MOTOR LEARNING AND SENSORY PLASTICITY IN HEALTHY ADULTS AND PARKINSON'S DISEASE

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ABSTRACT

We use multiple sources of sensory information to guide goal-directed movements, such as reaching. When information from multiple modalities (i.e. vision, proprioception) is incongruent, one learns to adapt his or her movements and recalibrate one sense to more closely match the other; simply put, one begins to perceive his/her hand where one sees it. This thesis attempts to better characterize this sensory recalibration (termed 'proprioceptive recalibration') following adaptation to a visuomotor distortion under a variety of contexts, and contributes to the existing literature that describes sensory plasticity associated with motor learning. Specifically, chapter two describes the effect of initial exposure to a visuomotor distortion and the dominance of the hand trained on proprioceptive recalibration. In this study, participants used their dominant right or non-dominant left hand to reach to targets with visual feedback of hand position that was abruptly rotated clockwise relative to their unseen hand. Proprioceptive recalibration was then assessed and found to be comparable in the two hands and consistent with previous studies employing a gradual perturbation; these findings suggest that neither the initial error signal nor dominance of the hand trained influence recalibration. Chapter three describes how the magnitude of the visuomotor distortion affects the magnitude of recalibration, and how this is related to changes in reach aftereffects. Changes in reach aftereffects and proprioception were measured following adaptation to increasingly misaligned visual hand feedback; these changes were found to increase systematically as a function of the distortion magnitude. However, while these changes were directly correlated with the distortion magnitude, they were not correlated with each other, which suggests that these two processes may be mediated by simultaneous yet separate underlying mechanisms. Chapter four similarly describes how the magnitude of a cross-sensory error signal (generated in the absence of a visuomotor signal derived from goal-directed movement)

affects the magnitude of recalibration, and how this is related to changes in reach aftereffects. Participants moved their unseen hand along a grooved path while viewing a cursor that moved towards a target; the position of the path was gradually rotated counter-clockwise with respect to the cursor. Following this cross-sensory adaptation, changes in reach aftereffects and proprioception were both found to saturate at a small distortion as no further changes were observed with training with increasing misalignment. Furthermore, these changes were not correlated with the magnitude of the misalignment. However, in contrast to the findings in chapter three, these changes were correlated with each other, suggesting that the cross-sensory discrepancy drives changes in both reach aftereffects (partially) and proprioception. This study helps to characterize the contribution of different error signals to changes in motor and sensory systems. Lastly, chapter five describes how damage to central nervous system structures integral to sensorimotor integration (i.e. the basal ganglia) affects proprioceptive recalibration. Patients with Parkinson's disease were able to learn to reach to targets with gradually rotated and translated visual feedback of hand positions comparably to healthy older adults. Patients also recalibrated proprioception comparably to healthy older adults, although the trend for greater recalibration in patients suggests that they may depend more on salient visual information of hand position than proprioceptive feedback to guide movement.

ACKNOWLEDGEMENTS

"Basic research is when I am doing what I don't know what I am doing."
— Wernher von Braun

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CHAPTER ONE

GENERAL INTRODUCTION

1.1 GENERAL INTRODUCTION

Movement is arguably the most important facet of human functioning and the primary means by which we interact with each other and negotiate our environment. While organisms possess innate and primitive motor behaviours and reflexes that allow them to respond to the environment, these motor programs are not sufficient for survival in a constantly changing environment. In order to succeed, organisms must constantly expand their motor repertoire and adapt well-learned movements to changing circumstances. Learning refers to the interaction of an organism with its environment and results in the organism acquiring new knowledge, which is stored in memory and can be recalled at later times. Motor learning can occur through two broad channels. The first is skill acquisition, where learning a new motor behaviour results in the acquisition and memory storage of a new skill. This process expands the repertoire of learned movements (Hallett, Pascual-Leone, & Topka, 1996). Many motor commands that are present in humans are obtained via skill acquisition; for example, learning to write with pen and paper. Alternatively, existing skills can be adapted when one is faced with an altered environment. In this case, writing on an upright chalkboard would require modifying the motor plan that is used when writing on paper on a desk. As one might expect, the first encounter with these environmental or contextual changes often leads to errors in the expected output (e.g. inconsistent letter size, line unevenness) but with practice, one is able to achieve the desired goal and perform the task at previous levels. Unlike skill acquisition, motor adaptation generally does not lead to an enhancement of the motor system's capabilities, but rather allows the system to function at a prior performance level in the face of changing environments.

Motor adaptation has been well-investigated in many situations; one of the best studied is during a goal-directed reaching task, where the desired movement and the actual movement are made incongruent through a

misalignment in the sensory information used by the brain. This misalignment occurs naturally, such as when reaching to an object underneath the water's surface; alternatively, this misalignment, can be induced artificially, such as when wearing goggles that displace the entire visual field. In cases of sensory misalignment, individuals will gradually adjust their movements so that the visual representation of the limb will achieve the desired movement endpoint. This type of learning is referred to as visuomotor adaptation. Recent evidence suggests that in addition to adapting movements, sensory systems undergo changes as well. Following adaptation to a visual-proprioceptive misalignment, such as those described above, individuals will proprioceptively perceive their limb as being in the same position as the visual estimate of the limb, even if the limb's actual position is displaced from its visual estimate. Simply put, individuals will feel their limb to be in the same position that they see it, even when it is not.

The motor changes that occur following visuomotor adaptation are well characterized; however, much remains to be elucidated about the sensory consequences of motor learning. The purpose of this research is to therefore characterize the sensory changes that occur following visuomotor learning. The projects contained herein investigate how both sensory and motor changes are affected by changes in the parameters of visuomotor learning and how damage to the central nervous system (CNS) affects these processes. Fundamentally, these studies provide novel insight into the signals the CNS uses to drive motor learning, and how these signals may contribute to the observed changes in movement and sensation following learning. Clinically, this information may have implications in the diagnosis, rehabilitation and/or treatment of patients suffering from CNS damage due to disease or stroke.

The following sections will provide the reader with the necessary background information to understand the experiments described in later chapters. Motor learning and its underlying neural mechanisms will be described,

with an emphasis placed on the sensory information that the CNS uses to generate movements and achieve learning. The use of internal models as a theory for the neural substrates of motor learning will then be briefly discussed. A discussion of the sensory changes that occur during motor learning will then be introduced in order to provide a foundation for the rational of the studies presented in later chapters. Damage to the CNS regions responsible for sensorimotor integration and its effects on motor learning and sensory processes will be included to establish the rationale for the study described in Chapter 5. Lastly, the specific objectives and rationales of the experiments described in the following chapters will be stated.

1.2 MOTOR CONTROL

Goal directed movement is especially important for human activity. While many repetitive and mundane actions such as reaching to a cup of coffee may seem easy to perform, the motor commands responsible for movement are generated by complex underlying processes. The sense of limb position is necessary for the execution and control of movement. To reach to an object or target, the CNS must first estimate the position of the hand relative to the target not only at the onset of movement, but throughout its duration. The difference between the current hand location and the desired hand location that results in successfully obtaining the object or target (called the difference vector) is fed back into the CNS, which then computes the necessary commands to bring the hand to the desired location (described later). This feedback is continuous and allows the system to make "on-line" corrections. Information can be derived from the visual percept of the limb's position (seen position), and positional information using proprioception (felt position). The brain combines these sensory signals to determine the current location and configuration of the limb in order to bring the

limb's effector (the hand) to the target. The roles of these sensory signals are now briefly discussed.

1.2.1 Vision

Based on data from neurophysiology, neuroimaging and clinical observation, scientists tend to view the higher cortical visual system of the brain as being separated into two functionally discrete processing streams: the dorsal (action) stream and ventral (perception) stream (Faillenot, Toni, Decety, Gregoire, & Jeannerod, 1997; Milner & Goodale, 1993; Milner & Goodale, 1995; Ungerleider & Mishkin, 1982). The ventral stream is associated with recognition and identification of objects and their features and contains neurons projecting from primary visual cortex (V1) through V2 and V4 to the posterior, central and anterior inferotemporal lobe. The dorsal stream is associated with localization of objects in space and the guidance of actions toward these objects, and contains neurons that project from V1 to various areas of the parietal lobe, such as MT and V5.

This anatomical two-stream model (Figure 1.1) was substantially based on the observation of a double dissociation of action and perception in patients with focal lesions. Patients with damage to the superior parietal cortex or parietal-occipital junction showed impaired reaching when asked to point to or grasp an object, while object identification and feature recognition was largely preserved (Karnath & Perenin, 2005). Conversely, patients with damage to the inferior temporal lobe showed marked deficits when tasked with identifying object features, while their reaching movements remained relatively intact (Adler, 1944; Milner & Goodale, 1995). The involvement of the dorsal stream in visually-guided reaching has been consistently demonstrated. The posterior parietal cortex (PPC) is involved in coding the location of targets, orienting attention towards those targets, and movement programming and execution (Corbetta, Kincade,

Ollinger, McAvoy, & Shulman, 2000; Culham & Kanwisher, 2001; Milner & Goodale, 1993; Mountcastle, Lynch, Georgopoulos, Sakata, & Acuna, 1975; Snyder, Batista, & Andersen, 1998). As previously mentioned, damage to areas along the dorsal stream has been shown to lead to marked impairments of reaching.
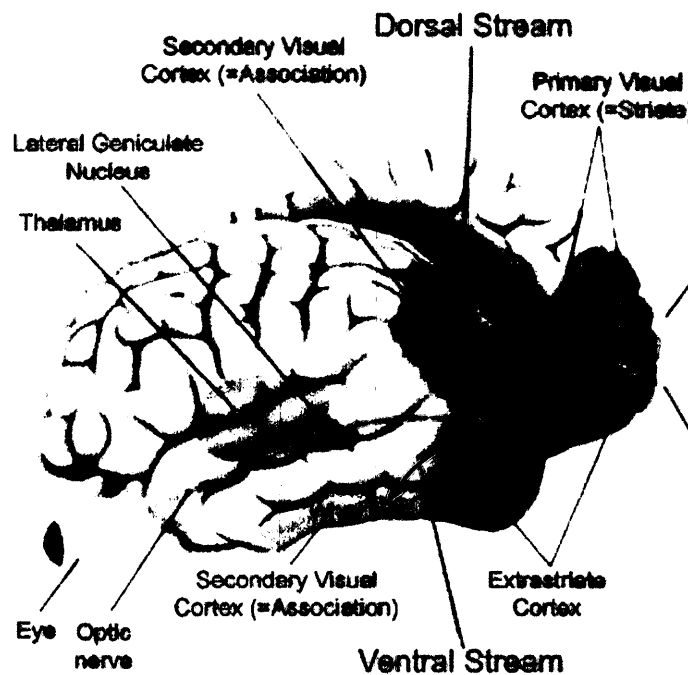
Figure 1.1 Diagrammatic representation of the two-stream hypothesis for visual association areas. Information arrives in the primary visual cortex of the occipital lobes via the optic nerve. Information is then communicated to association cortices: information regarding spatial location is communicated to the posterior parietal cortex (shaded in purple) while information regarding object properties is communicated to the inferior temporal cortex (shaded in orange). Image reprinted from http://quizlet.com/4415901/exam-3-flash-cards/.

The importance of the role of vision in executing movements was first demonstrated over a century ago (Woodworth, 1899) when movements towards targets were shown to be more accurate with vision than without vision. The role for vision in planning movements has since been shown to be important from early in life. Held and Bauer (1967) reared infant monkeys without visual feedback of the limb during the first month of life. When compared to control monkeys who were not restricted from viewing their limb, reared-restricted monkeys performed poorer during a reaching task with vision available, and even spent more time looking at the "new" limb. This suggests that early visual information of the limb is necessary in order to move and orient that limb toward a target accurately. Similar findings were observed when infant monkeys were reared in the dark (Held & Bauer, 1974). When compared to control monkeys, dark-reared monkeys performed poor during a reaching task, both when vision of the arm was available and unavailable. When human participants reached to targets without any visual information of the limb (termed "open-looped" reaches), errors were much greater than for reaches completed with visual limb feedback (Westwood, Heath, & Roy, 2001). Accuracy when reaching to targets was improved when even only initial visual feedback of the hand was available compared to when it was not (Prablanc, Echallier, Jeannerod, & Komilis, 1979; Prablanc, Echallier, Komilis, & Jeannerod, 1979). Pointing accuracy also has been shown to be highly influenced by available visual feedback of the hand (Admiraal, Keijsers, & Gielen, 2003) for both continuously displayed and remembered targets.

One of the most important findings to support the role of vision in movement planning and execution comes from studies in which the visual feedback of the limb is displaced from its actual location in space. In these tasks, visual limb feedback is provided in the form of a cursor. As expected, when participants initially reach to targets the errors are quite large. With practice,

however, participants are able to adjust their movements in order to bring the visual representation of the hand (the cursor) to the desired endpoint (Krakauer et al., 1999; Krakauer et al., 2000; Simani et al., 2007; Sainburg & Wang, 2002). This can occur without conscious awareness (in the case of gradually introduced visual-feedback misalignments) and demonstrates implicit reliance on visual information to influence movement. This paradigm also has been widely used to demonstrate motor learning and from here will be referred to as *visuomotor adaptation*. The consequences of visuomotor adaptation will be discussed in greater detail in later sections.

1.2.2 Proprioception

In addition to vision, the CNS uses another source of sensory information during movement planning and execution. Receptors located in muscles, joints and tendons are used to localize limb effectors and other body parts to develop a representation of the body's position in space. This sensory information is termed proprioception (Konczak et al., 2009; McCloskey, 1978; van Beers, Wolpert, & Haggard, 2002). Muscle spindles (Figure 1.2, left) are a type of proprioceptor located throughout the body of and in parallel to the extrafusal fibers of the muscle. Their role is the detection of changes to the length of a muscle. The intrafusal fibers located within the muscle spindle itself have filaments at each end that contract and expand with the muscle body; when the muscle is lengthened and the spindle is stretched, the afferent neuron sends an action potential to the brain to convey information regarding muscle state. The Golgi tendon organ (Figure 1.2, right) is another proprioceptor, located within the tendons that attach muscles to bones. The sensory dendrites of the Golgi organ are interwoven with the collagen fibres of the tendon; when the muscle is contracted, the collagen fibers are pulled taught and activate the afferent neuron to convey information about muscle tension. Together, these proprioceptors

provide information about muscle contraction and tension which, together with other mechanoreceptors throughout the body, are used by the CNS to deduce the position of the body's joints/limbs in space.
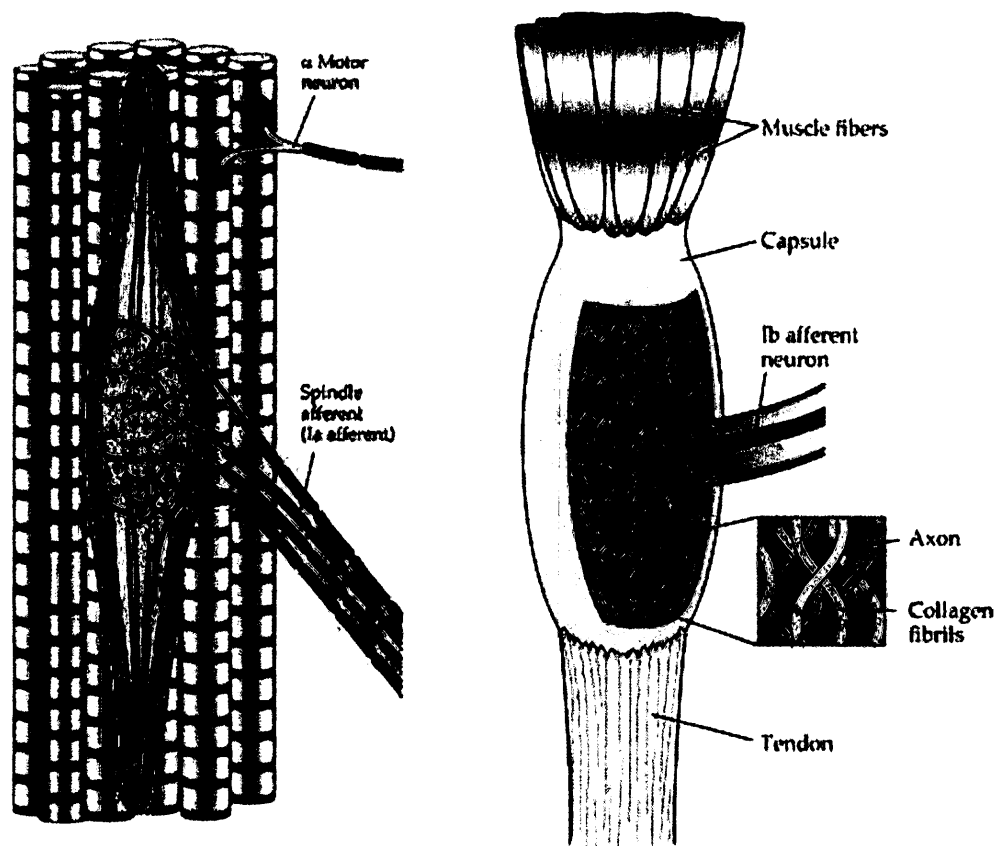
Figure 1.2 Muscle spindle (left) and Golgi tendon organ (right) are two of the body's proprioceptors. Image reprinted from http://grants.hhp.coe.uh.edu/clayne/6397/unit4a.htm.

Non-human primates that have had somatosensory input (including proprioception) to the CNS surgically ablated show marked impairments in

movement accuracy and coordination during reaches and in natural, unrestricted movements. In humans, this may occur due to large fiber sensory neuropathy which results in a loss of somatosensory input to the CNS (also called deafferentation). Deafferented patients have demonstrated impairments in several functions, including their ability to make movements in the absence of vision (Sainburg, Poizner, & Ghez, 1993). Reaching is also particularly affected and patients are unable to make accurate reaching movements towards visual targets when visual feedback of the limb is unavailable (Ghez, Gordon, & Ghilardi, 1995). These reaches tended to have both large directional and distance errors. In healthy humans in whom proprioceptive feedback of limb position was altered through tendon vibration, participants' movements were significantly deviated compared to when no vibration was applied (Larish, Volp, & Wallace, 1984). Taken together these findings suggest an important role of proprioception in computing and executing goal-directed movements.

1.2.3 Integrating sensory information with movement

When our eyes are open and we can see our hand, vision and proprioception simultaneously provide useful information about the hand's position that the CNS uses to plan and execute movements. Indeed, our movements become much more accurate when we use both sources of information compared to situations in which we must rely solely on vision or proprioception. So how does the CNS integrate this information to form a motor command and execute movement in a rapidly changing environment? To answer this question, the internal model theory of motor control has been posited.

1.3 NEURAL CONTROL OF MOVEMENT

1.3.1 Internal models

Learning a motor action requires the motor control system to link the sensory and motor information of a movement together. The internal model achieves this by simulating the response of the motor system in order to estimate the outcome of a particular motor command. When the brain generates a motor command, a prediction of the sensory consequences of that motor command is also produced. Simply put, the internal model predicts what will happen to the body for any given motor command and uses online feedback to make corrections to the movement. A motor command from the controller (i.e. the motor system) is transmitted to the effector (i.e. a limb) which results in muscle and joint motions that move the effector to the appropriate location (Kawato, 1999). Two varieties of internal models have been proposed: a) forward models mimic the causal flow of a process by predicting the effector's future state given information on its current state and the selected motor command; b) inverse models invert the causal flow by estimating the motor command that caused a transition in state (Figure 1.3).

Forward Model
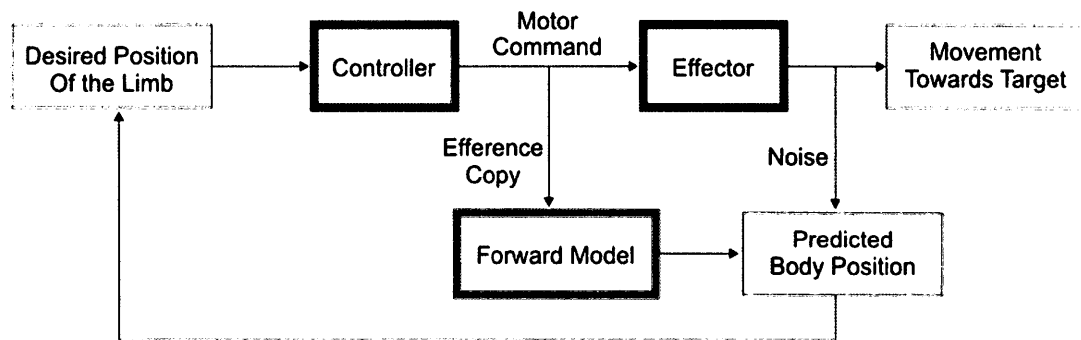
Inverse Model

Figure 1.3 Internal models of motor control. Forward (A) and Inverse (B) models.

In a forward model, the desired position of the limb is fed into the controller which generates a) a motor command to move the effector to the desired position and b) an efference copy of that movement, which is fed into the forward model. The forward model uses this efference copy to predict the outcome position of the effector, which is then compared with the actual position of the effector. The predicted and actual effector positions may differ (as in the case of motor adaptation, described later), in which case differences can be fed back into the system so that the motor plan can be adjusted to produce a new motor command to achieve a more desirable and accurate movement. In inverse models, the desired and actual position of the effector are input into the system to estimate the necessary motor command required to transform the current position into the desired position. The motor control system uses both forward

and inverse models to guide goal-directed movements, both before the movement occurs and on-line during the execution of the movement. The efference copy output (sensory feedback) of the inverse model can be used as input in a forward model to predict which motor commands will result in the desired outcome (Wolpert, Ghahramani, & Jordan, 1995; Wolpert & Kawato, 1998).

1.3.2 Internal models and sensorimotor adaptation

Evidence for the existence of internal models comes from behavioural studies of sensorimotor adaptation (including visuomotor adaptation). When participants make reaching movements to targets while feedback of the hand is manipulated (e.g. the position of the unseen hand is misrepresented by a cursor on a computer screen that is displaced from the hand's actual position), the hand path from the start position to the target is deviated from its normal trajectory. Instead of making straight lines, participants' movements may look like Cs or Ss, depending on how the cursor is distorted relative to the hand. Moreover, the position at which the hand stops moving may be significantly deviated from the target, resulting in large end-point error. However, following repeated trials, the trajectory paths start to resemble straight lines and the end-point error is reduced, suggesting that reaches become more accurate (Buch, Young, & Contreras-Vidal, 2003; Krakauer, 2009; Krakauer, Pine, Ghilardi, & Ghez, 2000; Sainburg & Wang, 2002). Furthermore, when the misrepresentation or distortion is removed, trajectories become deviated again and end-point errors increase in the direction opposite from the initial learning trials. These persistent deviations in movement are called aftereffects. The use of an internal model can explain these findings: under normal conditions the inverse model derives motor commands which compensate for arm dynamics and kinematics, while under altered conditions the inverse model derives motor commands that are

insufficient to compensate for misaligned visual feedback of the hand. With practice, the inverse model uses the misaligned feedback information derived from the distortion to correct the output of the effector on-line during the movement. That is, the motor plan is adjusted to yield motor commands that compensate for the distortion (Miall & Wolpert, 1996; Wolpert et al., 1995; Wolpert & Kawato, 1998). As well, learning this new 'mapping' between the visual feedback of the hand and the motor output can be applied to movement planning, resulting in improved accuracy right from the beginning of a movement. When the distortion is removed, the inverse model continues to generate the newly modified motor commands to compensate for the distortion and this results in the observed aftereffects (Kawato, 1999).

1.4 CHARACTERIZING SENSORIOMOTOR ADAPTATION

As previously described, sensorimotor adaptation occurs when conflicting sensory information is presented during motor tasks and the CNS must learn to adapt the movements to fit the new sensory context. Adaptation can occur under a variety of contexts which are described here.

1.4.1 Prism adaptation

Humans and monkeys have both been shown to adapt their movements to displacements of the visual field. When monkeys were forced to wear dove prism goggles which inverted the entire visual image 180° along the left-right plane, they were initially unable to reach to a target that they could accurately reach to prior to wearing the goggles. In fact, the monkeys could barely perform any movements at all. However, after 30 to 50 days the monkeys began to reach straight towards the target with smaller errors; indeed, performance began to approach baseline levels without distortion (Sugita, 1996). Thus, the monkeys

were able to adjust their arm movements such that a target appearing to be on the left side of a computer screen as viewed through the goggles would result in the monkey reaching to the right side of space. A prism study conducted in humans demonstrated similar findings (Sekiyama, Miyauchi, Imaruoka, Egusa, & Tashiro, 2000). Participants wore inverting prism goggles for 30 days. During the first days of use, participants could not perform activities of daily living particularly well (some participants were observed to hold walls as they walked down a corridor). After 30 days of wearing the goggles, participants were able to ride a bicycle, chop vegetables, and perform other tasks. In studies, when the prism goggles were removed, monkeys and humans made errors in the opposite direction when reaching to targets and performing tasks. These movement aftereffects were taken as evidence of adaptation, although they dissipated in less time than it took to generate them. However, when participants put the goggles back on during subsequent testing days, they quickly readapted. These findings suggest that a new kinematic map for altered vision was created and retained separately from a kinematic map for unaltered vision.

Adaptation to wedge prisms, which displace vision by only 5° to 25°, has been shown to occur even quicker than that of dove prisms, with accuracy approaching baseline levels requiring only a few trials. Moreover, the washout of aftereffects (deadaptation) requires roughly the same number of trials as initial adaptation (Kurata & Hoshi, 1999; Martin, Keating, Goodkin, Bastian, & Thach, 1996b). In several experiments, both humans and monkeys made reaches or throws towards targets, both while wearing the goggles and while not wearing the goggles (or while wearing goggles displacing vision to one direction followed by goggles displacing vision of the opposite direction). Following alternating visual feedback (i.e. with goggles, without goggles), participants were able to achieved first-trial accuracy in either feedback context after only two and a half weeks. These findings suggest that rather than acquiring new kinematic mappings, the

CNS adjusts the kinematic mapping for vision in the context of prisms, and that motor adaptation rather than skill acquisition is the process driving the observed motor learning.

1.4.2 Cursor adaptation

The mapping between vision and motor commands can also be adjusted by artificially manipulating visual feedback of the hand displayed on a screen, as previously described in earlier sections. One such visuomotor manipulation involves cursor distortion, where a cursor representation of the hand on the screen is displaced with respect to the actual location of the unseen hand. In these paradigms the cursor is most often rotated or laterally translated relative to the unseen hand. Unlike prism adaptation, cursor rotations do not displace the target location; only visual feedback of the hand is affected. (Krakauer, Ghilardi, & Ghez, 1999; Sainburg & Wang, 2002; Simani, McGuire, & Sabes, 2007). This method of inducing visuomotor adaptation is used in the experiments described in later chapters. Like prism adaptation, cursor adaptation results in individuals adjusting their movements to acquire a target and achieve the desired movement.

1.4.3 Force-field adaptation

Manipulation of visual feedback is not the only method of inducing a sensorimotor discrepancy. Proprioception also can be artificially manipulated by inducing mechanical or force disturbances during limb movement. Examples of this include changing the inertial properties of the moving limb (Bock, 1990) or by introducing a force perturbation during movement (Shadmehr & Mussa-Ivaldi, 1994). When reaching to a target with a force perturbation, participants initially make large errors but are able to rapidly align the cursor with the target in a few trials. Moreover, adaptation to these manipulations leads to aftereffects in which

the trajectories are in the direction opposite to the initial adaptation errors. As in other forms of sensorimotor adaptation, the aftereffects wash out after roughly the same number of trials required achieving initial adaptation.

1.5. PROPRIOCEPTIVE RECALIBRATION

Moving while visual feedback is distorted leads to a mismatch of the expected and actual outcomes that result in sensorimotor remapping and adaptation. However, this manipulation also induces a mismatch between vision and proprioception. How does the brain deal with this sensory conflict? Previous studies have suggested that visuomotor adaptation arises due to changes in proprioception, such that one's sense of felt hand position becomes aligned with the visual representation of the hand (Bernier, Chua, & Franks, 2005; Hay, Pick, & Ikeda, 1965; Redding, Rossetti, & Wallace, 2005; Redding & Wallace, 2004; Simani et al., 2007). Simply put, we begin to feel our hand where we see our hand. In order to examine if proprioception is recalibrated following visuomotor adaptation, previous studies have primarily used tasks that required participants to make self-generated movements. For example, participants reached to a proprioceptive target (i.e. body midline or the index finger of the untrained hand) using the hand that had adapted to the visuomotor distortion (Simani et al., 2007; van Beers et al., 2002). While these participants adapted their reaches to these proprioceptive targets following visuomotor adaptation, it is not clear if they did so due to cross sensory recalibration (i.e. proprioception was recalibrated to match vision) and/or simply motor recalibration (i.e. the internal model was updated). To clarify this, Henriques and colleagues examined proprioceptive recalibration in tasks in which participants did not employ any self-generated movements. Instead, participants provided a perceptual estimate of either the path the hand had travelled (Malfait, Henriques, & Gribble, 2008; T. Wong & Henriques, 2009)

or the location of the hand relative to a visual reference marker (Cressman & Henriques, 2009, 2010). This later paradigm involved moving participants' hands passively (the hand was pushed by a robot) or actively (the participants pushed the hand) along a grooved pathway with no target or visual feedback of the hand. Following the appearance of a reference marker, participants made a decision as to whether their hand was to the right or left of the reference marker. Using this hand position estimation task, Cressman and Henriques (2009) have shown that visuomotor adaptation to either a rotated or translated cursor led to recalibration of felt hand position relative to a visual reference marker, as well as body midline (a non-visual reference point), both when the hand was actively and passively moved. This recalibration was also shown to persist throughout the lifespan as older and younger adults recalibrated proprioception to a comparable extent (Cressman, Salomonczyk, & Henriques, 2010). Specifically, Cressman and Henriques observed a shift in felt sense of hand position of approximately 6°, which corresponded to 20% of the distortion introduced, suggesting that at least partial sensory recalibration took place. Thus, proprioception was shifted leftwards to match the leftwards movement induced by the visual distortion. In a follow-up study, Cressman & Henriques (2010) showed a similar change in felt hand position following mere exposure to a visual-proprioceptive discrepancy. In this case, during "training" participants' hands were either passively or actively moved along a constrained path while they saw a cursor that was displaced from their actual hand location; participants did not engage in reaching or any goal directed movement. In both conditions, participants still adjusted their subsequent open-loop reaches in the direction of the sensory discrepancy similar to those aftereffects observed following traditional sensorimotor learning, although these "aftereffects" were substantially smaller. Participants also recalibrated the position of their hand and, unlike aftereffects, this recalibration occurred to the same extent as that observed in Cressman and Henriques

(2009). Thus, visuomotor adaptation and cross-sensory recalibration appear to occur even without goal-directed movement, although proprioceptive recalibration may be due to a different aspect of visuomotor training than the persisting aftereffects.

Sensory recalibration has also been demonstrated following force field adaptation (Ostry, Darainy, Mattar, Wong, & Gribble, 2010). Participants trained to reach to targets while a velocity-dependent force perturbation was applied to the unseen hand. Following adaptation to the force perturbation, participants' perception of the location of their unseen hand was shifted in the direction of the adaptation to the perturbation. Moreover, this shift lasted for at least 24 hours following adaptation. Interestingly, these authors did not observe a perceptual shift when participants' hands were passively moved in the perceptual assessment task, as was observed by Cressman and Henriques (2010). Thus, sensory recalibration occurs during various adaptation paradigms in the presence of volitional movement due to an adaptation of sensorimotor and cross-sensory maps; however mechanisms underlying cross-sensory recalibration during passive movement remain less well understood.

1.5.1. Recalibration and adaptation

Visuomotor adaptation leads to at least partial proprioceptive recalibration, but this relationship remains poorly understood. One possibility is that visuomotor adaptation – specifically the resulting changes in hand movements made during trials when the distortion is removed – is at least partially due to cross-sensory recalibration. In other words, reaches are deviated in the direction of adaptation to the visuomotor distortion because the felt position of the hand has also shifted in that direction. Alternatively, the changes in sensory and motor components may be distinct. Reaches are deviated following training perhaps only because the desired motor command or internal model has been altered. In this case,

potential changes in estimates based on these sensory signals are not related to the resulting changes in movement that follow from visuomotor adaptation. Instead, visuomotor adaptation leads to a) changes in the movement but not proprioception, or b) simultaneous but separate, uncorrelated sensory and motor adjustments. The focus of this dissertation will be to further characterize proprioceptive recalibration and to help elucidate the contributions of different error signals responsible for adaptation and recalibration.

1.6 PARKINSON'S DISEASE AND ADAPTATION

Parkinson's disease (PD) is a neurodegenerative disorder affecting 1-2% of the population over the age of 65. The disorder is a result of the depletion of dopamine-producing neurons of the substantia nigra pars compacta, one of several nuclei located in the basal ganglia. The loss of these cells leads to reduced inhibition of the striatum and subsequent impairment to the direct pathway (a fronto-striatal circuit governing movement), which ultimately results in a reduction of excitatory signals to the cortex. Thus, the cardinal symptoms of PD are those of reduced movement, including rigidity, bradykinesia, hypokinesia, and postural instability (Jankovic, 2008). Tremor, which is observed in up to 70% of patients at the onset of disease, may be a result of hyperactivation of the thalamus via the indirect pathway.

Although typified primarily by motor dysfunction, sensory systems have been shown to be affected by PD as well. Thresholds for detection of olfactory stimuli has been shown to increase in patients with PD, suggesting that sense of smell is reduced, and as many as 50% of patients have shown evidence of complete loss of smell (Muller, Mungersdorf, Reichmann, Strehle, & Hummel, 2002). In addition to a disruption of olfactory sense, as many as 40% of PD patients report abnormal sensations and/or pain (Ford, 2010). Strong evidence

suggests that proprioception is particularly affected by PD. Patients have been shown to have elevated thresholds for detection of passive limb movement, an impairment that was correlated with disease severity and duration (Konczak, Krawczewski, Tuite, & Maschke, 2007; Maschke, Gomez, Tuite, & Konczak, 2003). Patients may also require greater movement velocity to detect limb motion. The perception of weight (Maschke, Tuite, Krawczewski, Pickett, & Konczak, 2006) and arm curvature (Konczak, Li, Tuite, & Poizner, 2008) are also impaired in PD. Proprioceptive deficits observed in PD may even result in patients becoming more reliant on visual cues as suggested by previous reports into reaching, especially when vision of the arm is unavailable and proprioception is the dominant sensory cue guiding movement (Adamovich, Berkinblit, Hening, Sage, & Poizner, 2001). Increased dependence on visual cues has also been demonstrated during sequential arm movements (Curra et al., 1997) and walking (G. N. Lewis, Byblow, & Walt, 2000).

1.6.1 The basal ganglia and adaptation

While the cerebellum has been strongly implicated in motor learning (Kawato, 1999) via error-driven signals (i.e. internal models), this discussion will focus on the basal ganglia and its role in motor learning and sensory integration for the purposes of the experiments contained in this dissertation.

The basal ganglia are a group of subcortical midbrain structures consisting of the caudate and putamen (collectively referred to as striatum), globus pallidus, substantia nigra, and subthalamic nucleus (Figure 1.4).
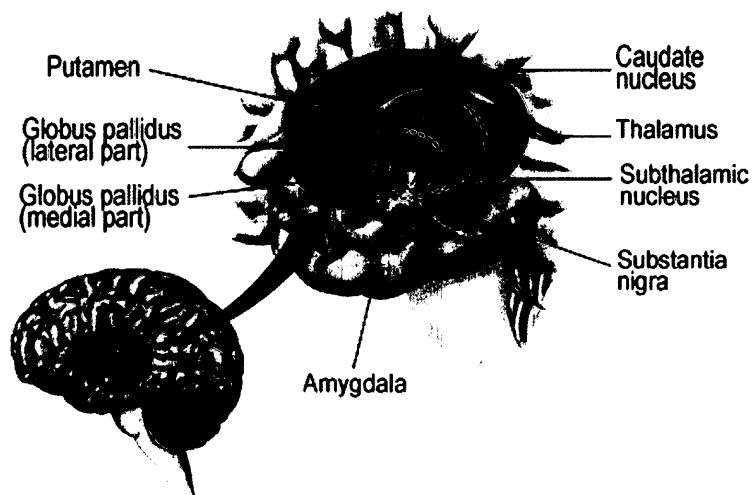
Figure 1.4 Illustration of the anatomy and location of the structures of the basal ganglia. Image reprinted from
http://cti.itc.virginia.edu/~psy220/kalat/JK246.fig8.15.basal_ganglia.jpg.

The basal ganglia are heavily involved in different aspects of motor control and therefore extensive connections exist between the basal ganglia, thalamus and cerebral cortex. A diagram of this circuitry is presented in Figure 1.5. The striatum is the main structure which accepts excitatory inputs from the motor areas of the cerebral cortex. Cortical inputs synapse with inhibitory medium spiny neurons in the striatum. Output neurons from the striatum project onto neurons of the internal globus pallidus via two pathways: the direct pathway and the indirect pathway. The indirect pathway consists of striatal projections to the inhibitory neurons of the external globus pallidus which in turn project to the excitatory neurons of the subthalamic nucleus. These neurons synapse on the external globus pallidus. In contrast, the direct pathway consists of inhibitory striatal projections to the internal globus pallidus. The external globus pallidus projects inhibitory neurons to the thalamus, which in turn projects excitatory neurons back to the cortex. This organization results in disinhibition of the neurons in the

thalamus (and subsequently excitation of the cortex) by the direct pathway and inhibition of the same structures by the indirect pathway (Y. Smith et al., 2009). Dopaminergic inputs from the substantia nigra pars compacta also project to the striatum and these projections have the effect of modulating the amplitude of the direct and indirect pathways, and will be an important consideration in the discussion of Parkinson's disease that follows.
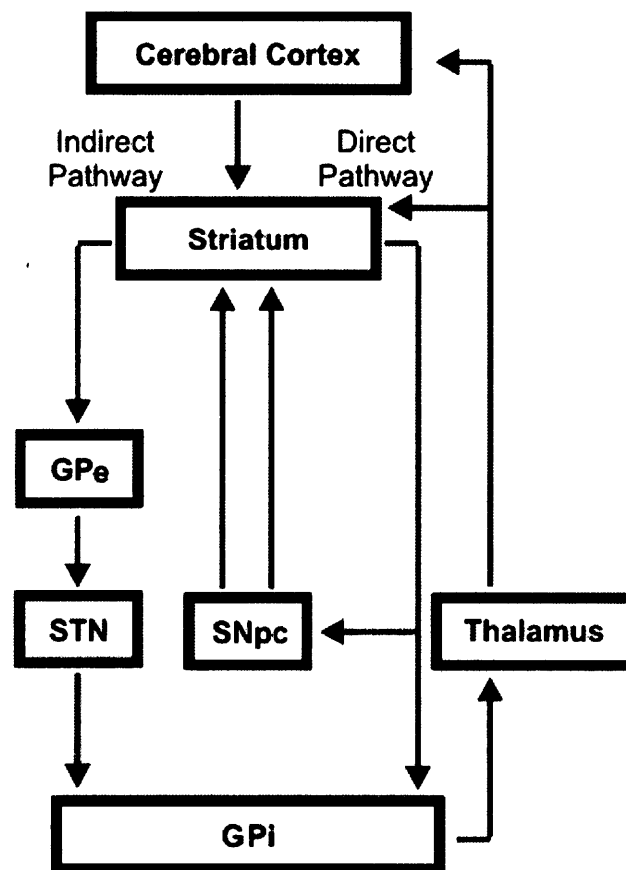
Figure 1.5 Circuitry of the basal ganglia. Green lines indicate excitatory projections, red lines indicate inhibitory projections. Globus pallidus external

segment (GPe), globus pallidus internal segment (GPi), subthalamic nucleus (STN), substantia nigra pars compacta.

