and proprioceptive recalibration following the first block of 99 reach training trials, there was no significant difference in reach aftereffects or proprioceptive recalibration following any of the three training blocks. These results suggest that both proprioceptive recalibration and reach adaptation saturated within 99 trials of reach training (Salomonczyk et al. 2011).

A similar estimation paradigm has also been used by Ostry and colleagues (2010) to assess sense of hand motion following training in a velocity-dependent force-field. In their estimation task, subjects pushed their hand out along a (constrained) force channel. Subjects did not receive any visual feedback with regards to the target or their hand position. After the subject’s hand had moved 15 mm, , the lateral position of the force channel was shifted to the right or to the left and continued on the right or left path until the hand was 20 cm from the start position. After moving 20 cm outward, the subject encountered a robot-generated barrier, and they were asked to provide a “yes” or “no” response to the question “Was your hand moved to the right?” The magnitude of the shift in lateral position of the force channel was adjusted across trials according to the subject’s response, using an adaptive staircase algorithm. Based on their estimation task, Ostry and colleagues (Ostry et al. 2010; Mattar et al. 2011, 2013; Vahdat et al. 2011, 2014) have reported shifts in sense of limb motion of up to 33% of the magnitude of reach adaptation (i.e. about 2-3 mm). They have also found that sensory changes are similar when a force-field is introduced gradually or abruptly, and that these changes persisted for 24 hours following training (Ostry et al. 2010).

5. Relationship between Motor and Sensory Plasticity

Although a vast number of studies have shown very robust changes in both the motor and sensory systems following training with distorted visual feedback of the hand and in a velocity-dependent force-field, the mechanisms underlying changes within these two systems is not fully understood. Recent research has found no correlation between proprioceptive recalibration and reach adaptation, as well as differences in how these two processes generalize to novel targets, leading to the suggestion that sensory and motor plasticity arise due to different processes (Cressman and Henriques 2009, 2010; Henriques and Cressman 2012; Salomonczyk et al. 2011).

The idea that reach adaptation and proprioceptive recalibration are independent processes is supported by studies that have found that visuomotor adaptation is still possible in deafferented patients (i.e. patients with no proprioceptive feedback), and when proprioceptive feedback is degraded with agonist-antagonist muscle vibration (Bernier et al. 2006; Bock and Thomas 2011; Ingram et al. 2000). Ingram et al. (2000) compared reach adaptation between a deafferented subject and a healthy control group of subjects after they reached while wearing prism goggles. Their findings demonstrated that the deafferented subject’s reaches were adapted to a similar extent as healthy controls. Similarly, Bernier et al. (2006) found that there was no difference in rate or extent of reach adaptation between a deafferented subject and healthy controls following training with a rotated cursor (i.e. as measured during aftereffect trials). Thus, they suggested that proprioception is not necessary for reach adaptation to occur. In other words, an internal model can still be updated in response to an environmental perturbation, even in the absence of proprioceptive input (Bernier et al. 2006). Finally, Bock and Thomas (2011) performed an experiment in which healthy subjects adapted to a visual distortion while receiving agonist-antagonist muscle vibration at the wrist, elbow, and shoulder. Results were compared to a control group that performed the same reaching movements in the absence of any muscle vibration, and the researchers found that vibration did not modify adaptation or lead to a reduction in aftereffects following the distortion (Bock and Thomas 2011).

Changes in the sensory system have also been shown to arise in the absence of motor changes in cerebellar patients. For example, Block and Bastian (2012) found that individuals with cerebellar damage were capable of sensory realignment of their hand (i.e. realignment of proprioceptive estimates of hand position to more closely match the visual estimates) in the absence of any motor adaptation. Additionally, Synofzik and colleagues (2006, 2008) found that patients with cerebellar damage and healthy controls were able to predict the sensory consequences of their movements, despite the patients' impaired ability to adapt to a visuomotor distortion. Overall, these findings suggest that reach adaptation and proprioceptive recalibration may be independent, such that they may be driven by different error signals. When proprioceptive information is available, it may be that the role of proprioceptive recalibration is to reduce the conflict between visual and proprioceptive information (i.e. cross-sensory error signal; Cressman and Henriques 2012), which may not be necessary for the adaptive processes that bring about reach aftereffects.

The proposed independence between reach adaptation and proprioceptive recalibration fits within the source-estimation model of Berniker and Kording (2008). This model claims that reach adaptation is dependent on how/where the central nervous system has attributed the source of the error. In other words, adaptation of the internal model representing a movement would differ depending on whether errors are attributed to changes in the limb (e.g. fatigue) or changes in the environment (e.g. external perturbations). Changes in proprioceptive estimates of hand position may arise due to errors being attributed to the limb itself, while further changes in movement may be due to an adapted internal model that represents changes in the environment (Cressman and Henriques 2012). Furthermore, these different error signals, and hence independent reach adaptation and proprioceptive recalibration, may arise in different areas of the brain. A recent review article by Shadmehr and Krakauer (2008) proposed that the cerebellum and parietal cortex have different roles in their involvement in motor learning. The cerebellum is thought to be involved in forming an internal model that predicts the sensory consequences of a motor command and correcting these motor commands through sensory feedback. The parietal cortex, on the other hand, is involved in integrating the predicted visual and proprioceptive feedback with sensory feedback in order to estimate the current state of the body and the environment. Proprioceptive changes involve an adaptation in the body's state estimate, and therefore may occur within the parietal cortex, while adapted motor commands directly affect the internal model of a movement, which would most likely occur within the cerebellum (Cressman and Henriques 2012).

In contrast to the proposed independence of reach adaptation and proprioceptive recalibration, Ostry and colleagues have suggested that proprioceptive recalibration is dependent on reach adaptation (Ostry et al. 2010; Mattar et al. 2013). Furthermore, they indicate that the results of Matter et al. (2013) support their proposal. Mattar et al. (2013) looked at the time course of motor and sensory changes during adaptation within a velocity-dependent force-field and found that motor changes arise much earlier than sensory changes. Based on these results it was suggested that motor adaptation likely drives changes in the sensory system. However, more recent work from the same lab has shown that completing perceptual training (i.e. receiving feedback as to the correctness of responses regarding hand motion estimates) improved subsequent motor adaptation (Darainy et al. 2013), and led to changes in frontal motor areas in the brain (Vahdat et al. 2014), which may indicate that sensory changes play a role in motor adaptation.

6. Specific Objectives

In the current research we will look at the time-course of proprioceptive recalibration while subjects train with a visuomotor distortion. As well, we will investigate the relationship between proprioceptive recalibration and reach adaptation by comparing their changes over time. Mattar et al. (2013) recently explored the relationship between motor and sensory plasticity by looking at the time-course of both motor adaptation and sensory recalibration within a velocity-dependent force-field paradigm. Specifically, they had subjects perform perceptual tests across six blocks of reach training trials, in order to determine how the perceptual boundary between left and right (i.e. the “felt” motion of the reaching hand) changed with changes in movement curvature. They found that reach adaptation began earlier and occurred at a much greater rate during the initial trials, as compared to sensory recalibration. They argued that this was because motor learning drives plasticity in the sensory system, and therefore motor adaptation must occur earlier, and with a greater rate of increase than sensory recalibration (Mattar et al. 2013).

While the work by Mattar et al. (2013) provides initial insight into the time-course of sensory recalibration, it is difficult to interpret their results in light of proprioceptive recalibration. Mattar et al. (2013) did not include a visuomotor distortion, and therefore did not introduce a discrepancy between proprioceptive and visual estimates of hand location (i.e. cross-sensory error signal; Sarlegna and Bernier 2010). Thus, one would not expect proprioception to be recalibrated. Furthermore, their “perceptual tests” looked to determine changes in perceived motion of the hand (i.e. subjects indicated if they felt that their hands were deviated to the left or right during a straight-ahead movement), which employs different sensory signals than those used to judge felt hand position. In addition, it is difficult to compare their changes in the sensory system to the changes they saw in the motor system over time as Mattar et al. (2013) only had subjects complete one block of aftereffect trials at the very end of their experiment. In other words, they did not perform separate aftereffect trials at different time points in the experiment. Instead, they used changes in movement curvature during their reach training trials as a measure of motor adaptation. As outlined above (Section 3.5), these changes in reaches do not provide true insight into motor adaptation and hence do not allow one to draw conclusions regarding the relationship between the time-course of proprioceptive recalibration and reach adaptation.

The proposed research will look at proprioceptive recalibration and reach adaptation following exposure to an abruptly introduced 30° counter clockwise visual rotation (i.e. visuomotor distortion). The experiment will include sequential blocks of a varying number of reach training trials and each block of trials will be followed by an aftereffect task and proprioceptive estimate task (as described above in Section 4.2) to determine reach adaptation and proprioceptive recalibration respectively, relative to baseline measures. Changes in the sensory and motor systems will therefore be analyzed and compared over trials, which will provide insight into the relationship between the processes that underline proprioceptive recalibration and reach adaptation. We hypothesize that reach aftereffects will increase rapidly within the first 20 trials, before reaching a plateau at 18°, or approximately

60% of the visuomotor distortion introduced. Furthermore, we hypothesize that changes in proprioceptive estimates of hand position will increase more slowly within the first 100 trials to about 6°, or approximately 20% of the visuomotor distortion introduced. Moreover, it is expected that these slow changes in the proprioceptive estimates of hand position will still occur even after changes in reach aftereffects have plateaued, suggesting that reach adaptation does not necessarily drive proprioceptive recalibration, and that changes in the motor and sensory systems while reaching with a visuomotor distortion are due to separate, independent processes.

Chapter II: Research Article

Distinct Time Courses for Proprioceptive Recalibration and Reach Adaptation

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Abstract

When subjects reach in a novel visuomotor environment (e.g., while viewing a cursor representing their hand that is rotated from their hand's actual position), they typically adjust their movements (i.e., bring the cursor to the target), thus reducing reaching errors. Additionally, research has shown that reaching with altered visual feedback of the hand results in sensory changes, such that proprioceptive estimates of hand position are shifted in the direction of the visual feedback experienced (Cressman and Henriques 2009). This study looked to establish the time course of sensory changes. Additionally, the time courses of sensory and motor changes were compared to determine the relationship between their underlying processes. Subjects reached to a single visual target while seeing a cursor that was either aligned with their hand position (50 trials), or rotated 30° clockwise relative to their hand (150 trials). Reach errors and proprioceptive estimates of felt hand position were assessed following the aligned reach training trials and at 7 different times during the rotated reach training trials by having subjects reach to the target without visual feedback, and provide estimates of their hand relative to a visual reference marker respectively. Results revealed a shift in proprioceptive estimates throughout the rotated reach training trials; however, significant sensory changes were not observed until after 70 trials. In contrast, results showed a greater change in reaches after a limited number of reach training trials with the rotated cursor. These findings suggest that reach adaptation and proprioceptive recalibration arise due to separate processes.

1. Introduction

When performing goal-directed reaches to objects in the environment, the central nervous system transforms visual and proprioceptive information about hand and target location into appropriate motor commands to move the hand to the desired location (Jeannerod 1988; Flanders et al. 1992; Desmurget et al. 1998). Although the visual and proprioceptive signals that indicate limb position are usually aligned, situations may arise in which the position at which one sees their hand differs from the position at which they feel their hand. When these signals conflict and one is reaching to a visual target, one tends to rely more on the visual estimate of the limb, rather than the actual or ‘felt’ position. Thus, movements are corrected based on the visual estimate, such that a new mapping between visual input and motor output is learned (i.e., visuomotor adaptation). For example, if subjects train to reach to a visual target while viewing a cursor that is distorted (e.g., rotated or translated) relative to their hand’s actual position, they initially produce deviated movements such that the cursor does not achieve the target. However, subjects rapidly learn to reach such that the cursor moves to the target (Krakauer et al. 1999; Sainburg and Wang 2002; Simani et al. 2007; Cressman and Henriques 2009). Moreover, when subjects reach in the absence of visual feedback, they continue to produce movements in the direction opposite to the visual distortion experienced. These persistent deviations in their movements reflect plastic changes (i.e., adaptation) in the motor system, and are referred to as reach aftereffects (Martin et al. 1996; Krakauer et al. 1999, 2000; Baraduc and Wolpert 2002; Buch et al. 2003). Similar findings have been reported in experiments which introduce distorted visual feedback of the hand using laterally-displacing prism goggles (i.e., subjects reach to targets while wearing goggles that produce a lateral shift in the entire visual field;

Von Helmholtz 1909/1962; Harris 1963, 1965; Redding and Wallace 1993, 2002, 2003) or perturb the dynamics of the hand's movement during its trajectory (e.g., subjects reach in a force-field with velocity-dependent loads applied to the reaching limb during movement), pushing the hand off its initial course (Shadmehr and Mussa-Ivaldi 1994; Scheidt et al. 2001; Ostry et al. 2010; Mattar et al. 2011, 2013; Vahdat et al. 2011, 2014).