The basal ganglia have been strongly implicated in motor control and learning, with a particular emphasis placed on the selection and inhibition of action commands (Alexander & Crutcher, 1990). This is thought to be achieved by the interaction between the two pathways: activation of the direct pathway is thought to lead to a reduction of inhibition of thalamocortical output and thus facilitate the intended movement, while activation of the indirect pathway would cause inhibition of thalamocortical output and thus suppress unintended movement (Y. Smith et al., 2009). The extensive neuronal convergence of the corticostriatal pathway suggests that the basal ganglia are involved in recognizing the context of a particular behavioural state. Performing a task with one part of the body, such as turning a doorknob with your hand, has implications for other body parts. The basal ganglia appear to be important for recognizing and minimizing these consequences and thus points to a role of the basal ganglia in context-dependent action (Horak, Nutt, & Nashner, 1992).The basal ganglia have also been shown to contribute to motor learning via reward-based mechanisms. Schultz and colleagues (1993) demonstrated that dopamine neurons in primate midbrains respond to rewards following successful trials. As the animal learns the task, the neurons instead become tuned to the conditioned visual stimulus rather than the actual reward. This mechanism has implications for visuomotor learning.

The role of the basal ganglia in sensorimotor integration is becoming increasingly recognized. Neurophysiological evidence shows that cells in the basal ganglia respond specifically to sensory stimuli. The basal ganglia contain many neurons that have proprioceptive receptive fields that respond to both passive and active joint motions (Crutcher & DeLong, 1984; DeLong, Crutcher, &

Georgopoulos, 1985). A large proportion of cells in the caudate and substantia nigra contain cells that respond to stimulation from multiple sensory modalities. These cells may integrate information from these different modalities in order to form a cohesive representation of the environment (Nagy, Paroczy, Norita, & Benedek, 2005). Putamen cells have been shown to respond to combined visual-tactile stimuli, suggesting further multiple sensory modality processing in this region (Graziano & Gross, 1993). Cells that selectively respond to sensorimotor stimuli (coupled sensory and motor stimuli) also have been observed within the basal ganglia. Activity of cells in the striatum of several non-human species has been shown to depend on whether the sensory information is linked to movement, and cells that are silent for a particular sensory event have been shown to fire when the same event is used as a cue for movement (Konczak et al., 2009). The greatest support for the role of the basal ganglia in sensorimotor integration comes from patients with impairments caused by damage to this region. Individuals with PD and Huntington's disease (which results from damage to the striatum) show deficits of sensorimotor integration in a variety of tasks and contexts (Lasker & Zee, 1997; Lueck, Tanyeri, Crawford, Henderson, & Kennard, 1990).

1.6.2 Sensorimotor integration in PD

Given the sensory impairments demonstrated in PD, and that brain regions involved in sensory integration are disrupted, it would be unsurprising to find that sensorimotor integration is impaired as well. Indeed, this appears to be the case. Proprioceptive-motor integration during grasping has been shown to be disrupted as patients tend to increase their grip force when holding an object, despite showing awareness of necessary or appropriate grip force for the task (Nowak & Hermsdorfer, 2006). Voluntary saccades require visual cues to be integrated with motor output, and these have been shown to be impaired in PD

patients (Briand, Hening, Poizner, & Sereno, 2001) whereas reflex saccades are generally spared. Instead of being considered solely a disorder of gain control of motor control, Konczak and colleagues (Konczak et al., 2009) suggest that PD may be considered partially as a disorder of gain control of sensorimotor integration.

Knowledge of deficits of sensorimotor integration in PD has led to increased interest in visuomotor adaptation in this population. Several studies suggest that visuomotor adaptation is impaired in PD relative to controls. Stern and colleagues (1988) assessed adaptation to displacing prisms in PD patients and normal controls. While the initial end point errors and rate of learning across trials were similar for both groups of participants, aftereffects were observed only in controls, suggesting that patients were unable to maintain (i.e. remember) the new learned sensorimotor mapping. Contreras-Vidal and Buch (2003) examined visuomotor adaptation to a 90° visuomotor rotation in PD patients and normal controls. The authors observed smaller aftereffects, greater directional error, and decreased smoothness of movement in the patient group relative to controls, suggesting that adaptation was slower and reduced and therefore impaired in PD. Reaching under 3D distortions also has been assessed in PD patients (Messier et al., 2007). Both initial learning and reversal learning (i.e. when the sign of the distortion was reversed) were markedly impaired in PD patients relative to controls, suggesting that learning novel visuomotor coordination is impaired.

Most studies have assessed performance of PD patients while they were medicated with primary drug therapy for PD: L-DOPA and other CNS dopamine boosting compounds. However, the effect of dopaminergic medication on sensory processing and visuomotor adaptation is not well understood. While dopaminergic medication is highly effective at improving motor function, some reports suggest that it does not improve sensory function in PD (Jacobs & Horak,

2006). O'Suilleabhain, Bullard and Dewey (2001) were among the first to report impaired proprioceptive functioning in PD patients who were taking dopaminergic medication. These authors observed impairments in matching the angle of the elbow joints and recalling these angles in PD patients in the "on" medicated state relative to PD patients in the "off" medicated state and normal controls. Mongeon and colleagues (2009) further examined the effect of dopaminergic medication on proprioception by having PD patients and controls reach to 3D targets under varying sensory availability conditions. The authors found that patients in the "on" medicated state made greater errors relative to controls, and that dopaminergic medication did not normalize these errors; in some patients it actually impaired it.

Given these findings, it is possible that proprioceptive acuity of the end-effector (i.e. the hand) may be impaired in PD; moreover, the change in positional estimates of hand position may be affected by degeneration of dopaminergic nigrostriatal pathways underlying PD. Lastly, the effect of dopaminergic medication on proprioceptive processing and sensorimotor integration deserves further investigation. Thus, the last chapter of this dissertation will consider these questions in patients with PD along with healthy, age-matched controls.

1.7 SPECIFIC OBJECTIVES

This work contributes to the general aim of understanding how the brain uses sensory information to guide motor action. This dissertation specifically addresses how different sensory signals contribute to motor learning and sensory recalibration and has the following objectives:

Objective 1:

- Determine how motor learning and sensory recalibration are affected by the size of the initial error during visuomotor adaptation (Chapter 2).

Objective 2:

- Determine if motor learning and sensory recalibration are consistent in the dominant and non-dominant hands by examining these processes in right-handed participants (Chapter 2).

Objective 3:

- Determine if the magnitude of the visuomotor distortion systematically affects the resulting changes to motor and sensory systems (Chapter 3).

Objective 4:

- Determine which sensory error signals contribute to motor changes and sensory recalibration following adaptation to a cross-sensory discrepancy (Chapter 4).

Objective 5:

- Determine how proprioceptive acuity is affected by nervous system pathology of structures integral to sensory and sensorimotor integration (Parkinson's disease; Chapter 5)

Objective 6:

- Determine how patients with Parkinson's disease adapt to visuomotor adaptations and recalibrate proprioception (Chapter 5)

Objective 7:

- Determine if pharmaceutical intervention restores visuomotor adaptation and proprioceptive recalibration to levels comparable to those with healthy nervous systems (Chapter 5).

The remaining chapters of this dissertation will describe the experiments used to achieve these objectives. The rationale, hypotheses, methods, results and discussion of findings will be articulated in detail in each of the following chapters.

CHAPTER TWO

PROPRIOCEPTIVE RECALIBRATION IN THE RIGHT AND LEFT HANDS FOLLOWING ABRUPT VISUOMOTOR ADAPTATION

Danielle Salomonczyk, Denise YP Henriques & Erin K Cressman

2.1 ABSTRACT

Previous studies have demonstrated that after reaching with misaligned visual feedback of the hand, one adapts his or her reaches and partially recalibrates proprioception, such that sense of felt hand position is shifted to match the seen hand position. However, to date, this has only been demonstrated in the right (dominant) hand following reach training with a visuomotor distortion in which the rotated cursor distortion was introduced gradually. As reach adaptation has been shown to differ depending on how the distortion is introduced (gradual vs. abrupt), we sought to examine proprioceptive recalibration following reach training with a cursor that was abruptly rotated $30°$ clockwise (CW) relative to hand motion. Furthermore, because the left and right arms have demonstrated selective advantages when matching visual and proprioceptive targets, respectively, we assessed proprioceptive recalibration in right-handed participants following training with either the right or left hand. On average, we observed shifts in felt hand position of approximately $7.6°$ following training with misaligned visual feedback of the hand, which is consistent with our previous findings in which the distortion was introduced gradually. Moreover, no difference was observed in proprioceptive recalibration across the left and right hands. These findings suggest that proprioceptive recalibration is a robust process that arises symmetrically in the two hands following visuomotor adaptation regardless of the initial magnitude of the error signal.

2.2 INTRODUCTION

The central nervous system (CNS) integrates visual and proprioceptive information when planning a movement. If these sensory cues conflict and one is reaching to a visual target, one tends to rely more on the visual estimate of the hand than on the actual or felt position to guide motor output. For example, participants reaching to a visual target with misaligned visual feedback of the hand (e.g. reaching in a virtual reality environment or while wearing prism goggles) adjust their movements in order for the visual representation of the hand to achieve the desired endpoint. Furthermore, participants reach with these adapted movement patterns following removal of the distortion (i.e. exhibit aftereffects; (Baraduc & Wolpert, 2002; Buch et al., 2003; Krakauer et al., 1999; Krakauer et al., 2000; Martin et al., 1996b). This form of motor learning is referred to as visuomotor adaptation.

In addition to visuomotor adaptation, reaching with misaligned visual feedback of the hand has been shown to result in changes in sense of felt hand position (i.e. proprioceptive recalibration). Specifically, proprioceptive recalibration has been suggested to arise following reaches made while wearing prism goggles, where the visual distortion is introduced immediately and in full (Harris, 1963; Hay & Pick, 1966; Simani et al., 2007), and following reaches made in a virtual-reality environment (Cameron, Franks, Inglis, & Chua, 2010; Cressman & Henriques, 2009; Harris, 1963; Hay et al., 1965; Ostry et al., 2010; Simani et al., 2007). Until recently, this sensory recalibration was demonstrated following visuomotor adaptation by asking participants to reach with the adapted hand to proprioceptive targets (Redding & Wallace, 1996; Simani et al., 2007; van Beers et al., 2002). While results from these tasks indicated that reaches to proprioceptive targets were adapted, it is unclear if these changes in reaches reflected proprioceptive recalibration per se. Given that participants used their adapted arm, these resulting reaching movements to localize proprioceptive

targets could have been influenced by motor adaptation. Thus, in attempt to assess proprioceptive recalibration independent of motor changes, Henriques and colleagues (Cressman & Henriques, 2009, 2010; Cressman et al., 2010; Salomonczyk, Cressman, & Henriques, 2011) and Ostry et al. (2010) designed sensory estimation tasks that do not require any goal-directed movement. Specifically, in Cressman and Henriques' (2009) estimation task, participants indicated the position of their hand relative to a visual or proprioceptive reference marker. In general, results revealed that participants shifted the position at which they felt their hand was aligned with a reference marker ~6° (or about 20% of the visuomotor distortion), in the direction that they adapted their movement following reaches with a gradually introduced visuomotor distortion (Cressman & Henriques, 2009, 2010; Cressman et al., 2010; Salomonczyk et al., 2011). This shift in felt hand position has been shown to be remarkably consistent across several parameters, including the type of distortion (rotation vs. lateral displacement), the magnitude of the distortion (up to 70°), the extent of reach training (up to 300 trials), the type of reference marker (visual vs. proprioceptive), method of hand positioning (active vs. passive placement of the hand), and even across different age groups (young adults vs. adults 60 years and older).

Previous work from our lab examining sensory changes following motor adaptation has introduced the visuomotor perturbation (e.g., a visuomotor rotation around the hand) gradually during adaptation trials. In the current study we sought to determine if the size of the initial error signal influences sensory recalibration. To address this question, we introduced the visuomotor distortion abruptly, such that participants initially experienced large reaching errors. To date, research comparing adaptation to large and small error signals has focused on examining resulting changes in movements, without a similar investigation into sensory changes. With respect to visuomotor adaptation, results indicate that motor learning (aftereffects) are frequently greater in participants who train to

reach with misaligned sensory feedback of the hand when the distortion is introduced gradually and participants experience small reaching errors compared to when the distortion is introduced abruptly and participants initially experience large reaching errors; after participants reach while wearing prism goggles (Michel, Pisella, Prablanc, Rode, & Rossetti, 2007), with a visuomotor rotation (Abeele & Bock, 2001; Kagerer, Contreras-Vidal, & Stelmach, 1997) or with a force perturbation (Criscimagna-Hemminger, Bastian, & Shadmehr, 2010). Furthermore, retention of motor learning is reportedly greater in participants that adapt to an incrementally introduced distortion compared with an abruptly introduced one (Klassen, Tong, & Flanagan, 2005). By establishing if proprioceptive recalibration arises following adaptation to an abrupt visuomotor distortion, we will be able to determine if the size of initial error signals experienced also affects sensory plasticity.

Additionally, we sought to determine if proprioceptive recalibration is comparable between the left and right hands of right-handed individuals. Previous studies examining proprioceptive recalibration have focused on assessing shifts in felt right hand position following motor learning of the right arm in right-handed individuals. Given that Goble and colleagues (Goble & Anguera, 2010; Goble & Brown, 2008) have recently shown that the left arm performs better for matching proprioceptive targets and the right arm for visual targets, reaching with misaligned visual feedback may have different effects on proprioceptive recalibration in the two arms. For example, the left arm, which has demonstrated an advantage for position-related proprioceptive sense in comparison to the right arm, may be more susceptible to sensory recalibration. If we do find an arm effect of proprioceptive recalibration it would suggest hemispheric asymmetry for encoding visual and proprioceptive information.

2.3 METHODS

2.3.1 Participants

Forty-six right-handed young adults (mean age = 21.0 years, SD = 3.58, 29 female) were recruited from York University and volunteered to participate in the tasks described below. Data from three participants were eliminated from analyses and hence not included in the results provided, as they were unable to consistently report the position of their hand in space (i.e. their uncertainty ranges (defined below) were greater than 3 times the average uncertainty range). Participants were pre-screened verbally for self-reported handedness and any history of visual, neurological, and/or motor dysfunction. Following pre-screening, participants were randomly assigned to either the right hand training (n = 20) or left hand training (n = 26; analysis with n = 23) groups. All participants provided informed consent in accordance with the ethical guidelines set by the York Human Participants Review Subcommittee.

2.3.2. General experimental set-up

A side view of the set up is provided in Figure 2.1A and is similar to the set-up used in Cressman and Henriques (2010) and Cressman, Salomonczyk and Henriques (2010). Participants were seated in a height adjustable chair so that they could comfortably see and reach to all target and marker locations presented on an opaque, reflective surface. Participants grasped the vertical handle of a two-joint robot manipulandum mounted in the horizontal plane (Interactive Motion Technologies). Visual stimuli were projected from a monitor (Samsung 510N, refresh rate 72Hz) installed 17 cm above the robot onto a reflective surface aligned in the same horizontal plane as the robot. The room lights were dimmed and participants' view of their hand was blocked by the reflective surface and a black cloth draped between the experimental set up and participants' shoulders.

Figure 2.1 Experimental set-up and design. A: Side view of the experimental setup. B-C Top view of the experimental surface visible to participants. B: Visuomotor distortion introduced in the rotated Reach Training Task. The green cursor (representing the hand) was rotated 30° clockwise with respect to the actual hand location (grey circle). Reach targets (yellow circles) were located at 0° in line with body midline and 30° left and right of body midline. C: Reference markers (yellow circles) were located at 30° left and right of midline. The grooved path along which the participants' unseen hand travelled is represented by the red rectangle.

2.3.3. General procedure

Similar to our previous study (Cressman & Henriques, 2009), the experiment consisted of two separate testing sessions completed on two separate days. Each testing session involved two tasks. On the first testing day participants completed the reaching trials outlined below while seeing a green cursor disc 1 cm in size that was aligned with their unseen hand. On the second testing day participants completed the reaching trials while viewing a cursor that was misaligned from the actual location of their unseen hand (Figure 2.1B). The misaligned cursor was rotated $30°$ clockwise (CW) relative to actual hand position, with the origin of the rotation at the starting hand position. The cursor was represented by a green disc 1 cm in diameter (Figure 2.1B). The descriptions and order of tasks is outlined below and in Figure 2.2.

2.3.3.1 Training and adaptation

While grasping the robot manipulandum with either the right or left hand, participants were instructed to reach to a yellow visual target disc, 1 cm in size, as quickly and accurately as possible while viewing either an aligned (first testing session) or misaligned (second testing session) cursor that moved with their hand. The reach targets were located radially 10 cm from the home position at $0°$ (centre), $30°$ left (CCW) and $30°$ right (CW) of centre (yellow circles in Figure 2.1B). The home position was located approximately 40 cm in front of the participants along their body midline (indicated by the black circle in Figure 2.1B). This position was not illuminated and visual feedback was provided only when the hand had travelled 4 cm outwards from the home position. The reach was considered complete once the centre of the cursor had moved to within 0.5 cm of the target's centre. At this point, both the cursor and target discs disappeared and participants moved their hands back to the home position in the absence of visual feedback along a linear route. If participants attempted to move outside of

the established path, a 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 path wall (Cressman & Henriques, 2009; Henriques & Soechting, 2003; Jones, Cressman, & Henriques, 2010).

Each session began with participants completing either 60 reaches with an aligned cursor (1st session) or 150 reaches with the misaligned cursor (2nd session) (box 1 in Figure 2.2). Afterwards, participants reached to the same targets 5 times each without cursor feedback for a total of 15 trials (box 2 in Figure 2.2) to assess visuomotor adaptation (i.e. aftereffects in the second testing session). Participants then reached again with the aligned or misaligned cursor for an additional 6 trials (box 3 in Figure 2.2). Following these reaching trials, we began to assess participants' estimates of hand position (box 4 in Figure 2.2) as described below.

2.3.3.2 Proprioceptive estimate trials and reach trials

A proprioceptive estimate trial began with the participant grasping the robot manipulandum at the home position, which was indicated by a 1 cm green disc. After 500 ms this disc disappeared and the participant was instructed to push his or her hand outward along a constrained robot-generated linear path (as described previously and shown by the red rectangle in Figure 2.1C). On all trials, once the hand reached the end of the path a reference marker located 30° left (CCW) or 30° right (CW) of center represented by a yellow circle 1cm in diameter appeared (yellow circles, Figure 2.1C) and participants made a two-alternative forced choice judgment about the position of their hand (left or right) relative to the reference marker. There was no time constraint for giving a response. After responding, the reference marker disappeared and the participant moved the robot directly back to the home position along a linear route to begin the next trial.

The position of the hand with respect to each reference marker was adjusted over trials using an adaptive staircase algorithm (H. Kesten, 1958; Treutwein, 1995) as described by Cressman and Henriques (2009). Participants alternated between 10 proprioceptive estimate trials and 6 reach trials with cursor feedback for a total of 100 proprioceptive estimate trials and 60 reaching trials (boxes 3-5 in Figure 2.2). Participants then reached 15 more times without the cursor (box 6 in Figure 2.2) as a final measure of reach adaptation.

Reach Task   Proprioceptive Estimate + Reach Task

Reach Training 60 Trials (Aligned) 150 Trials (Misaligned) 1	Reach Aftereffects (no cursor) 15 Trials (5/target) 2	Reach Training 6 Trials 3	Proprioceptive Estimates 10 Trials (5/marker) 4	Reach Training 6 Trials 5	Reach Aftereffects (no cursor) 15 Trials (5/target) 6

10 Times
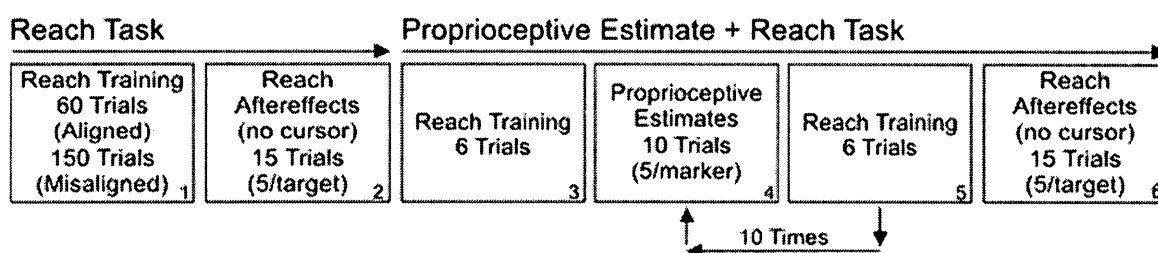
Figure 2.2 Breakdown of the testing sessions within the experiment. In the first testing session participants reached with an aligned cursor that accurately represented the position of their hand in the reach training trials. In the second testing session, participants reached with a misaligned cursor that was rotated 30° clockwise with respect to the actual hand location during the reach training trials. Using their right or left hand, participants began a testing session by reaching to visual targets with a green cursor that provided visual feedback of hand position (Box 1). After completing either 60 (aligned cursor) or 150 (misaligned cursor) reach training trials, participants next reached to each of the three targets 5 times without a cursor in order to assess visuomotor adaptation (reach aftereffects trials, Box 2). Participants then completed 6 reaches to the reach targets with the cursor present (Box 3). This was followed by 10 sets of 10 proprioceptive estimate trials (Box 4) and 6 visually guided reaches (Box 5) for a

total of 100 proprioceptive estimate and 60 reach training trials. Following this, participants again reached to each of the three targets 5 times without a cursor in order to assess maintenance of visuomotor adaptation (Box 6).

2.3.4. Data analysis

2.3.4.1 Visuomotor adaptation

Directional deviations of the hand made during reaching trials without visual feedback were analyzed to assess motor adaptation. Reach endpoint errors were defined as the angular difference between a movement vector (from the home position to reach endpoint) and a reference vector (from the home position to the target). Reach errors at peak velocity were defined as the angular difference between a movement vector joining the home position and the position of the hand at peak velocity and the reference vector. Both errors at reach endpoint and at peak velocity were analyzed to determine if participants adapted their reaches to the targets after aiming with a rotated cursor, and if there was any change in reach adaptation following the proprioceptive estimate trials. Analyses were conducted using separate 2 Group (right hand group vs. left hand group) x 2 Feedback condition (aligned vs. misaligned cursor) x 2 Epoch (preceding proprioceptive estimate trials vs. following proprioceptive estimate trials) x 3 Target ($30°$ CW vs. $0°$ vs. $30°$ CCW) mixed repeated measures analysis of variance (RM-ANOVA). Group was treated as a between-participants factor, while all others were treated as within-group factors. A Bonferroni correction was applied to post-hoc pair-wise comparisons.

2.3.4.2 Proprioceptive estimates of hand position

A logistic function was fitted to each participant's responses for each reference marker in each testing session in order to determine the location at which participants perceived their hand to be aligned with a reference marker.

From this logistic function we calculated the bias (the point at which the probability of responding left was 50%) and uncertainty (the difference between the values at which the probability of responding left was 25% and 75%). The bias value is a measure of participants' accuracy of proprioceptive sense of hand position, while the magnitude of the uncertainty range defines its precision (Cressman & Henriques, 2009; 2010). A 2 Group (right hand group vs. left hand group) x 2 Feedback condition (aligned vs. misaligned cursor) x 2 Marker location (30° CW vs. 30° CCW) mixed RM-ANOVA was used to compare bias and uncertainty values following reach training with the right and left hands. Group was treated as a between-participants factor, while all others were treated as within-group factors. Proprioceptive recalibration was examined by comparing the bias values after training with a misaligned cursor with those following an aligned cursor (baseline). A Bonferroni correction was applied to all post-hoc pair-wise comparisons.

2.4 RESULTS

2.4.1 Visuomotor adaptation

Directional endpoint reach errors made following reach training (i.e. before the proprioceptive estimation trials) are presented in Figure 2.3A. After training with an aligned cursor, participants in the left hand group (open squares) had reach errors that were on average 2° leftwards of the targets and participants in the right hand group (open triangles) made reach errors that were on average 1° to the right of the targets. This is consistent with estimates of hand position (see Figure 2.4A for bias results) and previous work suggesting that an inherent systematic bias exists in the two hands when reaching to targets (Jones et al., 2010; Wilson, Wong, & Gribble, 2010). After training with a rotated cursor (filled symbols), participants in both groups had reach errors that deviated more

leftwards than after training with an aligned cursor (filled symbols). Figure 2.3B depicts the mean changes in endpoint errors for the left and right hand groups preceding proprioceptive estimates trials (empty bars) and following the proprioceptive estimate trials (filled bars) relative to baseline performance (i.e. errors achieved on the first day of testing after training with an aligned cursor were subtracted from errors achieved after reaching with a rotated cursor), along with endpoint errors from Cressman and Henriques (2009). A significant change in average reach aftereffects from aligned to misaligned training was observed $(F(1,41) = 244.5, p < .001)$. Aftereffects observed in the left hand group did not differ from those observed in the right hand group $(F(1,41) = 1.63, p = .21)$. As well, these aftereffects are consistent with previous results following a gradually introduced misaligned reach cursor (Cressman & Henriques 2009). Analysis of the epoch factor revealed greater reach aftereffects following the proprioceptive estimate trials ($14°$ and $17°$ for the left and right hand groups, respectively) compared to those preceding the proprioceptive estimate trials ($12°$ and $13°$ for the left and right hand groups, respectively; $F(1,41) = 12.76, p = .001$). This pattern was consistent for both groups $(F(1,41) < 1, p = .35)$. While larger aftereffects were also observed in Cressman and Henriques (2009) following proprioceptive estimate trials compared to those preceding proprioceptive estimates trials, this difference did not achieve statistical significance. Lastly, there was a significant effect of target $(F(2,82) = 19.32, p < .001)$ such that reaching errors around the lateral targets were slightly compressed towards the central workspace (i.e. reaching errors tended to be to the left of the CW target and right of the CCW target), although this effect did not differ between aligned and rotated conditions $(F(2,82) = 2.63, p = .07)$.

Reach aftereffects at peak velocity were analysed and revealed a similar pattern of results (Figure 2.3B, circles). After training with a rotated cursor, participants reached significantly more leftwards of the target than after training

with an aligned cursor ($F(1,41) = 154.71$, $p < .001$). These aftereffects were comparable across groups ($F(1,41) = 3.07$, $p = .08$). As with endpoint aftereffects, aftereffects at peak velocity following proprioceptive estimates ($11.8°$ and $16.8°$ for the left and right hand groups, respectively) were greater than those preceding proprioceptive estimates trials ($9.1°$ and $11.0°$ for the left and right hand groups, respectively; $F(1,41) = 6.89$, $p = .01$). This pattern was again consistent for both groups ($F(1,41) < 1$, $p = .35$), although the compression of reaching errors around the targets towards the centre was only observed for reaches made following aligned training ($F(2,28) = 18.94$, $p < .001$). The similarity between directional reach errors at peak velocity and reach endpoint suggests that participants did not make online corrections to their reach trajectories in the absence of visual feedback of hand position.
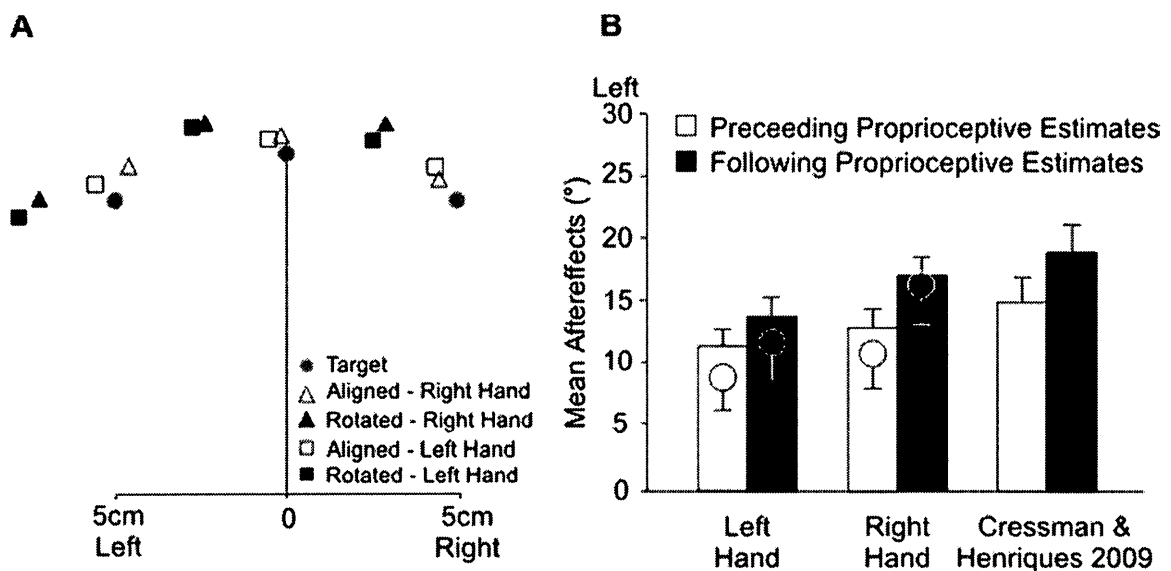
Figure 2.3 Reaching errors for the left and right hand groups. A: Mean 2-D representation of movement endpoint errors for the left (squares) and right (triangles) hand groups after training with aligned (empty symbols) and

misaligned (filled symbols) visual feedback of the hand. The target locations are represented as filled grey circles. B: Mean change in directional reach endpoint errors (bars) and errors at peak velocity (circles) after reaching with misaligned visual feedback of the hand for the left and right hand groups and data from Cressman and Henriques (2009). Values reflect baseline-subtracted aftereffect errors preceding proprioceptive estimate trials (empty bars and black outlined circles) and following proprioceptive estimate trials (filled bars and white outlined circles). Aftereffects of $30°$ would reflect 100% adaptation. Error bars reflect standard error of the mean.

2.4.2 Proprioceptive estimates of hand position

2.4.2.1 Bias

Figure 2.4A depicts the positions at which participants in the left and right hand groups perceived their hands to be aligned with the reference markers after training with an aligned (empty symbols) and misaligned cursor (filled symbols). Estimates of hand position following training with aligned cursor feedback significantly differed between left and right hand groups ($F(1,41) = 70.12$, $p < .001$). Specifically, participants in the left hand group judged their hand to be in line with the reference marker when it was $9°$ to the right of it, while participants in the right hand group estimated their hand to be in line with the reference marker when it was $3°$ to the left of it. These results are in agreement with previous hand biases observed when participants were asked to judge the position of their hand prior to any reach training: participants estimated their right hand was more rightwards than it actually was and their left hand was more leftwards than it actually was (Jones et al 2010). Figure 2.4B depicts the mean change in bias for the left (filled bar) and right (empty bar) hand groups. On average, the position at which participants' felt their hand coincided with the reference marker was shifted leftwards by $7.6°$ after training with a misaligned

cursor compared to after reaching with an aligned cursor ($F(1,37) = 69.56$, $p <$ .001). This shift is consistent with changes observed by Cressman and Henriques (2009; Figure 2.4B, patterned bar), in which participants estimated the position of their right hand following reach training trials in which the visuomotor distortion was gradually introduced. In the present study, post-hoc tests revealed that participants in both groups recalibrated their proprioceptive estimates of hand position around the $30°$ CW and $30°$ CCW reference markers ($p < .005$ for all contrasts). No differences in estimates between the left and right reference marker locations were observed between conditions for the right hand group, suggesting that recalibration was comparable across the locations; however, estimates following rotated training were different between the two reference marker locations for the left hand group, suggesting that participants experienced greater recalibration around the CCW marker ($11°$) than the CW marker ($4°$; $p =$ .01). This effect does not appear to be dependent on initial proprioceptive estimates as there was no difference in biases following reaches with the aligned cursor between the two reference markers for the left hand group (CCW marker = $8.9°$, CW marker = $9.0°$; $p = .95$).

A

B

5cm   0   5cm
Left   Right

Reference Marker
△ Aligned - Right Hand
▲ Rotated - Right Hand
□ Aligned - Left Hand
■ Rotated - Left Hand

■ Left Hand
□ Right Hand
▨ Cressman &
   Henriques (2009)
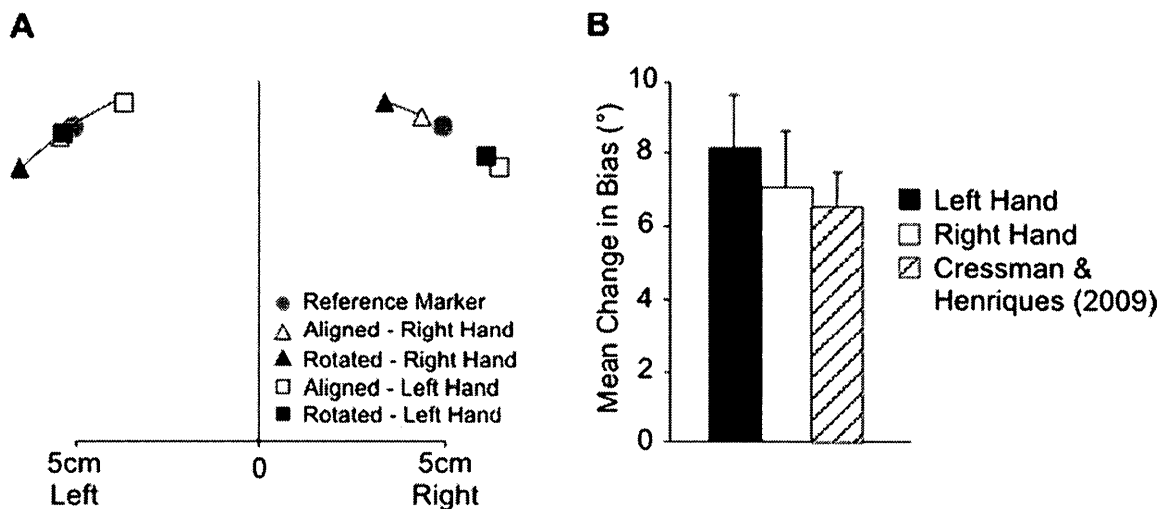
Figure 2.4 Proprioceptive estimates for the left and right hand groups. A: Mean angular biases in the proprioceptive estimate trials for the left (squares) and right (triangles) hand groups following training with aligned (empty symbols) and misaligned (filled symbols) visual feedback of the hand. The actual reference marker positions are represented as filled grey circles and a line connects each proprioceptive estimate of hand position after training with an aligned and rotated cursor for either the left or right hand with its corresponding reference marker. B: Mean changes in bias for the left and right hand groups, as well as from participants from Cressman and Henriques (2009), averaged across reference marker positions and participants. Error bars reflect standard error of the mean.

2.4.2.2 Uncertainty

Figure 2.5 depicts the magnitude of the uncertainty ranges for the left and right hand groups following reaches made with aligned (empty bars) and misaligned (filled bars) cursor feedback. Participants' levels of precision in estimating the location of their unseen hands were comparable after reach training with an aligned and misaligned cursor ($F(1,41)$ =< 1, p = .40), at all reference markers ($F(1,41)$ = <1, p = .93). Precision of estimates did not differ

between the two groups (F(1,41) < 1, p = .24). These results are in accordance with previous results following adaptation to a gradually introduced distortion (Cressman & Henriques, 2009).
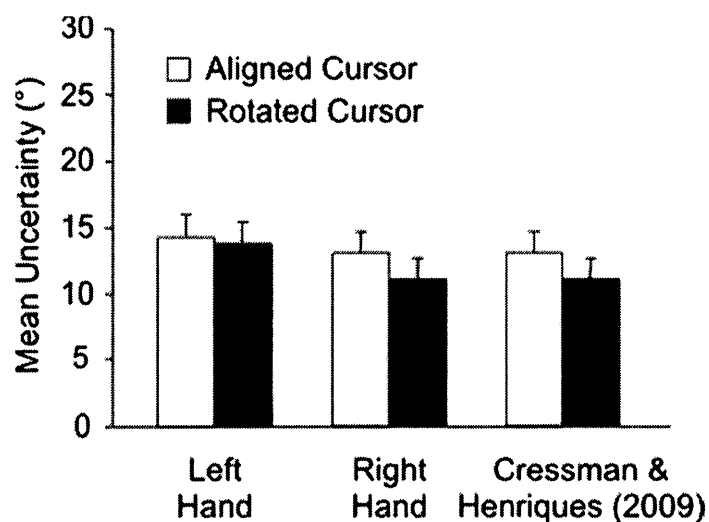
Figure 2.5 Magnitude of the uncertainty ranges in the proprioceptive estimate trials for the left and right hand groups and data from Cressman and Henriques (2009) averaged across reference marker positions and participants after reaching with an aligned cursor (empty bars) or misaligned cursor (filled bars). Error bars reflect standard error of the mean.