In addition to adaptation in the motor system, reaching with distorted visual feedback of the hand also results in changes to the sensory system. In particular, proprioceptive sense of felt hand position is recalibrated and shifted to match the visual representation of the hand experienced during the reach training trials (Efstathiou and Held 1964; Harris 1963, 1965; Craske and Gregg 1966; Hay and Pick 1966; Redding and Wallace 1988, 2002, 2003, 2006; Cressman and Henriques 2009). To assess sense of felt hand position after reaching in a virtual reality environment, Cressman and Henriques (2009) have devised a unique method that does not involve any goal-directed movements, such that subjects either move their hand out along a constrained path or have their hand moved out by a robot manipulandum to the goal location. Subjects then indicate the position of their hand relative to a visual or proprioceptive reference marker. Using this task, it has been demonstrated that, in general, subjects shift the position at which they feel their hand is aligned with a reference marker by about 20% of the visuomotor distortion introduced or 33% of the magnitude of motor adaptation (e.g., about 6° when a 30° hand-cursor distortion is introduced). This shift is in the same direction as the visual feedback experienced in the reach training trials, suggesting that it results from a recalibration of the proprioceptive sense of hand position in order to align it with the visual representation of the hand. Similar changes in felt hand position have been found across a wide range of experimental conditions, including: training hand (left or right), distortion type (rotated or translated cursor), distortion presentation (gradual or abrupt), reference marker (visual or proprioceptive), and age (young and older adults) (Cressman and Henriques 2009, 2010; Cressman et al. 2010; Salomonczyk et al. 2011, 2012). Using a similar sensory estimation task (i.e., subjects indicated if they felt their hand motion was deviated to the right or left during a straight ahead movement), Ostry and colleagues (Ostry et al. 2010; Mattar et al. 2011, 2013) have reported changes in felt limb motion following adaptation to a velocity-dependent force-field. In particular, they found shifts in sense of limb motion of approximately 33% of the magnitude of motor adaptation (i.e., about 2-3 mm).

While it is well established that proprioceptive recalibration arises after reaching with distorted visual feedback of the hand, it is unclear how quickly these changes arise in the sensory system and how quickly they arise relative to reach adaptation. Previous work has shown that motor changes arise quickly across motor adaptation paradigms. For example, in prism adaptation paradigms, reaching performance returns to near-baseline levels within as few as 15 reach training trials, such that subjects begin to point to the actual, rather than the visually-shifted target (Rossetti et al. 1993; Redding and Wallace 1993, 2000, 2006). Similarly, adaptation to visuomotor distortions and velocity-dependent force-fields in virtual reality environments has been shown to occur within approximately 20 reach training trials when reaching to a single target (Krakauer et al. 2000; Ostry et al. 2010; Mattar et al. 2011, 2013). However, while these previous studies have shown quick changes in motor adaptation, they typically determined the time course of motor adaptation by examining changes in performance during trials in which the perturbation was still present. It is unclear if motor adaptation follows a similar time course when assessed through reach aftereffect trials (i.e., trials in which subjects perform reaching movements in the absence of any perturbation), which have been suggested to assess implicit adaptive motor processes as opposed to strategic processes and hence provide a more accurate measure of reach adaptation (Weiner et al. 1983; Pisella et al. 2004; Redding et al. 2005).

The current study looked to first establish the time course of proprioceptive recalibration and reach adaptation (as assessed through reach aftereffect trials) while training to reach with distorted visual feedback of the hand in a virtual reality environment. Mattar et al. (2013) recently looked at the time courses of sensory and motor changes while subjects trained to reach in a velocity-dependent force-field. Specifically, they had subjects perform their sensory estimation task 6 times during reach training trials in a velocity-dependent force-field. They found that reach adaptation began earlier and occurred at a much greater rate during the initial trials, as compared to sensory changes. While these results provide initial insight into the time course of sensory changes in a motor learning paradigm, they may not be indicative of sensory changes following training with distorted visual feedback of the hand. Sensory changes following training within force-field paradigms are much smaller in magnitude than those typically seen in visuomotor adaptation studies, perhaps because reaching with a visuomotor distortion involves a discrepancy between proprioceptive and visual feedback, whereas force-field adaptation does not (Sarlegna and Bernier 2010). Therefore changes in felt hand position may occur earlier while training with a visuomotor distortion compared to a velocity-dependent force-field. Moreover, the study by Mattar et al. (2013) does not allow one to draw conclusions about the time course of reach adaptation in the absence of the perturbation, as Ostry and colleagues' (Ostry et al. 2010; Mattar et al. 2011, 2013) measure of motor learning was based on changes in movement curvature during their reach training trials, and not on aftereffect measures. As stated earlier, changes in performance during training may involve strategic rather than implicit adaptive processes, and therefore may not reflect a measure of true motor adaptation (Weiner et al. 1983; Pisella et al. 2004; Redding et al. 2005). The current study used aftereffect trials to determine the time course of reach adaptation.

After establishing the time course of proprioceptive recalibration and reach adaptation, we then looked to determine the relationship between these two processes. From previous work, it is clear that proprioceptive recalibration and reach adaptation of the trained hand arise together under experimental conditions (Cressman and Henriques 2009, 2010; Cressman et al. 2010; Salomonczyk et al. 2012, 2013; Mostafa et al. 2014**a**, 2014**b**; Ostry et al. 2010; Mattar et al. 2011, 2013). However, it has been suggested that they may be separate, independent processes. Specifically, it has been shown that proprioceptive recalibration is not correlated with reach adaptation (Cressman and Henriques 2009, 2010). Furthermore, Mostafa et al. (2014**a**) have demonstrated that these two processes show different patterns of generalization across target distances, such that proprioceptive recalibration generalizes to a lesser extent at farther distances as compared to reach adaptation. Reach adaptation has also been shown to transfer from the trained to the untrained limb while changes in felt hand position are only present in the trained hand (Mostafa et al. 2014**b**). Moreover, recent work has found that changes in the predicted sensory consequences of one's movements occur both in the absence and presence of reach adaptation in patients with cerebellar damage (Synofzik et al. 2006, 2008; Block and Bastian 2012; Izawa et al. 2012). Thus, taken together, these experiments suggest that sensory and motor changes may arise due to distinct neural processes.

To establish the time course of proprioceptive recalibration and its relation to changes in reach adaptation over time, we performed a similar experiment to that of Mattar et al. (2013). Specifically, subjects trained to reach to a visual target with rotated visual feedback of the hand (i.e., a 30° clockwise (CW) cursor rotation). We measured both proprioceptive recalibration and reach adaptation at seven time-points throughout the training trials. We then assessed and compared the time courses and rates of change of these two processes. We hypothesized that changes in felt hand position would arise slowly over the course of the reach training trials, because the sensory system has been shown to be robust and resistant to change (Mattar et al. 2013). Additionally, we hypothesized that reach adaptation would occur much earlier than proprioceptive recalibration and hence would have a greater rate of change.

2. Methods

2.1 Subjects

20 healthy, right-handed university students (5 female, 15 male; mean age = 21.2 years, SD 2.2 years) volunteered to participate in the following experiment. All subjects were verbally screened for history of sensory, neurological and motor dysfunction. Subjects had normal or corrected-to-normal vision and were right-handed according to their responses on the modified version of the Edinburgh handedness inventory (mean score = 84%, SD 15%; see Appendix A, Oldfield 1971).

All subjects were naïve to the hypotheses, and had never performed prior experiments that involved reaching with distorted visual feedback of the hand. This study was approved by the University of Ottawa's research ethics board (see Appendix B for ethics certificate), and all subjects provided informed consent before taking part in the experiment (see Appendix C).

2.2 General Experimental Setup

A side-view of the experiment is illustrated in FIG. 2A. Subjects were seated in a height-adjustable chair in front of the experimental apparatus. The chair’s height and distance from the apparatus were adjusted to ensure that subjects could comfortably see and reach to the visual target. Once adjusted, the chair remained in the same position for the entirety of the experiment. Subjects grasped the vertical handle of a two-joint robot manipulandum (BKIN technologies) with their right hand, and made reaching movements to a visual target within a 70 cm by 36 cm workspace. Subjects started with their hand at a home position (white circle; 1 cm in diameter), which was aligned with their midline and was approximately 20 cm in front of their chests. Visual stimuli were projected from a downward facing computer monitor (EzSign model 47LD452B; refresh rate: 60 Hz; LG, Seoul, South Korea) onto a reflective surface that was in the same horizontal plane as the robot handle. The visual target (blue circle; 2 cm in diameter) appeared 15 cm and 45° CW from the home position relative to straight ahead. The room was dimmed and subjects were prevented from seeing their hands by a black cloth that was draped between the apparatus and their shoulders.

2.3 Procedure

The experiment was divided into 8 testing blocks. A breakdown of each testing block can be found in FIG. 3. Subjects completed the testing blocks in two consecutive testing sessions; they completed the first block in the first testing session and the next seven blocks in the second testing session. Subjects took an extended break between the two sessions, ranging from 15 minutes to several days. Within each block subjects performed three experimental tasks, which are outlined in more detail below. The blocks included 50 (Block 1), 5 (Block 2), 5 (Block 3), 10 (Block 4), 20 (Block 5), 30 (Block 6), 30 (Block 7) and 50 (Block 8) reach training trials. Following the reach training trials, subjects completed 6 reach aftereffect trials (Time 1) followed by 50 proprioceptive estimate trials, and then an additional 6 reach aftereffect trials (Time 2). Thus, each subject completed a total of 200 reach training trials, 96 reach aftereffects trials, and 400 proprioceptive estimate trials over the course of the experiment.

2.3.1 REACH TRAINING TASK

The reach training trials involved subjects reaching to a single visual target. Subjects grasped the robot handle with a comfortable but firm grip. After maintaining the hand at the home position for 500 ms, the visual target appeared 15 cm and 45° CW from the home position relative to straight ahead, so that it could be easily achieved. It is important to note that the home position was not displayed during these trials. Subjects were instructed to move as quickly and accurately as possible to the target while holding onto the robot handle. Visual feedback of the unseen hand was represented by a cursor (green circle; 1 cm in diameter). This cursor appeared as soon as the robot handle moved 7 cm outward from the home position, corresponding to a position where subjects tended to achieve peak velocity. In Block 1, the cursor was aligned with the actual position of the hand, and in all remaining blocks (Blocks 2 – 8), the cursor was rotated 30° CW relative to the hand (see FIG. 2B). The reach was considered complete once the center of the green cursor had moved to within 0.5 cm of the target’s center. At this time, both the target and cursor were removed and the robot locked to a grooved path. This grooved path allowed subjects to guide their hand back to the home position via a direct linear route in the absence of visual feedback. If subjects attempted to move outside of the grooved path, a very small resistance force [proportional to the depth of penetration with a stiffness of 2 N/mm and a viscous damping of 5 N/(mm/s)] was generated perpendicular to the grooved wall (Henriques and Soechting, 2003). The position of the robot manipulandum was recorded throughout all reaching tasks at a sampling rate of 1000 Hz and a spatial accuracy of 0.1 mm.