2.4.3 Visuomotor adaptation vs. proprioceptive recalibration

Figure 2.6 shows a summary of the changes in proprioceptive recalibration (bias) and reach adaptation (aftereffects) following training with a misaligned cursor as a percentage of the visuomotor distortion introduced and with respect to the overall magnitude of the distortion introduced (i.e. 30°). Specifically, Figure 2.6 depicts the mean changes in proprioceptive biases (bars) and reach endpoint aftereffects (diamonds) following training with a misaligned

cursor compared to training with an aligned cursor for each group. From this figure, we see that on average, participants recalibrated proprioception by approximately 25% of the distortion introduced. As well, after training with the misaligned cursor, participants showed aftereffects equal to approximately 50% of the distortion introduced.
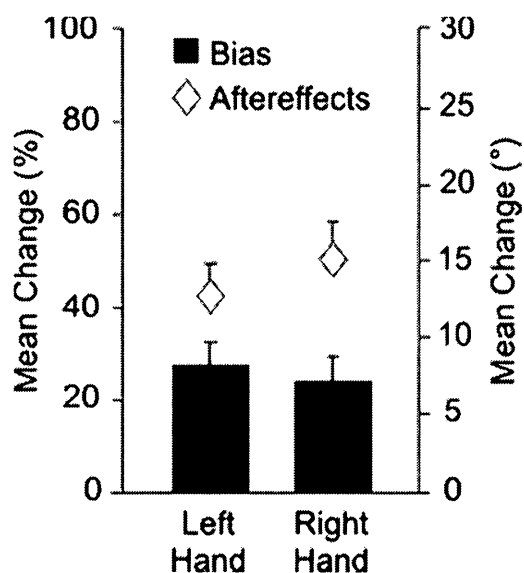
Figure 2.6 Mean changes in proprioceptive biases and aftereffects after reach training with a misaligned cursor compared to an aligned cursor. The mean change in bias (bars) is plotted along with the mean change in aftereffects (diamonds) for the left and right hand groups. Results are shown in degrees and as a percentage of the distortion introduced during reach training trials. Error bars reflect standard error of the mean.

We subsequently examined the relationship between the motor changes (aftereffects) and sensory changes (proprioceptive recalibration) expressed as a percentage of the visuomotor distortion introduced using a bivariate correlation (Figure 2.7). Consistent with previous work (Cressman & Henriques, 2009;

Salomonczyk et al., 2011) results revealed that all participants adapted their movements and recalibrated proprioception, though a significant relationship between these changes was not observed (r = .052, p = .74).
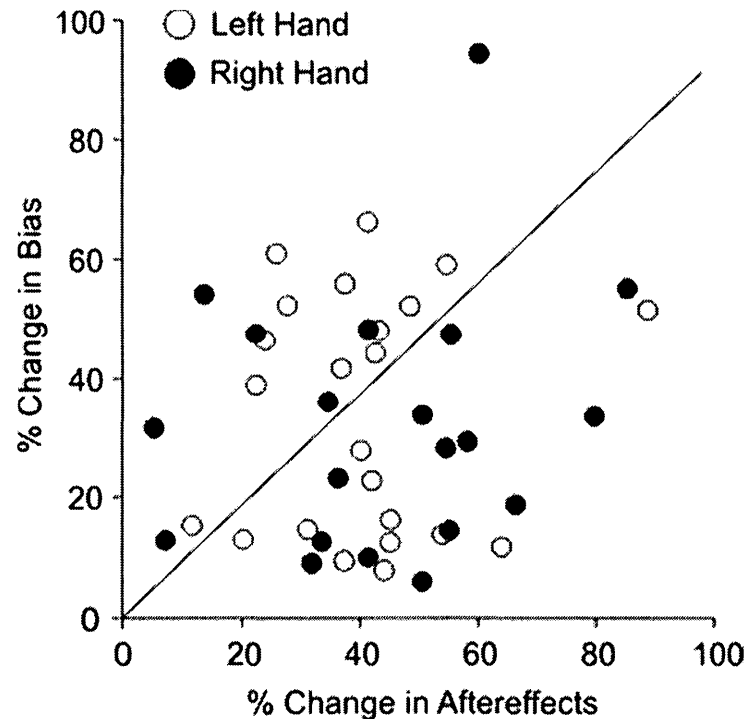
Figure 2.7 Changes in proprioceptive biases and aftereffects are expressed as a percentage of the visuomotor distortion introduced for the left (empty circles) and right hand groups (filled circles). The solid line is a unit slope and so indicates equivalent levels of proprioceptive recalibration and visuomotor adaptation.

2.5 DISCUSSION

The present study examined if proprioceptive recalibration occurs following visuomotor adaptation to an abrupt distortion and if this recalibration is comparable across the left and right hands of right handed-individuals. On

average, participants adapted their reaches by 14° and recalibrated the position at which they felt their hand was aligned with a reference marker by 7.6° after training with a rotated cursor compared to reach training with an aligned cursor. This change in felt hand position was in the same direction that participants' adapted their reaches during reach training and was approximately 25% of the magnitude of the visuomotor distortion introduced. These results address our first question of interest and suggest that proprioceptive recalibration does occur following visuomotor adaptation to an abrupt distortion. Given that participants in both groups adapted their reaches and recalibrated proprioception around all targets and reference markers indicates that proprioceptive recalibration occurs comparably in the left and right hands, which addresses our second question of interest. Furthermore, our findings for our right hand group replicate those of Cressman and colleagues (Cressman & Henriques, 2009; 2010) wherein proprioceptive recalibration was observed following adaptation to a visuomotor distortion that was introduced gradually. In fact, recalibration was comparable in magnitude across these studies (approximately 7° leftwards), regardless of both the hand used and whether the perturbation was introduced gradually or abruptly.

2.5.1 Effect of initial error on recalibration

We found similar changes in hand proprioceptive estimates and no-cursor (open-loop) reaches as we did in our previous studies where the cursor was gradually rotated during training. These findings are consistent with previous results that suggest adaptation is comparable between abrupt and gradual perturbations (Klassen et al., 2005). For example, Klassen and colleagues introduced a 30° visuomotor rotation either abruptly or gradually (in 0.125° increments) and found no difference in motor learning retention when participants were tested 24 hours later. However, Kagerer and colleagues (1997) introduced

a 90° visuomotor rotation either at once or in 10° increments and observed increased retention (aftereffects) in participants who reached with a gradually introduced 90° visuomotor perturbation compared to those in which the perturbation was abruptly introduced (43.1° and 28.22°, respectively). In contrast to these findings Buch and colleagues (2003) reported *decreased* aftereffects following gradual exposure to a 90° visuomotor rotation compared with abrupt exposure; however, this trend was only described for older adults. The differences in motor adaptation following reaches with an abruptly versus gradually introduced distortion appear to depend on the initial error signals experienced, such that differences in aftereffects following gradual or abrupt learning seem to occur only for visuomotor rotations greater than the 30° rotation used in our current study. According to Abeele and Bock (2001) different mechanisms are engaged when learning large (over 90°) versus small rotations and these separate mechanisms, which may further be differentially engaged when learning abrupt versus gradual rotations, lead to the inconsistency between findings of increased or decreased adaptation depending on the magnitude of the initial error signal. It could also be that adapting to a very large and thus difficult or less relevant perturbation may be easier to do when the error signals and overall difficulty increase gradually; for instance, correct credit assignment for reaching error in the case when the cursor is suddenly deviated from the hand movement by a rotation of 90° or more may be quite different than that for smaller or gradual deviations (Wei & Kording, 2009).

In instances when the distortion is introduced abruptly and large reach errors are initially experienced, it has been suggested that explicit, strategic control processes are engaged early in the learning process in order to produce rapid corrections in motor performance (Redding & Wallace, 1996). In contrast, when the distortion is introduced gradually and small reach errors are experienced, reach adaptation is proposed to arise through implicit processes

that reduce the discrepancies between vision and proprioception. The fact that we found similar changes in movements and sensory recalibration following abrupt-cursor adaptation compared to gradual-cursor adaptation suggests that these changes are not cognitively or strategically driven as proposed by previous research using prism adaptation paradigms (Redding & Wallace, 1996). In fact, given the results of Mazzoni and Krakauer (2006), the sensory and motor changes observed in the present study most likely arise implicitly rather than explicitly.

2.5.2 Arm Symmetry

It has been suggested that the two arms may be better at using different types of sensory information for localizing a target. For instance, Goble and Brown (2008) have suggested that the left limb is better at matching proprioceptive targets and the right limb for matching visual targets. In the current study, biases measured following reach-training with an aligned cursor did produce a small asymmetry across the two hands, where larger rightward biases were present in the left hand group and smaller leftward biases were present in the right hand group. These results are consistent with Goble and Brown's (2008) proposal, in that participants were able to more accurately localize their right hand relative to a visual reference marker compared to the left hand. Yet in our previous study, we found the same magnitude of proprioceptive biases when participants judged the position of the right hand with respect to body midline (i.e. proprioceptive reference) and a visual reference. Likewise, we found no differences in the magnitude of reaching errors to a visual target made without any cursor feedback following either right or left hand training with an aligned or rotated cursor; absolute reach endpoint errors were 1.5° on average following aligned-cursor training and were not different between the two groups. Differences in findings between our work and Goble's may arise due to the

nature of the task. Goble and Brown's findings were observed during a task that involved moving the arm around the elbow joint in order to match the angle of the opposite arm in a bimanual task or to match a visual reference. In contrast, our task was a unimanual task and we did not find similar asymmetries between the two arms in either our sensory or motor tasks. In the current study, and in our previous work (Jones et al., 2010), the extent of the misestimates of proprioceptive biases of the unseen hand position of the two arms were similar. Moreover, we have shown that proprioceptive biases and uncertainty ranges, measured without a preceding reach-training task, do not differ at all in magnitude (just in direction) across the two hands (Jones et al., 2010; Rincon-Gonzalez, Buneo, & Helms Tillery, 2011; Wilson et al., 2010). Thus, perhaps arm asymmetry is only observable when the two arms are working together to complete the same task.

While sense of felt hand position was shifted at all reference markers and movements adapted at all targets examined, proprioceptive recalibration was significantly less at the rightwards (CCW) marker than at the leftwards (CW) marker for the left hand group; this asymmetry was not observed in the right hand group. Previous results suggest that motor adaptation asymmetries may arise following reaches with prism goggles due to asymmetries in underlying attentional biases (Goedert, Leblanc, Tsai, & Barrett, 2010). However, given that we found that movement aftereffects were comparable in magnitude across all targets, suggests that the asymmetric proprioceptive recalibration we observed may not have arisen due to attentional biases. Moreover, no differences in bias between the two reference markers following aligned reach training were observed in the left hand group, further weakening the argument for an attentional bias underlying asymmetrical recalibration. An alternative explanation may involve asymmetries in encoding limb position and interactions with workspace locations. As discussed previously, Goble and Brown (2010) suggest

that the left hand is more accurate at matching proprioceptive targets than the right hand. Moreover, Goble (2010) recently demonstrated that joint matching is better when the tested joint is in the far-left workspace. That proprioceptive estimates of hand position were shifted following rotated training more so for a reference marker in the left workspace than the right may be a result of an inherent workspace bias for the left limb, which only becomes evident when information from proprioceptive and visual modalities are incongruent. More research is required in order to address this question specifically.

Proprioceptive Recalibration

While the precise relationship between sensory and motor changes arising from reaching with altered visual feedback of the hand remains to be determined, results from the current study (i.e. Figure 2.7) and previous studies from the Henriques' lab (Cressman & Henriques, 2009; Salomonczyk et al., 2011) and recent work by de Grave and colleagues (2011) suggest that these processes may occur simultaneously, yet independently of each other. Specifically, we find that proprioceptive recalibration is uncorrelated with motor changes (aftereffects) following visuomotor adaptation paradigms (Cressman & Henriques, 2009; Salomonczyk et al., 2011). Moreover, de Grave and colleagues (2011), recently demonstrated that visuomotor adaptation in response to a cursor perturbation that was shifted in depth relative to the body was not related to changes in the perceived "reachability" of a target (i.e. changes in participants reaches were not correlated with their perceptions regarding their ability to successfully reach a target). In accordance with these findings, recent work from Block and Bastian (2011) suggests that sensory realignment (i.e. proprioceptive recalibration) also arises independently of sensory weighting.

Recalibration of proprioception may arise because the central nervous system performs motor tasks optimally when a unified estimate of hand position is available. When sensory estimates of hand position are incongruent, the brain

may seek to resolve this sensory discrepancy by recalibrating a less salient sense (proprioception) to match the more reliable visual input. In the current study we only asked participants to estimate the position of their hand with respect to visual reference markers. Thus it could be argued that our results demonstrate sensory (visual-proprioceptive) realignment without providing evidence that proprioception was recalibrated, such that participants experienced an overall shift of sense of felt hand position that was independent of having to align one's hand with a visual cue. Based on our previous results, in which we demonstrate similar shifts in proprioceptive biases regardless of whether participants are required to judge the position of their hand relative to a visual or proprioceptive reference marker at the same location (Cressman & Henriques 2009), we are confident that the changes in felt hand position we observe at visual reference markers reflect a more global shift in felt hand position, as opposed to intersensory realignment. In addition, we have recently not only repeated these results using proprioceptive and visual reference markers, but also have shown similar shifts in proprioceptive biases when participants were required to indicate the position of their right (adapted) hand with their left hand (i.e. a proprioceptive-proprioceptive alignment task (Clayton, Cressman, & Henriques, 2011). Similar to the results we have reported previously, we again find a shift in proprioceptive biases that are reflective of proprioceptive recalibration.

CHAPTER THREE

**PROPRIOCEPTIVE RECALIBRATION FOLLOWING PROLONGED TRAINING
AND INCREASING DISTORTIONS IN VISUOMOTOR ADAPTATION**

Danielle Salomonczyk, Erin K Cressman and Denise YP Henriques

3.1 ABSTRACT

Reaching with misaligned visual feedback of the hand leads to reach adaptation (motor recalibration) and also results in partial sensory recalibration, where proprioceptive estimates of hand position are changed in a way that is consistent with the visual distortion. The goal of the present study was to explore the relationship between changes in sensory and motor systems by examining these processes following (1) prolonged reach training and (2) training with increasing visuomotor distortions. To examine proprioceptive recalibration, we determined the position at which participants felt their hand was aligned with a reference marker after completing three blocks of reach training trials with a cursor that was rotated 30° clockwise (CW) for all blocks, or with a visuomotor distortion that was increased incrementally across the training blocks up to 70° CW relative to actual hand motion. On average, participants adapted their reaches by 16° and recalibrated their sense of felt hand position by 7° leftwards following the first block of reach training trials in which they reached with a cursor that was rotated 30° CW relative to the hand, compared to baseline values. There was no change in these values for the 30° training group across subsequent training blocks. However, participants training with increasing levels of visuomotor distortion showed increased reach adaptation (up to 34° leftward movement aftereffects) and sensory recalibration (up to 15° leftwards). Analysis of motor and sensory changes following each training block did not reveal any significant correlations, suggesting that the processes underlying motor adaptation and proprioceptive recalibration occur simultaneously yet independently of each other.

3.2 INTRODUCTION

When reaching to a target with misaligned visual feedback of the hand (i.e. reaching in a virtual reality environment or while wearing prism goggles), individuals adjust their movements in order for the visual representation of the hand to achieve the desired endpoint. Moreover, when the distortion is suddenly removed, reach errors referred to as aftereffects are observed, as participants continue to make movements adapted to the distortion (Krakauer et al., 1999; Krakauer et al., 2000; Martin, Keating, Goodkin, Bastian, & Thach, 1996a; Redding & Wallace, 2000; Simani et al., 2007). It has been suggested that in addition to this motor adaptation, proprioception is also recalibrated following reaches made with altered visual feedback. This proposal is based on changes in reaches observed when participants are required to reach to visual and proprioceptive targets with their adapted hand following prism exposure (Harris, 1963; Hay & Pick, 1966; Redding & Wallace, 2000) and visuomotor adaptation, in which visual feedback of the hand position was displaced (Simani et al., 2007; van Beers et al., 2002). While participants' reaches are altered after reaching with altered visual feedback of the hand, it is unclear whether these changes reflect proprioceptive recalibration per se. Given that participants moved their adapted arm, errors may better reflect motor adaptation than cross-sensory recalibration (i.e. changes to the motor system rather than sensory changes). To avoid this potential motor confound, Henriques and colleagues (Cressman & Henriques, 2009; Cressman et al., 2010) and Ostry et al. (2010) have recently designed novel perceptual tasks to examine proprioceptive recalibration. In these tasks participants estimate the position of their hand with respect to a visual or proprioceptive (i.e. body midline) reference marker and hence do not perform any goal-directed movements with the adapted hand.

Results using this proprioceptive estimation task reveal that proprioceptive estimates of hand position are significantly shifted in the direction of motor

adaptation after participants reach with visual or force perturbations applied to the hand. Moreover, these changes in felt hand position do not differ in magnitude when estimates of hand position following visuomotor adaptation are made relative to visual or proprioceptive references (Cressman & Henriques, 2009), suggesting that these misestimates are due to recalibration of proprioception rather than any change in the visual percept. As additional support for the recalibration of proprioception, we have shown that changes in felt hand position do not transfer between limbs following visuomotor adaptation (Salomonczyk, Henriques, & Cressman, 2010). Specifically, if the visual representation of space had been recalibrated, we expect that changes in sensory alignment would have been present in both the trained and untrained hand, which we did not observe.

We have found that proprioceptive recalibration is a robust process that occurs along with motor changes under a variety of contexts, including when the hand is passively or actively displaced, when the visuomotor distortion is gradually or abruptly introduced, following training with a rotated or translated cursor, using either the left or right hand, and in both young and older adults (Cressman & Henriques, 2009; Cressman et al., 2010; Salomonczyk et al., 2010). While sensory changes are also observed in conjunction with motor changes following dynamic learning (Ostry et al., 2010) these changes are slightly smaller than those observed following visuomotor rotation training (11% vs. 33% of the deviation of the accompanying movement aftereffects). Surprisingly, we also found similar changes in felt hand position even in the absence of visuomotor adaptation training trials. In this task, participants were merely exposed to a sensory discrepancy between visual and proprioceptive signals while their hand was passively moved by a robot and they viewed a cursor that simultaneously travelled directly to the target (Cressman & Henriques, 2010). Because no goal-directed reach training was involved and no motor

commands were generated, the sensorimotor error signal was eliminated and participants experienced only a cross-sensory error signal derived from the discrepancy between visual and proprioceptive feedback. In addition to recalibrating proprioception, this cross-sensory error signal was sufficient to produce significant movement aftereffects when participants were asked to reach to targets with no visual feedback. While these aftereffects were only one third of the magnitude reported in previous studies where participants could use the additional sensorimotor error signal to adapt their reaches (i.e. 20% vs. 60% of the 30° visuomotor distortion; Cressman & Henriques, 2009), they were similar in magnitude to and correlated with the changes in proprioception. Given that movement aftereffects produced following cross-sensory discrepancy exposure were almost two thirds smaller than those produced following visuomotor adaptation learning trials, the larger aftereffects following visuomotor adaptation may be due to additional changes exclusive to the motor system derived from the sensorimotor error signal.

Based on these previous results, it is possible that motor and sensory recalibration following sensorimotor learning rely on different training signals. As with visual processing (Goodale & Milner, 1992; Milner & Goodale, 1993) separate cortical areas have been suggested to be involved in action-oriented proprioceptive processing (the posterior parietal cortex) vs. perception oriented proprioceptive processing (the insula (Dijkerman & de Haan, 2007)). Thus, perhaps the separate streams may be differentially involved in realigning proprioceptive and visual feedback of the hand and for providing a unified estimate of hand position for feedforward motor control. To study the relationship between motor and sensory changes, we sought to examine these processes following (1) prolonged reach training and (2) training with increasing levels of visuomotor distortion. While proprioceptive recalibration occurs under a variety of contexts following motor learning, it is unclear if proprioceptive recalibration

saturates in the same manner as movement aftereffects (as found by Krakauer and colleagues (2005) and Wong and Henriques (2009)) or whether prolonged training would lead to increased proprioceptive recalibration. For example, although we found proprioceptive recalibration to be much smaller than movement aftereffects following over 200 visuomotor adaptation trials (Cressman & Henriques, 2009), it is possible that proprioceptive recalibration requires more training in order to attain levels equivalent to those for motor adaptation. Based on previous findings demonstrating that the magnitude of the distortion affects motor learning (Abeele & Bock, 2001; Kagerer et al., 1997), we also examined whether adaptation to increasing distortions (and thus exposure to increasing sensorimotor error signals) would result in sensory changes consistent with those of the motor system. To address these questions, we used the same technique for measuring hand proprioception following visuomotor adaptation to a rotated cursor as described by Henriques and colleagues (Cressman & Henriques, 2009, 2010; Cressman et al., 2010; Salomonczyk et al., 2010).

3.3 METHODS

3.3.1 Participants

Twenty-three right-handed young adults (mean age = 22.58, SD = 4.09, 14 female) were recruited from York University and volunteered to participate in the experiments described below. Participants were pre-screened verbally for self-reported handedness and any history of visual, neurological, and/or motor dysfunction. Following pre-screening, participants were randomly assigned to either the $30°$ (n = 10) or $70°$ (n = 13) training groups. All participants provided informed consent in accordance with the ethical guidelines set by the York University Human Participants Review Sub-Committee.

3.3.2 General experimental set-up

A side view of the set up is provided in Figure 3.1A. Participants were seated in a height adjustable chair so that they could comfortably see and reach to all target and reference marker locations presented on an opaque, reflective surface. Participants grasped the vertical handle of a two-joint robot manipulandum mounted in the horizontal plane (Interactive Motion Technologies). Visual stimuli were projected from a monitor (Samsung 510N, refresh rate 72 Hz) installed 17 cm above the robot onto a reflective surface. The reflective surface was opaque and positioned so that images displayed on the monitor appeared to lie in the same horizontal plane as that of the robot handle. The room lights were dimmed and participants' view of their hand was blocked by the reflective surface and a black cloth draped between the experimental set up and participants' shoulders.

Figure 3.1 Experimental set-up and design. A: Side view of the experimental setup. B-C: Top view of the experimental surface visible to participants. B: Visuomotor distortion introduced in the rotated Reach Training Task. The 1 cm green cursor (representing the hand) was rotated 30° clockwise with respect to the actual hand location (white disk) during the first rotation training block and increased to 50° and 70° for the second and third rotation training blocks, respectively for the 70° training group. Reach targets (white rings) 1 cm in size were located 10 cm from the home position (black circle) at 5° and 30° left and right of body midline. C: In the proprioceptive estimate task, participants actively pushed their hand out 10 cm along a constrained linear path (depicted by the rectangle) from the home position and judged the position of their hand with respect to a reference marker. Reference markers (white rings) were located at 0° and 30° left and right of midline.

3.3.3 General procedure

The experiment consisted of two separate testing sessions completed on two testing days. Each testing session involved two tasks (comprising one block) and on the second day of testing these tasks were repeated three times (Figure 3.2). On the first testing day participants completed the reaching trials outlined below while seeing a cursor that was veridical, or aligned, with their hand. On the second testing day participants completed the reaching trials while viewing a cursor that was misaligned from the actual location of their unseen hand. The misaligned cursor was rotated 30°, 50° or 70° clockwise (CW) relative to the actual hand position and was represented by a green disc 1 cm in diameter (white disk, Figure 3.1B). The 30° training group completed all three blocks of the second session with a 30° rotated cursor, while the 70° training group completed the first block of the second session with a 30° rotated cursor, the second block with a 50° rotated cursor, and the third block with a 70° rotated cursor. For both groups, the 30° rotation was introduced gradually such that on the first trial the cursor was rotated 0.75° clockwise (CW) with respect to the hand. The rotation then increased by 0.75° each trial, until the full distortion was achieved. For the 70° training group, the cursor distortion in the 50° and 70° blocks was again introduced gradually by 0.75°/trial, starting from the rotation of the previous block (i.e. in block two the distortion was introduced at 30.75°, and increased by 0.75° per trial up to 50°; in block three the distortion was introduced at 50.75°, and increased by 0.75° per trial up to 70°).

3.3.3.1 Reach training and motor adaptation

While grasping the robot manipulandum with the right hand, participants were instructed to reach to a visual target (yellow circle, 1 cm in diameter) as quickly and accurately as possible while viewing either an aligned (first testing day) or misaligned (second testing day) cursor that moved with their hand. The

reach targets were located radially 10 cm from the home position at 5 and 30° left (CCW) and right (CW) of centre (white rings in Figure 3.1B). The home position was located approximately 40 cm in front of participants, in line with their body midline (indicated by the black circle in Figure 3.1B). This position was not illuminated and visual feedback was provided only when the hand had travelled 4 cm outwards from the home position. The reach was considered complete once the centre of the cursor had moved to within 0.5 cm of the target's centre. At this point, both the cursor and target disappeared and participants moved their hands back to the home position along a linear route in the absence of visual feedback. If participants attempted to move outside of the established linear path, a 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 (Cressman & Henriques, 2009, 2010; Cressman et al., 2010; Henriques & Soechting, 2003; Jones et al., 2010). The order of the reach trials was pseudo-randomized such that participants reached once to 3 of the reach targets, specifically the two peripheral targets and one of the pair of peri-central (5°) targets, before any target was repeated. Participants completed 99 reach trials (box 1, Figure 3.2).

After completing the 99 reach training trials, participants immediately completed 12 aiming movements, 3 reaches to each of 4 reach targets (i.e. both outer targets and the two peri-central targets), without the cursor (box 2, Figure 3.2). These trials were included to measure aftereffect reach errors to ensure that participants had adapted their reaches in response to the misaligned cursor on the second testing day. On these trials participants were instructed to aim to a target and hold their end position. Once this end position had been maintained for 500 ms, the visual target disappeared and the trial was considered complete. Participants were guided back to the home position by a linear grooved path. The

position of the robot manipulandum was recorded throughout all reaching trials at a sampling rate of 50 Hz and a spatial accuracy of 0.1 mm

3.3.3.2 Proprioceptive estimate trials and reach trials

In this task, proprioceptive estimates and reach trials (boxes 3-5 in Figure 3.2) were systematically interleaved. Participants began by completing an additional 12 reaching trials with an aligned (first testing day) or misaligned (second testing day) cursor (box 3). Participants reached once to 3 of the reach targets, specifically the two peripheral targets and one of the pair of peri-central (5°) targets, before any target was repeated. These reaches were then immediately followed by interleaving sets of 15 proprioceptive estimate trials (box 4) and 6 reaching trials (box 5). A proprioceptive estimate trial began with the participants grasping the robot manipulandum at the home position. The position of the hand at the home position was indicated by a 1 cm green disc. After 500ms this disc disappeared and the participant was instructed to push his or her hand outward along a constrained robot-generated linear path 10 cm in length (as described previously, rectangle in Fig 3.1C). On all trials, once the hand reached the end of the path (along the dotted arc in Fig 3.1C) a reference marker located at 0°, 30° left (CCW) or 30° right (CW) of center (white rings, Figure 3.1C) appeared and participants made a two-alternative forced choice judgment about the position of their hand (left or right) relative to the reference marker. There was no time constraint for giving a response. After responding, the reference marker disappeared and the participants moved the robot directly back to the home position along the same linear route to begin the next trial. The position of the hand with respect to each reference marker was adjusted over trials using an adaptive staircase algorithm (H. Kesten, 1958; Treutwein, 1995) as described by Cressman and Henriques (2009, 2010) and Jones et al. (2010). In particular, for each reference marker there were 2 staircases, one starting 20° to the left (CCW)

of the reference marker and one starting 20° to the right (CW). The 2 staircases were adjusted independently and randomly interleaved as outlined by Cressman and Henriques (2009). The test sequence of 15 proprioceptive estimates followed by 6 reaches was completed 10 times, for a total of 222 trials (150 proprioceptive estimate trials (50 at each reference marker) + 72 reach trials).

Participants completed 15 final no cursor reaches (box 6, Figure 3.2) immediately after completing the Proprioceptive Estimate + Reach Task in order to ensure that they were still reaching in a similar manner as before the proprioceptive estimate trials. These reaches were carried out like the previous 12 no cursor reach trials (box 2 in Figure 3.2) but now all 5 reach targets and reference marker positions were presented.

Aligned Cursor

Reach Training   Proprioceptive Estimate + Reach Task

| Reach Training (aligned cursor) 99 Trials (33/target) 1 | Reach Aftereffects (no cursor) 12 Trials (3/target) 2 | Reach Training (aligned cursor) 12 Trials (4/target) 3 | Proprioceptive Estimates 15 Trials (5/marker) 4 | Reach Training (aligned cursor) 6 Trials (2/target) 5 | Reach Aftereffects (no cursor) 15 Trials (3/target) 6 |

10 times

Rotated Cursor

Reach Training   Proprioceptive Estimate + Reach Task

| Reach Training (rotated cursor) 99 Trials (33/target) 1 | Reach Aftereffects (no cursor) 12 Trials (3/target) 2 | Reach Training (rotated cursor) 12 Trials (4/target) 3 | Proprioceptive Estimates 15 Trials (5/marker) 4 | Reach Training (rotated cursor) 6 Trials (2/target) 5 | Reach Aftereffects (no cursor) 15 Trials (3/target) 6 |

10 times

3 times

Figure 3.2 Breakdown of the testing sessions within the experiment. In the first testing session (top row) participants reached with an aligned cursor that accurately represented the position of their hand in the reach training trials. In the

second testing session (bottom row), participants first reached with a misaligned cursor that was rotated 30° clockwise with respect to the actual hand location during the reach training trials (first rotated block). Participants then completed two more training blocks during which time the cursor was rotated 30° or 50° (second rotated block) and 30° or 70° (third rotated block). After completing 99 reach training trials with an aligned (top row) or misaligned cursor (bottom row), participants next reached to each of four reach targets (the two outer targets and the two inner targets), 3 times each without a cursor in order to assess motor adaptation (reach aftereffects trials, Box 2 in top and bottom rows). Participants then completed 12 reaches to the reach targets with the cursor present (Box 3). This was followed by 10 sets of 15 proprioceptive estimate trials (Box 4) and 6 visually guided reaches (Box 5) for a total of 150 proprioceptive estimate and 60 reach trials. Following this, participants reached to all targets and reference markers 3 times without a cursor in order to assess maintenance of reach aftereffects (Box 6). In the first testing session, participants only completed one block of training trials with aligned visual feedback of the hand. In the second testing session, participants completed three training blocks with misaligned visual feedback of the hand.

3.3.4 Data analysis

3.3.4.1. Motor adaptation

We analyzed reaching errors (i.e. aftereffects) made in the no-cursor reach trials to (1) determine if participants adapted their reaches after aiming with a misaligned cursor and (2) ensure that participants maintained adaptation across the proprioceptive estimate and reach trials. Reach endpoint errors were defined as the angular difference between a movement vector (from the home position to reach endpoint) and a reference vector (joining the home position and the target). Reach errors at peak velocity (PV) were defined in a similar manner.

In particular, reach errors at PV were defined as the angular difference between a movement vector at peak velocity and a reference vector. To determine if participants had indeed adapted their reaches, we analyzed mean endpoint aftereffects and aftereffects at peak velocity separately using a RM-ANOVA with 2 Training Group (30 ° group vs. 70 ° group) x 4 Visual Feedback Block (aligned feedback vs. first block of rotated feedback (30°) vs. second block of rotated feedback (30° or 50°) vs. third block of rotated feedback (30° or 70°)) x 2 Time (trials completed following reach training vs. trials completed following the proprioceptive estimate and reach trials) factors. Training Group was a between-group factor while Visual Feedback Block and Time were within-group factors. Tukey's Honestly Significant Difference (HSD) post-hoc tests were administered to determine the locus of these differences (alpha = .05). In addition to revealing if participants adapted their reaches in response to the visuomotor distortion and maintained this level of adaptation across the testing session, this analysis allowed us to determine if reach adaptation increased with increasing practice and/or distortion following visuomotor learning.

3.3.4.2. Proprioceptive estimates of hand position

To examine the influence of prolonged reach training and the magnitude of visuomotor distortion on changes in proprioceptive recalibration, we determined the locations at which participants felt their hands were aligned with the reference markers. This location was determined by fitting a logistic function (solid black line, Figure 3.3B) to each participant's responses (Figure 3.3A) for each reference marker in each testing session. The point of responding "left" 50% of the time (i.e. responding "left" and "right" equally often) represents bias (Cressman & Henriques, 2009, 2010; Jones et al., 2010). In addition to calculating bias, we also determined participants' uncertainty (or precision) by finding the difference between the values at which the point of responding "left"

was 25% and 75% (dashed grey lines, Figure 3.3B). Bias and uncertainty related to a particular reference marker were excluded if the associated uncertainty was greater than the mean uncertainty across all reference markers + 2 standard deviations. Based on this analysis, only two proprioceptive estimates (less than 1% of total estimates) were excluded.
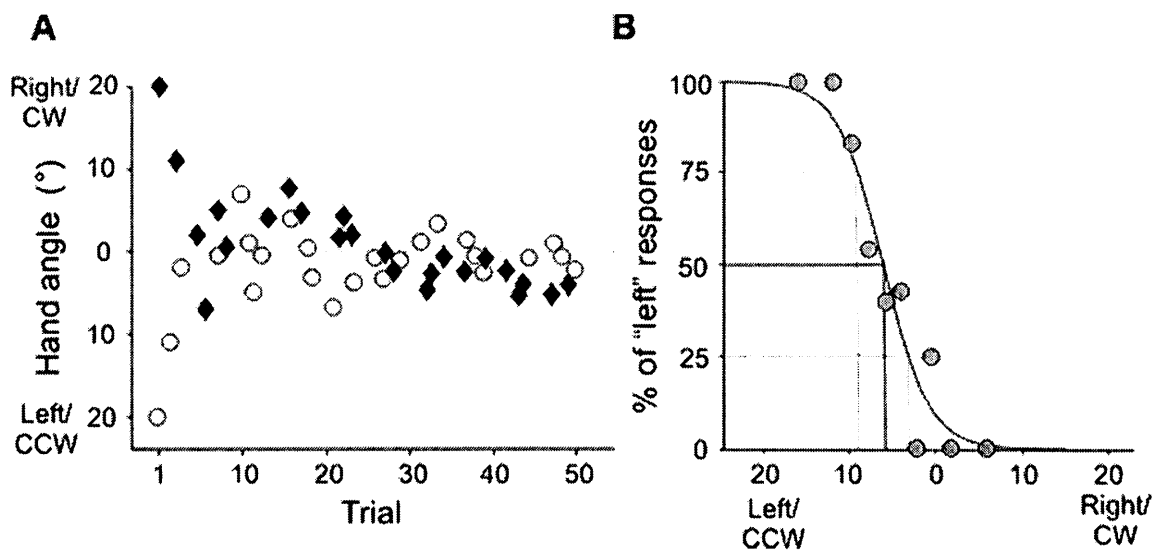
Figure 3.3 Angular position of the hand during proprioceptive estimate trials and percentage of left responses for a single participant when the 0° visual reference marker was displayed. A: The left (white circles) and right (black diamonds) staircases began with the participant's hand deviated by 20° from the reference marker (dashed line) and gradually converged over trials. B: A logistic function was fitted to the response data to define bias and uncertainty, where bias is the probability of responding left 50% of the time (dashed black line) and uncertainty is the difference between the values at which the probability of responding left was 25 and 75% (dashed grey lines).

Biases and uncertainty ranges were analyzed in a 2 Training Group (30 ° group vs. 70 ° group) x 4 Block (aligned feedback vs. first block of rotated feedback (30°) vs. second block of rotated feedback (30° or 50°) vs. third block of rotated feedback (30° or 70°)) x Marker Location (0° vs. 30° CW vs. 30° CCW) RM-ANOVA. Differences with a probability of less than .05 were considered to be significant. Tukey's Honestly Significant Difference (HSD) post-hoc tests were administered to determine the locus of these differences (alpha = .05).

3.4 RESULTS

3.4.1 Motor adaptation

Across groups, participants reached to the targets with an average movement time of 1.95 s ± .93 s (SD) and an average peak velocity of 16.4 cm/s ± 5.9 cm/s (SD) when no visual feedback of the hand was provided. Mean reach endpoint errors (i.e. aftereffects) for these no-cursor trials following training with an aligned cursor were on average 0.75° to the right of the target. These small reaching errors suggest that all participants were able to accurately reach to a target even without any visual feedback of their hand position. Mean aftereffects following training with misaligned visual feedback of the hand are displayed in Figure 3.4. In this figure we see that after training with a rotated cursor, endpoint errors deviated significantly more leftwards of the target ($F(3,63)$ = 78.104, $p <$ .001) for both training groups. Following the first block of 30° rotated cursor feedback training, reaching movements deviated on average 16° leftwards for all participants compared to aftereffects following aligned training. The training groups then differed on subsequent training blocks ($F(3,63)$ = 10.445, $p <$ .001). Specifically, aftereffects for those participants that trained with a 30° cursor rotation (white bars in Fig 4) remained constant and did not differ significantly with successive blocks of training ($p >$ .05 for all contrasts). In contrast,

aftereffects for participants that trained with a 50° and 70° rotation in rotated training Blocks 2 and 3 respectively (filled bars), increased to 27.6° and 33.8° respectively compared to training with an aligned cursor ($p < .001$). For the 70° training group, aftereffects following each training block differed significantly from the previous block (aligned block 1 vs. rotated block 1, $p < .001$; rotated block 1 vs. rotated block 2, $p < .001$, rotated block 2 vs. rotated block 3, $p = .006$). For both groups, aftereffects following reach training trials did not differ from aftereffects following proprioceptive estimates ($F(1, 21) < 1$). Thus, results from the 70° training group indicate that as the magnitude of the distortion of the visual cursor feedback became greater, so too did motor adaptation. However, the relative proportion of aftereffects was consistent for each training block and on average represented 51% of the visuomotor distortion: a one-way ANOVA revealed no differences between blocks ($F(2,38) < 1$, $p = .654$; 70° group: first rotated block, $\bar{x} = 49\%$, SD = 19.38; second rotated block, $\bar{x} = 55\%$, SD = 22.82; third rotated block, $\bar{x} = 48\%$, SD = 21.41). As well, participants in the 30° training group maintained a reach adaptation level of 61% of the visuomotor distortion across all training blocks, similar to that of the 70° training group (30° group: first rotated block $\bar{x} = 60\%$, SD = 24.78; second rotated block, $\bar{x} = 63\%$, SD = 23.47; third rotated block, $\bar{x} = 60\%$, SD = 17.04). Reach errors at peak velocity followed the same pattern of results as the reach endpoints described above, consistent with previous work from our lab suggesting that deviations at end point and peak velocity are comparable (Wong and Henriques, 2009).
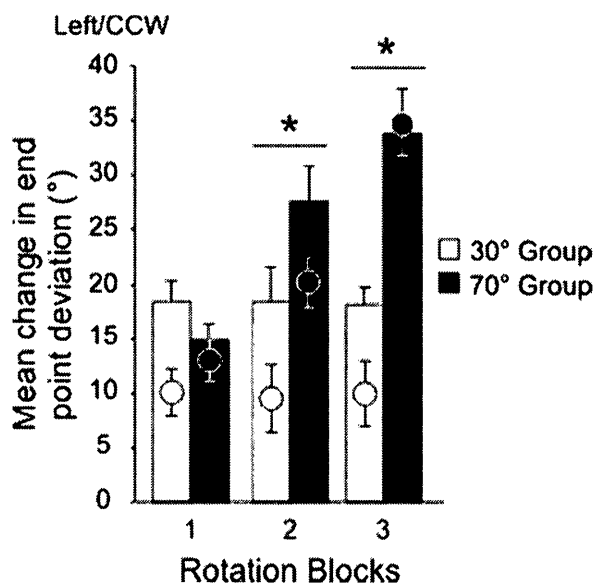
Figure 3.4 Aftereffects following training with misaligned visual feedback of the hand. Endpoint errors were calculated by subtracting angular reach endpoint errors in the no cursor reach trials after training with an aligned cursor from errors completed in the no cursor reach trials after training with a rotated cursor. Errors at peak velocity were calculated by subtracting angular reach errors at peak velocity in the no cursor reach trials after training with an aligned cursor from errors completed in the no cursor reach trials after training with a rotated cursor. Errors at reach endpoint (bars) and at peak velocity (circles) averaged across targets and participants for the 30° training group (open symbols) and the 70° training group (filled symbols) are shown for the no cursor reaches completed after the three consecutive rotated training blocks of trials. Asterisks indicate significant group differences ($p < .05$). Error bars reflect standard error of the mean.