2.3.2 REACH AFTEREFFECTS TASK

The reach aftereffects trials were used to determine how subjects reached (i.e. the extent of reach adaptation) as a result of the preceding reach training trials. Similar to the reach training task, subjects grasped the robot handle with a comfortable but firm grip. After maintaining their hand at the unseen home position for 500 ms, the visual target appeared 15 cm and 45° CW from the home position relative to straight ahead. Subjects were instructed to move as quickly and accurately as possible to the target while holding onto the robot handle. However, in this task, no visual feedback (i.e. no cursor) representing the hand was provided to subjects. Once the subjects had finished their reach (i.e. had maintained a final hand position for 1000 ms), the visual target disappeared and the trial was considered complete. The subject’s hand was then guided back to the home position by a linear grooved path.

2.3.3 PROPRIOCEPTIVE ESTIMATION TASK

The proprioceptive estimate trials were used to determine the position at which subjects perceived their unseen hand was aligned with a visual reference marker. This task began with subjects grasping the robot handle at the home position. The position of the hand at the home position was indicated by displaying a white circle (1 cm diameter) directly above the robot for 500 ms. After 500 ms, the home position disappeared and the subject's hand was guided by the robot to a position somewhere along the white dotted line seen in FIG. 2C (i.e. passive movement, note that the dotted white line in FIG. 2C was not visible to subjects). The hand was moved by the robot according to a bell-shaped velocity profile, and the movement was 1 second in duration. The duration of the passive movement was based on average active movement times to the same target achieved by 3 subjects in a pilot study. Once the subject's hand reached its final position, a visual reference marker (yellow circle; 1 cm in diameter) appeared 15 cm and 45° CW from the home position relative to straight ahead (the same position as the visual target subjects reached to in the reach training task and reach aftereffects task). Subjects then made a two-alternative forced-choice judgement about the position of their hand, indicating whether they felt that their hand was to the left or to the right of the visual reference marker. There were no time constraints during this task, and subjects were encouraged to take as much time as they needed before giving their answer verbally to the experimenter. Once their response had been entered, the reference marker disappeared and the robot moved the hand back to the home position along the same route, with a 1 second movement duration.

2.4 Data Analyses

2.4.1 PROPRIOCEPTIVE ESTIMATES OF HAND POSITION

To examine the time course of proprioceptive recalibration, we first determined the locations at which subjects felt their hands were aligned with a visual reference marker in each of the training blocks shown in FIG. 3. This location was determined by fitting a logistic function to each subject's responses during the corresponding proprioceptive estimation trials completed within the block. The point at which subjects responded "left"

50% of the time (i.e., responded “left” and “right” equally often) represents their proprioceptive bias and provides a measure of subjects’ accuracy of alignment of the hand and reference marker (i.e., the point at which subjects felt their hand was aligned with the reference marker). Additionally, we determined subjects’ uncertainty by finding the difference between the values at which the probability of responding “left” was 25% and 75%, which provides insight into subjects’ precision.

Biases and uncertainty ranges were analyzed in an 8 Block repeated-measures analysis of variance (RM ANOVA). Differences with a probability of less than 0.05 were considered significant and indicated that biases or uncertainty changed across block. Bonferroni post-hoc tests were administered to find the locus of these differences for pre-planned comparisons (alpha = 0.05).

2.4.2 REACH ADAPTATION

We determined angular reach errors at peak velocity (PV) in the reach training trials in order to determine if subjects showed rapid changes in reaches when the distortion was still present as has been shown previously. As well, we analyzed angular reach errors at both PV and movement endpoint (EP) in the no-cursor reach aftereffect trials to measure the time course of motor changes after training with a rotated cursor. PV angular reach errors were defined as the angular difference between a movement vector (from the home position to peak velocity) and a reference vector (joining the home position and the target). EP angular reach errors were defined as the angular difference between a movement vector (from the home position to movement endpoint) and a reference vector (joining the home position and the target).

To illustrate performance in the reach training trials, average angular error at PV for each reach training trial with the rotated cursor is plotted in FIG. 4A relative to average performance across the aligned training trials. As shown previously, we see that subjects quickly adapted to the cursor distortion within a few trials when reaching with the distortion (Krakauer et al. 2000). Given that reach aftereffects have been suggested to represent implicit motor adaptation, the following analyses are based on the no-cursor reach aftereffect trials. Performance in the training trials is shown for comparison purposes only.

Average errors at EP and PV for each set of 6 reach aftereffect trials (i.e. trials completed at Time 1 or Time 2 within each block) were determined for each subject. To determine if these average errors in the aftereffect trials at EP and PV followed a similar pattern across blocks, we first performed a 2 Error Score (EP vs. PV) x 8 Block x 2 Time (Time 1 vs. Time 2 relative to the proprioceptive estimate trials) RM ANOVA. A similar pattern of changes in reaching errors was seen for reach errors at PV and EP following training with a rotated cursor, such that ANOVA revealed no interaction between Error Score and Block [$F_{(7, 133)} = 1.233$, $P > 0.05$] or Error Score and Time [$F_{(1, 19)} = 0.063$, $P > 0.05$], as seen in FIG. 4B. Given that errors at peak velocity and movement endpoint reflect similar changes in reaches, additional analyses were based on movement endpoint angular reach error as movement endpoint errors (i) were smaller than errors at peak velocity [$F_{(1, 19)} = 4.604$, $P < 0.05$], and therefore provide a more conservative error to compare with the smaller changes in proprioceptive biases, (ii) avoid any angular deviations that arise during curved movements, and (iii) are determined at a similar location as the proprioceptive biases.

We analyzed changes in EP angular reach errors in an 8 Block x 2 Time RM ANOVA. Differences with a probability of less than 0.05 were considered significant.

Bonferroni post-hoc tests were administered to find the locus of these differences for pre-planned comparisons (alpha = 0.05).

2.4.3 RELATIONSHIP BETWEEN PROPRICOEPTIVE RECALIBRATION AND REACH ADAPTATION

To examine the relationship between proprioceptive recalibration and reach adaptation, we compared average EP angular reach errors in the reach aftereffect trials at Time 1 and Time 2 to proprioceptive estimates using a 2 Measure (Reach Error at Time 1 or Time 2 vs. Proprioceptive Bias) x 8 Block RM ANOVA.

To find differences in the rates of change for reach aftereffects (at Time 1 and Time 2) and proprioceptive biases, we fit exponential curves to the data using the curve fitting toolbox in MATLAB. The curves took the form of the following exponential function as used by Mattar et al. (2013):

$$\hat{y} = a \cdot [1 - (1 - b)^{x} + c] \qquad (1)$$

such that y represents angular error, x represents the number of reach training trials completed just prior to the no-cursor reach aftereffect trials or proprioceptive estimates, a represents the scale of the change, b represents the rate of change, and c represents the vertical offset of the function. Rates of change were considered significantly different if their 95% confidence intervals did not overlap. We also fit exponential curves to the reach training trials when (i) all reach training trials were included and (ii) when the first reach training trial of each set was removed, given the decay in reach errors seen at the start of each set of reach training trials or what Izawa and colleagues (2012) referred to as forgetting. In these analyses x represents the reach training trial number.

2.5 Control Experiment

In the main experiment described above, subjects performed a set of reach aftereffect trials before and after the proprioceptive estimation trials within each block. The two sets of aftereffect trials were completed to see if there was any change in reach errors after completing the proprioceptive estimation trials. As seen below, reach aftereffects decreased following the proprioceptive estimation trials. It is unclear if this decrease in reach aftereffects was due to the proprioceptive estimation task itself, or the interval of time between sets of reach aftereffect trials. Thus, we performed a separate control study involving seven subjects (4 female, 3 male; mean age = 20.14 years, SD = 0.38 years). This study was identical to the main experiment except subjects did not perform proprioceptive estimation trials, but instead sat quietly holding on to the robot handle for 5 minutes between sets of reach aftereffect trials (the average time that it took subjects to complete a set of 50 proprioceptive estimation trials in the main experiment). To assess differences between the experiments, we performed a 2 Time (Time 1 vs. Time 2) x 8 Block RM ANOVA, with Experiment as a between-subjects factor.

3. Results

3.1 Time Course of Proprioceptive Recalibration

Proprioceptive estimates immediately following aligned reach training revealed an initial bias, such that subjects felt their hands were at the reference marker when they were shifted approximately 9.6° left of the reference marker. As seen in FIG. 5, proprioceptive estimates then shifted further to the left of this baseline estimate after training with rotated visual feedback of the hand. In fact, estimates shifted 8.8° more left of the baseline estimates after 150 reach training trials, as seen in FIG. 6A. In accordance with these observations, ANOVA revealed a significant effect of Block [$F_{(7, 133)} = 7.513$, $P < 0.001$], indicating that the position at which subjects felt that their hand was aligned with the visual reference marker changed over the course of the reach training. In addition to demonstrating a change in proprioceptive bias over reach training trials, FIG. 5 also illustrates that this shift arose gradually over the course of the experiment, as the magnitude of the shift did not differ significantly between consecutive blocks. Moreover, as shown in FIG. 6B, there were very little changes in proprioceptive bias after only 5 rotated training trials (shift in proprioceptive estimate = 0.65°, n.s.). However, post hoc analyses revealed that proprioceptive bias was significantly different from performance following the aligned training trials by Block 6, or following 70 rotated training trials. These results suggest that proprioceptive recalibration arises gradually over the course of reach training trials.

Subjects' levels of precision in estimating the location of their unseen hand were comparable after the aligned reach training trials and after all sets of rotated reach training trials [$F_{(7, 133)} = 1.460$, $P > 0.05$]. The average uncertainty range across all blocks was 9°.

3.2 Time Course of Reach Adaptation

Mean angular reach errors at PV for the reach training trials are shown in FIG. 4A and mean angular reach errors in the no-cursor reach aftereffect trials are displayed in FIG. 4B following the aligned cursor reach training trials, and at the end of each of the 7 sets of rotated reach training trials. Specifically, in FIG. 4B, angular reach errors at movement endpoint (EP) are displayed before and after the proprioceptive estimation trials (at Time 1 and Time 2, respectively). From the reach training trials in FIG. 4A we see that subjects quickly altered their movements when the distortion was present, but that performance decayed at the start of each set of reach training trials, following the proprioceptive estimates and aftereffect trials. From FIG. 4B, we see that subjects reached such that their hand was to the left of the target after training with the aligned cursor (mean EP reach error = 3.1°, SD = 0.9°). Following training with rotated hand-cursor feedback, reach errors increased rapidly, such that subjects aimed significantly more to the left of the target after training with a rotated cursor compared to an aligned cursor [$F_{(7, 133)} = 63.718$, $P < 0.001$]. Specifically, the total change in EP reach errors following 150 rotated reach training trials relative to baseline at Time 1 was 22.3° and at Time 2 was 14.7°, as seen in FIG 6A. Analysis also revealed a significant interaction between Block and Time [$F_{(7, 133)} = 17.383$, $p < 0.001$]. Thus, we will consider changes in reaching performance at both Time 1 and Time 2 separately when discussing the remainder of our results.

As discussed above and shown in FIG. 4 and 6, reaching errors at Time 1 and Time 2 increased significantly over Block. ANOVA revealed a main effect of Block for errors at Time 1 [$F_{(7, 133)} = 67.752$, $p < 0.001$] and Time 2 [$F_{(7, 133)} = 36.952$, $p < 0.01$]. Post-hoc analyses revealed that even though errors were smaller at Time 2 compared to Time 1, angular reach errors at Time 1 and Time 2 were both significantly greater relative to their respective baselines following Block 2 (i.e., after 5 reach training trials with the rotated hand-cursor feedback), indicating that changes in the motor system occurred very rapidly (see FIG. 6B). The time course of Time 1 angular reach errors showed a great initial increase which then plateaued at Block 5 (i.e., after 40 rotated cursor trials), such that there were no further significant changes across consecutive blocks. The time course of changes in angular reach errors at Time 2 showed a smaller initial increase, with gradual increases until errors saturated following Block 6 (i.e., after 70 rotated cursor trials) and there were no more significant changes between consecutive blocks.