3.4.2 Proprioceptive recalibration

3.4.2.1 Bias

Figure 3.5A displays mean proprioceptive biases at all three reference marker locations (circles) for both the 30° (top panel) and 70° training groups (bottom panel). The diamonds indicate biases following training with an aligned cursor, while the three sets of triangles indicate biases following the three training blocks with a rotated cursor (white = 1st block, grey = 2nd block, black = 3rd block). For both groups of participants we see that, on average, estimates of unseen hand location were slightly biased to the left after reaching with an aligned cursor. In fact, the mean bias collapsed across all participants and reference markers was 5.1° left of the reference marker (previous studies in our lab have shown that this is merely a hand bias, Jones, Cressman & Henriques, 2010). More importantly however, following reach training with misaligned cursor feedback of the hand, biases were shifted further left for both training groups. Figure 3.5B displays the mean changes in bias following visuomotor adaptation training. Following training with a 30° rotated cursor, biases were shifted on average 7.3° more leftwards for all participants compared to estimates following training with an aligned cursor ($F(3,63) = 42.39$, $p < .001$). However, the training groups differed on subsequent blocks ($F(3,63) = 4.771$, $p = .005$). Similar to the aftereffects errors discussed above, biases for the 30° training group did not change across successive blocks of reach training trials with a cursor rotated 30° CW with respect to the hand ($p > .05$ for all contrasts). Moreover, the average biases for the 70° training group following training with a 50° and 70° rotated cursor increased leftwards by 12.2° and 14.7° respectively, relative to performance following training with an aligned cursor. For the 70° training group, changes in bias following each rotated training block were different from the previous block (rotated block 1 vs. 2, $p = .001$; block 2 vs. 3, $p = .048$). Changes in bias were similar across all reference marker locations ($F(2,42) < 1$ for both

groups). Thus, as the magnitude of the visuomotor distortion became greater, so too did proprioceptive recalibration. However, the relative proportion of changes in bias for the 70° training group were consistent for each training block and on average represented 24% of the visuomotor distortion (first rotated block, $\bar{x}$ = 26%, SD = 18.04; second rotated block, $\bar{x}$ = 24%, SD = 10.10; third rotated block, $\bar{x}$ = 21%, SD = 9.32). Participants in the 30° training group also maintained a change in bias equivalent to 28% of the visuomotor distortion across all training blocks consistent with that of 70° training group (first rotated block $\bar{x}$ = 29%, SD = 20.22; second rotated block, $\bar{x}$ = 29%, SD = 19.18; third rotated block, $\bar{x}$ = 26%, SD = 15.93).

A   **30° Group**

B Left/CCW

○ Reference marker
◇ Aligned
△ Rotated Block 1 (30°)
▲ Rotated Block 2 (30°)
▲ Rotated Block 3 (30°)

5 cm
left
0
5 cm
right

70° Group

○ Reference marker
◇ Aligned
△ Rotated Block 1 (30°)
▲ Rotated Block 2 (50°)
▲ Rotated Block 3 (70°)

5 cm
left
0
5 cm
right

Mean change in bias (°)

20

15

10

5

0

*

*

□ 30° Group
■ 70° Group

1   2   3
Rotation Blocks
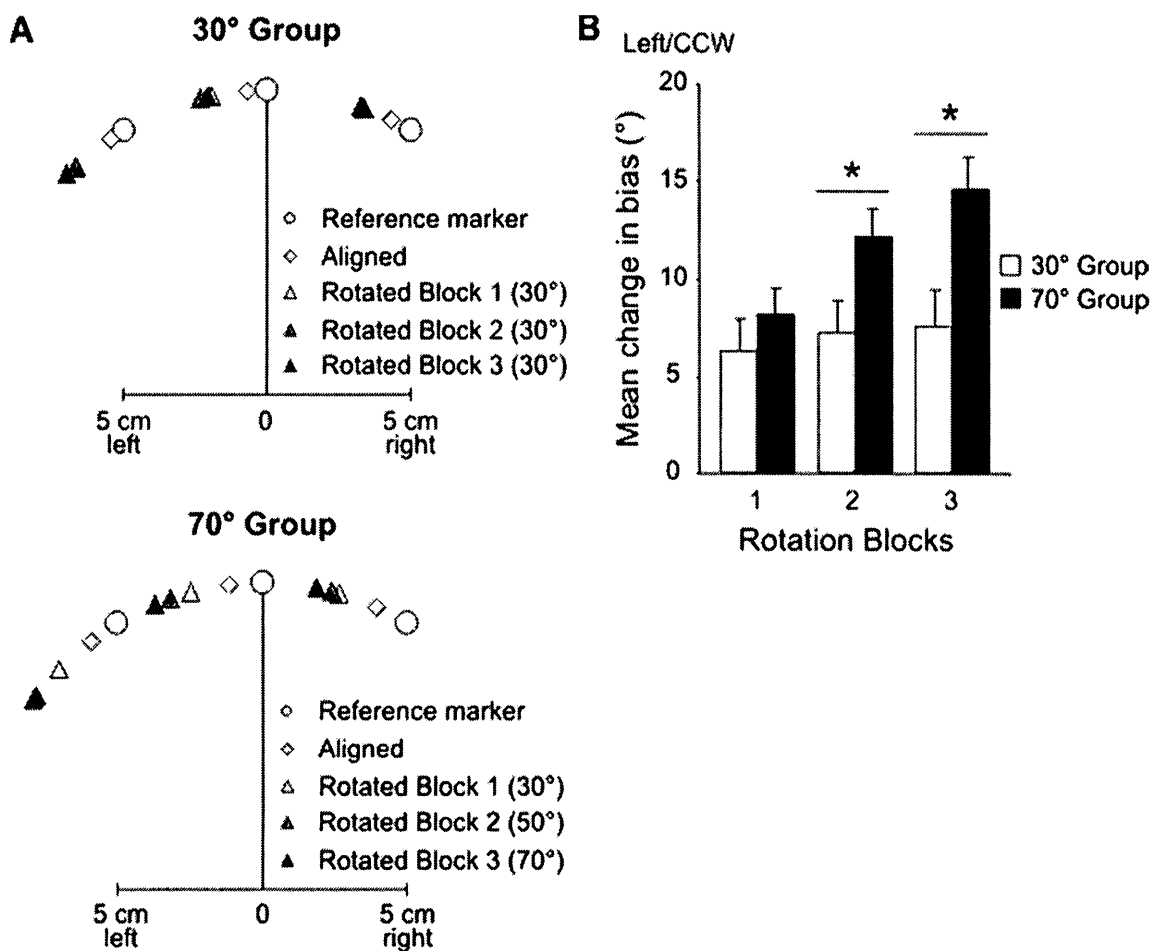
Figure 3.5 Proprioceptive biases following training with aligned and misaligned visual feedback of the hand. A: Mean 2-D proprioceptive biases following training with an aligned (diamonds) or misaligned (after the first rotated block: white triangles; second rotated block: grey triangles; third rotated block: black triangles) cursor for participants in the 30° (upper panel) and 70° (lower panel) training groups. The actual reference marker positions are represented as circles. B: Mean changes in biases after training with a misaligned cursor compared to an aligned cursor were averaged across reference markers for the 30° (open bars)

and 70° (filled bars) training groups. Asterisks indicate significant group differences ($p < .05$). Error bars reflect standard error of the mean.

3.4.2.2 Uncertainty

Figure 3.6 depicts the magnitude of the uncertainty ranges for both the 30° (white bars) and 70° (filled bars) training groups following reaches with an aligned and misaligned cursor. Uncertainty levels were on average 9.5° for each reference marker. Participants' levels of precision in estimating the location of their unseen hand were comparable after reach training with aligned and misaligned cursor feedback ($F(3,63) = 2.455$, $p = .071$). While no overall differences were observed between groups ($F(1,21) < 1$) or reference marker locations ($F(2,42) = 2.26$, $p = .117$), a significant interaction was observed, wherein participants in the 70° training group demonstrated greater precision (7.8°) when estimating hand position relative to the centre reference marker compared with the markers located 30° left and right of center (12° and 10.2°, respectively; $F(2,42) = 4.423$, $p = .018$). No other differences were observed.
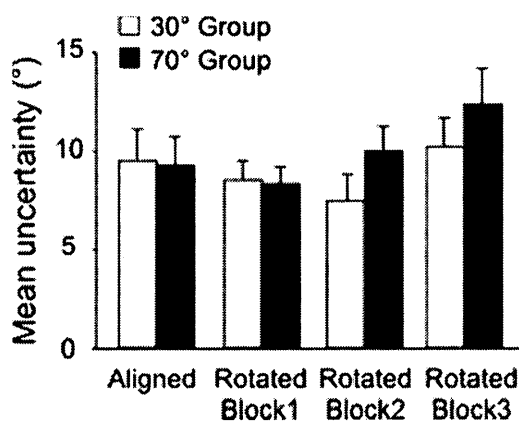
Figure 3.6 Magnitude of the uncertainty ranges in the proprioceptive estimate trials were averaged across participants and reference marker positions following reach training with an aligned cursor or with a misaligned cursor (after rotated

training block 1, 2 and 3) for participants in the 30° (open bars) and 70° (filled bars) training groups. Error bars reflect standard error of the mean.

3.4.3 Motor adaptation vs. sensory recalibration

Figure 3.7A displays mean changes in bias and aftereffects following training with a misaligned cursor compared to an aligned cursor. From this figure we see that participants adapted their reaches and recalibrated proprioception, and that proprioceptive recalibration was less than reach adaptation for both groups of participants across all training blocks. In fact, on average, both groups of participants recalibrated proprioception by roughly 45% of the movement aftereffects achieved on all training blocks. Furthermore, from Figure 3.7A we see that the 70° training group demonstrated a continual increase in changes in bias and aftereffects following training with an increasing visuomotor distortion, while the 30° training group did not show any changes in either bias or aftereffects following repeated training with a 30° cursor rotation.

From Figure 3.7A it appears that the magnitude of proprioceptive recalibration increased coincidentally with increasing aftereffects. In Figure 3.7B and 7c we plot the changes in proprioceptive recalibration and reach adaptation as a percentage of the visuomotor distortion for the 30° training group and 70° group, respectively. We found no significant relationship between the magnitude of proprioceptive recalibration and the extent of aftereffects (when expressed as a percentage of the visuomotor distortion) for either the 30° training group, Figure 3.7B: $\beta 1 = .225$, $p = .154$) group, or for the 70° training group, Figure 3.7C: $\beta 1 = .026$, $p = .896$; or when values from all participants and all blocks of trials were included in the analysis ($\beta 1 = .123$, $p = .154$). Likewise, individual analyses of each training block for both groups of participants did not reveal any significant relationships between the percentage of proprioceptive recalibration and reach adaptation achieved (30° training group: first rotated block, $\beta 1 = .026$, $p = .931$;

second rotated block, $\beta 1$ = .397, p = .155; third rotated block, $\beta 1$ = .313, p = .344; 70° training group: first rotated block, $\beta 1$ = .306, p = .272; second rotated block, $\beta 1$ = -.118, p = .378; third rotated block, $\beta 1$ = -.087, p = .514). Given that these coincident sensory and motor changes were not correlated, we hypothesized that the trend of increasing proprioceptive recalibration with increasing reach adaptation in the 70° training group, as shown in Figure 3.7A, was due to the size of the error signal. To determine if the magnitude of the visuomotor distortion was driving these changes, we analyzed the actual mean changes in bias (in degrees) of the 70° training group (as these participants experienced an increase in the visuomotor distortion) in a regression in which actual changes in aftereffects (in degrees) and magnitude of the visuomotor distortion were used as predictor variables. While the overall correlation was significant ($F(2,36)$ = 4.67, p = .019), it was only the magnitude of the visuomotor distortion that was a significant predictor of the changes in bias ($\beta 1$ = .193, p =.007). Changes in aftereffects did not significantly predict changes in bias for this training group ($\beta 2$ = -.057, p = .494) or when all participants were included in analyses ($\beta 2$ = .021, p = .499).
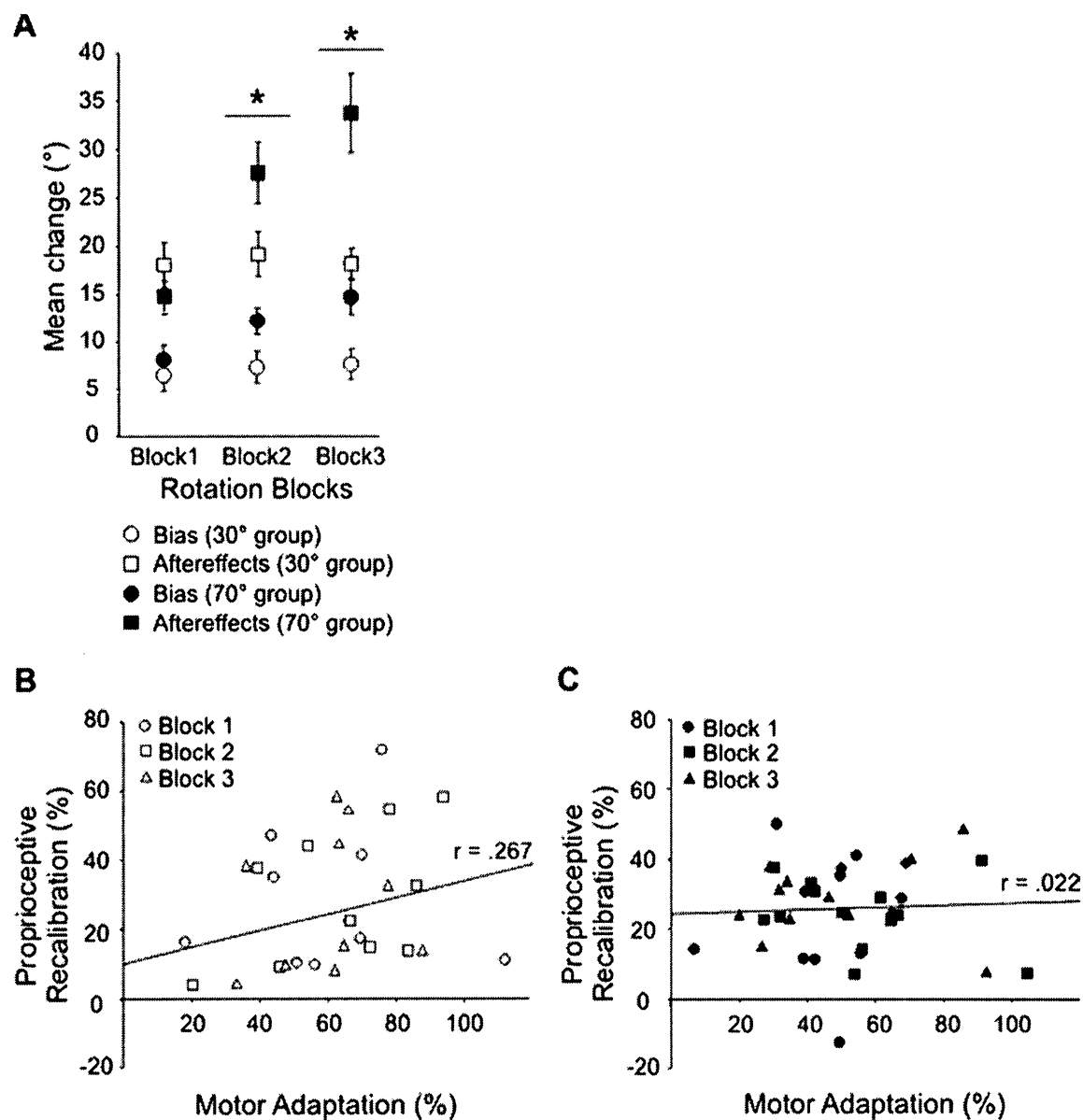
Figure 3.7 Comparison between changes in bias and aftereffects across the two training groups. A: Angular changes in bias (circles) and aftereffects (squares), averaged across participants and locations, following reach training with misaligned visual feedback of the hand in the three training blocks are shown for participants in the 30° (open symbols) and 70° (filled symbols) training groups. Asterisks indicate significant group differences ($p < .05$). Error bars reflect

standard error of the mean. B-C: Changes in sensory and motor recalibration as a percentage of the visuomotor distortion introduced during each training block for participants in the $30°$ training group (B) and $70°$ training group (C) following rotated blocks 1 (circles), 2 (squares) and 3 (triangles). Each symbol represents the percentage change in bias and % change in aftereffects averaged across marker and target locations for each participant. Solid line indicates the line of best fit for all data points.

Finally, to compare the relationship between sensory and motor recalibration across the 2 groups of participants and training blocks, we divided the actual change in bias by the change in aftereffects for each participants following all three rotated feedback training blocks to derive a ratio of sensory to motor recalibration. We then subjected these values to a 2 Group ($30°$ training group vs. $70°$ training group) x 3 Block (first block of rotated feedback ($30°$) vs. second block of rotated feedback ($30°$ or $50°$) vs. third block of rotated feedback ($30°$ or $70°$)) RM-ANOVA to determine if these ratios remained consistent across training blocks. No significant differences between blocks ($F(2,42) = 1.92$, $p = .174$) or groups ($F(1,21) < 1$) were observed. Thus, the proportion of sensory to motor recalibration remained consistent across blocks for both groups. Altogether these findings indicate that while the relationship between sensory and motor recalibration remains constant following prolonged training or reaching with a greater visuomotor distortion, results suggest that these two processes may be independent and due to two separate adaptation processes.

3.5 DISCUSSION

The goal of the present study was to examine the relationship between changes in sensory and motor systems following visuomotor adaptation. To do so we asked if prolonged reach training with distorted visual feedback of the

hand or training with an increasing visuomotor distortion leads to increased motor adaptation and proprioceptive recalibration. Participants completed one block of reach training trials with an aligned cursor and three blocks of reach training with a misaligned cursor that a) was rotated 30° clockwise relative to the participants's unseen hand for all three blocks, or b) was incrementally rotated 30°, 50° and 70° clockwise across three subsequent training blocks. After each training block we assessed reach adaptation and sense of felt hand position. We found that following initial training to a cursor rotated 30° CW with respect to the hand, participants adapted their reaches by 16° or approximately 55% of the distortion compared to when they reached with aligned visual feedback of the hand. Participants also shifted the position at which they felt their hand was aligned with a reference marker leftwards by 7° or roughly one quarter of the visuomotor distortion. Prolonged reach training with a 30° rotation did not lead to any further motor adaptation or proprioceptive recalibration, suggesting that both motor recalibration and sensory recalibration saturated within the first 100 trials of reach training. Conversely, reach adaptation increased to 28° and 34° following training with a 50° and 70° cursor rotation, respectively, while changes in bias increased to 12° and 15° following the same rotations. Overall, the magnitude of proprioceptive recalibration was approximately 45% of the observed reach adaptation across all conditions for both groups.

The magnitude of the visuomotor distortion was correlated with both changes in proprioceptive bias and movement aftereffects; however, no relationship between these sensory and motor changes was observed overall or within training blocks. In contrast to changes in proprioceptive biases and movement aftereffects, the precision of participants' estimates of hand position did not change across training blocks. Thus participants responded in a similar manner regardless of the magnitude of the distortion or the number of reach training trials completed. In accordance with these findings, Cressman et al.

(2010) also found that uncertainty in felt hand position remained consistent across training sessions and hence was not related to changes in proprioceptive bias and reach aftereffects in both young and older adults. Taken together, these findings suggest that the size of the distortion has a similar effect on both sensory and motor changes but does not affect the precision of participants' estimates of hand position.

Following the first block of learning trials and throughout subsequent blocks, participants in both groups began to feel their hand near the position that it was visually represented by a cursor. In the current study, this was demonstrated by asking participants to estimate the location of their unseen hand with respect to a visual reference marker. Previous work has also shown recalibration of felt sense of hand position with respect to an internal reference as defined by the participants' body midline (Cressman & Henriques, 2009). Moreover, this recalibration was not different from recalibration observed when a visual reference marker was displayed at the same location. These results strongly suggest that proprioception is recalibrated following visuomotor adaptation such that proprioceptive estimates of hand position are shifted to match the visual percept of hand position. Furthermore, given that proprioceptive recalibration failed to transfer from the trained hand to the untrained hand following visuomotor adaptation training (Salomonczyk et al., 2010) provides additional evidence that our method assesses proprioceptive recalibration rather than a visual shift, or combination of the two.

3.5.1 The influence of reach training

While more extensive training has been hypothesized to contribute to greater perceptual changes (Ostry et al., 2010), we found that this was not the case. Changes in bias and aftereffects after subsequent training trials with the same distortion were no larger than those following the first block of training with

misaligned visual feedback of the hand. This is consistent with reach adaptation findings from Krakauer and colleagues (2005), who showed that prolonged training with a cursor that was rotated with respect to the hand did not result in an increase in the magnitude of motor adaptation. Based on their findings, Krakauer et al. suggested that motor learning saturates within the first block of reach training. Results from our lab (T. Wong & Henriques, 2009) also indicate that prolonged training over subsequent testing days does not result in increased motor learning as we found no differences between aftereffects following an initial day of reach training (250 trials) and subsequent testing days in which 750 additional trials were performed.

Several authors have suggested a multi-rate model of motor learning wherein one system is highly sensitive to error but learning is rapidly forgotten, while the other system is less sensitive to error but retains learning much more robustly (Kording, Tenenbaum, & Shadmehr, 2007; Shadmehr, Smith, & Krakauer, 2010; M. A. Smith, Ghazizadeh, & Shadmehr, 2006). The latter slow-learning process is associated with long-term stable motor changes in the effector (Criscimagna-Hemminger & Shadmehr, 2008), likely because errors that drive this long-term slow learning may be attributed to more long-lasting changes in the plant or effector, like those resulting from fatigue, damage or development. For example, errors due to growth of the arm during childhood would require a more enduring change in estimating the state of the plant than those errors produced when using a new tool. Since sensory information like proprioception are critical for state estimates, it may be that changes in proprioceptive estimates or proprioceptive recalibration may be associated more with a slower learning process than those that lead to changes in movements (aftereffects) which tend to be greater in magnitude. However, further studies are necessary to properly test this possibility. So far, the multi-rate model of motor learning has not been

explored for visuomotor adaptation, only for saccade adaptation and force-field learning.

3.5.2 Mechanisms contributing to motor adaptation and proprioceptive recalibration

Results from our lab do indicate that learning rates during closed loop reaches are dependent on the magnitude of the visuomotor distortion (Balitsky-Thompson & Henriques, 2010; Dionne & Henriques, 2008). The increase in aftereffects or deviations in open loop reaches and the increase in bias observed in the present study were systematically shown to be related to the magnitude of the visuomotor distortion, suggesting that changes in the sensory and motor systems are tied directly to the magnitude of the distortion rather than practice. Consistent with previous work from our lab (Cressman & Henriques, 2009; Cressman et al., 2010; Salomonczyk et al., 2010), sensory and motor changes were not significantly correlated, suggesting that these changes arose via coincident yet separate mechanisms. Differences in changes in sensory and motor systems could arise due to the source of error signals used to generate adaptive responses in the two systems. Sensory prediction errors, or the difference between the actual sensory feedback and expected sensory feedback for a given motor command, are considered to be the predominant error signal driving motor adaptation (Miall & Wolpert, 1996; Tseng, Diedrichsen, Krakauer, Shadmehr, & Bastian, 2007). While previous studies suggest that this error signal also contributes to changes in proprioception (Simani et al., 2007; van Beers et al., 2002), studies from our lab have shown that a cross-sensory error signal (visual-proprioceptive discrepancy) is sufficient and more likely to be responsible for updating proprioceptive estimates of hand position(Cressman & Henriques, 2010). As well, this cross-sensory error signal may even be partially responsible for changes in movements following visuomotor adaptation. To investigate the

role of cross-sensory error signals in both sensory and motor recalibration, Cressman and Henriques (2010) eliminated sensory prediction errors by having a robot manipulandum passively guide participants' hands while they viewed a cursor rotated 30° CW with respect to their hand move directly to a target (i.e. the cursor moved to target so there was no discrepancy in desired/predicted and actual movement). Following exposure to this cross-sensory discrepancy between seen and felt hand movement, proprioceptive estimates of the hand were shifted in the direction of the distortion and by the same magnitude as that produced following adaptation to a visuomotor rotation of 30° CW when participants actively and voluntarily directed their reaches toward the target (Cressman & Henriques, 2009). Moreover, when participants reached to the same targets following exposure to this cross-sensory discrepancy, their open-loop reaches were also significantly deviated. However, these aftereffects were only about a third of the size of aftereffects typically following adaptation. Indeed, the aftereffects in this study were about the same size as, and were significantly correlated with, proprioceptive misestimates of hand position. This is in contrast to the lack of correlation between aftereffects and proprioceptive recalibration following visuomotor adaptation reported previously (Cressman & Henriques, 2009) and in the present study. Thus, aftereffects following mere exposure to cross-sensory discrepancy may be due to a change in felt hand position rather than any real motor recalibration and sensory prediction errors may not be the only training signal responsible for motor recalibration (i.e., movement aftereffects) produced during visuomotor adaptation. In the present study we explored how the magnitude of the distortion would affect proprioceptive recalibration and motor adaptation. In previous research, the magnitude of the distortion (and thus the sensory prediction error signal) has been shown to affect motor learning (Abeele & Bock, 2001; Kagerer et al., 1997). Here, we observed that an increase in the magnitude of a visuomotor distortion resulted in

proportional increases to both proprioceptive and motor recalibration. These results suggest that the magnitude of the cross-sensory error signal gives rise to changes in proprioception directly.

Like in our previous studies, a visual cue indicated the initial start position of the hand for the proprioceptive estimation trials so that we could ensure that our observed changes in proprioceptive estimates were not due to a drift in proprioception (Brown, Rosenbaum, & Sainburg, 2003). Given that participants were provided with a visual representation of their hand position at the beginning of these estimation trials, it is possible that this cue may also have been used to recalibrate proprioceptive estimates of hand position (this time to a visually-aligned location) and minimize the proprioceptive bias which was measured at the endpoint of the movement trajectory located 10 cm away, thus reducing the overall changes in felt hand position following visuomotor adaptation. Nonetheless, we did find a significant change in proprioceptive estimate of hand position. While the role of this initial visual hand feedback on proprioceptive recalibration remains to be determined, the results of the present study provide valuable insight into how the size of the visuomotor distortion and the length of training affect both sensory and motor changes.

3.5.3 Vision and proprioception

Both vision and proprioception have been shown to play integral roles in sensorimotor adaptation (Simani et al., 2007; van Beers et al., 2002). Sensory information from these modalities may be processed in a similar manner within the brain as it has been suggested that both visual (Goodale & Milner, 1992; Milner & Goodale, 1995) and proprioceptive signals (Dijkerman & de Haan, 2007) are processed within two distinct streams - dependent on whether the information is to be used to guide action or for perception. Furthermore, Dijkerman and de Hann suggest that the two proprioceptive processing streams may even be

represented in different areas of the brain such that action-oriented processing occurs in the posterior parietal cortex (PPC) and perception-oriented processing occurs in the insula as well as the PPC. The processing of proprioception necessary for re-aligning proprioceptive and visual feedback of the hand (i.e. resolving the cross-sensory error signal) may therefore be separate from the processing of proprioception necessary for providing a unified estimate of hand position for feedforward motor control (i.e. resolving the sensory prediction error signal). This segregated processing could explain how sensory and motor recalibration could arise as two related yet distinct processes in the brain. Further evidence for the possibility of distinct processes comes from findings of visuomotor adaptation in deafferented individuals who have been shown to adapt their reaches following reaching with misaligned visual feedback of the hand (Bernier, Chua, Bard, & Franks, 2006; Ingram et al., 2000).

Proprioceptive recalibration may arise because the central nervous system requires a unified estimate of hand position for motor control. Previous research has shown that motor performance is better when one has access to information from multiple sensory modalities compared to a single one, even though vision and proprioception sometimes provide naturally conflicting information (van Beers et al., 2002). Thus, one way for the brain to resolve conflicting information in order to provide a unified estimate is to recalibrate one sense so it better matches the other. In the present case, proprioception is recalibrated to match visual estimates of hand position.

3.5.4 Conclusions

While the precise relationship between cross-sensory error and sensory prediction error signals on reach adaptation and proprioceptive recalibration remains to be determined, our results provide further evidence of sensory plasticity after learning to reach with misaligned visual feedback of the hand. Our

method of assessing proprioceptive recalibration allows us to examine the influence of cross-sensory recalibration processes directly, independent of motor adaptation. With our method, proprioceptive recalibration has been observed in a variety of contexts, including following learning with translated and rotated cursor distortions (Cressman & Henriques, 2009, 2010) and force field perturbation (Ostry et al., 2010) when estimating the position of the hand relative to both proprioceptive and visual stimuli (Cressman & Henriques, 2009), following adaptation of both the left and right hands (Salomonczyk et al., 2010), across the lifespan (Cressman et al., 2010), and following prolonged reach training and training to increased distortions. With our method, we possess the requisite tools to investigate the role of distinct error signals in motor and sensory plasticity and with further studies we hope to gain insight into the contribution of these signals to recalibration processes. At present, results indicate that the magnitude of the visuomotor rotation predicts the magnitude of sensory and motor changes following adaptation.

CHAPTER FOUR

THE ROLE OF THE CROSS-SENSORY ERROR SIGNAL IN VISUOMOTOR ADAPTATION

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4.1 ABSTRACT

Reaching to targets with misaligned visual feedback of the hand leads to changes in proprioceptive estimates of hand position and reach aftereffects. In such tasks subjects are able to make use of two error signals: the discrepancy between the desired and actual movement, known as the sensorimotor error signal, and the discrepancy between visual and proprioceptive estimates of hand position, which we refer to as the cross-sensory error signal. We have recently shown that mere exposure to a sensory discrepancy in the absence of goal-directed movement (i.e., no sensorimotor error signal) is sufficient to produce similar changes in felt hand position and reach aftereffects. Here we sought to determine the extent that this cross-sensory error signal can contribute to proprioceptive recalibration and movement aftereffects by manipulating the magnitude of this signal in the absence of volitional aiming movements. Subjects pushed their hand out along a robot-generated linear path that was gradually rotated clockwise (CW) relative to the path of a cursor. On all trials subjects viewed a cursor that headed directly towards a remembered target while their hand moved out synchronously. After exposure to a 30° rotated hand-cursor distortion, subjects recalibrated their sense of felt hand position and adapted their reaches. However, no additional increases in recalibration or aftereffects were observed following further increases in the cross-sensory error signal (e.g., up to 70°). This is in contrast to our previous study where subjects freely reached to targets with misaligned visual hand position feedback, hence experiencing both sensorimotor and cross-sensory errors, and the distortion magnitude systematically predicted increases in proprioceptive recalibration and reach aftereffects. Given these findings, we suggest that the cross-sensory error signal results in changes to felt hand position which drive partial reach aftereffects, while larger aftereffects that are produced after visuomotor adaptation (and that vary with the size of distortion) are related to the sensorimotor error signal..

4.2 INTRODUCTION

When reaching with a visuomotor distortion (i.e., when wearing prism goggles or in a virtual-reality environment), one adjusts his or her movements in order to bring the visual representation of the hand to the desired target (Martin et al. 1996b; Krakauer et al. 1999; Krakauer et al. 2000; Redding and Wallace 2000; Simani et al. 2007). In general, it is proposed that motor adaptation arises primarily due to error-based learning (Tseng et al. 2007; Berniker & Kording 2008; Wei & Kording 2009; Hinder et al. 2010; Shadmehr et al. 2010), where the difference between one's desired performance and actual performance, or between the predicted and actual sensory consequences of one's movements, is reduced. Specifically, if the "seen" hand movement does not reach the desired goal or differs from the predicted outcome, then the brain uses this *sensorimotor error signal* (Wong & Shelhamer 2011) to change one's motor performance on subsequent movements. Moreover, these movements continue to deviate even when (misaligned) visual feedback of hand position is removed (Martin et al. 1996a; Krakauer et al. 1999; Krakauer et al. 2000; Redding & Wallace 2000; Simani et al. 2007). These persistent movement deviations, known as aftereffects, are robust evidence that the central nervous system (CNS) has learned a new visuomotor mapping in response to the sensorimotor error signal.

Evidence suggests that in addition to motor changes observed following visuomotor adaptation, sensory changes occur as well. More specifically, one's sense of felt hand position shifts in the direction of the visual feedback provided. This has been demonstrated following adaptation to prism goggles, in which the entire visual field is displaced (Harris 1963; Hay & Pick 1966; Redding& Wallace 1996, 2004) and more recently following adaptation in a virtual setup, where only the visual feedback of hand position is displaced (van Beers et al. 2002; Simani et al. 2007). Using this second paradigm we have shown that this shift is

approximately 20% of the visuomotor distortion introduced, or roughly one-half to one-third of the extent of reach adaptation achieved (Cressman & Henriques 2009; Salomonczyk et al. 2011; Salomonczyk et al. 2012). While this shift in felt hand position, which we term proprioceptive recalibration, is small, it is robust and occurs coincidentally with motor changes under a variety of contexts. For example, we have observed this shift in felt hand position following motor adaptation to rotated and translated cursor distortions (Cressman & Henriques 2009), during active and passive hand placement (Cressman & Henriques 2009), in both the left and right hands (Salomonczyk et al. 2012), and in healthy young and older adults (Cressman et al. 2010).

Recently we have suggested that a second error signal arising from the discrepancy between seen and felt positions of the reaching hand (what we term the cross-sensory error signal), may contribute to sensory and motor adaptation (Cressman & Henriques 2010; Henriques& Cressman 2012). In particular we have proposed that this cross-sensory error signal leads to the observed changes in perceived hand position, such that sensory signals are recalibrated to provide a unified state estimate of the hand/effector. To investigate the role of this cross-sensory error signal in motor learning, we devised a novel learning paradigm that isolated the visual-proprioceptive discrepancy (and thus this cross-sensory error signal) from the usual visuomotor discrepancy (Cressman & Henriques 2010). In particular, we employed a paradigm where subject did not make free, goal-directed reaches to the target during training, but instead moved their hand (active movement condition), or had their hand passively moved by the manipulandum (passive movement condition), along a robot-constrained pathway while they viewed a cursor that moved directly towards a remembered target. The pathway that the unseen hand travelled was gradually rotated with respect to the cursor-target pathway over trials, creating a discrepancy between the seen and felt motion of the hand. Since the actual direction of the hand

motion was not under the control of the subject, and the hand-cursor always headed toward the target, subjects did not experience any reaching errors or sensory consequences of a goal-directed action and hence any sensorimotor error. Furthermore, those in the passive exposure training condition experienced no volitional movement as their hand was passively moved for them. However, like previous adaptation paradigms, subjects in both active and passive movement conditions experienced a cross-sensory error signal as their felt sense of hand position was gradually misaligned from the cursor representation of their hand. Following active or passive exposure to this cross-sensory error signal, we found that all subjects still recalibrated proprioception, and the magnitude of this proprioceptive shift was comparable to that achieved following typical learning paradigms in which subjects were able to reach freely to targets with the visuomotor distortion (and utilize both the cross-sensory and sensorimotor error signals). Additionally, we found that following active and passive exposure training, subjects adapted their movements such that reaches made without visual feedback of their hand position were deviated in the direction opposite the cursor distortion. However, these movement aftereffects were two-thirds smaller than those observed following typical training with a visuomotor discrepancy. As well, unlike any of our previous studies, the observed proprioceptive recalibration and motor aftereffects were correlated with each other, suggesting that they may have been driven by the same mechanism (Cressman & Henriques 2010). Taken together, the findings of this study suggest that exposure to a sensory discrepancy alone is sufficient to form a new visuomotor mapping in the absence of a sensorimotor error signal. More importantly, results imply that the cross-sensory error signal alone may drive partial motor learning.

In the present study we looked to investigate the extent that this cross-sensory error signal can contribute to motor learning by determining if induced changes in perceived hand position can be used in computing subsequent motor

commands. To do so, we examined motor and sensory changes following exposure to a cross-sensory error signal that was systematically increased and compared these results to those from a previous study that examined motor and sensory changes following typical visuomotor adaptation (Salomonczyk et al. 2011). The influence of the size of the sensorimotor error (and hence combination of increases in the sensorimotor error signal and cross-sensory error signal) on motor learning and sensory plasticity has been previously characterized (Marko et al.; Abeele & Bock 2001; Wei & Kording 2009; Salomonczyk et al. 2012), yet the influence of the cross-sensory error signal on its own remains to be determined. Thus, we sought to determine the extent that proprioception can be recalibrated with an increasing cross-sensory error signal and further characterize its role in motor control.