3.3 Comparison of Proprioceptive Recalibration and Reach Adaptation

Reaching errors at Time 1 and Time 2 compared to proprioceptive estimates across blocks of trials revealed significant interactions (Time 1: [$F_{(7, 133)} = 13.594$, $p < 0.001$] and Time 2: [$F_{(7, 133)} = 3.161$, $p < 0.01$]), suggesting that changes in reaches followed a different time course compared to changes in proprioceptive estimates. The changes over time are shown by the exponential curves fitted to the data (see Equation 1) in FIG. 7. Changes in reach error at Time 1 and Time 2 over blocks of training trials, as well as proprioceptive bias were captured well by exponential curves, with r^2 values indicating that the curves accounted for 95.80% (Reach errors at Time 1), 97.07% (Reach errors at Time 2), and 98.70% (Proprioceptive biases) of the variance of the curves. From FIG. 7, it is evident that reach adaptation assessed at both Time 1 and Time 2 arose much earlier than proprioceptive recalibration. This early increase in reach adaptation is reflected in the associated large rates of change (or slope) shown in FIG. 8 (Time 1 rate of change = 0.25 and Time 2 rate of change = 0.09). In contrast, proprioceptive estimates did not change as quickly (rate of change = 0.02) and the 95% confidence intervals for the rates of change of reach adaptation do not overlap with the confidence interval for the rate of change of the proprioceptive bias. The rate of change of reach errors in the reach training trials is also displayed in FIG. 8 for comparison purposes when an exponential curve was fitted to (i) all reach training trials (rate of change = 0.28; $r^2 = 37.8\%$) and (ii) trials in which the first trial of each set was excluded (rate of change = 0.60; $r^2 = 77.7\%$).

3.4 Control Experiment

In the control experiment subjects sat quietly, holding onto the robot handle for 5 minutes in between sets of reach aftereffect trials. FIG. 9 shows the difference in endpoint reaching errors between Time 1 and Time 2 in all 8 training blocks for both the Control and Main experiment discussed above. Results revealed that there was no significant main effect of Experiment [$F_{(1, 25)} = 0.199$, $p > 0.05$], nor was there an interaction between Time and Experiment [$F_{(1, 25)} = 0.548$, $p > 0.05$]. In other words, the difference between reaching errors at Time 1 and Time 2 was not affected by whether subjects completed the proprioceptive estimation task, or merely held the robot handle for 5 minutes. Additionally, while we found a Time by Block interaction [$F_{(7, 175)} = 10.417$, $p < 0.001$], post hoc tests did not reveal a difference between the rotated reach training blocks, indicating that the difference between Time 1 and Time 2 did not change when subjects were training to reach with the rotated cursor.

4. Discussion

The goal of the present experiment was to determine the time course for changes in the sensory system during visuomotor adaptation to a 30° CW cursor rotation. Additionally, we were interested in comparing the time course of the proprioceptive changes with changes in the reach adaptation assessed through aftereffect trials. Subjects completed 150 reaches with a rotated cursor that were divided into 7 blocks. The number of reach training trials completed prior to the proprioceptive estimate trials and reach aftereffect trials increased over blocks, allowing us to assess early changes in the sensory and motor systems with a high resolution and look for rapid changes (as has been suggested to arise in the motor system; Krakauer et al. 2000; Ostry et al. 2010; Mattar et al. 2011, 2013). We found an overall change in proprioceptive bias of 8.8° following the 150 reach training trials, which corresponds to about 30% of the magnitude of the visuomotor distortion. These changes were slow to arise and did not differ from baseline performance until after 70 training trials with the rotated cursor, after which we found no significant differences between consecutive blocks (i.e., the changes levelled off). In contrast, changes in reach aftereffects arose after only 5 training trials with the rotated cursor, and continued to increase until errors of 22.3° and 14.7° were achieved, before (Time 1) and after (Time 2) the proprioceptive estimate trials respectively. These slow changes in the sensory system versus rapid changes in the motor system provide evidence that they arise from distinct processes during visuomotor adaptation.

4.1 Proprioceptive Recalibration

Our data show a relatively large initial proprioceptive bias of about 9.6° to the left of the visual reference marker following reach training with an aligned cursor. This bias is consistent with previous literature, which has shown that proprioceptive estimates of limb position are biased to the left for the right hand and to the right for the left hand (Cressman and Henriques 2010; Jones et al. 2010; Wilson et al. 2010). Thus, in general, subjects feel their right hand is more rightward than it actually is and their left hand is more leftward than it actually is. This is also true in studies that require subjects to reach to their opposite limb, such that subjects reach too far rightward when reaching to their right hand with their left hand (Crowe et al. 1987; van Beers et al. 1998; Haggard et al. 2000; Jones et al. 2010, 2012).

We found that this initial bias was then shifted more leftwards following training with the rotated cursor, such that subjects recalibrated proprioception by approximately 9° following 70 reach training trials. The current data are consistent with previous studies from our lab which have found that proprioceptive estimates of hand position shift by about 25% of the magnitude of the distortion when interleaved reach training trials are included between sets of proprioceptive estimates (Cressman and Henriques 2009; Salomonczyk et al. 2011, 2012). Specifically, Salomonczyk et al. (2011) found that subjects recalibrated their proprioceptive sense by 7° leftwards following training with a cursor that was rotated 30° CW relative to the hand after 99 trials. The current data extends Salomonczyk et al.'s (2011) findings by demonstrating that proprioceptive recalibration can saturate even earlier than 100 trials (at least when there is only one reach training target and reference marker). These results further suggest that, while the proprioceptive system is slow to change, no further changes are seen with additional training (e.g., another 80 trials). In accordance with this suggestion, Salomonczyk et al. (2011) found that prolonged training with the visuomotor distortion did not result in further changes in proprioceptive estimates, such that changes that had saturated within 99 reach training trials with the rotated cursor and did not increase even following 198 more reach training trials.

Despite designing the experiment to try and introduce fast changes in the sensory system (e.g. by introducing the distortion abruptly and having only 1 reach training target and reference marker), the time course of proprioceptive changes found in the current study reflects a slow, gradual leftward shift in proprioceptive bias over the course of 70 training trials with the rotated cursor (rate of change = 0.0225). These changes were captured well by the exponential curve shown in Equation 1, such that the curve accounted for 98.70% of the variance of the data. These results are consistent with work by Mattar et al. (2013), which found that changes in the sensory system increased exponentially during reaches in a velocity-dependent force-field (rate of change = 0.017). Specifically, an exponential fit accounted for 93.3% of the variance for their sensory changes, which provided a reliably better fit than a linear function. Thus, proprioceptive changes appear to follow a relatively slow exponential increase after training with either a visual distortion or in a velocity-dependent force-field. Interestingly, these slow rising proprioceptive changes have shown to be robust, such that they persist up to 24 hours following training with a velocity-dependent force-field (Ostry et al. 2010) and a visuomotor distortion (Nourouzpour et al. 2015).

4.2 Reach Adaptation

We found that large changes in the motor system arose quickly in the reach training trials and aftereffect trials (16.9° after 5 training trials with a 30° cursor rotation), which confirms previous findings which have found that reach performance returns to near baseline levels within 20 training trials with a 30° cursor rotation (Krakauer et al. 2000; Neva and Henriques 2013) and within 30 training trials with a 40° cursor rotation (Yamamoto et al. 2006). However, the rapid changes observed in the current study exhibited some decay, such that after approximately 5 minutes, reach aftereffects at Time 2 were only 5.1° (or 11.8° less than what was seen at Time 1) and performance at the start of each set of reach training trials differed from what was seen at the end of the previous set of reach training trials (as shown by Izawa et al. (2012) and Mattar et al. (2013)).

Changes in angular reach errors before (Time 1) and after (Time 2) proprioceptive estimate trials were well captured by exponential fits. Specifically, an exponential fit accounted for 95.80% and 97.07% of the variance of EP reach errors at Time 1 and Time 2, respectively. Previous studies have also characterized motor adaptation to a visuomotor rotation (Krakauer et al. 1999, 2004) or a velocity-dependent force-field (Smith et al. 2004; Mattar et al. 2013) as following exponential functions. However, these studies have typically looked at the rate of adaptation during training trials (i.e., trials when the perturbation is still present), such that explicit strategies could influence performance (Weiner et al. 1983; Pisella et al. 2004; Redding et al. 2005; Taylor and Ivry 2014; Taylor et al. 2014). On fitting an exponential function to our reach training trials, we found that it accounted for only 37.8% of the variance of reach errors when all reach training trials were included in the analysis. However, when the first trial of each set of reach training trials was excluded from analysis, thus accounting for forgetting as suggested by Izawa et al (2012), the fit was much better, accounting for 77.7% of the variance of reach errors. Our study is one of the first to show that motor changes follow an exponential curve when motor learning is assessed through a reach aftereffect task, which removes the distortion completely and that this fit is better than when evaluating performance across all trials in which the distortion is still present.

Interestingly, the 95% confidence interval for the reach training trials did not overlap with the aftereffect trials at Time 1 or Time 2 (as seen in FIG. 8), when the first trial was removed from each training block. The differences in performance between reach training and aftereffect trials may be explained by the two separate adaptive processes proposed by Redding and Wallace (1996, 2002, 2003, 2006) based on results achieved using a prism adaptation paradigm. Specifically, they suggest that (1) strategic control and (2) spatial realignment contribute to motor adaptation. Strategic control has been suggested to capture the rapid development of adaptive motor behaviour, which results in a rapid reduction of errors during prism exposure. Spatial realignment, however, represents a more implicit visuomotor remapping which persists into aftereffect trials when the prisms are removed. More recently, reach adaptation to a visuomotor rotation has been suggested to also involve an explicit component, such that subjects consciously correct their movements to quickly bring the cursor to the target, and an implicit component which involves an error-based updating of an internal forward model (Benson et al. 2011; Taylor et al. 2014). The difference in results between our reach training trials and aftereffect trials may reflect the different contributions of explicit and implicit processes between the different types of trials.

In the current study motor adaptation was primarily assessed through aftereffect trials, which have been suggested to provide insight into more permanent motor changes, and hence potentially reflect changes observed in our proprioceptive estimate trials. Reach aftereffects assessed immediately following each set of reach training trials (Time 1) were greater than after a 5 minute delay (Time 2) over the course of the experiment which was introduced by having subjects complete the proprioceptive estimation task. Specifically, reach aftereffect trials at Time 1 resulted in a greater overall magnitude of reach adaptation following all sets of training trials. This decay of reach adaptation was also observed in a control experiment in which we replaced the proprioceptive estimation task with a 5 minute rest interval in which subjects sat stationary, gripping the robot handle. Thus, it appears that reach adaptation decays over a 5 minute time interval, regardless of whether subjects are completing a perceptual task or resting quietly. Moreover, while the rates of adaptation were not different between Time 1 and Time 2, their 95% confidence intervals only slightly overlapped with one another; suggesting that there may be a difference in the neural processes involved in reach adaptation at these different time points. Given that motor adaptation at Time 1 and Time 2 was assessed through aftereffect trials, differences in reach adaptation between the two time points does not represent differences in strategic versus implicit learning, but perhaps reflect differences in the contribution of a faster, labile component and a slower, temporally stable component of learning as put forth recently by Smith and colleagues (Hadjiosif and Smith 2013**a,** 2013**b**; Miyamoto et al. 2014). Specifically, decreases in motor adaptation within a few aftereffect trials in Time 1 (as shown by Nourouzpour et al. 2015 and seen in the current data (not shown)), would reflect a decay of the faster, labile component, which has been shown to decay after about 16.5 s (Hadjiosif and Smith 2013**a**). Motor adaptation during Time 2, on the other hand, would be more represented by the temporally stable component of learning and hence may be a more accurate representation of long-term motor changes which result from an internal visuomotor remapping.

Interestingly, continuous training with the visuomotor distortion, either during the short time scale of the present study or even longer time scales, does not appear to lead to larger reach aftereffects, as motor adaptation has been shown to saturate within 100 training trials (Wong and Henriques 2009; Salomonczyk et al. 2011; Barkley et al. 2014). Additionally, studies have demonstrated that reach adaptation is relatively long-lasting, as subjects have shown substantial retention of adapted movements for days and months following visuomotor training (Klassen et al. 2005; Bock et al. 2001; Tong et al. 2002; Caithness et al. 2004; Krakauer et al. 1999, 2005). Specifically, subjects showed retention of reach aftereffects after 24 hours (Nourouzpour et al. 2015) and partial retention following 48 hours (Caithness et al. 2004) following training with a 30° visuomotor rotation. Additionally, Yamamoto et al. (2006) found substantial retention of reach aftereffects for one year following visuomotor training with a joystick tracking task.

4.3 Comparison of Proprioceptive Recalibration and Reach Adaptation

Here we have shown that changes in the sensory and motor systems arise with different time courses during visuomotor adaptation. The motor system undergoes large, rapid changes after only 5 training trials with the rotated cursor. The sensory system, on the other hand, undergoes slower and more gradual changes, such that changes are not observed until after a number of training trials (e.g., 70 trials with the rotated cursor). In accordance with these findings, exponential fits to the data reveal a significantly greater rate of change for reach adaptation as compared to proprioceptive recalibration.

These findings are similar to Mattar et al. (2013), who showed that motor changes occurred much earlier as assessed during trials in which the perturbation was still present, and with a greater rate of increase compared to sensory changes. Based on their results, Mattar et al. concluded that motor changes occur earlier and therefore drive sensory changes during adaptation. However, work from the same lab has also found that completing perceptual training (i.e., receiving feedback as to the correctness of responses regarding position estimates) improved both the rate and extent of motor adaptation (Darainy et al. 2013), and lead to changes in frontal motor areas in the brain (Vahdat et al. 2014), pointing to a role for sensory changes in motor adaptation. Similar findings have been shown by Cressman and Henriques (2010), who suggest that while sensory changes can result in changes in the motor system, they are not usually solely responsible for motor adaptation. Given the different time courses observed in the current study, even when a more stable measure of motor adaptation was used (i.e., aftereffects measured after a 5 minute delay), we conclude that while sensory changes may partially contribute to motor adaptation, for the most part, proprioceptive recalibration and reach adaptation are driven by different error signals present during visuomotor adaptation. Reach adaptation may arise due to error-based learning, which involves the reduction of the difference between the predicted and sensory consequences of a subject’s movements (i.e., reducing the difference between desired and actual performance; Tseng et al. 2007; Berniker and Kording 2008; Wei and Kording 2009). In contrast, proprioceptive recalibration may arise due to a cross-sensory error signal which depends on differences between visual and proprioceptive estimates of limb position (Cressman and Henriques 2010; Henriques and Cressman 2012; Salomonczyk et al. 2013; Henriques et al. 2014). From the results of the current study, it appears that it takes longer for the brain to resolve this sensory conflict and does not resolve it to the same extent as a visuomotor error signal.

In support of the proposal that sensory and motor changes arise independently, visuomotor adaptation has been shown to be possible in deafferented patients (i.e., patients with no proprioceptive feedback), and when proprioceptive feedback is degraded with agonist-antagonist muscle vibration (Ingram et al. 2000; Bernier et al. 2006; Bock and Thomas 2011). For example, Bernier et al. (2006) found that there was no difference in the rate or extent of reach adaptation between a deafferented subject and healthy controls following training with a rotated cursor (i.e., as measured during aftereffect trials). Thus, visuomotor adaptation can arise in the absence of a cross-sensory error signal and proprioceptive recalibration. Changes in the sensory system have also been shown to arise in the absence of motor changes in cerebellar patients. For example, Block and Bastian (2012) found that individuals with cerebellar damage were capable of sensory realignment of their hand (i.e., realignment of proprioceptive estimates of hand position to more closely match the visual estimates) in the absence of any motor adaptation. Additionally, Synofzik and colleagues (2006, 2008) found that patients with cerebellar damage and healthy controls were able to predict the sensory consequences of their movements, despite the patients' impaired ability to adapt to a visuomotor distortion.

The different errors signals giving rise to proprioceptive recalibration and reach adaptation may arise in different areas of the brain. A recent review article by Shadmehr and

Krakauer (2008) proposed that the cerebellum and parietal cortex have different roles in their involvement in motor learning. The cerebellum is thought to be involved in building an internal model that predicts the sensory consequences of a motor command, as well as in correcting these motor commands through sensory feedback. The parietal cortex, on the other hand, is involved in integrating the predicted visual and proprioceptive feedback with sensory feedback in order to estimate the current state of the body and the environment. Proprioceptive changes involve an adaptation in the body's state estimate, and therefore may occur within the parietal cortex, while adapted motor commands directly affect the internal model of a movement, which would most likely occur within the cerebellum (Cressman and Henriques 2012). In support of different brain areas being responsible for resolving different error signals, Vahdat et al. (2011) found distinct motor and sensory networks of brain activation during adaptation to a velocity-dependent force-field using fMRI. Specifically, they found that changes in the cerebellar cortex, primary motor cortex, and dorsal premotor cortex were associated with the motor component of adaptation, while changes in the second somatosensory cortex, ventral premotor cortex, and supplementary motor cortex were associated with the sensory component of adaptation.

5. Conclusion

In the current study, we found slow, gradual changes in the sensory system, which occurred later in time compared to changes in the motor system. Based on these results and other findings in our lab, we suggest that proprioceptive recalibration and reach adaptation are distinct neural processes that arise simultaneously during visuomotor learning. The visuomotor system appears to be quicker to change than the sensory system, perhaps because we are required to adjust our movements on a daily basis while interacting with a dynamic environment. The sensory system on the other hand is very rarely required to adapt, potentially leading to its resistance to change.

Figures

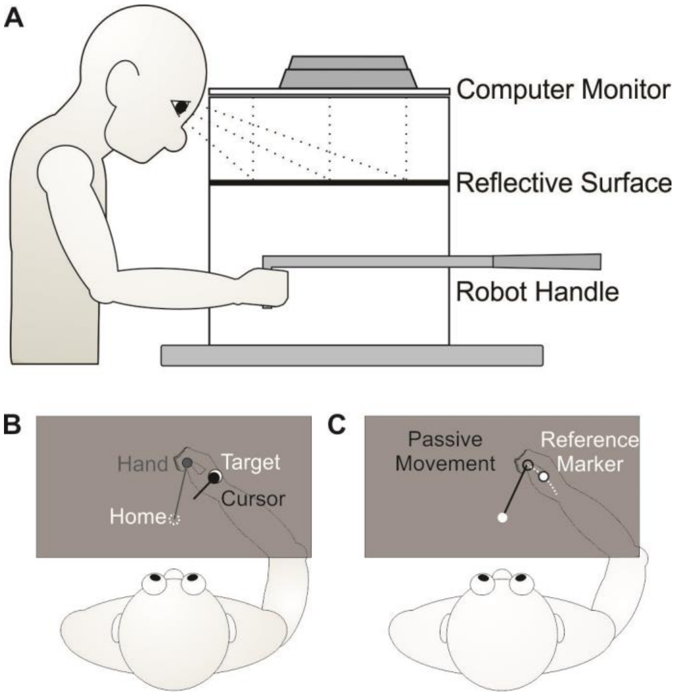

FIG. 2. Experimental set-up.

Side-view of experimental apparatus **(A)**. Top view and dimensions of experimental surface visible to subjects during the reach training **(B)** and proprioceptive estimation **(C)** tasks. **B:** Visuomotor distortion introduced in the rotated reach training task. The home position was not shown to subjects (dotted white circle). In the rotated reach training trials, the cursor representing the hand's position (white circle, 1 cm in diameter; represented at the end of the black arrow) was rotated 30° CW relative to the actual position of the hand (represented by the grey arrow). The reach target (white circle, 2 cm in diameter) was located 15 cm and 45° CW from the home position relative to straight ahead. **C:** For the proprioceptive estimation trials, the home position was only visible at the start of the movement (light grey circle, 1 cm in diameter). The reference marker (white circle, 1 cm in diameter) was located 15 cm and 45° CW from the home position relative to straight ahead. The hand was passively moved to a position along the white dotted line (shown for reference) using an adaptive staircase algorithm as described in the text.

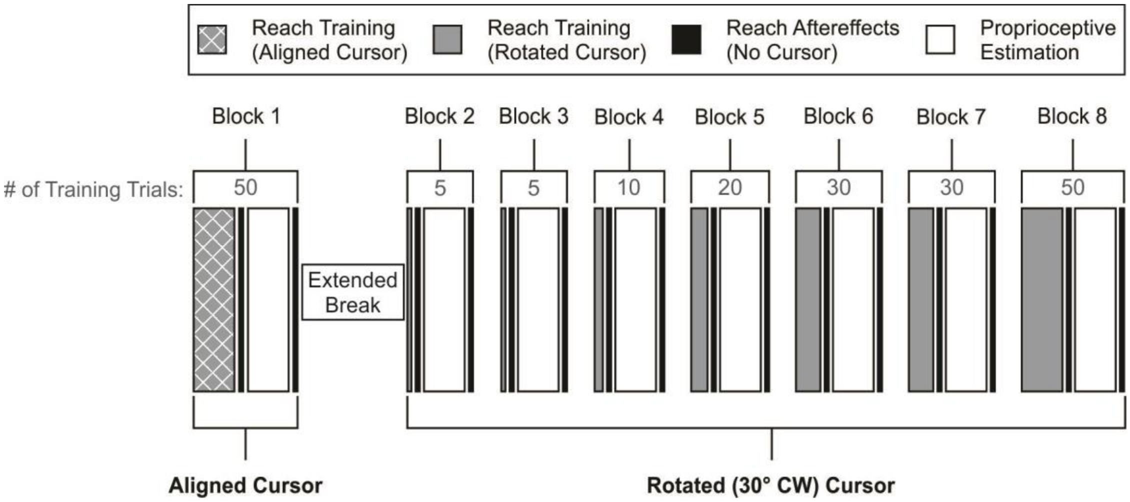

FIG. 3. Experimental design.

A breakdown of the testing blocks completed within the experiment. Gray bars represent sets of reach training trials; the grey bar with the crossed pattern indicates trials in which the cursor was aligned with the hand and the solid grey bars indicate trials in which the cursor was rotated 30° CW relative to the hand. The gray numbers indicate the number of reach training trials within each block. Black bars represent sets of 6 aftereffects trials and white bars represent sets of 50 proprioceptive estimate trials. In each block, subjects completed a set of reach aftereffect trials (Time 1) followed by proprioceptive estimate trials, and then an additional set of reach aftereffect trials (Time 2).