4.3 METHODS

4.3.1 Participants

Twenty-three healthy, right-handed young adults (mean age = 20.58, SD = 3.08 years, 11 females) volunteered to participate in the experiment described below. All subjects were pre-screened verbally for self-reported handedness and a history of visual, neurological and/or motor dysfunction. Subjects were then randomly assigned to either the $50°$ or $70°$ training groups ($50°$ group: n = 12; $70°$: n = 11). All subjects provided informed consent and the study was conducted in accordance with the ethical guidelines approved by the York University Human Participants Review Subcommittee.

4.3.2 General experimental set-up

A side-view of the setup is illustrated in Figure 1a, and is similar to that used by Cressman and Henriques (2009, 2010). Subjects were seated at a table

such that the distance of the chair from the table and the height of the chair were adjusted in order to ensure that each subject could comfortably see and reach to all target positions. Once the chair was adjusted it remained in the same position for the entire experiment. Subjects were instructed to grasp the vertical handle of a two-joint robot manipulandum (Interactive Motion Technologies) with their right hand such that their thumb was positioned on a top marker (1.4 cm in diameter). The position of the robot manipulandum was recorded throughout trials at a sampling rate of 50 Hz and a spatial accuracy of 0.1 mm. Visual stimuli were projected from a monitor (model: Samsung 510N, refresh rate: 72 Hz) installed 17 cm above the robot and viewed by subjects as a reflected image. The reflective surface was opaque and positioned so that the imaged displayed on the monitor appeared to lie in the same horizontal plane as the robot handle. The room lights were dimmed and subjects' view of their right hands were blocked by the reflective surface and a black cloth draped between the experimental setup and subjects' right shoulders.

Figure 4.1 Experimental set up and design. (A) Side view of the experimental set up. (B and C). Top view of the experimental surface visible to subjects. (B) Cross-sensory discrepancy introduced in the rotation exposure training task and target locations. The unseen hand's constrained pathway was rotated 30° clockwise (CW) with respect to the cursor-target pathway during the first rotation exposure training block and increased to 50° or 70° CW for the second rotation exposure training block for the 50° training group and 70° training group, respectively. Targets (yellow rings) 1 cm in size were located 10 cm from the home position (black circle) at 0° and 30° left and right of midline. (C) In the proprioceptive estimate task, subjects actively pushed their hand out 10 cm along

a constrained linear path (depicted by the red rectangle) from the home position and judged the position of their hand with respect to a reference marker. Reference markers (yellow rings) were located at 0° and 30° left and right of midline.

4.3.3 General procedure

The experiment consisted of two separate testing sessions completed on two testing days. Each testing session involved four tasks (comprising one block) and on the second day of testing these tasks were repeated two times (i.e., subjects completed two blocks, Figure 2). On the first testing day subjects completed the exposure training trials outlined below while viewing a cursor that was veridical, or aligned, with their unseen hand. On the second testing day subjects completed the exposure training trials while viewing a cursor that was misaligned from the actual location of their unseen hand (grey circle, Figure 1B). Specifically, a subject's unseen hand moved out along a path that was gradually rotated to 30°, 50° or 70° clockwise (CW) relative to the cursor position, that was represented by a green disc 1 cm in diameter (green circle, Figure 1B). The 50° training group completed the first block of trials of the second testing session such that their hand moved out along a path that was rotated 30° CW relative to the cursor and in the second block of trials their hand was rotated 50° CW relative to the cursor motion. The 70° training group completed the first block of trials of the second testing session with the same 30° CW hand-cursor distortion as the 50° training group, however they were exposed to a 70° CW hand-cursor discrepancy during the second block of training trials. For both groups, the 30° hand-cursor rotation was introduced gradually such that on the first trial the path that the unseen hand moved out along was rotated 0.75° CW with respect to the cursor. The rotation then increased by 0.75° each trial, until the full 30° distortion was achieved. The distortions in the 50° and 70° blocks (i.e., second blocks of

trials of the second testing session) were also introduced gradually by 0.75° per trial, starting from the rotation of the previous block (i.e., in the first trial of block two the distortion was introduced at 30.75°, and increased by 0.75° per trial up to 50° or 70°).

4.3.3.1 Exposure training

At the start of each trial, the robot manipulandum was positioned below the home position, which was indicated by a green circle 1 cm in diameter and located approximately 25 cm directly in front of subjects' midline. This circle then disappeared and a yellow target circle 1 cm in diameter (yellow circle in Figure 1B) was presented for 500 ms. The targets were located radially 10 cm from the home position at 0° (in line with subjects' midline), 30° right (CW) and 30° left (CCW) from center. Once the target disappeared, subjects were instructed to actively push the robot manipulandum out along a robot-generated constrained linear path (red rectangle, Figure 1B) while viewing a cursor that represented their unseen hand position. On all trials, the cursor headed directly to the remembered target position. If subjects attempted to move outside of the established path, a 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 channel wall (Henriques and Soechting 2003). In each session, the trials were pseudo-randomized such that each target was displayed at least once before any target was repeated.

To ensure that subjects paid attention to the cursor, we had them both 1) stop their movement when they felt their hand had reached the remembered target location, and 2) after stopping their movement, indicate via a key press if the cursor had 'blinked' during the movement (for 50% of trials the cursor was extinguished (i.e., blinked) for 30 ms in the middle portion of its trajectory). Thus,

subjects controlled the distance that their hand moved outwards away from their body, but not the lateral direction that the hand travelled.

Subjects completed 150 training trials with a cursor that was aligned with their hand (first testing session; Figure 2, Part 1, Box 1), 150 training trials with a gradually introduced $30°$ hand-cursor path discrepancy (second testing session, block 1; Figure 2, Part 2, Box 1), and 200 trials with a gradually introduced $50°$ or $70°$ hand-cursor path discrepancy (second testing session, block 2). Thus, subjects were exposed to the full $50°$ or $70°$ hand-cursor path discrepancy on 173 or 146 trials respectively. This is a greater amount of training trials at the full hand-cursor discrepancy compared to our previous paradigms (e.g. Cressman and Henriques, 2010; Salomonczyk et al. 2011). Given this large number of trials we had subjects complete in the current experiment and the fact that we have previously shown that there are no further changes in performance after training with misaligned visual hand feedback for 160 trials versus 60 trials (i.e., motor adaptation and proprioceptive recalibration do not increase after training for more than 60 trials), we are confident that the results discussed below are not due to the slightly different number of exposure trials at the full exposure completed by our $50°$ and $70°$ training groups.

4.3.3.2 Reach aftereffects to assess visuomotor adaptation

This task was performed twice in each block, immediately after the exposure training task and immediately after the proprioceptive estimate task (boxes labelled 2 and 4 in Figure 2). During these trials the robot-generated constrained pathway was removed and subjects could freely move the robot. A trial would start with the robot handle illuminated at the home position. One of three reach targets located at $0°$, $30°$ right (CW) and $30°$ left (CCW) of centre (Figure 1B) would then appear and after 500 ms the home position would disappear. This was the cue for subjects to reach to the visible target using the

robot handle without any visual cursor feedback of their hand position. Once subjects believed they were at the target, they were to hold their final position. Once the final position was held for 250 ms, the reach movement was deemed complete. The target would then disappear and subjects were to return their hand to the home position guided by a robot-generated constrained linear path. Subjects completed 5 trials to each of the three targets for a total of 15 trials.

4.3.3.3 Proprioceptive estimates to assess perceived hand position

To evaluate sensory changes resulting from motor adaptation, previous studies have typically employed tasks which required subjects to make goal-directed reaches using the adapted hand (Simani et al. 2007, van Beers et al. 2002). Reach errors arising in these paradigms could be due to changes in felt hand position resulting from proprioceptive recalibration, changes in motor commands resulting from an updated internal model, or a combination of sensory and motor changes. The present task was designed to isolate subjects' sense of felt hand position from goal-directed movement by removing any visual feedback during hand movement and having subjects make an estimate of their hand's static position with respect to a visual or proprioceptive (body midline) reference marker. We have previously shown that subjects' estimates are similar regardless of whether they actively guide their hand into position along a robot-generated constrained linear path or their hand is moved along the same path into position by the robot (Cressman & Henriques 2009). Moreover, estimates appear to be similar regardless of the path taken by the hand to its final position (Jones et al. 2012), suggesting that subjects use final hand position information to estimate the location of their hands, independent of how the hand was moved into position and the path taken. Due to time constraints associated with passive movement and the number of trials completed by subjects in the current

experiment, we employed the active version of the proprioceptive estimate paradigm described below.

A trial began with the subject grasping the robot manipulandum at the home position indicated by a green circle. After 500 ms this circle disappeared and the subject was instructed to push his or her hand outward along a robot-generated constrained linear path 10 cm in length (as described in task 1, red rectangle in Figure 1C). Once the hand arrived at the end of the path (along the dotted arc shown in Figure 1C), a visual reference marker located at 0°, 30° left (CCW) or 30° right (CW) of centre (yellow circles, Figure 1C) appeared and subjects made a two-alternative forced choice judgment about the position of their hand (left or right) relative to the visual reference marker. A visual reference marker appeared on 75% of the proprioceptive estimate trials, while for the remaining 25% of trials subjects were instructed to judge the location of their hand with respect to their body midline (indicated by the dashed vertical line in Figure 1C). For all trials, there was no time constraint for giving a response. The body midline trials were indicated with a brief sound cue (beep). After responding, the visual reference marker (for all non-body midline trials) disappeared and the subject moved the robot directly back to the home position along the same linear route to begin the next trial. The position of the hand with respect to each reference marker was adjusted over trials using an adaptive staircase algorithm (Kesten 1958; Treutwein 1995) as described by Cressman and Henriques (2009, 2010) and Jones et al. (2010). In particular, for each reference marker there were 2 staircases, one starting 20° to the left (CCW) of the reference marker and one starting 20° to the right (CW). The 2 staircases were adjusted independently and randomly interleaved as outlined by Cressman and Henriques (2009). Thus, if subjects responded consistently (i.e., associated a given felt hand position with a given reference marker), the two staircases converged.

Part 1: Baseline

Exposure Training Task Aligned Cursor 150 Trials (50 trials/target) 1	Reach Aftereffects No cursor 15 Trials (5 trials/target) 2	Proprioceptive Estimate Task 200 Trials (50 trials/marker) 3	Reach Aftereffects No cursor 15 Trials (5 trials/target) 4

Part 2: Misaligned Cursor

Exposure Training Task 30°CCW Cursor 150 Trials (50 trials/target) 1	Reach Aftereffects No cursor 15 Trials (5 trials/target) 2	Proprioceptive Estimate Task 200 Trials (50 trials/marker) 3	Reach Aftereffects No cursor 15 Trials (5 trials/target) 4

Exposure Training Task 50° or 70°CCW Cursor 200 Trials (67 trials/target) 1	Reach Aftereffects No cursor 15 Trials (5 trials/target) 2	Proprioceptive Estimate Task 200 Trials (50 trials/marker) 3	Reach Aftereffects No cursor 15 Trials (5 trials/target) 4

Figure 4.2 Breakdown of the testing sessions within the experiment. In the first testing session (top row) subjects moved the robot arm with an aligned cursor that accurately represented the position of their hand during the exposure training trials. In the second testing sessions (second and third rows), subjects' unseen hand path was increasingly misaligned from the cursor-target pathway by 30° (first rotated block) up to 50° or 70° clockwise (second rotated block). After completing 150 exposure trials with an aligned or misaligned cursor, subjects next reached freely to each of three reach targets 5 times each without a cursor in order to assess motor adaptation (reach aftereffect trials, Box 2 in each row). Subjects then completed 200 proprioceptive estimate trials (Box 3 in each row) followed by another set of free, no-cursor reaches (Box 4 in each row) to examine the maintenance of reach aftereffects. In the first testing session, subjects only completed one block of exposure training trials with aligned visual

feedback of the hand. In the second testing session, subjects completed two training blocks with misaligned visual feedback of the hand.

4.3.4 Data analysis

Before examining motor adaptation and proprioceptive recalibration, we first wanted to ensure that subjects were 1) moving out smoothly with minimal lateral deviation from the force channel and 2) paying attention to the cursor during the aligned and misaligned exposure training trials. To ensure that subjects were moving smoothly with minimal lateral deviation from the force channel, we calculated the perpendicular deviations of the hand for all trials when the target was located at $0°$. We observed a mean perpendicular deviation of 0.33 mm (with a mean SD across trials = .44 mm) which is within the 3 mm of the robot-generated channel. Averaged across all subjects, the maximum deviations were 1.3 mm left and 1.4 mm right of the home-target vector, which is again within the confines of the channel, suggesting that subjects stayed well within the confines of the force channel.

We found that, on average, the robot was stopped 10.08 cm (SD .70 cm) after movements were initiated, which is very close to the 10 cm movement target goal. In addition, subjects correctly reported whether the cursor had blinked or not on 90% of all trials. A one-way ANOVA comparing the percentage of correctly reported blinks across training blocks revealed a non-significant block effect $(F(2,75) = 1.54, p = .22)$, suggesting that subjects attended to the cursor in a similar manner across aligned and rotated training blocks.

4.3.4.1 Motor adaptation

We analyzed reaching errors (i.e., aftereffects) made in the reach aftereffects trials in which no visual cursor was presented (Task 2) to 1) determine if subjects adapted their reaches after exposure to misaligned visual-

proprioceptive feedback of their hand position and 2) examine whether subjects maintained this adaptation across the proprioceptive estimate trials. Reach endpoint errors were defined as the angular difference between a movement vector (from the home position to reach endpoint) and a reference vector (joining the home position and the target). To determine if subjects had indeed adapted their reaches, we analyzed mean endpoints in aftereffect trials using a 2 Training Group (50° group vs. 70° group) x 3 Visual Feedback Block (aligned feedback vs. first block of rotated feedback (30∘) vs. second block of rotated feedback (50∘ or 70∘)) x 3 Target (0° vs. 30° CW vs. 30° CCW) repeated-measures analysis of variance (RM-ANOVA). Training Group was a between-group factor while Visual Feedback Block and Target were within-group factors. Post-hoc pair-wise comparisons were used to explore the loci of these differences and a Bonferonni correction was applied (alpha = .05). In addition to revealing if subjects adapted their reaches following exposure training, this analysis allowed us to determine if reach adaptation increased with the increasing hand-cursor distortion.

To determine if subjects maintained their reach adaptation following proprioceptive estimate trials, we compared aftereffects between reaches following exposure training and those following proprioceptive estimate trials. To do so, we subtracted the reach errors following aligned exposure training from the two rotated exposure training blocks. These baseline-subtracted aftereffects were compared using a 2 Training Group (50∘ group vs. 70∘ group) x 2 Visual Feedback Block (30° rotated feedback vs. 50° or 70° rotated feedback) x 2 Time (reach aftereffects following exposure trials vs. reach aftereffects following proprioceptive estimate trials) RM-ANOVA. Post-hoc pair-wise comparisons were used to explore the loci of these differences and a Bonferonni correction was applied (alpha = .05).

4.3.4.2 Proprioceptive estimates of hand position

To examine the influence of the magnitude of the cross-sensory error signal on changes in proprioceptive recalibration, we determined the location at which subjects felt their hands were aligned with each reference marker after each block of exposure training trials (Cressman & Henriques 2009; Cressman and Henriques 2010; Cressman et al. 2010; Jones et al. 2010; Salomonczyk et al. 2011; Salomonczyk et al. 2012). This location was determined by fitting a logistic function to each subject's responses for each reference marker during each testing session. The position at which subjects responded "left" 50% of the time (i.e., responded "left" and "right" equally often) represents their bias. In addition to calculating bias, we also determined subjects' uncertainty (or precision) by finding the difference between the values at which the point of responding "left" was 25% and 75%. Bias and uncertainty related to a particular reference marker were excluded if the associated uncertainty was greater than the mean uncertainty across all reference markers + 2 standard deviations. Based on this analysis, only 1 proprioceptive estimate (less than 0.01% of total estimates) was excluded. Biases and uncertainty ranges were analyzed in a 2 Training Group (50∘ group vs. 70∘ group) x 3 Visual Feedback during the exposure trials (aligned feedback vs. first block of rotated feedback (30∘) vs. second block of rotated feedback (50∘ or 70∘)) x 4 Marker Location (0∘ vs. 30∘ CW vs. 30∘ CCW vs. body midline) RM-ANOVA. Post-hoc pair-wise comparisons were used to explore the loci of these differences and a Bonferonni correction was applied (alpha = .05). In addition to revealing if subjects recalibrated proprioception following exposure training, this analysis allowed us to determine if recalibration increased with an increasing hand-cursor distortion (i.e., cross-sensory error signal).

4.4 RESULTS

4.4.1 Motor adaptation

Following exposure training with an aligned cursor, mean reach endpoint errors were on average $1.0°$ to the left of the target. These small reaching errors suggest that subjects were able to accurately reach to a target without visual feedback of their hand position after having been forced to repeatedly move their hands to the targets along a constrained path. Mean baseline-subtracted aftereffects following exposure training with a rotated cursor are displayed in Figure 3 alongside results from Salomonczyk (2011; filled bars). Mean reach endpoint errors differed significantly between the exposure training conditions $(F(2,42) = 17.82, p < .001)$. Post-hoc analysis revealed that after exposure training with a hand-cursor discrepancy of $30°$ (empty bars, Figure 3), all subjects on average made reaching errors significantly more rightwards of the targets compared to after training with a cursor that was aligned with their hand position (mean difference = $8.9°, p < .001$). The magnitude of these errors is considerably less than those from 2011 results, in which subjects trained by making unconstrained reaching movements towards targets while visual feedback of the hand was rotated $30°$ CW with respect to the unseen hand. Following exposure training with either a $50°$ or $70°$ misaligned cursor, reaches were still more rightwards of the target compared to after training with an aligned cursor (mean difference = $9.9°, p < .001$); however, they were not any greater than those following $30°$ misaligned exposure training (mean difference between first and second rotated blocks = $1.0°, p > .99$). Furthermore, no difference in training group $(F(1,21) < 1, p = .42)$ or interaction between exposure condition and training group was observed $(F(2,42) < 1, p = .42)$. This is in contrast to our previous findings in which subjects showed increasing aftereffects after they reached voluntarily with a visuomotor distortion that increased in magnitude. These results suggest that reach adaptation following exposure to misaligned

visual-proprioceptive feedback saturates, such that no further increase in aftereffects occurs with distortion magnitudes greater than 30°.

There was an overall main effect of target location, such that reaches tended to fall to the right of the 30° CW and 0° targets and slightly to the left of the 30° CCW target (F(2,42) = 36.34, p < .001), indicating that subjects slightly expanded the workspace (consistent with previous work). Importantly, no interaction effects were observed between targets and training groups (F(2,42) = 2.40, p = .12) or targets and visual feedback conditions (F(4,84) < 1, p = .62), suggesting that reach adaptation occurred comparably between training groups and was not dependent on the location of the target in the workspace.

Analysis of baseline-subtracted endpoint errors using a RM-ANOVA revealed that the magnitude of these aftereffects decreased with time, such that those aftereffects measured following proprioceptive estimates were on average 5° smaller compared to those measured immediately following exposure training (F(1,21) = 12.14, p < .01). However, previously described results revealed a significant difference between the aligned and both the first and second rotated blocks (F(2,42) = 17.82, p < .001, see above), suggesting that while aftereffects may have diminished following proprioceptive estimates compared to those following exposure training, they were still present. No interaction effects were observed between time and rotated exposure training blocks (F(1,24) < 1, p = .62) or time and group (F(1,21) = 1.32, p = .50). Thus, aftereffects measured following proprioceptive estimates, while smaller, still showed a comparable pattern of effects as those aftereffects measured following exposure training.

Figure 4.3 Aftereffects following exposure training with misaligned visual feedback of the hand. Endpoint errors were calculated by subtracting angular reach endpoint errors in the no cursor reach aftereffect trials after training with an aligned cursor from errors completed in the no cursor reach aftereffect trials after training with a misaligned cursor. Errors at reach endpoints were averaged across targets and subjects and are shown for the no cursor reaches completed after the two consecutive rotated training blocks. Empty bars reflect aftereffects following the exposure training paradigm while filled bars reflect aftereffects following visuomotor reaching from Salomonczyk and colleagues (2011). Error bars reflect SEM.

4.4.2 Proprioceptive recalibration

4.4.2.1 Bias

Mean proprioceptive biases at each reference marker location (grey circles) for both training groups are displayed in Figure 4A. The diamonds indicate bias values following exposure training with aligned visual feedback of

hand position, while the triangles indicate biases following exposure training with a 30° misaligned cursor (empty triangles) or a 50° or 70° misaligned cursor (grey filled triangles). Bias estimates for the proprioceptive midline marker (dashed line) are displayed above visual marker estimates as dashed symbols. For both training groups we see that estimates of unseen hand position were biased following aligned cursor-hand exposure training slightly towards the left (6°). Previous studies in our lab have suggested that this directional bias arises due to a systematic hand bias (Jones et al. 2010; Salomonczyk et al. 2012), where subjects overestimate how far right their right hand is, resulting in a leftward bias. Mean bias estimates differed significantly between the exposure training conditions $(F(2,42) = 17.73, p < .001)$. Post-hoc analysis revealed that after exposure training with a 30° misaligned cursor, biases were shifted significantly rightwards (mean difference across all subjects = 5.3°, $p < .001$), consistent with the direction of motor adaptation (aftereffects, Figure 3). These results are also consistent with the magnitude of proprioceptive recalibration observed in results from Salomonczyk et al. (2011), shown as filled bars in Figure 4B. Following exposure training with either a 50° or 70° misaligned cursor, bias estimates were still more rightwards of the target compared to after training with an aligned cursor (mean difference = 6.4, $p < .001$); however, they were not any greater than those following 30° misaligned exposure training (mean difference between first and second rotated blocks = 1.1°, $p = .45$). Furthermore, no difference in group $(F(1,21) < 1, p = .76)$ or interaction between exposure condition and training group was observed $(F(2,42) < 1, p = .47)$. These results suggest that proprioceptive recalibration following exposure to misaligned visual-proprioceptive feedback saturates, such that no further increase in aftereffects occurs with distortion magnitudes greater than 30°.

Proprioceptive estimates of hand position were comparable across all visual reference and body midline (Figure 4A and 4B, lighter insets) marker

locations (F(3,63) = 1.96, *p* = .13), and no interaction between marker location and exposure block was observed (F(3,63) = 1.21, *p* = .31).

Altogether, these results suggest that proprioception is recalibrated around both visual and midline reference markers following exposure to misaligned visual-proprioceptive hand feedback, although this sensory change saturates within a 30° distortion. This then indicates that a cross-sensory error signal available during exposure training on its own is not enough to drive additional sensory recalibration when the error signal increases above 30° cursor-hand misalignment.
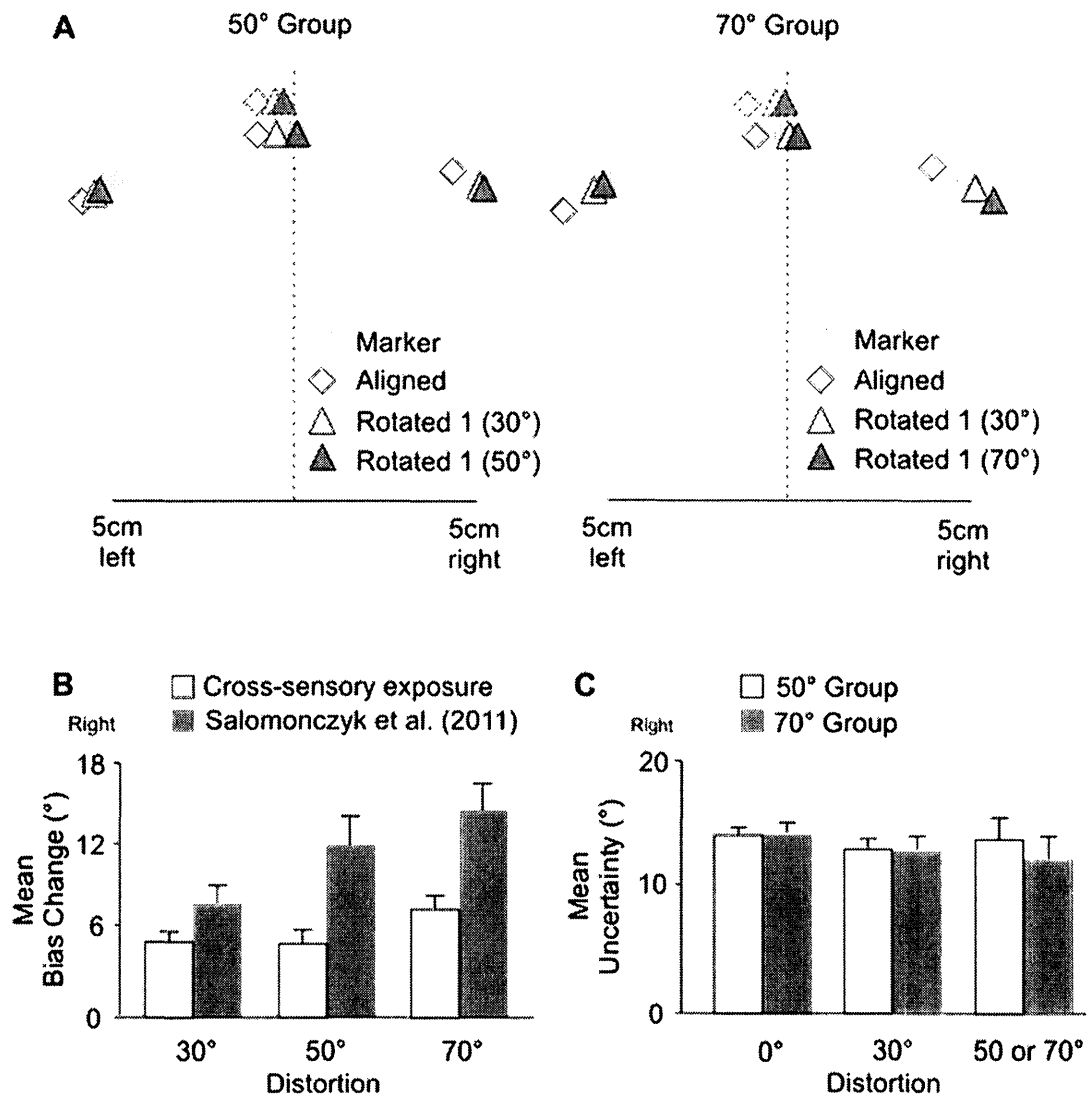
Figure 4.4 Proprioceptive biases following training with aligned and misaligned visual feedback of the hand. (A) Mean 2-D proprioceptive biases following training with an aligned (empty diamonds) or misaligned (after the first 30° rotated block: empty triangles; after the second rotated block: filled triangles) cursor for subjects in the 50° training group (left panel) and 70° training group (right panel). The actual reference marker positions are represented as grey

circles. Estimates around the midline (dashed line) are depicted on top of the estimates around the central visual marker and are outlined with a dashed line. (B) Mean changes in biases after training with a misaligned cursor compared to an aligned cursor were averaged across reference markers and subjects. Empty bars reflect proprioceptive recalibration following the exposure training paradigm while filled bars reflect proprioceptive recalibration following visuomotor reaching from Salomonczyk and colleagues (2011). (C) Mean uncertainty of proprioceptive estimates following training with an aligned ($0°$) or misaligned ($30°$, $50°$ and $70°$) cursor for the $50°$ training group (open bars) and $70°$ training group (filled bars). Error bars reflect SEM.

4.4.2.2 Uncertainty

Mean uncertainty is displayed in Figure 4C. On average, the overall magnitude of the uncertainty range was $13.2°$ and is consistent with measures of precision reported in previous exposure training paradigms (Cressman & Henriques, 2010) and results from Salomonczyk et al. (2011). Uncertainty was comparable across all training blocks ($F(2,42) < 1$, $p = .48$) and reference marker locations ($F(3,63) = 1.61$, $p = .20$). There were no differences in uncertainty between training groups ($F(1,21) < 1$, $p = .53$). No interaction effects were observed ($p > .34$). Thus, subjects' precision in estimating the location of their unseen hand relative to the markers was not affected by the magnitude of the cross-sensory error signal experienced or the marker location.

Figure 4.5 Changes in sensory recalibration (bias) and motor adaptation (aftereffects) as a percentage of the visuomotor distortion introduced during each exposure training block for subjects in the 50° training group (filled symbols) and 70° training group (empty symbols) following rotated exposure training trials. Each symbol represents the percentage change in bias and percentage change in aftereffects averaged across marker and target locations (respectively) for each subject. The solid line indicates the line of best fit for all data points.

4.4.3 Relationship between aftereffects and recalibration

Taken together, results indicate that subjects adapted their reaches and mis-estimated the position of their hand after viewing a rotated cursor that moved

synchronously with their unseen hand. Both reach aftereffects and proprioceptive estimates were shifted clockwise by approximately 9° and 5°, respectively, regardless of the magnitude of the visuo-proprioceptive distortion experienced. A paired-samples t-test did not reveal a significant difference between the magnitude of aftereffects and proprioceptive recalibration (t(45) = .80, p = .43). To examine the possibility that both aftereffects and bias rely on the cross-sensory error signal, we applied a step-wise regression procedure with the percent change in bias and the size of the distortion as predictors of percent change in aftereffects. Change in bias was selected as the predictor as we hypothesized that changes in felt hand position contributed to updates in the motor plan, resulting in adaptive reach movements (aftereffects). This relationship is displayed in Figure 5. Results revealed that the change in bias significantly predicted the change in aftereffects (β = .48, p =. 001, one-tailed), though the magnitude of the distortion did not (β = -.193, p = .08, one-tailed). We observed that change in bias was a significant predictor of change in aftereffects for both training groups (50° group: β = .39, p = .02, one-tailed; 70° group: β = .71, p = .004, one-tailed). This correlation was also present at each training block (first rotated block: β = .42, p = .03, one-tailed; second rotated block: β = .50, p = .02, one-tailed). These results, along with the observation that changes in bias and aftereffects were very similar, suggest that a similar error signal is underlying these processes. These findings are consistent with a previous study examining the relationship between changes in bias and aftereffects following exposure training (Cressman & Henriques 2010). However, these findings are in contrast to previous studies employing free reaching during visuomotor training (Cressman & Henriques 2009; Cressman et al. 2010; Salomonczyk et al. 2011; Salomonczyk et al. 2012), including our study investigating the role of the magnitude of the sensorimotor error signal (Salomonczyk et al. 2011). In these studies, bias and aftereffects were uncorrelated and in our 2011 study the

magnitude of the error signal did predict changes in bias and aftereffects. These results suggest that the cross-sensory error signal, on its own, exerts an initial effect on sensory and motor changes (potentially up to when the distortion is 30°). Further changes in response to distortions greater than 30° appear to be driven by the sensorimotor error signal or a combination of the two.

4.5 DISCUSSION

The goal of the present study was to examine the extent that a cross-sensory error signal can contribute to proprioceptive recalibration and motor adaptation. To do so, we exposed subjects to a cross-sensory error signal, such that subjects viewed a cursor that travelled towards a remembered target location, while their hand travelled along a constrained, robot-generated channel that was increasingly misaligned from the cursor-target pathway. The robot-generated channel only allowed subjects to move volitionally in the forward direction and not in the lateral direction, where the discrepancy between the senses (and the error signal) was introduced. This ensured that subjects did not experience an error in their reaching direction as the visual representation of their hand was always in line with the target. We found that subjects adapted their reaches and recalibrated their sense of felt hand position after exposure to this visuo-proprioceptive discrepancy, which occurred in the absence of the typical sensorimotor error signal associated with error-dependent learning. Specifically, after viewing a cursor that misrepresented the location of their hand by 30° during a constrained movement, subjects mis-reached in the same direction that their hand had moved during exposure training trials (9° change), and began to feel that their hand had shifted in the direction opposite the cursor distortion (6° change). Furthermore, subjects in the present study demonstrated a proprioceptive shift at both the visual reference markers and around their body

midline, suggesting that hand proprioception rather than vision (or a visuomotor mapping) was recalibrated. Interestingly, reach aftereffects and proprioceptive recalibration achieved early saturation, such that no further motor or sensory changes were observed after subjects were exposed to distortions greater than 30°.

Subjects completed a greater number of training trials in the current experiment than in previous paradigms (i.e. Salomonczyk et al. 2011). Thus, in order to ensure that we minimized subjects' fatigue and in attempt to keep subjects engaged in the task, we chose to have subjects actively push their hand out along a constrained pathway during the exposure training trials (as opposed to the passive exposure training in our previous study (Cressman & Henriques, 2010). Our previous exposure study, which compared active (subject-generated) and passive (robot-generated) movement during training, showed no differences in subsequent motor adaptation or proprioceptive recalibration between the two types of training (Cressman & Henriques 2010). This suggests that subjects were exposed to the same cross-sensory error signal in both paradigms. We believe that present results obtained with an active paradigm continue to reflect a purely cross-sensory error based on the following findings: firstly, present results are consistent with those of our 2010 study, in which small yet persistent aftereffects were observed following exposure training with either an actively or passively placed hand. Thus, while the motor commands generated to push the hand along the contrained path may be used by forward models to predict sensory consequences of these movements, this contribution appears to be minimal since the absence of such motor commands (when the hand is passively led by the robot) leads to similar results for both exposure training and proprioceptive estimation. Second, present findings reflect saturation of reach aftereffects and proprioceptive recalibration following exposure training with distortions greater than 30°, which is inconsistent with results from Salomonczyk et al. (2011) as

discussed below. Lastly, subjects' movements during exposure training were constricted in the lateral direction by a robot-generated force channel, yet we observed persistent changes in movements in this direction following misaligned exposure training. Altogether these findings suggest that the present results reflect subjects' change in performance after exposure to a cross-sensory error signal, rather than a change in the forward model resulting from a sensorimotor error signal.

4.5.1 Role of error signals in adaptation and recalibration

In the present study, we systematically increased the discrepancy between the hand path and the cursor path over trials. While subjects initially showed motor aftereffects and proprioceptive recalibration following exposure to a $30°$ visuo-proprioceptive discrepancy, subjects did not show any further motor aftereffects or proprioceptive recalibration following exposure training with an increased cross-sensory error signal (up to $70°$). Regression analysis further revealed that while changes in reaches and bias were highly correlated, the magnitude of this cross-sensory error signal did not predict changes in reaches or proprioceptive bias. In contrast, in a previous study in which subjects made unconstrained reaching movements towards targets with increasingly misaligned visual feedback of hand position (Salomonczyk et al. 2011), subjects' motor aftereffects and proprioceptive changes increased accordingly; furthermore, the magnitude of visuomotor distortion (including both sensorimotor and cross-sensory error signals) linearly predicted the magnitude of these motor and sensory changes. Thus, while the cross-sensory error signal appears to drive partial proprioceptive recalibration and movement adaptation even when there is no opportunity for goal-directed movement (or any volitional movement as demonstrated presently and previously (Cressman & Henriques 2010), the influence of this signal saturates at a relatively small ($30°$ or less) distortion due

to limits in how the CNS can update felt hand position and/or modify body image. Additional work examining how the size of the sensorimotor error signal can influence motor changes has shown that adaptation to increasing visuomotor distortions results in greater motor aftereffects (Abeele & Bock, 2001). However, Abeele and Bock also found that motor learning began to saturate with greater distortions such that facilitation from previously learned rotations was no longer observed with visuo-proprioceptive distortions greater than 80°. Moreover, Wei and Kording (2009) demonstrated that visuomotor adaptation (defined as subsequent-trial error) was linearly related to the error signal only at small distortion magnitudes (i.e. ± 2cm), but sub-linearly related at larger ones. Finally, using subsequent-trial errors, Marko and colleagues (2012) also found that adaptation to increasingly larger force-field distortions saturated, such that training with additional increases in the force-field distortion did not lead to additional increases in reach error magnitude. The authors also observed that sensitivity to the distortion magnitude was reduced for larger distortions. Taken together, these findings suggest that motor adaptation may saturate with larger distortions (e.g., greater than 70°), such that there is an upper limit to how much the sensorimotor and/or cross-sensory error signals can influence sensory and motor adaptation, both separately and in combination.

In accordance with the observation of non-linear motor changes as a function of error size, results from the present study also suggest (early) saturation for proprioceptive recalibration and motor changes when just the cross-sensory error signal is available (at or less than 30°) Following the present exposure training paradigm, reach aftereffects and proprioceptive recalibration did not increase with increases in the cross-sensory error signal, and were considerably smaller than (roughly half) those produced after performing voluntary movements on trials in which misaligned visual feedback of the hand was introduced and the sensorimotor error signal was also present (Krakauer et

al. 1999; Krakauer et al. 2000; Cressman & Henriques 2009; Salomonczyk et al. 2011; Salomonczyk et al. 2012). While it has been demonstrated that on-line corrective movements are not necessary for motor adaptation since straight and fast "shooting" hand movements (where the hand doesn't decelerate at the target) lead to similar adaptation as regular reaching movements (Tseng et al. 2007), the discrepancy between the actual movement and the desired movement (sensorimotor error signal) is still visible for all subject to use to adjust subsequent reaches in these studies. Moreover, in the present study where this signal was not present, movement aftereffects were more closely related in magnitude to changes in proprioceptive estimates than when following visuomotor adaptation with both the sensorimotor and cross-sensory error signals. Thus, changes in felt hand position derived from the cross-sensory error signal may initially drive motor adaptation, while the sensorimotor error signal contributes to greater motor adaptation and is responsible for motor adaptation with increasing distortions. Although the cross-sensory error signal only contributes to small adaptive changes, the functional implications could be quite significant as a few degrees can have large consequences.