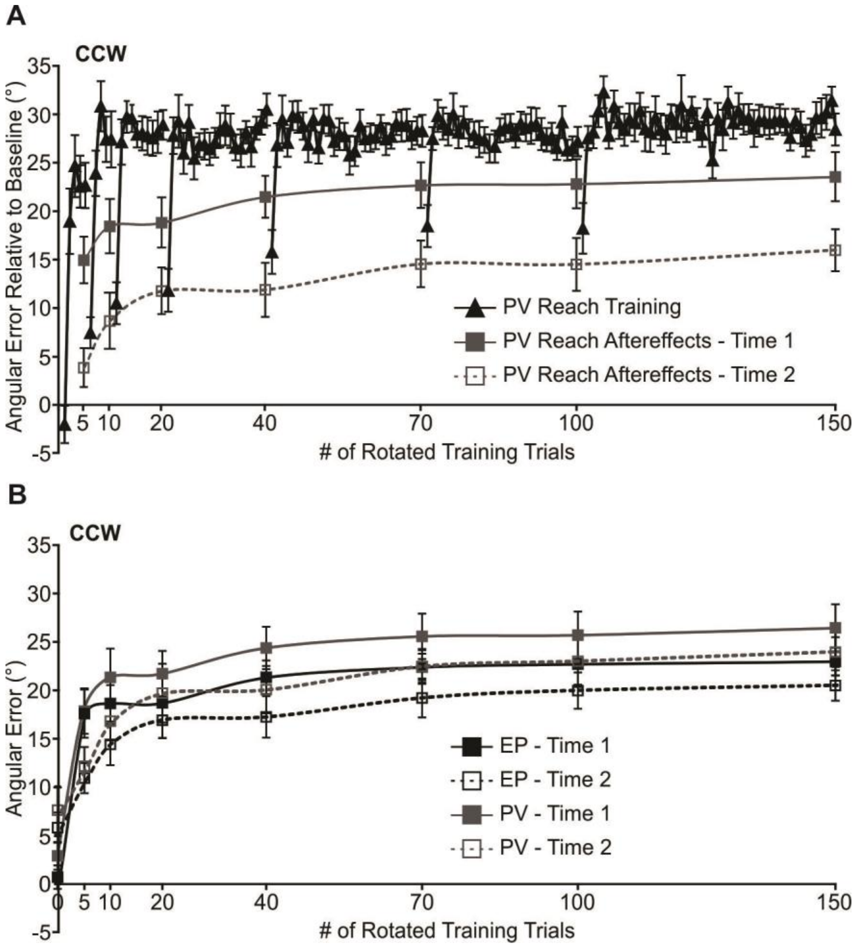

FIG. 4. Time course of changes in angular reach error.

Mean angular reach errors during reach training trials and reach aftereffect trials. **A:** Mean PV angular reach errors for each reach training trial completed with the rotated cursor relative to angular reach errors during reach training with an aligned cursor (black triangles). Mean PV angular reach errors for reach aftereffect trials at Time 1 (filled grey squares) and Time 2 (hollow squares) are also displayed relative to errors achieved following training with an aligned cursor. **B:** Mean PV (grey) and EP (black) angular reach errors for the 6 aftereffect trials at Time 1 (filled squares) and Time 2 (hollow squares) as a function of reach training trials with the 30° CW rotated cursor. Data points at 0 rotated training trials reflect baseline performance.

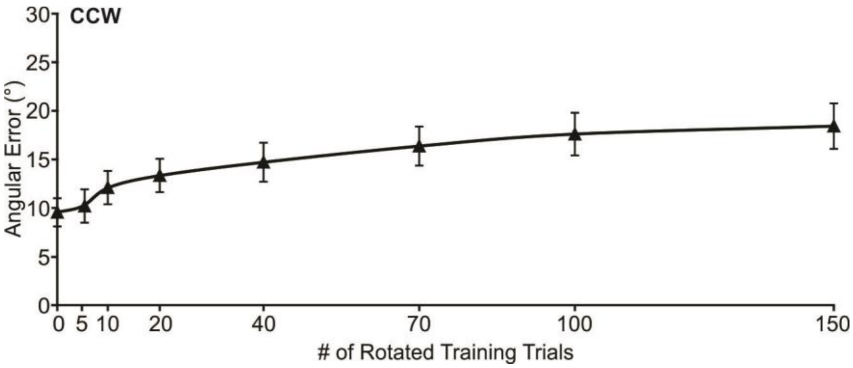

FIG. 5. Time course of changes in proprioceptive bias

Mean proprioceptive biases (represented as angular errors) relative to the reference marker as a function of reach training trials with the 30° CW rotated cursor. The data point at 0 rotated training trials represents the proprioceptive bias following reach training with the aligned cursor (i.e., baseline).

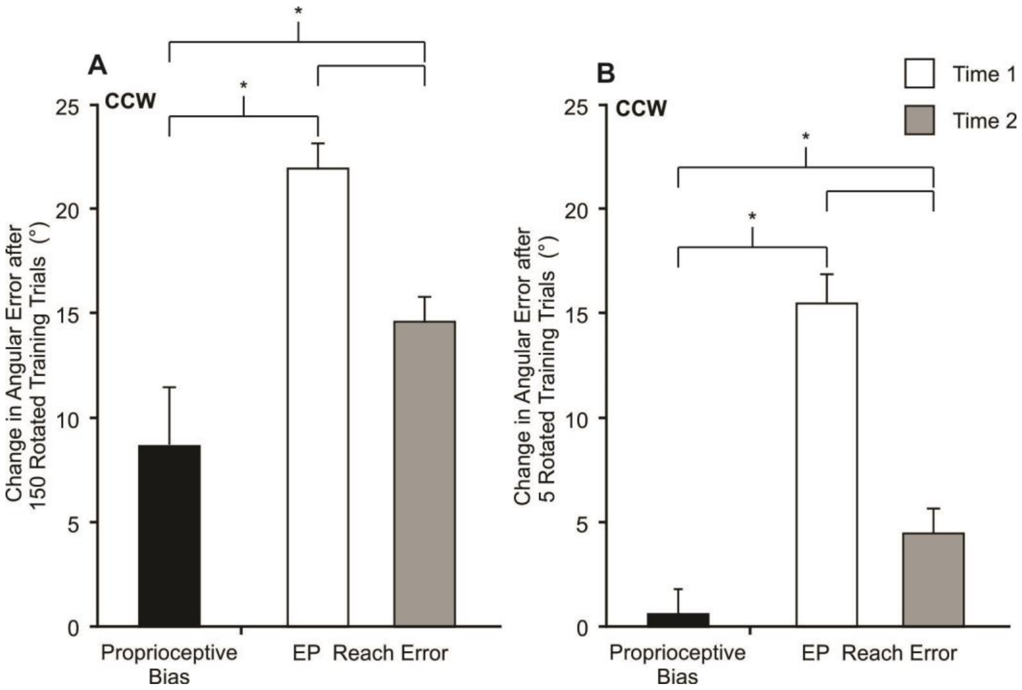

FIG. 6. Final and initial change in angular error.

Mean changes in proprioceptive biases (black bars) and angular reach errors at movement endpoint (Time 1: white bars, Time 2: grey bars) following 150 reach training trials **(A)** and following 5 reach training trials **(B)** with the 30° CW rotated cursor relative to angular errors achieved following aligned reach training. Stars denote a significant difference, such that confidence intervals do not overlap.

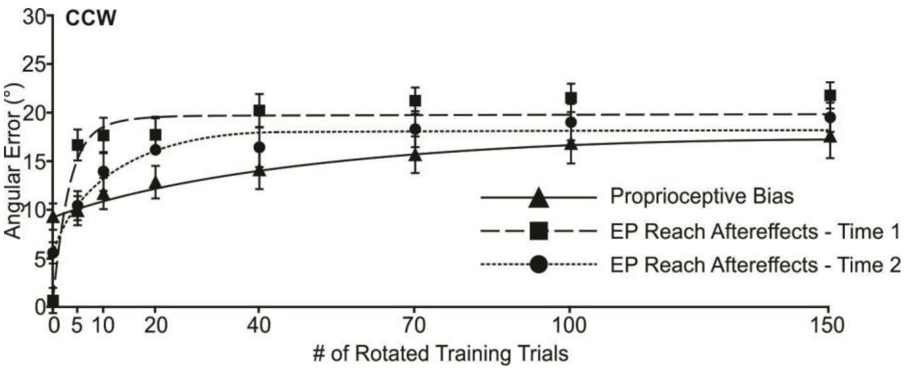

FIG. 7. Exponential fits.

Mean movement endpoint angular reach error at Time 1 (squares) and Time 2 (circles), as well as angular error for proprioceptive bias (triangles) as a function of training trials with the 30° CW rotated cursor. Data points at 0 rotated training trials reflect performance following training with an aligned cursor (i.e., baseline). Smooth curves indicate exponential fits to the data, according to Equation 1.

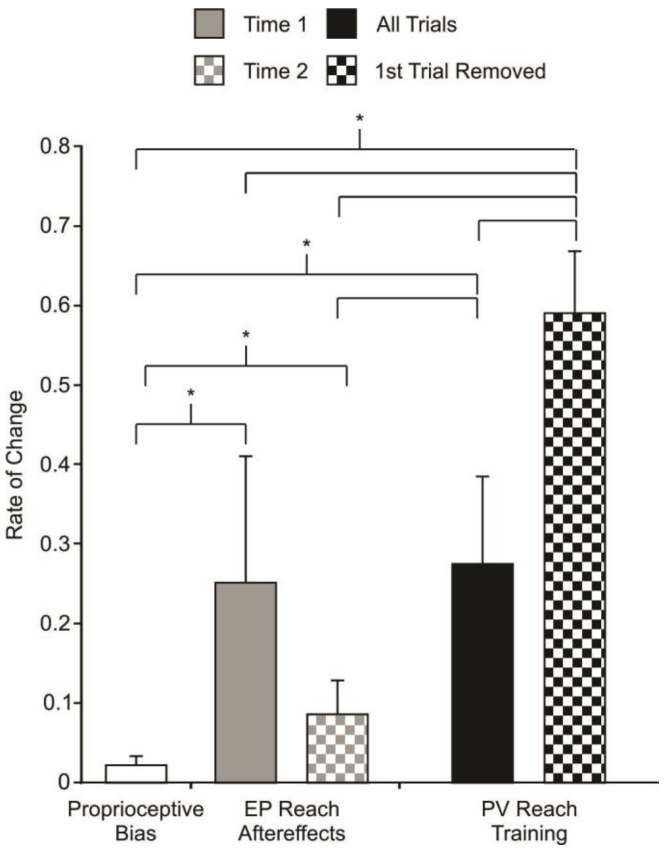

FIG. 8. Rates of change.

Rates of change of the exponential functions shown in FIG. 6 for proprioceptive biases (white bar) and reach errors at movement endpoint (Time 1: grey bar, Time 2: grey checkered bar). Rates of change of exponential functions fit to the reach training trials shown in FIG. 3A are also provided with (black bar) and without (black checkered bar) the very first trial of each set included. Bars represent 95% confidence intervals. Stars denote a significant difference, such that confidence intervals do not overlap.

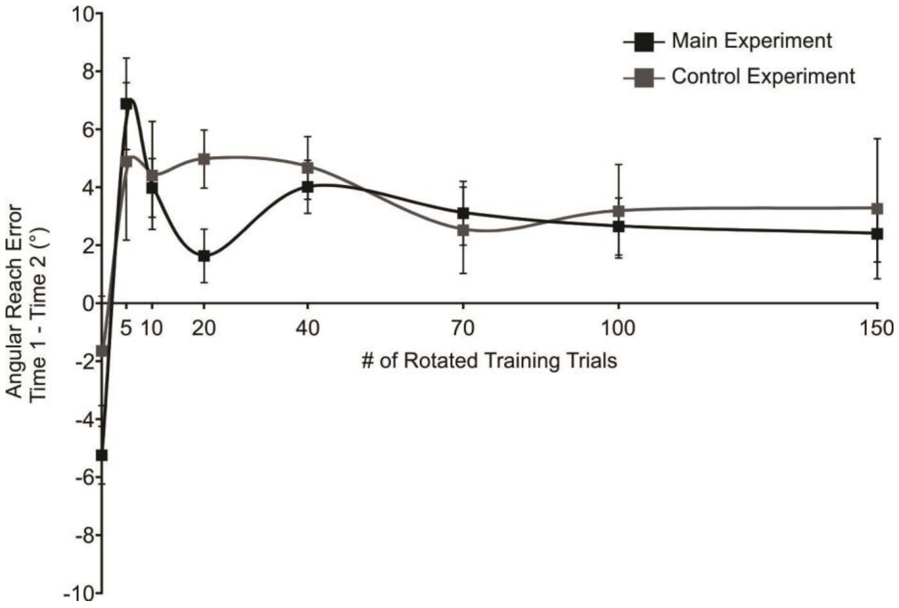

FIG. 9. Differences in reach aftereffects at Time 1 and Time 2 for main and control experiments.