4.5.2 Current models of adaptation

4.5.2.1 Error-based learning

The most commonly accepted mechanism underlying visuomotor adaptation relies on error-based (or goal-directed) learning using internal models. Typically, visual and proprioceptive signals are aligned and the inverse model derives appropriate motor commands which compensate for arm dynamics and kinematics. Under altered conditions (e.g., when visual and proprioceptive feedback of the hand are misaligned), the inverse model initially derives motor commands that are insufficient to compensate for the altered visual feedback of the hand position. With practice however, performance errors arising because of

the distortion introduced are used to correct the position of the hand during the movement and/or for the subsequent trial. That is, the motor plan is adjusted to compensate for the distortion and align the actual movement with the desired motor command (Wolpert et al. 1995; Miall & Wolpert 1996; Wolpert & Kawato 1998). When the distortion is removed, the inverse model continues to generate the newly modified motor commands to compensate for the distortion, resulting in reach aftereffects (Kawato 1999).

When the brain generates a motor command, a prediction of the sensory consequences of that motor command is also produced. The forward model compares the desired and actual limb position using sensory information which is then fed back to the CNS to generate motor commands that will meet the given conditions (i.e., update the inverse model). Updating of the forward model has recently been implicated in the sensory (perceptual) changes associated with motor learning (Synofzik et al. 2008; Izawa et al. 2012). For example, by examining the role of sensory prediction errors on motor learning in cerebellar patients, Synofzik and colleagues (2008) showed that damage to the cerebellum resulted in impairments in linking sensory prediction errors to movements. In their task, subjects made pointing movements in the absence of visual feedback with the right hand and perceptual judgements of those movements were made with the left hand using a cursor manipulated by a joystick. Results indicated that while motor adaptation for patients and controls was comparable, the perceived pointing direction was recalibrated to a lesser extent in patients than controls. Based on these results, the authors suggested that updates to the internal predictions of motor commands (i.e., the forward model) were responsible for perceptual changes and that this process was impaired in cerebellar patients. Furthermore, Izawa and colleagues (2012) recently showed that cerebellar patients are unable to learn to predict the visual sensory consequences of their motor commands. Realignment of perceived hand position was estimated

following adaptation in a task in which subjects moved their right hand to a position within a circle (no explicit target was given) and then had their hand guided back to a start position. With their left hand, subjects then pointed to the location at which they perceived their right hand had crossed the circle. While motor adaptation was comparable, patients showed less perceptual realignment than controls, further suggesting the role for a forward model in sensory changes.

4.5.2.2 Sensory plasticity in motor learning

While an update in the forward model has been implicated in the sensory changes observed during visuomotor adaptation (Synofzik et al. 2008; Izawa et al. 2012), our results suggest that this sensory recalibration involves a shift in proprioception, rather than a learned association between one's movements and sensory consequences. We have previously suggested that sensory recalibration may occur coincidentally, though separate from motor adaptation, as we have shown that changes in movements and sensory recalibration are uncorrelated (Cressman & Henriques 2009; Cressman et al. 2010; Salomonczyk et al. 2011; Salomonczyk et al. 2012). Indeed, Izawa and colleagues (2012) failed to observe a relationship between the perceptual and motor changes in their subjects. Moreover, in accordance with our suggestion, cerebellar patients have been shown to recalibrate proprioception such that proprioceptive estimates are shifted to match visual estimates of target positions in the absence (or lack) of motor adaptation (Block & Bastian 2012). In this task, subjects made reaching movements to visual and proprioceptive targets when visual and proprioceptive information were gradually misaligned. The authors found that following reach training, when endpoint feedback was not available, patients and controls realigned proprioceptive endpoints to the same extent; again, this realignment was independent of motor adaptation. Altogether, these findings indicate that the forward model may not have a role in realigning visual and proprioception, and

instead suggest that proprioceptive recalibration may be used to update the state estimate for motor commands and thus lead to partial motor adaptation in some contexts.

For accurate and effective motor control, the CNS must consider the properties of the environment and objects we interact with, as well as our own effectors. This information is derived from sensory afferents. When faced with incongruence in sensory information (i.e. vision and proprioception), we have shown that the CNS recalibrates one sense to better match the other; in our case, proprioception is recalibrated to better align with visual estimates of hand position. Conversely, when an error in motor performance is experienced, the CNS may attribute these errors to internal misestimates (e.g. of effector location), but also to external or environmental causes. The CNS will then take into consideration both the updated body or effector percept and the adapted environmental percept when planning subsequent movements (Berniker & Kording 2012). In our present paradigm, subjects did not experience a performance error and thus we would not expect the environment percept to have been adapted. In other words, subsequent open-loop reach errors therefore reflected only an update in the body percept that did not increase with increasingly discrepant visuo-proprioceptive feedback. In contrast, subjects in our previous paradigms experienced both a cross-sensory discrepancy and motor performance errors, and subsequent open-loop reach errors could therefore have reflected a combination of the updated body and environment percepts that increased linearly with increasingly misaligned visual hand feedback. Thus, present findings suggest that proprioceptive recalibration may be used to update the state estimate for motor commands, resulting in motor adaptation in the absence of error-based learning. However, results suggest that the body percept or state estimate can only be updated to a certain extent, reflected by the saturation of proprioceptive recalibration and motor commands observed

following exposure training with increasingly discrepant visuo-proprioceptive feedback.

In summary, these and other recent results suggest the need for a more comprehensive model of visuomotor learning that accounts for the role of visually-driven proprioceptive recalibration in forming a new visuomotor mapping and subsequent use in movement planning, as well as the magnitude of the error signals that drive these motor and sensory changes.

CHAPTER FIVE

MOTOR LEARNING AND SENSORY RECALIBRATION IN PARKINSON'S DISEASE

Danielle Salomonczyk

5.1 ABSTRACT

Healthy individuals have been shown to adapt their reaches to novel visuomotor perturbations. Moreover, they recalibrate their proprioceptive sense of felt hand position to match the provided visual estimate of their hand after reaching with altered visual feedback of the hand; that is, they begin to feel their hand where they see it. These processes require sensory integration, which is heavily dependent on basal ganglia structures; to test the role of the basal ganglia in proprioceptive recalibration following visuomotor adaptation, we sought to determine if patients with Parkinson's disease recalibrate proprioception after reaching with altered visual feedback of their hand. Stage II-III PD patients tested during the "on" and "off" medication states and age-matched healthy controls made reaching movements to visual targets while visual feedback of their unseen hand was gradually rotated $30°$ CW or translated 4 cm to the right of their actual hand. Analysis of aftereffects trials (completed without a cursor) revealed that patients adapted their reaches at levels comparable to control participants. Estimates of proprioceptive sense of hand position after training with an aligned cursor revealed a small leftward bias, also consistent with controls; accuracy and precision of these hand estimates did not differ between patients and controls. Following visuomotor adaptation, both patients and controls showed an average leftwards recalibration in hand position estimates; the magnitude of this recalibration was again comparable between controls and patients. No differences in medication status for any parameters assessed were observed. Results suggest that patients are able to adjust their sensorimotor mappings and recalibrate proprioception following adaptation to a gradually-introduced visuomotor perturbation, and that dopaminergic intervention does not affect performance in these parameters. Results of this study suggest that sensory recalibration may not involve dopaminergic striatal pathways.

5.2 INTRODUCTION

In Parkinson's disease (PD), the basal ganglia circuitry is compromised due in part to the progressive degeneration of dopaminergic neurons in the substantia nigra. While the motor symptoms of PD typically characterize the disorder, evidence suggests that sensory and perceptual processing may be impaired as well (Herting, Schulze, Reichmann, Haehner, & Hummel, 2008; Maschke et al., 2006; Snider, Fahn, Isgreen, & Cote, 1976). Proprioception appears to be particularly impaired in PD such that patients are less accurate in single-joint position matching tasks, including matching their elbow angle to a reference elbow angle (Zia, Cody, & O'Boyle, 2000; Zia, Cody, & O'Boyle, 2002), detecting single-joint movement (Konczak et al., 2007), evaluating weight thresholds, (Maschke et al., 2006) and judging arm curvature (Konczak et al., 2008). Proprioceptive deficits in PD have been suggested to result in patients placing greater reliance on visual cues in a variety of tasks including reaching (Adamovich et al., 2001), grasping (Muratori, McIsaac, Gordon, & Santello, 2008), sequential arm movements (Curra et al., 1997) and walking (G. N. Lewis et al., 2000).

Moreover, sensory impairments have been linked to motor deficits (Adamovich et al., 2001) and impairments with sensorimotor integration in patients (Nowak & Hermsdorfer, 2006). In particular, PD patients have difficulties adapting to novel visuomotor environments. For example, adaptation studies using displacing prisms to distort the entire visual field revealed that, while initial reaching errors and the rate of learning were similar for patients and healthy age-matched adults, aftereffects were not present in patients. These findings suggest that patients are able to reach in a novel visual environment while visual feedback is present, yet are unable to consolidate the new sensorimotor mapping (Stern et al., 1988). Additionally, adaptation to a visuomotor rotation in which visual feedback of the hand is distorted has been shown to be impaired in PD

compared to control participants. Several studies have reported smaller aftereffects and greater directional errors in patients compared to controls (Contreras-Vidal & Buch, 2003; Venkatakrishnan, Banquet, Burnod, & Contreras-Vidal, 2011). While more recent studies have elucidated comparable aftereffects between PD and healthy adults using modified paradigms, retention of this newly-learned sensorimotor mapping remains virtually absent in patients, even when tested just 24 hours later (Bedard & Sanes, 2009; Isaias et al., 2011; Marinelli et al., 2009). These results further demonstrate that while patients are able to use visual feedback to adapt reaching movements, they are unable to consolidate the new sensorimotor mappings.

Many of the studies described above examined sensory and sensorimotor processing in medicated patients, yet few studies have examined the effect of dopaminergic medication on sensorimotor processing in PD. Moreover, previous studies examining the influence of medication on sensorimotor processing have yielded conflicting results. Some reports suggest that dopaminergic medication improves sensorimotor performance during locomotion and proprioceptive acuity of the arm and wrist (Almeida et al., 2005; Li, Pickett, Nestrasil, Tuite, & Konczak, 2010; Rickards & Cody, 1997), while others suggest that dopaminergic medication does not alleviate performance (Jacobs & Horak, 2006; Maschke et al., 2006; Mongeon et al., 2009) and may even worsen observed sensorimotor deficits. Mongeon and colleagues (2009) examined the effect of dopaminergic medication on proprioception and sensory integration by comparing the performance of PD patients and healthy adults during a reaching task to 3D targets while visual and proprioceptive information about limb and target position were systematically manipulated. The authors found dopaminergic medication did not normalize performance in PD patients; in some patients it actually worsened it. Furthermore, O'Suilleabhain, Bullard and Dewey (2001) reported a

worsening of proprioceptive functioning during elbow joint matching and spatial recall tasks in medicated PD patients.

Given the impairments in proprioceptive processing and sensorimotor integration reported in PD and the questions surrounding the influence of dopaminergic medication on sensorimotor processing, we sought to examine sensory changes following reaches with a visuomotor distortion in patients during both medicated and non-medicated states. We have previously shown that sensorimotor adaptation leads not only to changes in movements (aftereffects) but to changes in proprioception as well (Cressman & Henriques, 2009, 2010; Cressman et al., 2010; Ostry et al., 2010; Salomonczyk et al., 2011; Salomonczyk et al., 2012). These sensory changes, which we term proprioceptive recalibration, reflect adjustments in sense of felt hand position arising due to the realignment of proprioception onto the new visuomotor coordinate system in order to eliminate the spatial discrepancy between visual and proprioceptive signals (i.e. participants begin to feel their hand is shifted in the direction that they see it). Reported deficits in proprioceptive processing may result in patients becoming more susceptible to proprioceptive recalibration following exposure to a visuomotor distortion compared with healthy older adults who have intact proprioceptive information, possibly due to an increased reliance on available visual information; patients may perceive their hand as though it was shifted in the direction that it was visually perceived. Therefore, we sought to examine 1) how patients learn and adapt to a novel visuomotor perturbation (rotation or translation of visual hand feedback); 2) how changes in movement affect proprioceptive perception of hand position; and 3) how dopaminergic medication normalizes or hinders these processes. The paradigm employed in the present study also allowed us to examine proprioceptive acuity of the hand (as opposed to a joint) in patients along with any effect that dopaminergic medication may have.

5.3 METHODS

5.3.1 Participants

Seventeen adults diagnosed with Parkinson's disease (mean age = 61.0 years, range = 40 to 78 years, 5 female) recruited from Toronto Western Hospital Movement Disorders Clinic and York University participated in this study. Thirteen (rotated visual feedback experiment) and fourteen (translated visual feedback experiment) age-matched, healthy adults (rotated: mean age = 63.4 years, range = 43 to 80 years, 9 female; translated: mean age = 58.1 years, range = 42 to 71 years, 5 female) also participated in the study described below. All participants provided informed consent in accordance with the institutional ethics review boards. Participants were screened for depression and dementia using the Beck Depression Inventory II (BDI-II) and the Mini-Mental State Examination (MMSE), respectively. All participants were free of other neurological or psychological disorders and had normal or corrected-to-normal vision. All PD patients were treated with dopaminergic medications (Table 1). To assess the impact of dopaminergic medication, each patient was tested during the practically defined Off state, i.e. at least 12h following the last intake of antiparkinsonian medication, and in the On state, 1-2h after taking the first dose of antiparkinsonian medication of the day. During each testing session patients were evaluated by a movement disorders specialist using the Unified Parkinson's Disease Rating Scale (UPDRS (Fahn & Elton, 1987)) and found to have mild to moderate PD (Stages II-III (Hoehn & Yahr, 1967)). Patients PD9 and PD10 were excluded from analyses due to extreme reach and hand estimate profiles and patients PD11 and PD15 failed to complete all sessions. Data from these participants were excluded and results include data from the remaining 13 patients.

Table 1. Clinical features of patients with Parkinson's disease

Participant	Sex	Age	Affected Side	UPDRS Motor Score OFF	ON	H & Y Stage	Duration of Disease (years)	Medication[a]
PD1	M	57	R	39	31	2	4	LC E P
PD2	M	65	R	40	26	2	8	LC P S
PD3	F	71	L	39	18	2.5	11	LC R
PD4	M	52	L	45	23	2.5	7	LC P
PD5	M	52	R	38	16	2.5	9	LC
PD6	M	47	R	49	22	2.5	10	LC A RO
PD7	F	78	R	36	22	2	3	LC
PD8	M	68	R	49	36	3	5	LC R RO
PD9[b]	M	73	L	49	39	3	6	LC
PD10[b]	F	59	L	25	16	2	6	ET P
PD11[b]	F	67	R	41	29	3	5	LC
PD12	M	40	L	25	18	2	3	LC P
PD13	M	69	L	38	30	2	3	LC
PD14	M	65	L	23	13	2	1	LC
PD15[b]	F	63	R	25	NA	2	4	LC R
PD16	F	60	R	16	14	2	6	LC P
PD17	M	64	L	31	25	2.5	7	LC LB R RO
Mean		61.7		35.8	23.6	2.3	5.8	

[a]LC = levodopa + carbidopa; LB = levodopa + benserazide; A = amantadine; E = entacapone; ET = ethopropazine; P = pramipexole; R = rasagiline; RO = ropinirole; S = selegiline
[b]participants were excluded from analyses

5.3.2 General experimental set-up

A side view of the experimental set up is provided in Figure 5.1A. Participants were seated in a height adjustable chair so that they could comfortably see and reach to all target and marker locations presented on an opaque, reflective surface. With the right hand participants grasped the vertical handle of a two-joint robot manipulandum mounted in the horizontal plane (Interactive Motion Technologies). Visual stimuli were projected from a monitor (Samsung 510N, refresh rate 72Hz) installed 17cm above the robot onto a reflective surface positioned between the monitor and the manipulandum, thus appearing to lie in the same horizontal plane as the robot. The room lights were dimmed and the participant's view of their hand was blocked by the reflective surface and a black cloth draped between the experimental set up and the participant's right shoulder.
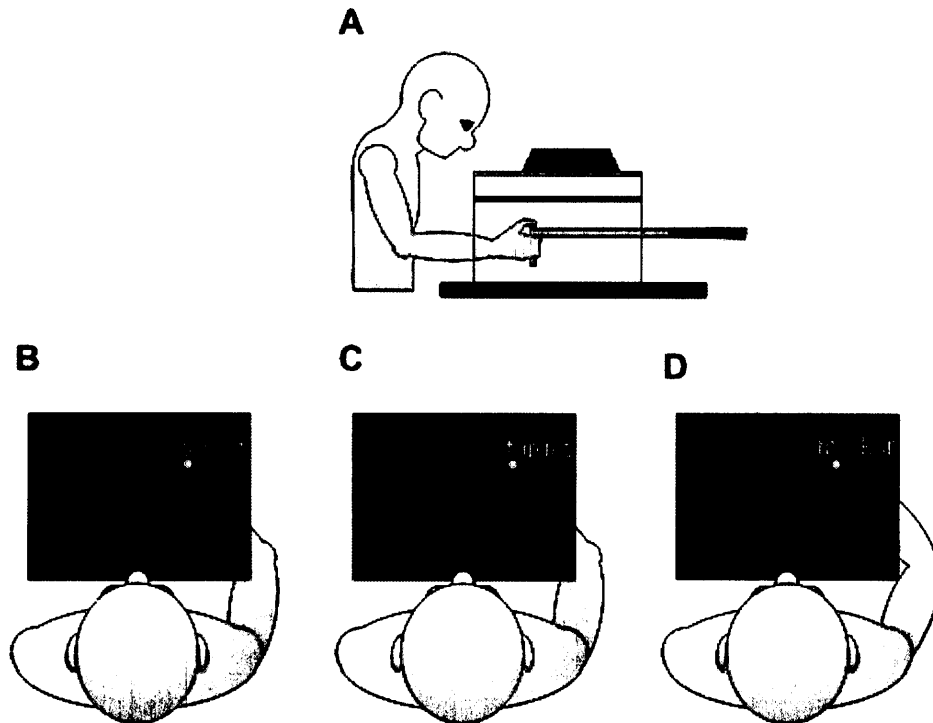
Figure 5.1 Experimental set up and design. (A) Side view of the experimental set up. (B, C and D). Top view of the experimental surface visible to participants. (B-C) Visuomotor distortion introduced in the rotation and translation training task and target locations. The cursor representing the unseen hand was gradually rotated 30° clockwise (rotated experiment, B) or translated 4 cm rightwards (translated experiment, C) with respect to the actual hand position. Targets (yellow rings) 1 cm in size were located 10 cm from the home position (black circle) at 5° and 30° left and right of midline. (D) In the proprioceptive estimate task, participants actively pushed their hand out 10 cm along a constrained linear path (depicted by the rectangle) from the home position and judged the position of their hand with respect to a reference marker. Reference markers (yellow rings) were located at 0° and 30° left and right of midline (depicted for the rotated experiment).

5.3.3 General procedure

The experiment consisted of three visuomotor conditions for both on and off states, completed during six testing sessions. Sessions were completed over 3 to 6 visits. Each testing session involved two tasks (Figure 5.2). During the baseline condition sessions participants completed reach training trials outlined below while seeing a cursor that was veridical, or aligned, with their hand. During the rotated and translated condition sessions participants completed the reach training trials while viewing a cursor that was misaligned from the actual location of their unseen hand. During the rotated reaching trials the cursor was rotated 30° clockwise (CW) relative to the hand position and this distortion was introduced gradually by 0.75° per trial (Figure 5.1B). During the translated reaching trials the cursor was translated 4cm leftwards relative to the hand position and this distortion was introduced gradually by 0.1cm per trial (Figure 5.1C). The cursor was represented by a green disc 1cm in diameter in all conditions. A minimum interval of 2 weeks separated the rotated and translated sessions to ensure sufficient wash-out of visuomotor learning.

5.3.3.1 Reach Training and Adaptation

While grasping the robot manipulandum with the right hand, participants were instructed to reach to a visual target as quickly and accurately as possible while viewing either an aligned (first two sessions) or misaligned (subsequent four sessions) cursor that moved with their hand. The reach targets were located radially 10cm from the home position at 5° and 30° left (CCW) and right (CW) of centre (yellow circles in Figure 5.1B and 5.1C). The home position was located approximately 40cm in front of the participants along their body midline (indicated by the black circle in Figure 5.1B and 5.1C). This position was not illuminated and visual feedback was provided only when the hand had travelled 4cm outwards from the home position. The reach was considered complete once the

centre of the cursor had moved to within 0.5cm of the target's centre. At this point, both the cursor and target disc would disappear and participants moved their hands back to the home position in the absence of visual feedback along a linear route. If participants attempted to move outside of the established path, a 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 (Cressman & Henriques, 2009, 2010; Cressman et al., 2010; Henriques & Soechting, 2003; Jones et al., 2010). The order of the reach trials was pseudo-randomized such that participants reached once to 3 of the reach targets, specifically the two peripheral targets and one of the pair of peri-central (5°) targets, before any target was repeated. Participants completed 99 reach training trials (box 1, Figure 5.2).

After completing reach training, participants immediately completed 12 aiming movements, 3 reaches to each of the 4 reach targets without the cursor (box 2, Figure 5.2). These trials were included to determine if participants adapted their reaches in response to the misaligned cursor (i.e. exhibited aftereffects). On these trials participants were instructed to aim to a target and hold their end position. Once this end position had been maintained for 500 ms, the visual target disappeared and the trial was considered complete. Participants were guided back to the home position by a linear grooved path. The position of the robot manipulandum was recorded throughout all reaching trials at a sampling rate of 50 Hz and a spatial accuracy of 0.1 mm

5.3.3.2 Proprioceptive estimate trials + reach trials

In this task, proprioceptive estimates and reach trials (boxes 3-5 in Figure 5.2) were systematically interleaved. Participants began by completing an additional 12 reaching trials with a cursor as described above (box 3). These reaches were then immediately followed by interleaving sets of 15 proprioceptive

estimate trials (box 4) and 6 reaching trials (box 5). The test sequence of 15 proprioceptive estimates followed by 6 reaches was completed 10 times, for a total of 222 trials (150 proprioceptive estimate trials (50 at each target) + 72 reach trials). A proprioceptive estimate trial began with the participant grasping the robot manipulandum at the illuminated home position located in the same position and represented by the same disc as that during reach training trials (though the home position was not illuminated in these trials). After 500 ms this disc disappeared and the participant was instructed to push his or her hand outward along a constrained robot-generated linear path (as described previously and shown by the red rectangle in Figure 5.1D). On all trials, once the hand reached the end of the path a reference marker located at $0°$, $30°$ left (CCW) or $30°$ right (CW) of center and represented by a yellow circle 1cm in diameter appeared (yellow circles, Figure 5.1D). Participants then made a two-alternative forced choice judgment about the position of their hand (left or right) relative to the reference marker. There was no time constraint for giving a response. After responding, the reference marker disappeared and the participant moved the robot directly back to the home position along a linear route to begin the next trial. The position of the hand with respect to each reference marker was adjusted over trials using an adaptive staircase algorithm (H. Kesten, 1958; Treutwein, 1995). For each reference marker there were 2 staircases, one starting 20° to the left (CCW) of the reference marker and one starting 20° to the right (CW). The 2 staircases were adjusted independently and randomly interleaved as outlined in Cressman and Henriques (2009, 2010).

Participants completed 15 final no cursor reaches, 3 reaches to each of the 4 previously described reach targets and 3 reaches to a target located at $0°$ (box 6 in Figure 5.2) immediately after completing the Proprioceptive Estimate + Reach Task in order to ensure that they were still reaching in a similar manner as before the proprioceptive estimate trials (box 2 in Figure 5.2).

Reach Task		Proprioceptive Estimate + Reach Task			
Reach Training 99 Trials ₁	Reach Aftereffects (no cursor) 12 Trials ₂	Reach Training 12 Trials ₃	Proprioceptive Estimates 15 Trials ₄	Reach Training 6 Trials ₅	Reach Aftereffects (no cursor) 15 Trials ₆

10 Times
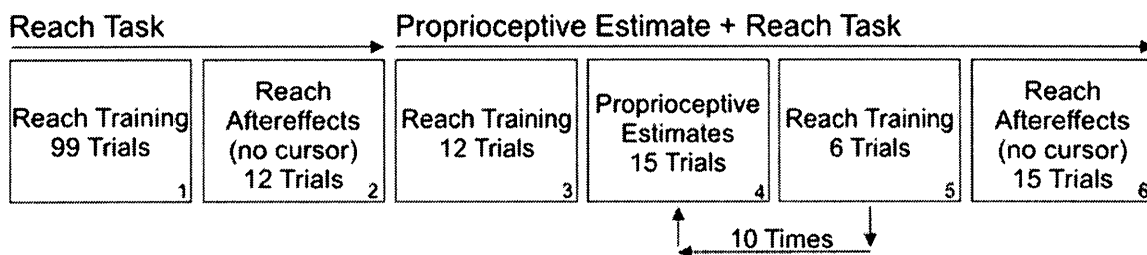
Figure 5.2 Breakdown of the testing sessions within the experiment. In the first testing session participants reached with an aligned cursor that accurately represented the position of their hand in the reach training trials. In the second testing session, participants reached with a misaligned cursor that was rotated 30° clockwise or translated 4 cm rightwards with respect to the actual hand location during the reach training trials. Using their right hand, participants began a testing session by reaching to visual targets with a green cursor that provided visual feedback of hand position (Box 1). After completing either 99 reach training trials, participants next reached to each of the four targets 3 times without a cursor in order to assess visuomotor adaptation (reach aftereffects trials, Box 2). Participants then completed 12 reaches to the reach targets with the cursor present (Box 3). This was followed by 10 sets of 15 proprioceptive estimate trials (Box 4) and 6 visually guided reaches (Box 5) for a total of 150 proprioceptive estimate and 60 reach training trials. Following this, participants again reached to each of the four targets, plus a central target, 3 times without a cursor in order to assess maintenance of visuomotor adaptation (Box 6).

5.3.4 Data Analysis

5.3.4.1 Visuomotor adaptation

5.3.4.1.1 Learning. To examine if disease influenced participants' reaching movements, we calculated angular deviations of the hand for all reach training

trials completed with cursor feedback. Hand deviations were defined as the angular difference between a reference vector joining the centre home position and the target and the vector joining the centre home position and position of the reaching hand at peak velocity (PV). Hand deviations completed during reach training trials were averaged over three consecutive trials such that 33 blocks of reaches were completed by each participant. To determine if participants reached in a similar manner when reaching with an aligned cursor across all trials, average hand deviations were analyzed in a 3 Group (between: PD off vs. PD on vs. control) x 33 (within: blocks) repeated measures analysis of variance (RM-ANOVA). We also examined differences in reach variability between the groups of participants by performing a one-way ANOVA on the standard deviation of participants' hand deviations across reaching trials.

To determine if disease influenced the rate at which participants adapted their reaches in response to the gradually introduced visuomotor distortion, average hand deviations over blocks of trials when participants reached with a rotated (experiment 1) or translated (experiment 2) cursor were analyzed with a 3 group (between: PD off vs. PD on vs. control) x 33 (within: blocks) RM-ANOVA. For both patients and controls, we then used pair-wise comparisons with a Bonferroni correction to compare hand deviations for each of the 32 blocks of reaching with a misaligned cursor to the average hand deviations achieved in the last 33rd learning block to determine at which block hand deviations reached saturation. Differences in reach variability between groups of participants were examined using an independent t-test on the standard deviation of participants' reaching movements. In order to determine each participant's standard deviation during misaligned cursor-feedback reaches, we computed the standard deviation of the cursor position at peak velocity across trials.

5.3.4.1.2 Aftereffects. The extent of visuomotor adaptation was examined by looking at the angular deviation of the hand at peak velocity in the first set of reaches made without a cursor, as no difference in reaches completed before and after the proprioceptive estimate trials was observed during the rotated experiment for PD off (t(12) = 1.34, *p* = .20), PD on (t(12) = < 1, *p* = .96) or control participants (t(12) = 1.80, *p* = .10), or during the translated experiment for PD off (t(12) < 1, *p* = .68) , PD on (t(12) < 1, *p* = .70) or control participants (t(13) = 1.88, *p* = .08). To determine if participants had indeed adapted their reaches following reach training with a misaligned cursor following proprioceptive estimate trials, we analyzed mean aftereffects in a 3 Group (between: PD off vs. PD on vs. control) x 2 Visual Feedback Condition (within: aligned vs. misaligned) x 4 Target (within: 5° CW vs. 5° CCW vs. 30° CW vs. 30° CCW) RM-ANOVA. Pair-wise comparisons with a Bonferroni correction were administered to determine the locus of these significant differences (alpha = .05).

5.3.4.2 Proprioceptive estimates of hand position

To determine if participants recalibrated their sense of felt hand position following reach training with a misaligned cursor, we first determined the locations at which participants felt their hands were aligned with the reference markers. This location was determined by fitting a logistic function to each participant's responses for each reference marker in each testing session and calculating the bias (the point of 50% probability). In addition to calculating bias, we also determined participants' uncertainty (or precision) by finding the difference between the values at which the response probability was 25% and 75%. Bias and uncertainty related to a particular reference marker were excluded if the associated uncertainty was greater than the mean uncertainty across all reference markers + 2 standard deviations. Based on this analysis, only 6 hand-reference marker estimates (3% of total estimates) were excluded. Biases and

uncertainty ranges were analyzed in a 3 Group (between: PD off vs. PD on vs. control) x Visual Feedback during reach training (within: aligned vs. misaligned x Marker Location (within: left vs. right vs. centre) RM-ANOVA. Pair-wise comparisons with a Bonferroni correction were administered to determine the locus of these significant differences (alpha = .05).

5.4 RESULTS

Before we explored the main questions in the study, we first wanted to describe the movement parameters of the PD patient group as another method to assess their symptoms and compare them to control participants. Movement parameters during reach training trials were examined with one-way ANOVAs in order to characterize movement impairments in patients. Results revealed that during the last 10 reach training trials with an aligned cursor, PD patients had slower reaction times (PD off: 231.7 ms; PD on: 214.5 ms; control: 133.6 ms; $F(2, 38) = 5.06$, $p = .01$), longer movement time to acquire the target (PD off: 2483 ms; PD on: 2312 ms; control: 1507 ms; $F(2, 38) = 5.01$, $p = .01$) and decreased peak velocity (PD off: .014 m/s; PD on: .016 m/s; control: .022 m/s; $F(2, 38) = 9.82$, $p < .001$) than control participants. Post-hoc analysis did not reveal differences in medication status in any parameter; while patients' measures of various movement parameters improved slightly with medication, these changes were not significant and were not sufficient to reach comparable levels with control participants. Thus, patients exhibited impairments in movements consistent with their diagnosis and staging. On average, PV was achieved approximately 682 ms into the movement (PD off: 821 ms; PD on: 759 ms; control: 466 ms) and the hand had travelled an average of 3.96 cm when PV had been achieved (PD off: 4.13 ms; PD on: 4.21 cm; control: 3.54 cm). Visual feedback of the hand was not provided until the hand had travelled 4 cm

outwards from the home position, which allowed for the determination of initial movement planning errors before participants had the opportunity to use visual feedback of their hand to correct trajectory errors. Despite the slower reaction times, longer movement times and later achievement of peak velocity during movement, patients were as accurate as controls with respect to their hand direction at peak velocity (as can be seen by the empty symbols presented in Figure 5.3). This is especially important given that the primary measure of motor learning involved the examination of movement deviations following reaches made with displaced visual feedback of the hand.

EXPERIMENT 1: ROTATED FEEDBACK

5.4.1. Visuomotor adaptation

5.4.1.1. Learning

To explore learning we first examined participants' reaching trajectories. Figure 5.3 displays mean angular deviations of the hand over blocks of reaching trials for the 99 reaches completed during the reach training task. Hand deviations for the PD off, PD on and control participants are represented by the triangles, circles and diamonds symbols, respectively (empty symbols denote reaches completed with aligned cursor feedback and filled symbols denote reaches completed with rotated cursor feedback).
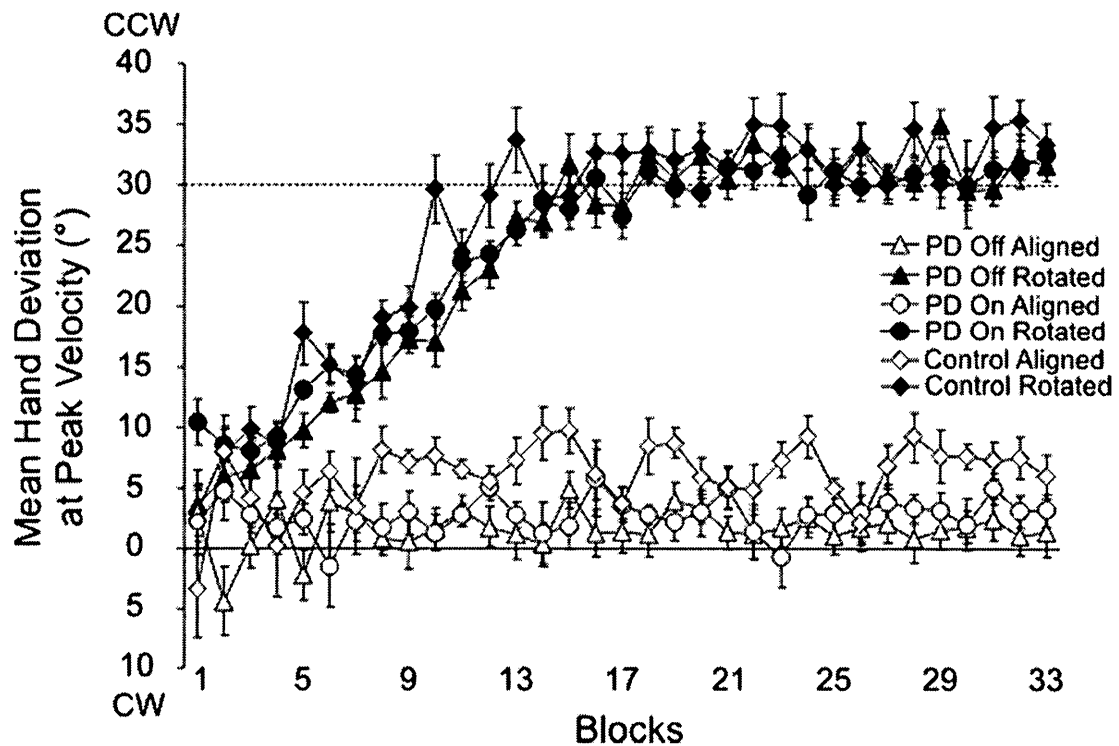
Figure 5.3 Visuomotor adaptation during reach training trials. Here we present the mean angular deviation of the hand at peak velocity for each block (3 trials) of training when PD patients off meds (triangles), on meds (circles) and controls (diamonds) reached with an aligned (empty symbols) and rotated (filled symbols) cursor. Error bars reflect standard error of the mean.

5.4.1.1.1 Aligned cursor. For the most part, all participants reached such that their hand travelled along a fairly linear path towards the target across all trials (i.e. hand deviations were minimal). In accordance with this observation, RM-ANOVA revealed no differences between the groups with respect to hand deviations (F(2,36) = 3.04, p = .06; mean deviations were 2°, 3° and 5° for the PD off, PD on and control groups, respectively). Moreover, there was no effect of block (F(32, 1152) < 1, p = .537) or a Block x Group interaction (F(64, 1152) = 1.10, p = .277). A one-way ANOVA of the standard deviations in reach errors,

averaged across all reach trials made with a cursor, revealed no overall difference in variability between groups (PD off: 10°; PD on: 9°; control: 13°; $F(2,36) = 2.08$, $p = .14$).

5.4.1.1.2 Rotated cursor. We see from the solid symbols in Figure 5.3 that all participants began to reach to the targets such that their hand movement was increasingly deviated leftwards with the increasing visuomotor distortion. Moreover, we see that for all participants, it appears as though deviations of the hand from the target vector gradually increased in magnitude across the first 12-13 blocks of learning trials as the visuomotor distortion was increased. This is supported by RM-ANOVA ($F(32, 1152) = 89.70$, $p < .001$) and suggests that participants increased their hand deviations in order to bring the cursor to the target in a more direct path. There was a significant Block x Group interaction ($F(64, 1152) = 1.35$, $p = .04$) that revealed differences between the groups in the first block of rotated training, such that PD on had greater initial baseline errors than PD off or control participants ($p = .02$). The point at which saturation was achieved was similar for all groups (block 12, block 13 and block 12 for PD off, PD on and controls, respectively). After these blocks, participants reached with similar trajectories throughout the rest of the training trials and achieved full and comparable levels of adaptation. A one-way ANOVA of the standard deviations in reach errors, averaged across all reach trials made with a cursor once saturation had been achieved (i.e. blocks 12 through 33), revealed no overall difference in reach variability between groups (PD off: 10°; PD on: 10°; control: 12°; $F(2,36) = 2.03$, $p = .15$).

5.4.1.2 Aftereffects

Figure 5.4A displays mean 2D reach endpoint errors at each of the four target locations for PD patients off meds, patients on meds and control

participants. Figure 5.4B displays the mean changes in reach error between aligned and rotated cursor conditions for the three groups. RM-ANOVA revealed that, on average, all participants reached 12° more to the left of the targets following training with a misaligned cursor compared with an aligned cursor (F (2,36 = 85.70, p < .001), such that these aftereffects representing approximately 40% of the induced distortion (Figure 5.4B). No difference between groups was observed (F(2,36) < 1, p = .717). This suggests that patients regardless of medication status persisted in making deviated hand movements without visual feedback comparable with controls.

A significant target effect was observed (F(3,108) = 6.50, p < .001) such that aftereffects were greater for the eccentric CW target than for the eccentric CCW target. Analysis of hand deviations at reach end point revealed similar results, such that participants' mean aftereffects were on average 13° more leftwards of the targets (Figure 5.4A). A paired t-test revealed no difference between aftereffects at peak velocity and those at reach end point (t(38) = 1.32, p = .19). This finding suggests that reaches made without cursor feedback were fairly straight with minimal correction for all participants.