Mean change in movement endpoint angular reach errors between Time 1 and Time 2 as a function of training trials with the 30° CW rotated cursor. Data points at 0 rotated training trials reflect performance following training with an aligned cursor (i.e., baseline). In the main experiment (black squares), subjects completed the proprioceptive estimation trials between Time 1 and Time 2. In the control experiment (grey squares), subjects sat stationary while holding the robot handle for 5 minutes between Time 1 and Time 2.

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Chapter III: General Discussion

When subjects perform reaches to a visual target with distorted visual feedback of their hand (e.g. a cursor representing their hand that is rotated relative to their hand's actual position), they adapt their reaches to reduce the error between the cursor and target, and recalibrate their felt hand position to more closely match the visual feedback (Cressman and Henriques, 2009, 2010; Cressman et al., 2010; Salomonczyk et al., 2011, 2012). The first objective of the current research was to establish the time course of these sensory changes. We then looked to determine the relationship regarding the processes underlying proprioceptive recalibration and reach adaptation by comparing changes in felt hand position and reach errors over time. Overall, we found an 8.8° shift in proprioceptive estimates of hand position following 150 reach training trials with a rotated cursor, corresponding to approximately 30% of the magnitude of the visuomotor distortion. Moreover, estimates did not differ significantly from baseline until after 70 reach training trials with the rotated cursor. Motor changes, on the other hand, arose much more quickly, such that there was a significant leftward shift in reaches after only 5 reach training trials with the rotated cursor compared to baseline measures. The overall magnitude of reach errors achieved after each block of rotated reach training trials differed depending on if aftereffect trials were completed before or after the proprioceptive estimate trials. For example, the overall magnitude of reach adaptation achieved was 22.3° for aftereffect trials completed before proprioceptive estimate trials and 14.7° for aftereffect trials completed after proprioceptive estimate trials (or 74% and 49% of the magnitude of the visuomotor distortion, respectively) following the 150 reach training trials with the rotated cursor. Additionally, we found that the rates of change of reach adaptation and proprioceptive recalibration differed significantly. Thus, this data suggests that distinct neural processes underlie motor and sensory changes during reach training with a rotated visual cursor.

In the current study we found a slow, gradual change in proprioceptive estimates of hand position during training with distorted visual feedback of the hand. Previous studies have found a similar overall magnitude of proprioceptive recalibration following 100 to 150 reach training trials (Cressman and Henriques, 2009; Cressman et al., 2010; Salomonczyk et al., 2011, 2012), and suggested that these plastic, sensory changes are driven by resolving a cross-sensory error signal between proprioceptive and visual estimates of hand position, such that the proprioceptive estimate is recalibrated in order to match the distorted visual feedback experienced during the reach training trials. In support of this proposal of a cross-sensory error signal driving proprioceptive recalibration, Cressman and Henriques (2010) have shown that proprioceptive recalibration arises in the absence of any goal-directed movements (or visuomotor error signal), when subjects are merely exposed to a cross-sensory error signal. In their paradigm, Cressman and Henriques (2010) had a robot passively move subjects' hands along a fixed path to a visual target while they viewed a cursor representing the position of their hand. The fixed path was gradually rotated relative to the path of the cursor, but subjects always saw the cursor move directly to the target during their passive movements. Subjects shifted the position at which they felt their hand was aligned with a visual reference marker by about 6° relative to baseline, which is similar in magnitude to the changes in felt hand position estimates found following active, goal-directed movements with rotated visual feedback of the hand (Cressman and Henriques, 2009, 2010). Interestingly, the cross-sensory error signal was also shown to produce partial reach adaptation, such that subjects reached about 6° more leftward relative to baseline following exposure to the cross-sensory error signal.

In the present research we discuss the observed changes in hand position as reflecting proprioceptive recalibration as opposed to visual recalibration. We think that it is unlikely that vision is being recalibrated based on our experimental manipulation and results across several previous studies. First, the current study only manipulated visual feedback of the hand position, rather than the entire workspace (as would occur in prism adaptation paradigms), which avoids recalibration of the visual system. Moreover, changes in felt hand positions have been shown to be similar when subjects estimated the position of their hand relative to a proprioceptive reference marker (e.g. body midline) and a visual reference marker, suggesting that recalibration was not dependent on vision (Cressman and Henriques 2009; Clayton et al. 2014; Mostafa et al. 2014**a**). Along the same lines, shifts in propricoeptive estimates have also been shown when subejcts reached to their unseen trained hand with the seen untrained hand (Clayton et al., 2014). Finally, if vision was recalibrated, we would expect changes in proprioceptive estimates to transfer between hands, which does not occur (Mostafa et al. 2014**b**).

Mattar et al. (2013) have also recently shown slow, gradual changes in the sensory system during reaches in a velocity-dependent force-field. In their task, subjects had to learn to reach to a straight-ahead target while velocity-dependent loads were applied on their reaching limb during movement. Although their task does not produce the cross-sensory error signal discussed above, subjects showed significant changes in reaching performance and sensory estimates of limb motion following training, suggesting that perturbing limb dynamics also leads to gradual changes in the sensory system. It is interesting to note that the sensory changes found by Mattar et al. (2013) following 150 trials were much smaller than those seen in the current study (e.g. only about 16% of the magnitude of the motor changes compared to the 40-60% seen in the current study). These different results between paradigms may arise due to differences in sensory coding for position versus movement sense (Allen and Proske, 2006), as Mattar et al. (2013) assessed proprioceptive estimates of hand motion, rather than assessing final hand position as we did in the current study. As well, differences may arise due to the cross-sensory error signal driving sensory changes to a greater extent than force perturbations alone, which creates a conflict between the expected sensory feedback and motor output (i.e. sensorimotor error signal) (Sarlegna and Bernier, 2010). In the future, it may be of interest to assess whether there is an additive contribution from both a cross-sensory error signal and sensorimotor error signal experienced in force perturbations to sensory changes, or whether these signals merely drive sensory recalibration to different extents.

The changes in sensory estimates over time in the paradigm by Mattar et al. (2013) were compared to changes in reaches on trials in which the force perturbation was present. Mattar et al. found very rapid changes in reaches across the reach training trials. However, trials in which the perturbation is present may capture explicit rather than implicit adaptive processes (Weiner et al., 1983; Pisella et al., 2004; Redding et al., 2005). In the present experiment we focused on assessing reach adaptation through aftereffect trials. Although we used aftereffect trials to assess reach adaptation as opposed to reach training trials used by Mattar, our results are similar. Again, our results showed very rapid changes in the motor system following as few as 5 reach training trials with the rotated visual feedback. However, we found that these changes decayed fairly quickly, as reach adaptation assessed after the proprioceptive estimation trials (which took approximately 5 minutes to complete) was significantly less than adaptation assessed immediately following reach training trials. A similar decay in motor changes was also found in a control experiment in which the proprioceptive estimation task was replaced with a 5 minute stationary rest interval, suggesting that a 5 minute interval results in reach adaptation decay, regardless of whether subjects complete a proprioceptive estimation task or rest quietly during this time. We suggest that this difference in reaching performance between the two intervals reflects differing contributions of two separate processes to reaching performance, as put forth by Smith et al. (2006) and Redding and Wallace (1996, 2000, 2002, 2003, 2006). Reach performance immediately following reach training may involve a greater contribution from the faster (strategic) learning mechanism which quickly decays, compared to reach performance following a 5 minute rest interval, which may be reflective of a slower (implicit) error-based learning mechanism.

We found that proprioceptive changes were much slower to arise in comparison to reach adaptation as assessed by aftereffect trials. Based on these results we conclude that proprioceptive recalibration and reach adaptation arise due to distinct neural processes. Mattar et al. (2013) also found similar findings, such that reach adaptation occurred earlier during training in a velocity dependent force-field, with a significantly greater rate of change, as compared to sensory changes. However, they concluded that motor changes occur earlier and therefore drive changes in the sensory system during adaptation. The different interpretations of similar data are hard to reconcile. Recent research from their lab has found that improving subjects' ability to estimate the movement direction of their limb in space (i.e. perceptual testing) improved both the rate and extent of reach adaptation in subsequent training trials within a velocity-dependent force-field (Darainy et al., 2013). Additionally, perceptual testing was found to produce changes to frontal motor areas of the brain which were not involved in motor adaptation (Vahdat et al., 2014). Based on these results, Ostry and colleagues have changed the manner in which they interpret their findings. In particular, they now suggest that while motor adaptation may arise before sensory changes, as shown by Mattar et al. (2013), sensory changes may directly contribute to a portion of motor adaptation during force-field adaptation and do not speak of motor adaptation driving sensory changes.

Work using a visuomotor distortion supports the notion that sensory changes may contribute to motor changes under specific circumstances (Cressman and Henriques, 2010; Salomonczyk et al., 2013). However, the contribution of sensory changes to motor changes has been shown to be minimal, suggesting that while proprioceptive recalibration may contribute to reach adaptation, it is not primarily responsible for reach adaptation. Moreover, recent research from our lab has provided additional evidence for reach adaptation and proprioceptive recalibration being distinct processes. For example, bimanual transfer from the trained to the untrained hand for reach adaptation and proprioceptive recalibration has been shown to results in different generalization patterns. Specifically, Mostafa et al. (2014**b**) found that reach adaptation transfers from the trained to the untrained hand, while proprioceptive recalibration does not. Mostafa et al. (2014**a**) also showed that there was complete generalization of reach errors to novel targets at various distances, but only partial generalization of proprioceptive estimates to the same targets following training with a rotated cursor. Specifically, subjects' estimates of hand position did not shift to the same extent when they indicated the felt position of their hand relative to a far novel target, as compared to relative to the trained and close novel targets, while reach adaptation was similar in magnitude to targets at all distances. Pilot data from our lab has also found different generalization patterns for reach adaptation and proprioceptive recalibration. Specifically, we have found that subjects demonstrate substantial generalization of proprioceptive estimates across the workspace to novel targets in new directions, while reach adaptation appears to be specific to the trained movement direction. In conjunction with the current study's finding, these experiments provide evidence that different neural processes give rise to reach adaptation and proprioceptive recalibration during reaches with distorted visual feedback of the hand.

Overall, we find that the sensory system is more robust and resistant to change in comparison to the motor system. Motor adaptation in response to a novel visual environment is a very common occurrence in everyday activities (e.g. adjusting to novel mouse-computer interfaces), perhaps contributing to its quick occurrence. On the other hand, humans rarely experience situations in which they are required to update the perceived position of their limbs, and thus this process requires a greater degree of interaction with the novel visual environment. Based on the different time courses for sensory and motor changes observed in the present study we also suggest that motor and sensory changes arise due to distinct neural processes during training with distorted visual feedback of the hand. Thus, regimens used to treat individuals with sensorimotor dysfunction should consider spending more time on sensory or perceptual training compared to motor training, and should cater their tasks to specifically target the system (e.g. motor or sensory) which requires most attention, rather than using a one-size-fits-all program for rehabilitation.

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Appendix A

Edinburgh Handedness Inventory (Oldfield, 1971)

Name: ____________ Date:____________

Please indicate with a check (✓) your preference in using your left or right hand in the following tasks.