A

PD Off
10 cm

PD On
10 cm

Control
10 cm

Marker
Aligned
Rotated

5 cm
left

5 cm
right

5 cm
left

5 cm
right

5 cm
left

5 cm
right

B

n.s.
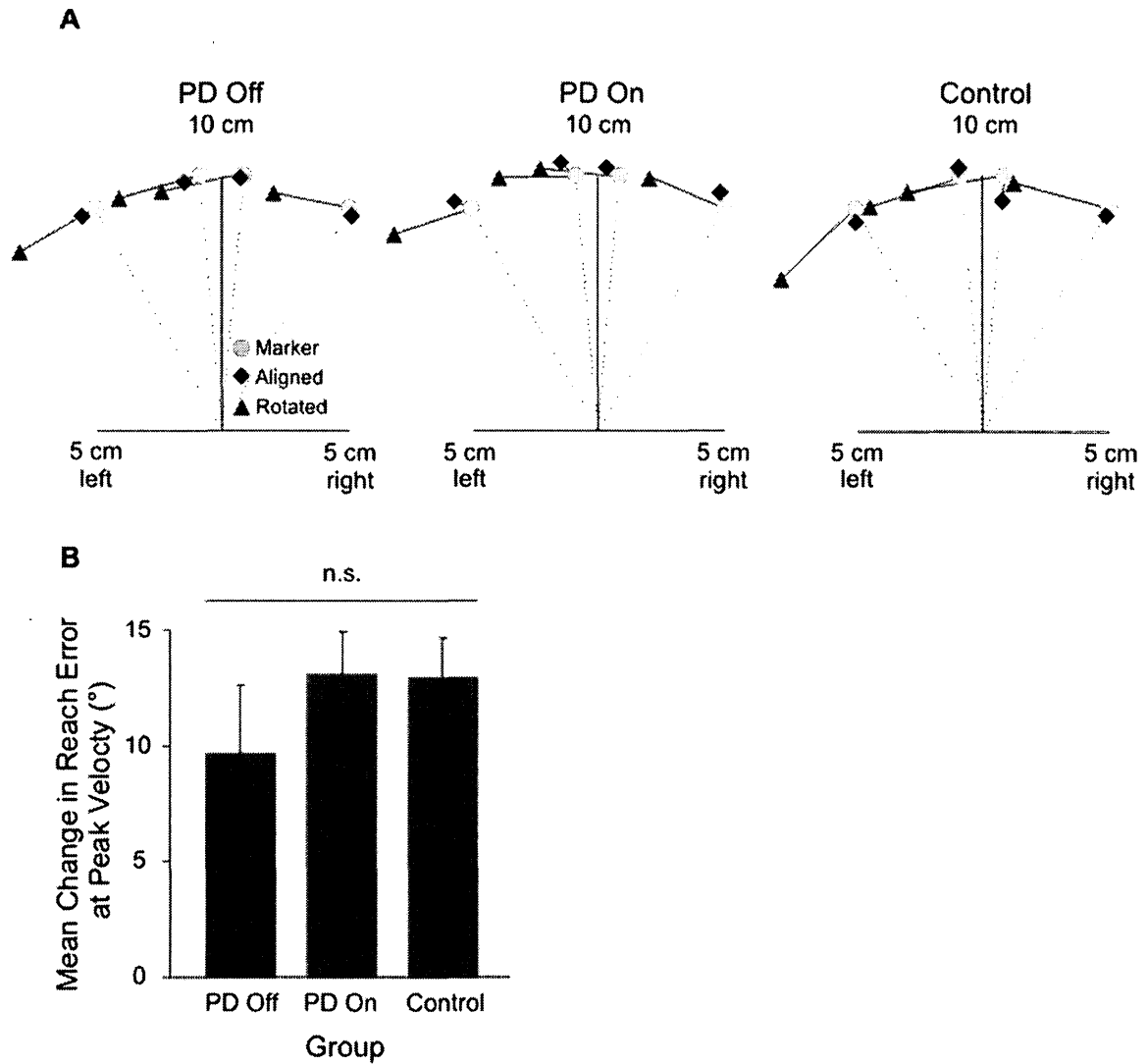
Figure 5.4 (A) Mean 2-D hand deviations at reach endpoint for participants following reach training with an aligned (diamonds) and rotated (triangles) cursor. (B) Mean baseline-subtracted aftereffects at peak velocity were calculated by subtracting the angular error during no-cursor reach trials following rotated reach training from those following aligned reach training. Error bars reflect standard error of the mean.

5.4.2 Proprioceptive recalibration

5.4.2.1 Bias

Figure 5.5A displays mean 2D biases at each of the three reference marker locations for PD patients off meds, patients on meds and control participants. Grey circles denote marker locations, diamonds denote biases following reach training with an aligned cursor and triangles denote biases following reach training with a rotated cursor. For all participants we see that, on average, estimates of hand location were biased slightly to the left after reaching with an aligned cursor (diamonds). The mean bias collapsed across all reference markers was 6°, 5° and 3° leftwards of the marker for patients off meds, patients on meds and control participants, respectively; Post-hoc analysis revealed no differences between groups in these leftward biases $(F(2,36) < 1, p > .05$ for all comparisons). In addition to finding that participants had similar levels of proprioceptive acuity regardless of disease or medication state under baseline conditions, we found that all participants recalibrated proprioception. Specifically, after reaching with a cursor that was rotated with respect to actual hand position, participants perceived their hand to be aligned with the visual reference marker when it was shifted significantly to the left of the aligned estimates by an average of 7° $(F(1,36) = 50.85, p < .001)$. This leftward shift in magnitude was comparable across all marker locations $(F(2,72) = 1.40, p = .49)$. As shown in Figure 5.5B, while there was a trend for greater recalibration in patients than controls, this difference was not statistically significant (PD off: 8.6°; PD on: 7.8°; control: 5.5°; $F(2,36) < 1, p = .46)$.
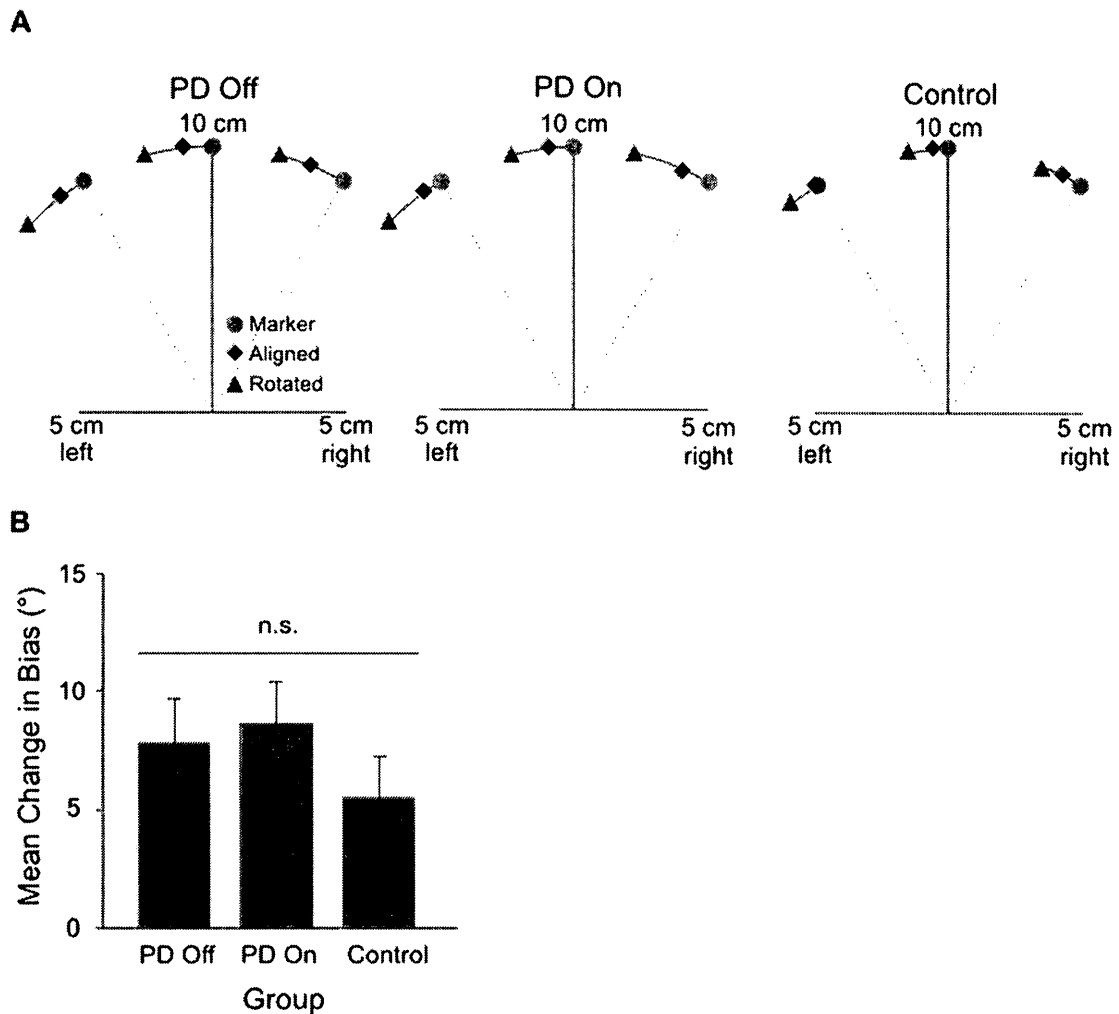
Figure 5.5 Proprioceptive biases following training with aligned and rotated visual feedback of the hand. (A) Mean 2-D proprioceptive biases following training with an aligned (diamonds) or rotated (triangles) cursor. The actual reference marker positions are represented as grey circles. (B) Mean changes in biases after training with a rotated cursor compared to an aligned cursor were averaged across reference markers. Error bars reflect standard error of the mean.

5.4.2.2 Uncertainty

Figure 5.6 depicts the mean uncertainty following reaches with an aligned cursor (empty bars) and rotated cursor (filled bars). Analysis did not reveal any difference between groups ($F_{(2,36)} < 1$, $p = .91$). Participants' level of precision in estimating the location of their unseen hands was comparable after reach training with an aligned and misaligned cursor ($F_{(1,36)} = 1.25$, $p = .27$) at all reference markers ($F_{(2,72)} = 2.49$, $p = .09$). These results suggest that PD patients and controls are comparably precise in estimating the location of their unseen hand.

☐ Aligned
■ Rotated

n.s.
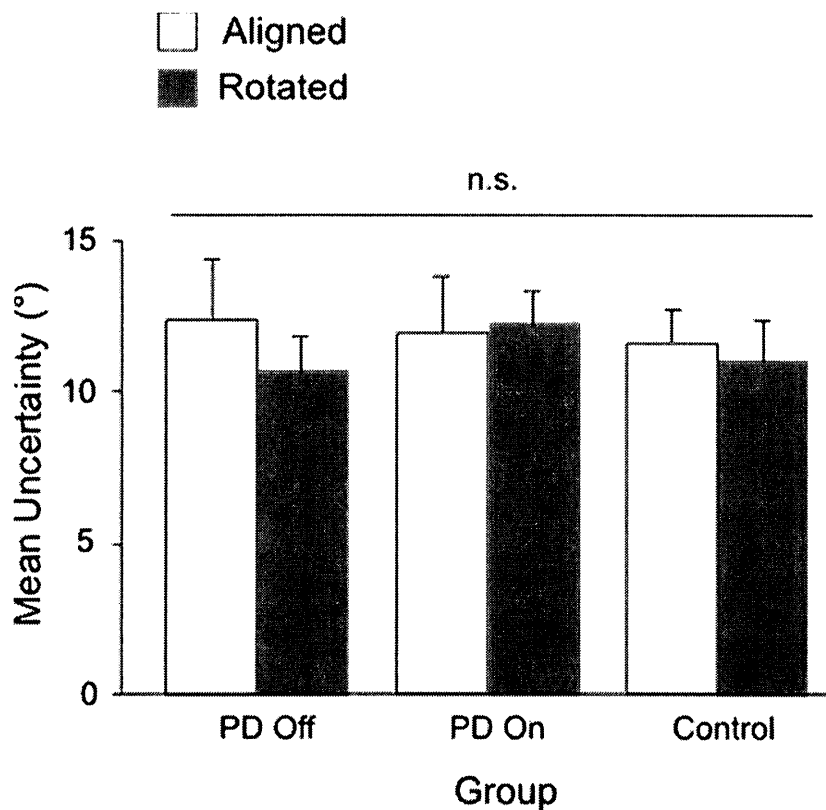
Figure 5.6 Magnitude of the uncertainty ranges in the proprioceptive estimate trials were averaged across participants and reference marker positions following

reach training with an aligned cursor (empty bars) and rotated cursor (filled bars). Error bars reflect standard error of the mean.

5.4.3 Relationship between Adaptation and Recalibration

Overall, proprioceptive recalibration was approximately 60% of the motor adaptation observed. A one-way ANOVA was used to examine the proportion of changes between groups. Results revealed that the proportion of changes did not differ between patients on and off meds and controls (F(2,36) < 1, p = .79; PD off: 62%; PD on: 73%; controls: 60%). To determine if the magnitude of proprioceptive recalibration was predicted by the magnitude of visuomotor adaptation, we regressed adaptation as a proportion of the induced visuomotor distortion on the recalibration as a proportion of the induced visuomotor distortion for patients. Results did not reveal a significant relationship between motor aftereffects and proprioceptive recalibration in patients (F(1,24) < 1, p = .489, R^2 = .02) or controls (F(1,12) < 1, p = .86, R^2 = .003).

EXPERIMENT 2: TRANSLATED FEEDBACK

5.4.4 Visuomotor adaptation

5.4.4.1 Learning

We first examined participants' reaching trajectories. Figure 5.7 displays mean distance deviations (as opposed to angles) of the hand over blocks of reaching trials for the 99 reaches completed during the reach training tasks. Hand deviations for the PD off, PD on and control participants were represented by the triangles, circles and diamonds symbols, respectively (empty symbols denote aligned cursor feedback and filled symbols denote translated cursor feedback).

5.4.4.1.1 Aligned cursor. Data from PD patients presented in Figure 5.7 (empty triangles and empty circles) and compared with data from the second group of control participants who participated in Experiment 2 (empty diamonds). RM-ANOVA revealed no differences between the groups with respect to hand deviations at peak velocity (F(2,37) = 2.06, *p* = .14; mean deviations were 0.15 cm left, 0.05 cm right and 0.05 cm right for the PD off, PD on and control groups, respectively) following training with an aligned cursor. Moreover, there was no effect of block (F(32, 1184) = 1.82, *p* = .07) or a Block x Group interaction (F(64, 1184) = 1.10, *p* = .28). A one-way ANOVA revealed no difference in variability between groups in hand deviations across trials (F(2,37) = < 1, *p* = .93; Mean PD off: 2.58cm; PD on: 2.64 cm; control: 2.62 cm).
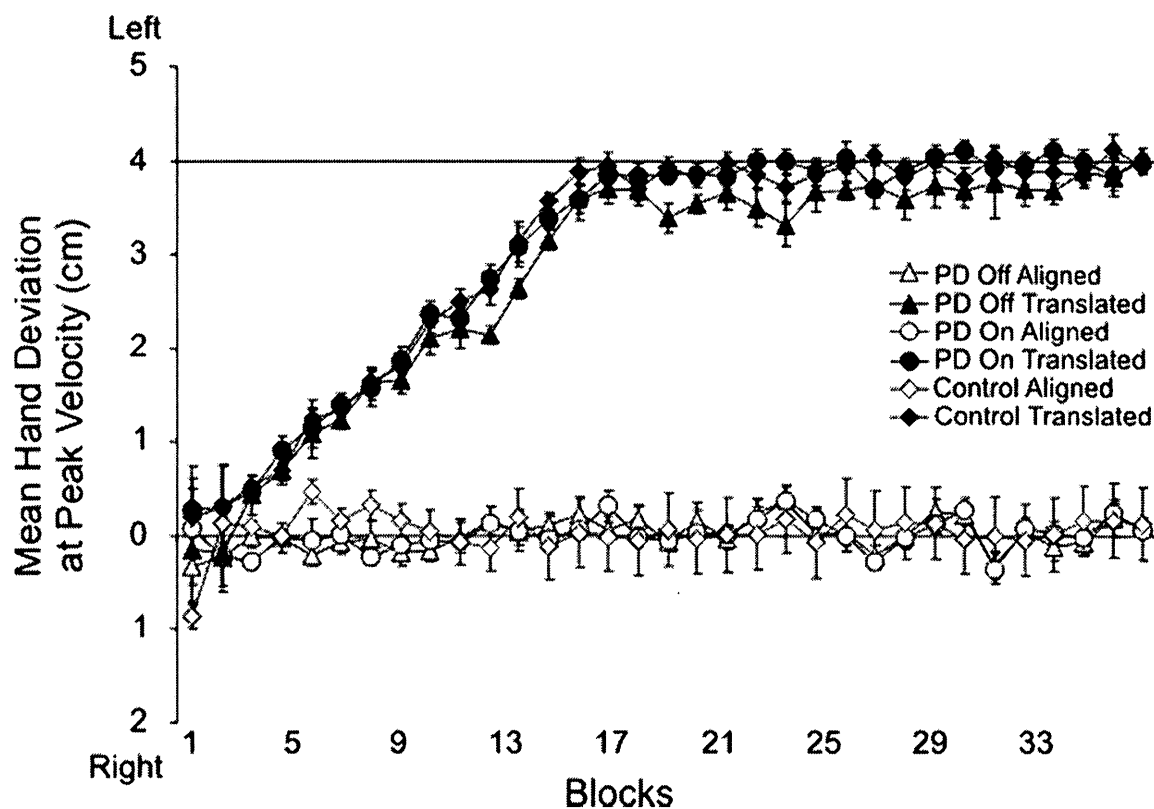
Figure 5.7 Visuomotor adaptation during reach training trials. Here we present the mean hand deviation at peak velocity for each block (3 trials) of training when PD patients off meds (triangles), on meds (circles) and controls (diamonds) reached with an aligned (empty symbols) and translated (filled symbols) cursor. Error bars reflect standard error of the mean.

5.4.4.1.2 Translated cursor. We see from the solid symbols in Figure 5.7 that all participants began to reach to the targets such that their hand was increasingly deviated leftwards with the increasing visuomotor distortion. As with adaptation to a rotated cursor (Figure 3), we see that for all participants, deviations of the hand from the target vector gradually increased in magnitude across the first 14 blocks of learning trials as the visuomotor distortion was increased. This is supported by RM-ANOVA (F(32, 1184) = 239.74, *p* < .001) and

suggests that participants increased their hand deviations in order to bring the cursor to the target in a more direct path. No Block x Group interaction (F(64, 1184) < 1, p = .94) or overall group differences (F(2,37) = 1.52, p = .23) were observed. Saturation of adaptation was achieved at approximately the fourteenth block for all groups, after which participants reached with similar trajectories throughout the rest of the training trials and achieved full and comparable levels of adaptation. There was no difference in variability between groups with respect to hand deviations across trials (F(2,37) = < 1, p = .59; Mean PD off: 3.00 cm; PD on: 3.09 cm; control: 3.10 cm).

5.4.4.2 Aftereffects

Figure 5.8A displays mean 2D reach endpoint errors at each of the four target locations for PD patients off meds, patients on meds and control participants. The differences in hand deviations at peak velocity during open-loop reaches following training with a misaligned cursor compared to an aligned cursor are shown as grey bars in Figure 5.8B. RM-ANOVA revealed that, on average, all participants reached 3.4 cm more to the left of the targets following training with a misaligned cursor (F(1,37 = 979.52, p < .001), such that these aftereffects represent approximately 80% of the induced distortion. A significant target effect was observed (F(3,111) = 1774.71, p < .001) such that aftereffects were largest for the 30° CW target. No difference between groups was observed (F(2,37) = 2.23, p = .12

Analysis of hand deviations at reach end point revealed similar results, such that participants' mean aftereffects were on average 2.9 cm more leftwards of the targets following translated cursor training compared to aligned cursor training, however no difference in aftereffects between targets was observed (F(3,111) = 1.33, p = .27). Aftereffects measured at reach endpoint were found to

be significantly smaller than those at peak velocity (t(39) = 3.83, p < .001), suggesting a very slight (0.5cm) movement correction
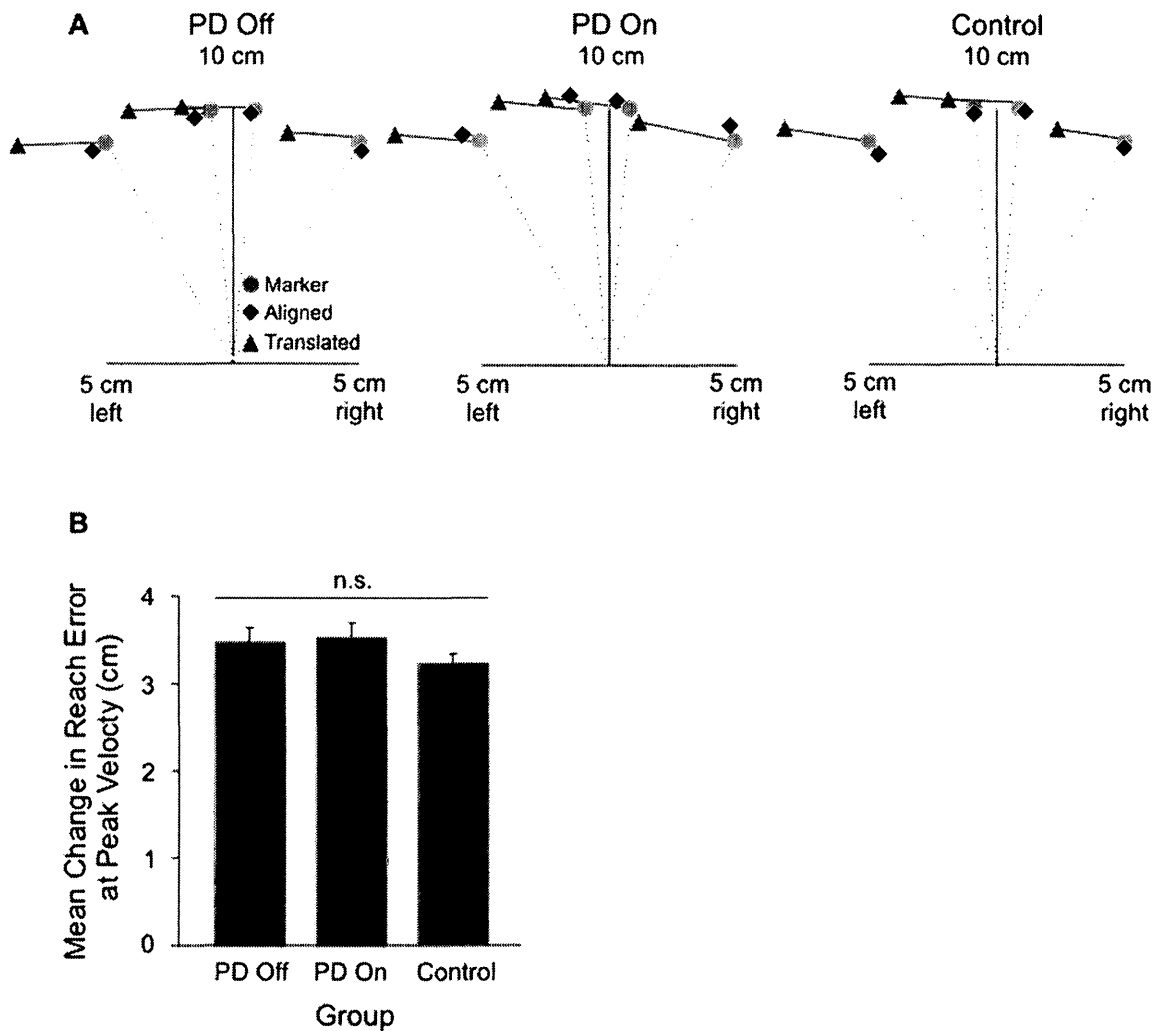
Figure 5.8 (A) Mean 2-D hand deviations at reach endpoint for participants following reach training with an aligned (diamonds) and translated (triangles) cursor. (B) Mean baseline-subtracted aftereffects at peak velocity were calculated by subtracting the distance error during no-cursor reach trials following translated reach training from those following aligned reach training. Error bars reflect standard error of the mean.

5.4.5 Proprioceptive recalibration

5.4.5.1 Bias

Figure 5.9A displays mean 2D biases at each of the three reference marker locations for PD patients off meds, patients on meds and control participants. Grey circles denote marker locations, diamonds denote biases following aligned cursor reach training and triangles denote biases following translated cursor reach training. As previously observed, for all participants we see that average estimates of hand location were slightly biased to the left after reaching with an aligned cursor (diamonds). The mean bias collapsed across all reference markers was 1.09 cm, 0.91 cm, and 1.31 cm leftwards of the marker for patients off meds, patients on meds and control participants, respectively. Post-hoc analysis revealed that patients and control participants had comparable leftward biases $(F(2,37) < 1, p > .05$ for all comparisons). In addition to finding that participants had similar levels of proprioceptive acuity regardless of disease or medication state under baseline conditions, we found that participants recalibrated proprioception. After reaching with translated cursor feedback of hand position participants perceived their hand to be aligned with the visual reference marker when it was shifted significantly to the left of the aligned estimates by an average of 1.18cm $(F(1,37) = 23.57, p < .001)$. This leftward shift in magnitude was comparable across all marker locations $(F(2,74) < 1, p = .35)$. Importantly, as can be seen in Figure 5.9B, these biases did not differ between groups $(F(2,37) < 1, p = .95)$.
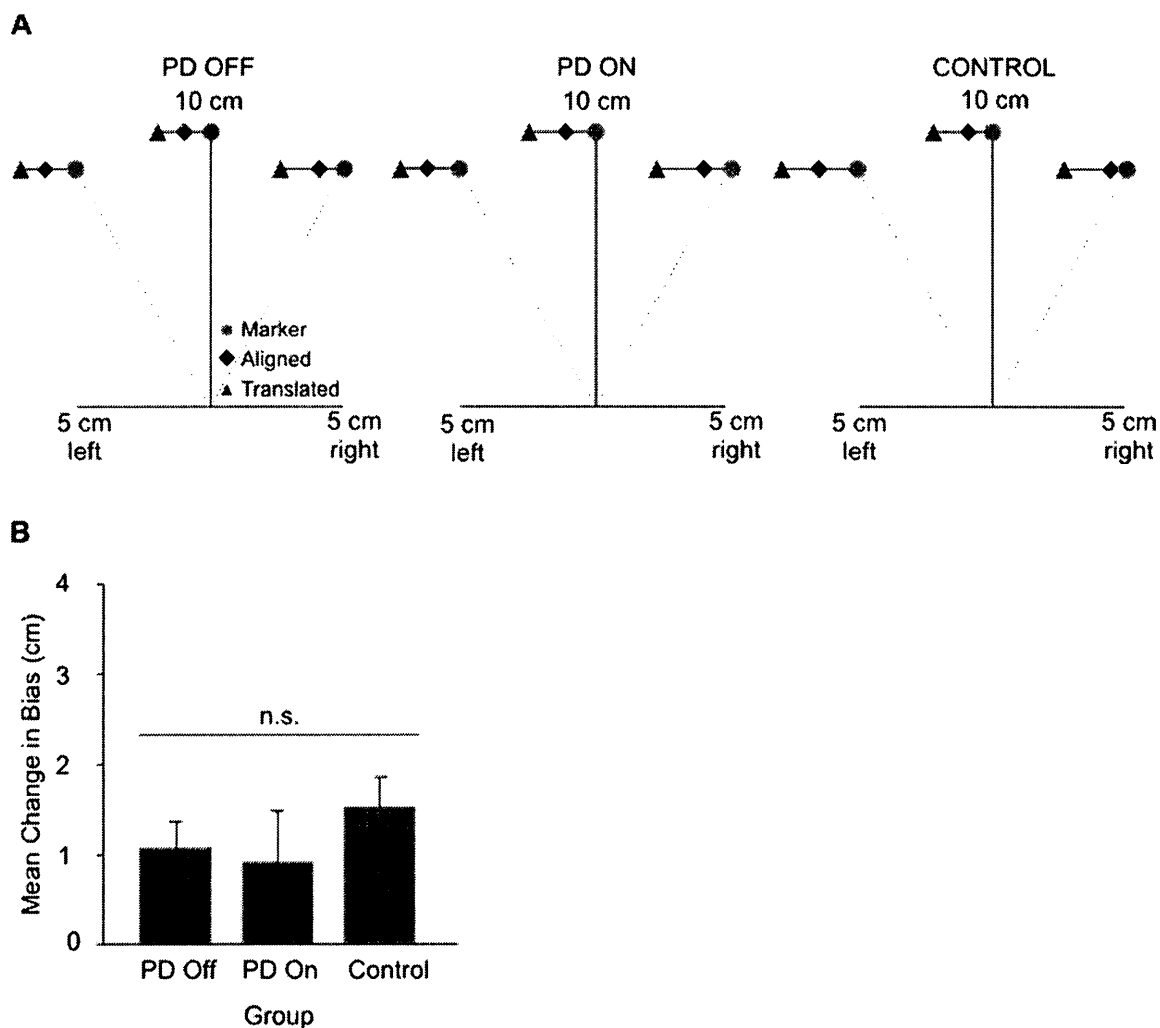
Figure 5.9 Proprioceptive biases following training with aligned and translated visual feedback of the hand. (A) Mean 2-D proprioceptive biases following training with an aligned (diamonds) or translated (triangles) cursor. The actual reference marker positions are represented as grey circles. (B) Mean changes in biases after training with a translated cursor compared to an aligned cursor were averaged across reference markers. Error bars reflect standard error of the mean.

5.4.5.2 Uncertainty

Figure 5.10 depicts the mean uncertainty following reaches with an aligned cursor (empty bars) and misaligned cursor (filled bars). Participants' level of precision in estimating the location of their unseen hands were comparable after reach training with an aligned and misaligned cursor ($F(1,37) < 1$, $p = .95$) at all reference markers ($F(2,74) < 1$, $p = .60$). Analysis did not reveal any difference in group ($F(2,37) = 1.17$, $p = .32$). These results suggest that patients and controls have similar levels of precision when estimating the location of their unseen hand.
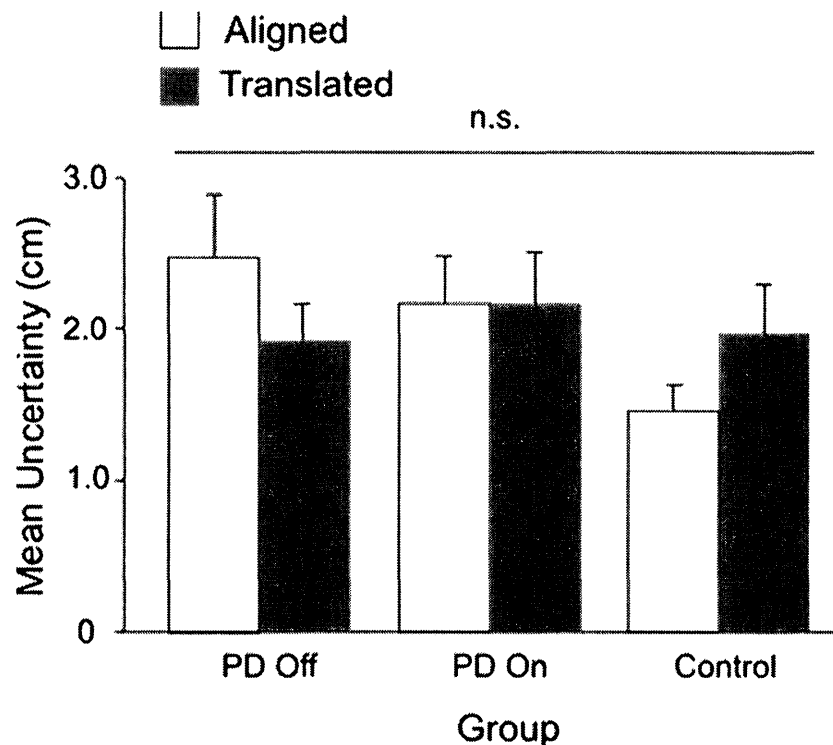
Figure 5.10 Magnitude of the uncertainty ranges in the proprioceptive estimate trials were averaged across participants and reference marker positions following reach training with an aligned cursor (empty bars) and translated cursor (filled bars). Error bars reflect standard error of the mean.

5.4.6 Relationship between Adaptation and Recalibration

Overall, proprioceptive recalibration was approximately one-third of the motor adaptation observed. A one-way ANOVA was used to examine the proportion of changes between groups. Results revealed that the proportion of changes did not differ between patients on and off meds and controls ($F_{(2,37)} <$ 1, p = .56; PD off: 30%; PD on: 24%; controls: 40%). To determine if the magnitude of proprioceptive recalibration was predicted by the magnitude of visuomotor adaptation, we regressed adaptation as a proportion of the induced visuomotor distortion on the recalibration as a proportion of the induced visuomotor distortion for patients. Results did not reveal a significant relationship between motor aftereffects and proprioceptive recalibration in patients ($F_{(1,24)}$ = 1.24, p = ..10, R^2 = .11) or controls ($F_{(1,13)}$ = 1.13, p = .31, R^2 = .09).

5.6 DISCUSSION

The present study addressed several questions. Firstly, we wished to examine if and how individuals with Parkinson's disease adapt their movements to a novel visuomotor distortion. Results revealed that mild to moderately affected PD patients learned to reach to targets with a cursor that was gradually displaced (either rotated or translated) from their unseen hand's position. Deviational errors made during learning trials were comparable to control participants, indicating that patients' rate of adaptation and point of saturation were not necessarily impaired. Reaches made to targets without cursor feedback revealed that patients persisted in making deviated movements, and these aftereffects were the same magnitude as age-matched control participants. Secondly, we wished to determine if after making deviated movements in response to a visuomotor distortion patients would perceive their hand as having "shifted" in the direction of motor adaptation. We found that after adapting to the

distortions, patients' estimates of their unseen hand position shifted leftwards compared to their estimates following training with an aligned cursor. Moreover, this shift occurred in the direction consistent with adaptation and was comparable to the shift observed in control participants, suggesting that processes underlying proprioceptive recalibration are retained in PD patients. Consistent with previous work in our lab (Cressman & Henriques, 2009; Cressman et al., 2010; Salomonczyk et al., 2011; Salomonczyk et al., 2012), no relationship between motor aftereffects and proprioceptive recalibration was observed suggesting further that these processes are served by separate underlying mechanisms. We were also able to examine patients' proprioceptive acuity at the effector end point (i.e. the hand). On average, patients' were fairly accurate in estimating the position of their hand such that they aligned their hand with the reference markers comparably to control participants. Lastly, we examined the impact of dopaminergic medication on these motor and sensory changes. No differences in any measures obtained during the clinically defined "on" and "off" medicated states suggest that dopaminergic medication neither improves nor worsens proprioceptive and sensorimotor processing in mildly to moderately affected PD patients. Altogether, these results suggest that at smaller distortions that are introduced gradually (i.e. up to 30° or 4 cm), PD patients are able to adapt to a visuomotor distortion and recalibrate proprioception at levels comparable to healthy adults.

5.6.1 Visuomotor adaptation in PD

Present results showed that PD patients adapted their movements to a visuomotor distortion in a similar manner as healthy adults following adaptation to gradually misaligned visual hand feedback, despite different movement patterns and slower movement execution. This learning occurred by participants reaching further and further to the left of the targets, such that the participants achieved

the target location with the visual cursor with increased hand deviations over trials. Results also revealed persistent deviated movements in the absence of visual feedback of hand position, suggesting that patients were able to at least temporarily maintain this new visuomotor mapping. Our findings are consistent with previous studies in which a gradually introduced visuomotor distortion was utilized, however previous studies have shown differential adaptation to gradually versus suddenly introduced visuomotor distortions in patients with PD (Contreras-Vidal & Buch, 2003; Venkatakrishnan et al., 2011). These authors observed reduced aftereffects following training with an abruptly introduced visuomotor distortion compared with a gradually introduced distortion. This effect has been observed across several experimental paradigms, including those utilizing a digitizing tablet and tracking ball, and suggests that different movements are not differentially affected by the initial error experienced. As suggested by these authors, it is possible that learning a gradually introduced distortion recruits cerebellar-dependent mechanisms typical of error-based learning (i.e. updating internal models), thus bypassing basal ganglia mechanisms that are involved in the contextual learning that would be utilized during learning of an abruptly introduced distortion.

Although patients with PD have been shown to adapt to gradual perturbations comparably to controls, previous studies have reported impaired retention and recall of these newly learned sensorimotor mappings. For example, after a period of washout, patients consistently failed to show recollection of adaptation or savings in subsequent learning trials, even as little as 24 hours after initial training (Bedard & Sanes, 2011; Isaias et al., 2011; Marinelli et al., 2009). Although dopaminergic transmission has been shown to be necessary in facilitating motor learning (McEntee, Mair, & Langlais, 1987; Seidler et al., 2010) and coding prediction errors involved in learning (Galea, Bestmann, Beigi, Jahanshahi, & Rothwell, 2012), evidence seems to suggest that dopaminergic

pathways are responsible for the maintenance, and not formation, of updated sensorimotor mappings in response to gradually learned distortions.

Another aspect of learning that appears to be impaired in PD is intermanual transfer. While patients are able to initially adapt to a visuomotor rotation comparably with controls, they fail to show not only sustained aftereffects following learning, but transfer of adaptation to the opposite, untrained hand observed in healthy controls (Isaias et al., 2011). These authors were even able to discern a relationship between the level of intermanual transfer and dopamine transporter (DAT) binding. In patients, SPECT analysis revealed a positive correlation between transfer (but not adaptation) and DAT binding in the right caudate and putamen. The authors suggest that because levels of transfer were also strongly correlated with the level of retained aftereffects that this observation may be due to an overall deficit in memory processes that underlie learning, consolidation and retrieval (Isaias et al., 2011).

While our results cannot directly speak to the magnitude of long-term learning of adaptation or transfer in PD, we have demonstrated the novel finding that patients are able to adapt to a variety of cursor distortions (i.e. rotated or translated), and this adaptation is comparable to controls and not dependent on the medication status. Moreover, the comparable level of learning and aftereffects observed between patients and healthy controls subsequently allowed us to directly investigate changes in proprioceptive sense of hand position.