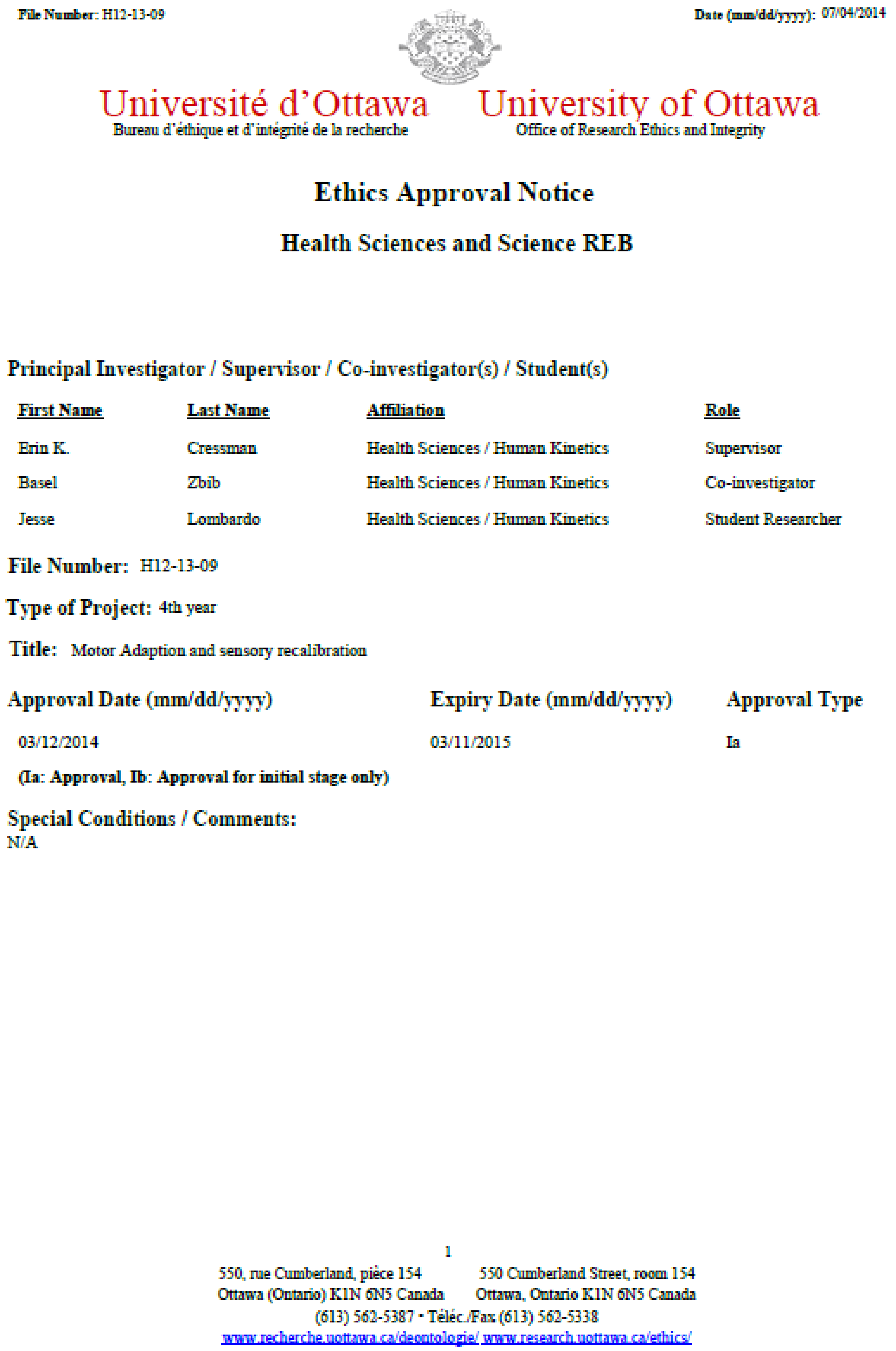
Where the preference is so strong you would never use the other hand, unless absolutely forced to, put two checks (✓✓).

If you are indifferent, put one check in each column (✓|✓).

Some of the activities require both hands. In these cases, the part of the task or object for which hand preference is wanted is indicated in parentheses.

Task / Object	Left Hand	Right Hand
1. Writing		
2. Drawing		
3. Throwing		
4. Scissors		
5. Toothbrush		
6. Knife (without fork)		
7. Spoon		
8. Broom (upper hand)		
9. Striking a Match (match)		
10. Opening a Box (lid)		
Total checks:	LH =	RH =
Cumulative Total	CT = LH + RH =	
Difference	D = RH – LH =	
Result	R = (D / CT) × 100 =	
Interpretation: (Left Handed: $R < -40$) (Ambidextrous: $-40 \le R \le +40$) (Right Handed: $R > +40$)		

Appendix B



File Number: H12-13-09 **Date (mm/dd/yyyy):** 07/04/2014

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Office of Research Ethics and Integrity

Ethics Approval Notice

Health Sciences and Science REB

Principal Investigator / Supervisor / Co-investigator(s) / Student(s)

First Name	Last Name	Affiliation	Role
Erin K.	Cressman	Health Sciences / Human Kinetics	Supervisor
Basel	Zbib	Health Sciences / Human Kinetics	Co-investigator
Jesse	Lombardo	Health Sciences / Human Kinetics	Student Researcher

File Number: H12-13-09

Type of Project: 4th year

Title: Motor Adaption and sensory recalibration

Approval Date (mm/dd/yyyy)	Expiry Date (mm/dd/yyyy)	Approval Type
03/12/2014	03/11/2015	Ia

(Ia: Approval, Ib: Approval for initial stage only)

Special Conditions / Comments:
N/A

1

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File Number: H12-13-09

Date (mm/dd/yyyy): 07/04/2014

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University of Ottawa
Office of Research Ethics and Integrity

This is to confirm that the University of Ottawa Research Ethics Board identified above, which operates in accordance with the Tri-Council Policy Statement (2010) and other applicable laws and regulations in Ontario, has examined and approved the ethics application for the above named research project. Ethics approval is valid for the period indicated above and subject to the conditions listed in the section entitled "Special Conditions / Comments".

During the course of the project, the protocol may not be modified without prior written approval from the REB except when necessary to remove participants from immediate endangerment or when the modification(s) pertain to only administrative or logistical components of the project (e.g., change of telephone number). Investigators must also promptly alert the REB of any changes which increase the risk to participant(s), any changes which considerably affect the conduct of the project, all unanticipated and harmful events that occur, and new information that may negatively affect the conduct of the project and safety of the participant(s). Modifications to the project, including consent and recruitment documentation, should be submitted to the Ethics Office for approval using the "Modification to research project" form available at: http://www.research.uottawa.ca/ethics/forms.html.

Please submit an annual report to the Ethics Office four weeks before the above-referenced expiry date to request a renewal of this ethics approval. To close the file, a final report must be submitted. These documents can be found at: http://www.research.uottawa.ca/ethics/forms.html.

If you have any questions, please do not hesitate to contact the Ethics Office at extension 5387 or by e-mail at: ethics@uOttawa.ca.

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Appendix C

Background information and consent form

Motor adaptation and sensory recalibration

Supervisor: Dr. Erin Cressman,
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Principal Investigator:

Jesse Lombardo, 4th Year Honours Project, School of Human Kinetics, University of Ottawa

Basel Zbib, MSc Student, School of Human Kinetics, University of Ottawa

Funding: National Science and Engineering Research Council (NSERC)

Background

Most of us perform goal directed actions – i.e. reaching for a cup of coffee – without thought or effort. It is only after something goes wrong (i.e. damage to part of the brain), that we begin to appreciate how complex a job the brain has in transforming sensory signals (e.g. visual input) into appropriate action plans. The overall goal of the research being undertaken in my laboratory is to understand how the brain transforms sensory input into motor output in the “healthy” brain. This research has important implications for people suffering from neurological disorders, as it is only after we gain a fundamental understanding of the normal mechanisms underlying goal directed action that we can begin to design effective rehabilitation programs, targeted at individuals with damage to certain areas of the brain.

Purpose

The purpose of this research is to determine how the brain combines multiple sources of sensory information so that it can plan an appropriate movement and form a coherent estimate of where the limb is in space. In particular we are looking at the integration of visual and proprioceptive information in the brain, where proprioceptive input arises from sensory receptors inside the body that enable us to localize various parts of the body in relation to each other (e.g. proprioception is the sense that allows you to touch your index finger to your nose when your eyes are closed).

Subject Profile

To be a participant you must be a right-handed, healthy (no history of neurological, and/or motor dysfunction) adult with normal or corrected to normal visual function, aged between 16 and 40 years.

Study Procedures

In order to examine how visual and proprioceptive inputs are integrated in the brain you will be asked to point to targets (i.e. a visual dot) with your right/left hand and indicate where your hand is relative to a target (i.e. left or right). Your task will be to move and report your position as accurately as possible to the target. In order to record your hand movement, you will hold onto a robot handle (KINARM, Kingston, ON, Canada). We do not need to do any preparation of the skin. It is important to note that this robot system only captures the position of the handle (it does not capture your image (i.e. personal features) in any form).

Experimental Session

The entire experiment will be completed in Room 403 in Monpetit Hall in two testing sessions on different days, and each session will take between an hour and an hour and a half to complete. Upon completion of the testing session the experimenter will provide additional details on the visual information displayed and the hypothesized results.

Risks and discomforts

The risks involved in participating in this experiment are minimal. That is, the risks are no greater than the risks experienced in everyday life. However, you might experience slight fatigue, as you will be asked to maintain focused attention throughout the experiment and perform multiple reaching movements. In attempt to ensure that you do not become fatigued, we have scheduled 5 minute breaks approximately every 15 minutes. As well, please let us know if you require longer or more frequent periods of rest.

Benefits

Thank you for taking the time to participate in this study. While there are no direct benefits to you from participating in this study, this research has important implications for people suffering from neurological disorders. It is only after we gain a fundamental understanding of the normal mechanisms underlying sensory guided action that we can begin to design effective rehabilitation programs, targeted at individuals with damage to certain areas of the brain.

Anonymity and Confidentiality

All information and data collected are coded to maintain confidentiality. Specifically, raw data will be stored using an alphanumeric coding system so that no one will be able to identify you as your name will not appear on these files. The data will be analyzed on password protected computers that only the researchers directly involved in this study will have access to. Once analyzed the data will be kept in Room 403, Montpetit Hall, in locked filing cabinets and only the researchers directly involved in this study will have access to your data.

No records bearing your name will leave the institution. You are encouraged to request and discuss the results of the experimental trials at any time.

The data collected in this study will be published in scientific journals, as well as in a University of Ottawa MSc thesis. The data will kept for a period of 10 years post-publication and will subsequently be destroyed by the physical resources service of the University of Ottawa.

For the entire duration of the study, it is fully understood that you may refuse to participate or withdraw from the study at any time, without question. As well, you can ask the researcher any question about any part of the research being conducted at any time.

Data of participants who withdraw from the study will be destroyed immediately.

INFORMED CONSENT OF PARTICIPANT

Research involving human subject require written consent of the participants.

I, __________________________, hereby volunteer to participate as a subject in the study entitled **“Motor adaptation and sensory recalibration”**. I have read the information presented in the above background information and I had the opportunity to ask questions to the investigators. I understand that my participation in this study, or indeed any research, may involve risks that are currently unforeseen.

I recognize that there will be no direct benefit to me from my participation in this study.

I understand that if I have any questions regarding the study, I may contact Dr. Erin Cressman. If I have any questions or complaints with regards to the ethical conduct of this study, I may contact the Protocol Officer for Ethics in Research, University of Ottawa, Tabaret Hall, 550 Cumberland Street, Room 154, Ottawa, ON K1N 6N5, tel.: 613-562-5387, email: ethics@uottawa.ca .

I have been given a copy of this Background Letter and Consent Form for me to keep.

Signature of participant: _________________________ Date: ___________________

Signature of Researcher: _________________________ Date: ___________________

Research Summary/Debriefing text

The overall goals of this research are to examine how information from different sensory systems is integrated in order to perform an accurate movement and form a coherent estimate of where one's limb is in space.

The specific goals of this experiment were to look at the impact of motor learning on sensory recalibration (or sensory plasticity). To examine this, we had you reach to targets when provided with false visual feedback of the hand (e.g. reaching to a target while seeing a cursor that was rotated with respect to the hand's actual location). We then had you (1) reach to targets without any feedback to assess motor learning/adaptation, and (2) estimate where you felt your hand was located in space to determine sensory recalibration of felt hand position. Your results from the motor and sensory perceptual tasks will be compared in order to determine whether the sense of hand position was recalibrated following motor adaptation.

The second goal of the project was to examine generalization of motor and sensory changes. Specifically, we examined how motor and sensory systems change when you moved from novel start positions, to determine if the path your hand took influenced your perception of its position.

After having been briefed on the purpose of this research, do you consent to have your data included in this study?

Signature of participant: _________________________ Date: ___________________

Signature of Researcher: _________________________ Date: ___________________