5.6.2 Proprioception in PD

Following reach training with an aligned cursor, patients perceived their hand as being aligned with a reference marker when it was slightly biased to the left. This leftward bias was consistent with controls' estimates of hand-reference marker alignment as well as with previous work that suggests estimates made

with the right hand are naturally biased towards the left (Jones et al., 2010; Salomonczyk et al., 2012); that is, individuals feel their right hand is more rightwards than it actually is. This effect was not modulated by dopaminergic medication. Additionally, the precision with which patients judged their hand position was comparable to controls; that is, no deficits in proprioceptive acuity or precision were observed, which is in contrast to previous studies. Previously, the sense of felt limb position in PD was measured using single-joint matching tasks. Specifically, patients were asked to match a remembered target joint angle (the elbow) in the absence of vision with the previously displaced limb or by matching a concurrently held limb position with the opposite limb (O'Suilleabhain et al., 2001; Zia et al., 2000; Zia et al., 2002). These studies revealed impairments such that patients made greater errors in angle matching than controls regardless of active or passive limb placement.

It is possible that joint-angle proprioception is processed differently than proprioception of the end-effector by the CNS. Fuentes and Bastian (2010) recently showed that end-effector proprioception is more precise than proprioception of a joint angle (i.e. the elbow), possibly due to CNS optimization resulting from the greater need for estimating hand position in daily activities. That present results did not indicate impairment in end-effector position estimation could be due to potential CNS optimization in estimating end-effector position. However, end-effector (fingertip) proprioception has been shown to be impaired in PD patients as well (O'Suilleabhain et al., 2001) though these authors employed a task that required matching the position to a remembered spatial location.

Another plausible explanation to explain contradictory findings is the cognitive demand inherent in matching remembered positions. Matching a remembered joint angle using the ipsilateral limb requires working memory resources that are impaired in PD (S. J. Lewis, Slabosz, Robbins, Barker, &

Owen, 2005; Owen, Iddon, Hodges, Summers, & Robbins, 1997). Conversely, contralateral matching tasks require the transfer of information across the corpus callosum. While the corpus callosum was shown to remain structurally intact in early to moderate PD (Wiltshire, Foster, Kaye, Small, & Camicioli, 2005), functional deficits including interlimb coordination are present (Swinnen et al., 1997; Verschueren, Swinnen, Dom, & De Weerdt, 1997). More recently, Isaias and colleagues (2011) demonstrated impaired interlimb transfer of visuomotor adaptation in PD patients that directly related to DAT binding in basal ganglia nuclei, directly implicating the basal ganglia in tasks requiring interlimb transfer and attention/memory. Together, these findings may implicate memory or central processing impairments in joint-angle matching deficits previously observed. Our present proprioceptive task does not place demand on proprioceptive memory or hemispheric communication of interlimb information, thus providing an accurate assessment of one's ability to localize the endpoint position of the limb without additional interference from cognitive demands.

Another difference between previously reported findings and our present results is the modality of the reference around which proprioception is assessed. In elbow matching studies, the reference (elbow joint-angle) was proprioceptive. In our paradigm, patients had to match their hand to an external, visual reference marker. While it remains unknown whether PD patients are differentially impaired at spatial encoding around visual or proprioceptive spatial locations, indirect evidence supporting impaired egocentric processing in PD comes from findings of disrupted representations of body size relative to space (Lee, Harris, Atkinson, & Fowler, 2001). Previous work in our lab revealed no differences in proprioceptive acuity or precision between visual and egocentrically encoded proprioceptive (i.e. body midline) markers (Cressman & Henriques, 2009) in healthy control participants. However, evidence suggests that perception of body midline is impaired in PD (Davidsdottir, Wagenaar, Young, & Cronin-Golomb,

2008) which could subsequently effect judgements of effector position around this type of reference marker. To explore this further, proprioceptive acuity around both visual and proprioceptive markers should be explored. From the present study, we can only conclude that multi-joint, end-effector proprioceptive acuity is around visual markers is retained in PD.

5.6.3 Proprioceptive Recalibration in PD

Following reaches with altered visual feedback (either rotated or translated) of hand position, patients recalibrated their sense of hand-reference marker alignment more leftwards, in the direction opposite the distortion and consistent with their reach adaptation. For adaptation to a rotated cursor, this shift was roughly 8° or 25% of the induced 30° distortion; for a translated cursor, this shift was roughly 1 cm or 25% of the induced 4 cm distortion. Moreover, the magnitude of this change was comparable to controls. From previous work described earlier suggesting that proprioception is impaired in PD, we may have expected that patients would recalibrate their proprioceptive sense of hand position to a greater extent than healthy adults. This may arise from an overreliance on visual information resulting in patients perceiving their hand to feel as though it had shifted in the direction they saw it (Simani et al., 2007; van Beers et al., 2002). This was not the case.

Results from our lab and others have consistently shown that healthy adults recalibrate proprioception by roughly one-third of the visuomotor adaptation achieved (Cressman & Henriques, 2009; Ostry et al., 2010). In the present study we observed recalibration that was roughly one-third (translated paradigm) to one-half of the visuomotor adaptation achieved. While the overall magnitude of proprioceptive recalibration remained comparable between paradigms, the proportion of proprioceptive recalibration was slightly, though not significantly, greater in patients than controls. This seems to suggest that

patients may rely more on visual information to guide movement (Adamovich et al., 2001) and thus become more susceptible to proprioceptive shift. However, that proprioceptive recalibration and motor aftereffects are again observed to be unrelated further supports the role for separate underlying mechanisms governing these processes.

In summary, this study represents the first attempt at examining sensory recalibration in Parkinson's disease. The results indicate that patients are able to recalibrate their proprioceptive sense of hand position as accurately and precisely as healthy age-matched control participants. Moreover, dopaminergic therapy was not shown to improve (or worsen) proprioceptive acuity or recalibration. These results do not provide evidence to suggest a role of striatal dopaminergic pathways of the basal ganglia in this process. Future work remains to be done to further elucidate the neural substrates involved in visuomotor adaptation and proprioceptive recalibration.

CHAPTER SIX

GENERAL DISCUSSION

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6.1 SUMMARY OF FINDINGS

6.1.1 Visuomotor adaptation and recalibration

While the motor consequences of visuomotor adaptation have been well characterized, only recently has attention been paid to the sensory consequences that follow. In order to examine the extent that sensory (and motor changes) contribute to visuomotor adaptation, we have developed a novel perceptual task to assess proprioceptive recalibration. Specifically, we have designed a perceptual task in which participants provide estimates regarding the position of their hand in the absence of any goal-directed movement. These proprioceptive estimates provide insight into sensory changes that are independent of any possible motor changes (or changes in the motor representation). The results of these studies suggest that proprioception, specifically felt hand position, is recalibrated following visuomotor adaptation (Cressman & Henriques, 2009, 2010; Cressman et al., 2010; Jones et al., 2010; Salomonczyk et al., 2011; Salomonczyk et al., 2012). As well, results provide further insight into the sensory plasticity observed in conjunction with changes to the motor system.

In all our studies to date, we have observed significant shifts in proprioceptive estimates of hand position (proprioceptive recalibration) in the direction of movement adaptation following visuomotor adaptation training (Cressman & Henriques, 2009, 2010; Cressman et al., 2010; Salomonczyk et al., 2011). On average, healthy participants recalibrate their felt sense of hand position by roughly $6°$, representing approximately 20% of the $30°$ visuomotor distortion. This shift has been observed at both visual and proprioceptive reference markers located in different positions of the workspace, which suggests that visual recalibration is not responsible for the observed shifts in felt hand position. Moreover, from chapter two we saw that this proprioceptive shift was observed in both the left and right hands of right-handed participants and is

of similar magnitude in the two limbs (Salomonczyk et al., 2012). Given that proprioceptive recalibration around visual markers occurs in both the left and right hands, and that the extent of recalibration is comparable across reference marker modalities (i.e. visual and proprioceptive markers (Cressman & Henriques, 2009), it appears that proprioceptive recalibration is not subject to limb-modality specialization, which has been observed in localization tasks (Goble & Brown, 2008).

In this study we also evaluated the role of the initial magnitude of the visuomotor distortion in driving proprioceptive recalibration following reach training with an abruptly introduced distortion and observed similar proprioceptive recalibration to that observed by Cressman and Henriques (2009) and Salomonczyk et al. (2011) when a gradually introduced distortion was introduced with the same final 30° clockwise hand-cursor error discrepancy. These findings from chapter two suggest that learning processes engaged during gradual and abrupt adaptation of small (< 90°) visuomotor rotations do not affect the sensory consequences of such learning, suggesting further that motor adaptation is separate from proprioceptive recalibration. To further investigate the role of the visuomotor distortion, we examined the relationship between proprioceptive recalibration and the magnitude of the sensorimotor discrepancy (i.e. the difference between the desired or expected movement outcome and the actual movement outcome) experienced during visuomotor adaptation. As described in chapter three, we systematically manipulated the magnitude of the cursor distortion presented during reach training trials. Specifically, we examined if an increase in the size of the distortion would result in a consistent increase in the extent of proprioceptive recalibration (Salomonczyk et al., 2011). Participants completed three blocks of reach training trials with a rotated cursor that was displaced 30°, 50° and 70° clockwise with respect to the hand. Participants estimated the location of their unseen hand with respect to visual reference

markers as described previously after each reach training block. We found that participants' estimates of hand position were deviated more leftwards following reach training with an increasingly distorted cursor, such that after training with a 70° distortion, participants' sense of felt hand position had shifted 15° leftwards in the direction of movement adaptation (which represents approximately 20% of the magnitude of the hand-cursor distortion). Moreover, the motor aftereffects observed following each training block were consistent with those observed by Cressman and Henriques (2009) and Salomonczyk et al. (2012) and represented approximately 50% of the magnitude of the hand-cursor distortion. While the magnitude of the distortion predicted the relative changes in proprioceptive recalibration and movement aftereffects, no correlation between the two effects was observed. This was also the case in other work (Cressman & Henriques, 2009; Cressman et al., 2010; Salomonczyk et al., 2012). Thus, while both sensory and motor changes occur following visuomotor adaptation, and these changes are directly related to the magnitude of the visuomotor distortion, evidence strongly indicates separate, yet simultaneous, mechanisms underlying proprioceptive recalibration and movement adaptation.

6.1.2 Visuo-proprioceptive misalignment and recalibration

All of the findings discussed thus far suggest that proprioceptive recalibration arises from mechanisms independent of motor adaptation. Moreover, this independence holds true when the distortion consists of a cursor that is rotated or laterally displaced, both during active and passive hand displacements and across a wide variety of other parameters (Cressman & Henriques, 2009). Thus, differences between proprioceptive and motor recalibration may arise due to different error signals that each drive distinct changes in the CNS's representation of the body and world. To better investigate the differences in sensory recalibration and motor aftereffects following

adaptation to altered visual feedback of the hand (chapter four), we employed a learning paradigm that isolated the discrepancy between vision and proprioception (what we refer to as the *cross-sensory error* signal) from the sensorimotor error signal that is thought to drive visuomotor adaptation (Cressman & Henriques, 2010). In particular, participants' movements were constricted during reach training trials, such that the motor component and resulting sensorimotor error signal were removed. This was achieved by guiding participants' unseen hands towards a briefly presented target while they were exposed to discrepant visual and proprioceptive information regarding their hand position. Specifically, participants always saw the cursor move in the direction of the target but the position of the unseen hand was gradually deviated such that the path the hand actually travelled was eventually rotated 70° counter-clockwise from the cursor. Given that there was no goal-directed movement, participants did not experience a sensorimotor error signal as they never experienced a discrepancy between their intended and actual movement outcomes. Thus, with this paradigm, we could effectively explore whether mere exposure to a cross-sensory error signal is sufficient to induce changes to sensory and motor systems and if increasing the magnitude of the discrepancy affects motor and sensory changes as described in chapter three. Unlike our previous study (Salomonczyk et al., 2011), in which participants trained with an increasing visuomotor discrepancy when freely reaching to similar targets, participants exposed to only a cross-sensory error signal did not show greater recalibration or motor aftereffects following exposure training with an increased cross-sensory distortion (up to 70°). Regression analysis further revealed that while changes in reaches and bias were highly correlated, the magnitude of this cross-sensory error signal did not predict changes in reaches or proprioceptive bias. Thus, while the cross-sensory error signal appears to drive partial proprioceptive recalibration and movement adaptation even when there is no opportunity for voluntary

movement, the influence of this signal saturates at a relatively small (30° or less) distortion due to limits in how the CNS can update felt hand position (or modify body image).

6.1.3 Recalibration in Parkinson's disease

In addition to characterizing the relationship between proprioceptive recalibration and visuomotor adaptation along with the contribution of the sensorimotor and cross-sensory error signals to these processes, we sought to investigate the neural substrates underlying sensory and motor plasticity. The cerebellum has been strongly implicated in driving error-driven learning (including visuomotor adaptation to gradual perturbations), although this region has since been shown to not be involved in sensory adaptation (Block & Bastian, 2012). Given the evidence supporting the role of the basal ganglia in integrating sensory and motor information, along with consolidation of visuomotor adaptation, we chose to assess this region and its relationship to proprioceptive recalibration. To investigate the role of the basal ganglia in proprioceptive recalibration, we compared proprioceptive recalibration following adaptation to a gradually introduced perturbation between healthy older adults and patients with Parkinson's disease. That proprioceptive acuity has been reported to worsen following dopaminergic therapy (O'Suilleabhain et al., 2001) led us to also examine the role of dopaminergic therapy on motor adaptation and sensory recalibration by assessing performance in patients during the clinically defined "on" state (60 minutes following administration of medication) and "off" state (abstaining from medication for 12 hours). Results revealed that patients and healthy controls shared similar levels of adaptation consistent with recent findings). Moreover, patients shifted the position at which their hand felt aligned with the reference marker by nearly 8° during regardless of medication state, while age-matched controls shifted the position at which their hand felt aligned

with the reference marker by 5°, although this difference was not statistically different. Lastly, there was no difference in the precision of these estimates between patients and controls. Thus, we concluded that visuomotor adaptation and proprioceptive recalibration are retained in patients with PD and that the basal ganglia may not underlie this sensory shift. However, that a trend for greater recalibration was observed in patients suggests that these individuals may be relying more on salient visual information than proprioceptive input to guide movement (Adamovich et al., 2001). This may be due to impaired proprioceptive acuity that has been reported in PD. Further research is needed to better characterize and examine the processes underlying proprioceptive recalibration in patients with Parkinson's disease; for example, while aftereffects assessed < 1 hour following visuomotor adaptation indicate preserved function, previous studies suggest that savings or retention of learning is not retained even as little as 24 hours after learning (Marinelli et al., 2011). While the basal ganglia may not be involved in the initial learning of new sensorimotor mappings or proprioceptive shifts that accompany them, this region does appear involved in the retention and consolidation of motor learning. Thus, retention of proprioceptive recalibration deserves particular attention within this population and should be a target for future work.

6.2 CONCLUSIONS

Together, the present results suggest that one recalibrates proprioception in the trained hand following learning of a new visuomotor mapping. This recalibration is a robust phenomenon that occurs under a variety of contexts: in the left and right hands, following adaptation to gradual and abrupt perturbations, following adaptation to increasing visuomotor distortions, following visuomotor adaptation and exposure to a visuo-proprioceptive discrepancy, and even in

patients with neurodegenerative disease of the basal ganglia (PD). These proprioceptive changes in the estimates of hand position are only a fraction of the motor changes observed in the adapted hand. In fact, it is only when the sensorimotor error signal is removed during training trials, that we observe a correlation between sensory and motor plasticity. This suggests that the cross-sensory error signal gives rise to sensory changes and is able to influence motor adaptation (i.e., aftereffect reaches) to a certain extent. That motor adaptation can occur without corresponding recalibration of hand path geometry and even in individuals with no proprioceptive afferents (Bernier et al., 2005; Ingram et al., 2000) further suggests that mechanisms underlying the two processes are distinct and that proprioceptive recalibration of hand path and hand position may themselves be mediated by distinct mechanisms (Malfait et al., 2008; T. Wong & Henriques, 2009). While the sensorimotor error signal has been shown to predict changes in motor learning and proprioceptive recalibration, recent evidence also implicates the cross-sensory error signal in these processes; indeed, this signal may itself be sufficient to induce motor learning at small distortions. The role of this error signal should be considered in subsequent models of motor learning. Lastly, results from the PD study suggest that the basal ganglia and/or dopaminergic striatal pathways are not integral in mediating proprioceptive recalibration; thus, future targets of investigate include other regions involved in sensorimotor transformations (i.e. the parietal cortex). Importantly, current models of visuomotor adaptation must take into consideration the shift in felt sense of hand position in driving observed changes to subsequent motor commands.

While this body of work has provided considerable evidence to better characterize and understand how and why proprioception may be shifted to better match visual estimates of limb position, some questions remain to be answered. While the results from Chapter two suggest that proprioceptive

recalibration is not subject to limb specialization, the question of hemispheric involvement is still unanswered. The intermanual transfer of visuomotor adaptation suggests that each hemisphere may encode specific information, and this effect depends on which hand is trained with the visuomotor distortion (Wang & Sainburg, 2003). Could intermanual transfer of proprioceptive recalibration be possible? If so, is it bidirectional? Answers to such questions may provide valuable information as to how the brain handles the sharing of positional proprioceptive information in the context of visuomotor adaptation.

We have shown from previous work (Cressman & Henriques, 2009) and from Chapter four that proprioceptive recalibration is comparable around visual and proprioceptive markers; however, the type and location of markers could be expanded to include other proprioceptive markers (for example, using the untrained hand to estimate the location of the trained hand) and visual markers in other locations of the workspace. Such information would provide us with a better understanding of how proprioception and proprioceptive recalibration vary within the workspace environment and with markers of different sensory modalities. This is especially important for studies with clinical populations, including PD, as proprioceptive estimation around proprioceptive markers may differ from that around salient, visual markers.

Lastly, our evidence for the underlying mechanisms supporting visuomotor adaptation and proprioceptive recalibration are derived from behavioural methods. To better understand the neural substrates underlying these conditions, other techniques including neuroimaging, cellular recording and temporary lesion induction (i.e. with transcranial magnetic stimulation (TMS)) could be employed.

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APPENDIX A: INFORMED CONSENT FORMS

Study Name: Multisensory Interaction In Motor Control And Learning

Purpose of the Research: Our research team is interested in how people adapt movement of the arm towards visual targets or proprioceptive (felt but unseen hand) target, or estimate of the location or motion of their hand, under various circumstances and using multisensory information.

What You Will Be Asked to Do in the Research: You will be asked to reach or point toward visual targets displayed on a screen and/or point to your unseen other hand (felt target). In most tasks, you will be sitting comfortable in a chair, but some tasks, you will sit in a chair that swivels left and right while you aim your hand to a target.

Risks and Discomforts: We do not foresee any risks or discomfort from your participation in the research.

Benefits of the Research and Benefits to You: You will receive 3 credits for participation in this study.

Voluntary Participation: Your participation in the study is completely voluntary and you may choose to stop participating at any time. Your decision not to volunteer will not influence your relationship with us or anyone else at York University either now, or in the future.

Withdrawal from the Study: You can stop participating in the study at any time, for any reason, if you so decide. If you decide to stop participating, you will still be eligible to receive the promised pay for agreeing to be in the project. Your decision to stop participating, or to refuse to answer particular questions, will not affect your relationship with the researchers, York University, or any other group associated with this project. In the event you withdraw from the study, all associated data collected will be immediately removed from our computers.

Confidentiality: All information you supply and recording of your arm movements or judgments about hand location during the experiment will be held in confidence, your name will not appear in any report or publication of the research. Your data will be safely stored password protected computers in our locked laboratory and only research staff will have access to this information. We will keep your information and recording will be destroyed after the study has

been published. Confidentiality will be provided to the fullest extent possible by law.

Questions About the Research? If you have questions about the research in general or about your role in the study, please feel free to contact Dr. Denise Henriques either by telephone at (416) 736-2100, extension 77215 or by e-mail (deniseh@yorku.ca). This research has been reviewed and approved by the Human Participants Review Sub-Committee, York University's Ethics Review Board and conforms to the standards of the Canadian Tri-Council Research Ethics guidelines. If you have any questions about this process, or about your rights as a participant in the study, please contact the Sr. Manager & Policy Advisor for the Office of Research Ethics, 5th Floor, York Research Tower, York University (telephone 416-736-5914 or e-mail ore@yorku.ca).

Legal Rights and Signatures:

I_____, consent to participate in this study conducted by Dr. Denise Henriques and her research team. I have understood the nature of this project and wish to participate. I am not waiving any of my legal rights by signing this form. My signature below indicates my consent.

Signature_____   **Date**_____
Participant

Signature_____   **Date**_____
Principal Investigator

Study Name: Motor Control Deficits in Parkinson's Disease

Purpose of the Research: To assess reaching movements to visual and proprioceptive targets to better understand the possible deficits in processing proprioceptive information (felt sense) of arm position in generating movements.

What You Will Be Asked to Do in the Research: You will be seated and asked to grip the handle of a robot manipulandum to move a mouse cursor on a computer screen between different visual targets in one condition. In a second condition, you will be asked to estimate the location of your unseen hand after moving it along a robot-generated boundary. To assess the stage of your disease, you will also complete the motor exam of the Hoehn & Yahr Parkinson's Disease rating scale. This exam will take 15 min, and should be familiar to you.

Risks and Discomforts: We do not foresee any risks or discomfort from your participation in research.

Benefits of the Research and Benefits to You: You will be paid $20/hour for your time in the lab and will be reimbursed for travel expenses.

Voluntary Participation: Your participation in the study is completely voluntary and you may choose to stop participating at any time. Your decision not to volunteer will not influence the relationship you have with the researchers or with York University either now, or in the future.

Withdrawal from the Study: You can stop participating in the study at any time, for any reason, if you so decide. If you decide to stop participating, you will still be eligible to receive the promised pay for agreeing to be in the project. Your decision to stop participating, or to refuse to answer particular questions, will not affect your relationship with the researchers, York University, or any other group associated with this project. In the event you withdraw from the study, all associated data collected will be immediately destroyed.

Confidentiality: All information you supply during the research will be held in confidence and unless you specifically indicated your consent, you name will not appear in any report or publication of the research. We will measure your arm movements during the reaching conditions, and keep these data on computers for analysis; these computers are located in our locked laboratories and only the research staff will have access to this information. Once we have published the results, the data will be destroyed. Confidentiality will be provided to the fullest extent possibly by law.

Questions About the Research? If you have questions about the research in general or about your role in the study, please feel free to contact Dr. Denise Henriques either by telephone at (416) 736-2100, extension 77215 or by e-mail (deniseh@yorku.ca). This research has been reviewed and approved by the Human Participants Review Sub-Committee, York University's Ethics Review Board and conforms to the standards of the Canadian Tri-Council Research Ethics guidelines. If you have any questions about this process or about your rights as a participant in the study, please contact Ms. Alison Collins-Mrakas, Manager, Research Ethics, 309 York Lanes, York University (telephone 416-736-5914 or e-mail acollins@yorku.ca).

Legal Rights and Signatures:

I _____ consent to participate in the Motor Control Deficits in Parkinson's Disease study conducted by Dr. Henriques and her lab. I have understood the nature of this project and wish to participate. I am not waiving any of my legal rights by signing this form. My signature below indicates my consent.

Signature _____   **Date** _____
Participant

Signature _____   **Date** _____
Principal Investigator

University Health Network

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Title	Motor Control Deficits in Parkinson's Disease
Investigator	Dr. Anthony E. Lang
Co-Investigators	Dr. Denise Henriques, Dr. Howard Poizner, Danielle Salomonczyk, Dr. Alina Constantin, Dr. Janis Miyasaki, Dr. Elena Moro, Dr. Robert Chen, Dr. Antonio Strafella, Dr. Susan Fox, Dr. Connie Marras
Sponsor	York University

Introduction

You are being asked to take part in a research study. Please read this explanation about the study and its risks and benefits before you decide if you would like to take part. You should take as much time as you need to make your decision. You should ask the study doctor or study staff to explain anything that you do not understand and make sure that all of your questions have been answered before signing this consent form. Before you make your decision, feel free to talk about this study with anyone you wish. Participation in this study is voluntary.

Background and Purpose

Although the motor symptoms of Parkinson's (PD) are the most obvious, PD patients also exhibit loss of sensation, an impairment that can contribute to problems in controlling movements. The extent of this loss of sensation in PD and its relationship to observed motor impairment remains unclear. It is also unclear whether sensory function is improved or, as a recent report suggests, is even worsened by dopaminergic medications. This study will assess reaching movements to visual and proprioceptive targets to better understand the possible deficits in processing proprioceptive information (felt sense) of arm position in

generating movements. The project will also assess whether dopamine replacement therapy worsens body awareness as some research has suggested. You have been asked to take part in this research study because you are between the ages of 40 and 80 years old and you have been diagnosed with Parkinson's disease. About 20 patients from the Toronto Western Hospital – Movement Disorders Centre and 20 age-matched control participants will take part in this study.

Study Visits and Procedures

During the study you will be seated and asked to grip the handle of a robot manipulandum to move a mouse cursor on a computer screen between different visual targets in one condition. In a second condition, you will be asked to estimate the location of your unseen hand after moving it along a robot-generated boundary. To assess the stage of your disease, you will also complete the motor exam of the Hoehn & Yahr Parkinson Disease rating scale. This exam will take 15 min, and should be familiar to you.

This study involves 4 to 6 visits to York University. You will be required to travel to York University for all study procedures. Again you will be reimbursed for your travel costs. Each visit will last for 1 hour to 2.5 hours.

Half of the visits will be carried out during the practically defined "off" medication state. In the "off state" you will be asked to stop taking your Parkinson's medications the night before your study visit. You will re-start your medication once the visit is over. The practically defined "off" state is safely and routinely done for the evaluation of PD patients undergoing pre-surgical evaluations. You will be off your Parkinson's medication for no more than 15 hours. Half of the visits will be done when you are in the "on state". The "on state" is when you feel you have the best response after taking your Parkinson's medication.

Risks Related to Being in the Study

It is not expected that you will be exposed to any greater risks to your personal wellbeing than at a regular clinic visits. The possible risks encountered during the course of this study may be associated to discomfort related with not taking Parkinson's medications overnight prior to the study visit and during testing. These discomforts include increased stiffness, rigidity, and tremor.

Benefits to Being in the Study

You will not receive any direct benefit from being in this study. Information

learned from this study may help other people with Parkinson's disease in the

future.

Voluntary Participation

Your participation in this study is voluntary. You may decide not to be in this study, or to be in the study now and then change your mind later. You may leave the study at any time without affecting your care.

If you decide to stop participating, you will still be eligible to receive the promised pay for agreeing to be in the project. Your decision to stop participating, or to refuse to answer particular questions, will not affect your relationship with the researchers, York University, or any other group associated with this project.

We will give you new information that is learned during the study that might affect your decision to stay in the study.

Confidentiality

If you agree to join this study, the study doctor and his/her study team will look at your personal health information and collect only the information they need for the study. Personal health information is any information that could be used to identify you and includes your:
- name,
- address,
- date of birth,
- new or existing medical records, that includes types, dates and results of medical tests or procedures.

The information that is collected for the study will be kept in a locked and secure area by the study doctor for 10 years. Only the study team or the people or groups listed below will be allowed to look at your records. Your participation in this study also may be recorded in your medical record at this hospital.

The following people may come to the hospital to look at the study records and at your personal health information to check that the information collected for the study is correct and to make sure the study followed proper laws and guidelines:
- Representatives of the study organizing committee.
- University Health Network Research Ethics Board.

All information collected during this study, including your personal health information, will be kept confidential and will not be shared with anyone outside the study unless required by law. Any information about you that is sent out of the hospital will have a code and will not show your name or address, or any information that directly identifies you. You will not be named in any reports, publications, or presentations that may come from this study.

If you decide to leave the study, the information about you that was collected before you left the study will still be used. No new information will be collected without your permission.

In Case You Are Harmed in the Study

If you become ill, injured or harmed as a result of taking part in this study, you will receive care. The reasonable costs of such care will be covered for any injury, illness or harm that is directly a result of being in this study. In no way does signing this consent form waive your legal rights nor does it relieve the investigators, sponsors or involved institutions from their legal and professional responsibilities. You do not give up any of your legal rights by signing this consent form.

Expenses Associated with Participating in the Study

You will not have to pay for any of the procedures involved with this study. You will be paid $20/hour for your time in the lab and will be reimbursed for travel expenses.

Questions About the Study

If you have any questions, concerns or would like to speak to the study team for any reason, please call: the Principal Investigator, Dr. Anthony Lang at (416) 603-6422 or the Co-investigator, Dr. Denise Henriques, (York University) at (416) 736-2100, extension 77215.

If you have any questions about your rights as a research participant or have concerns about this study, call Ronald Heslegrave, Ph. D., Chair of the University

Health Network Research Ethics Board (REB) or the Research Ethics office number at 416-946-4438. The REB is a group of people who oversee the ethical conduct of research studies.These people are not part of the study team. Everything that you discuss will be kept confidential.

Consent

This study has been explained to me and any questions I had have been answered.
I know that I may leave the study at any time. I agree to take part in this study.

_____   _____   _____

Print Study Participant's Name   Signature   Date

(You will be given a signed copy of this consent form)

My signature means that I have explained the study to the participant named above. I have answered all questions..

_____   _____   _____

Print Name of Person Obtaining Consent   Signature   Date

Was the participant assisted during the consent process? ☐ **YES** ☐ **NO**

If **YES**, please check the relevant box and complete the signature space below:

☐ The person signing below acted as a translator for the participant during the consent process and attests that the study as set out in this form was accurately translated and has had any questions answered..

_____   _____   _____

Print Name of Translator   Signature   Date

_____   _____

Relationship to Participant   Language

☐ The consent form was read to the participant. The person signing below
attests that the study as set out in this form was accurately explained to, and
has had any questions answered.

_____   _____   _____
Print Name of Witness   Signature   Date

_____
Relationship to Participant

APPENDIX B: AUTHOR CONTRIBUTIONS

Chapter 2:

Salomonczyk, D., Henriques, D.Y.P., & Cressman, E.K. (2012). Proprioceptive recalibration in the right and left hands following abrupt visuomotor adaptation. *Experimental Brain Research, 217* (2), 187-196.

Danielle Salomonczyk: Conceived and designed the experiments; performed the experiments; analyzed the data; contributed materials/analysis tools; wrote the manuscript.

Denise Henriques: Conceived and designed the experiments; contributed materials/analysis tools, assisted with preparation of the manuscript.

Erin Cressman: Conceived and designed the experiments; contributed materials/analysis tools, assisted with preparation of the manuscript.

Assistance with data collection provided by Orysia Kachmarchuk; materials and/or analysis tools provided by John Stemberger.

Chapter 3:

Danielle Salomonczyk: Conceived and designed the experiments; performed the experiments; analyzed the data; contributed materials/analysis tools; wrote the manuscript.

Denise Henriques: Conceived and designed the experiments; contributed materials/analysis tools, assisted with preparation of the manuscript.

Erin Cressman: Conceived and designed the experiments; contributed materials/analysis tools, assisted with preparation of the manuscript.

Assistance with data collection provided by Mohsin Mian; materials and/or analysis tools provided by John Stemberger, Edgar Edj.

Chapter 4:

Danielle Salomonczyk: Conceived and designed the experiments; performed the experiments; analyzed the data; contributed materials/analysis tools; wrote the manuscript.

Denise Henriques: Conceived and designed the experiments; contributed materials/analysis tools, assisted with preparation of the manuscript.

Erin Cressman: Conceived and designed the experiments, contributed materials/analysis tools, assisted with preparation of the manuscript.

Materials and/or analysis tools provided by Ivan Djokic.

Chapter 5:

Danielle Salomonczyk: Conceived and designed the experiments; performed the experiments; analyzed the data; contributed materials/analysis tools; wrote the manuscript.

Denise Henriques: Conceived and designed the experiments; contributed materials/analysis tools, assisted with preparation of the manuscript.

Erin Cressman: Conceived and designed the experiments; contributed materials/analysis tools, assisted with preparation of the manuscript.

Materials and/or analysis tools provided by Ivan Djokic, John Stemberger, Kemar Trenchfield; Critical feedback for manuscript provided by Howard Poizner

Chapter 6:

Salomonczyk, D., Cressman, E.K., Henriques, D.Y.P. (2013). Motor Adaptation and Proprioceptive Recalibration. in *Plasticity in Sensory Systems*, ed. M. Jenkin, J.K.E. Steeves, and L.R. Harris. Cambridge University Press.

Danielle Salomonczyk: Wrote the paper with assistance of Erin Cressman and Denise Henriques

APPENDIX C: RELEVANT OFFPRINTS

RESEARCH ARTICLE

Proprioceptive recalibration in the right and left hands following abrupt visuomotor adaptation

Danielle Salomonczyk · Denise Y. P. Henriques ·
Erin K. Cressman

Abstract Previous studies have demonstrated that after reaching with misaligned visual feedback of the hand, one adapts his or her reaches and partially recalibrates proprioception, such that sense of felt hand position is shifted to match the seen hand position. However, to date, this has only been demonstrated in the right (dominant) hand following reach training with a visuomotor distortion in which the rotated cursor distortion was introduced gradually. As reach adaptation has been shown to differ depending on how the distortion is introduced (gradual vs. abrupt), we sought to examine proprioceptive recalibration following reach training with a cursor that was abruptly rotated 30° clockwise relative to hand motion. Furthermore, because the left and right arms have demonstrated selective advantages when matching visual and proprioceptive targets, respectively, we assessed proprioceptive recalibration in right-handed subjects following training with either the right or the left hand. On average, we observed shifts in felt hand position of approximately 7.6° following training with misaligned visual feedback of the hand, which is consistent with our previous findings in which the distortion was introduced gradually. Moreover, no difference was observed in proprioceptive recalibration across the left and right hands. These findings suggest that proprioceptive recalibration is a robust process that arises symmetrically in the two hands following visuomotor adaptation regardless of the initial magnitude of the error signal.

Keywords Proprioception · Visuomotor adaptation · Sensory recalibration · Vision · Learning · Plasticity

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Introduction

The central nervous system (CNS) integrates visual and proprioceptive information when planning a movement. If these sensory cues conflict and one is reaching to a visual target, one tends to rely more on the visual estimate of the hand than on the actual or felt position to guide motor output. For example, subjects reaching to a visual target with misaligned visual feedback of the hand (e.g. reaching in a virtual-reality environment or while wearing prism goggles) adjust their movements in order for the visual representation of the hand to achieve the desired endpoint. Furthermore, subjects reach with these adapted movement patterns following removal of the distortion (i.e. exhibit aftereffects; Martin et al. 1996; Krakauer et al. 1999; Krakauer et al. 2000; Baraduc and Wolpert 2002; Buch et al. 2003). This form of motor learning is referred to as visuomotor adaptation.

In addition to visuomotor adaptation, reaching with misaligned visual feedback of the hand has been shown to result in changes in sense of felt hand position (i.e. proprioceptive recalibration). Specifically, proprioceptive recalibration has been suggested to arise following reaches made

while wearing prism goggles, where the visual distortion is introduced immediately and in full (Harris 1963; Hay and Pick 1966), and following reaches made in a virtual-reality environment (Cressman and Henriques 2009; Cameron et al. 2010; Ostry et al. 2010; Simani et al. 2007). Until recently, this sensory recalibration was demonstrated following visuomotor adaptation by asking subjects to reach with the adapted hand to proprioceptive targets (Redding and Wallace 1996; van Beers et al. 2002; Simani et al. 2007). While results from these tasks indicated that reaches to proprioceptive targets were adapted, it is unclear whether these changes in reaches reflected proprioceptive recalibration per se. Given that subjects used their adapted arm, these resulting reaching movements to localize proprioceptive targets could have been influenced by motor adaptation. Thus, in attempt to assess proprioceptive recalibration independent of motor changes, Henriques and colleagues (Cressman and Henriques 2009, 2010; Cressman et al. 2010; Salomonczyk et al. 2011) and Ostry et al. (2010) designed sensory estimation tasks that do not require any goal-directed movement. Specifically, in Cressman and Henriques' (2009) estimation task, subjects indicated the position of their hand relative to a visual or proprioceptive reference marker. In general, results revealed that subjects shifted the position at which they felt their hand was aligned with a reference marker ~6° (or about 20% of the visuomotor distortion), in the direction that they adapted their movement following reaches with a gradually introduced visuomotor distortion (Cressman and Henriques 2009, 2010; Cressman et al. 2010; Salomonczyk et al. 2011). This shift in felt hand position has been shown to be remarkably consistent across several parameters, including the type of distortion (rotation vs. lateral displacement), the magnitude of the distortion (up to 70°), the extent of reach training (up to 300 trials), the type of reference marker (visual vs. proprioceptive), method of hand positioning (active vs. passive placement of the hand), and even across different age groups (young adults vs. adults 60 years and older).

Previous work from our laboratory examining sensory changes following motor adaptation has introduced the visuomotor perturbation (e.g. a visuomotor rotation around the hand) gradually during adaptation trials. In the current study, we sought to determine whether the size of the initial error signal influences sensory recalibration. To address this question, we introduced the visuomotor distortion abruptly, such that subjects initially experienced large reaching errors. To date, research comparing adaptation to large and small error signals has focused on examining resulting changes in movements, without a similar investigation into sensory changes. With respect to visuomotor adaptation, results indicate that motor learning (aftereffects) is greater in subjects who train to reach with misaligned

sensory feedback of the hand when the distortion is introduced gradually and subjects experience small reaching errors compared to when the distortion is introduced abruptly and subjects initially experience large reaching errors after subjects reach while wearing prism goggles (Michel et al. 2007), with a visuomotor rotation (Kagerer et al. 1997; Abeele and Bock 2001) or with a force perturbation (Criscimagna-Hemminger et al. 2010). Furthermore, retention of motor learning is reportedly greater in subjects that adapt to an incrementally introduced distortion compared with an abruptly introduced one (Klassen et al. 2005). By establishing whether proprioceptive recalibration arises following adaptation to an abrupt visuomotor distortion, we will be able to determine whether the size of initial error signals experienced also affects sensory plasticity.

Additionally, we sought to determine whether proprioceptive recalibration is comparable between the left and right hands of right-handed individuals. Previous studies examining proprioceptive recalibration have focused on assessing shifts in felt right-hand position following motor learning of the right arm in right-handed individuals. Given that Goble and colleagues (Goble and Brown 2008; Goble and Anguera 2010) have recently shown that the left arm performs better for matching proprioceptive targets and the right arm for visual targets, reaching with misaligned visual feedback may have different effects on proprioceptive recalibration in the two arms. For example, the left arm, which has demonstrated an advantage for position-related proprioceptive sense in comparison with the right arm, may be more susceptible to sensory recalibration. If we do find an arm effect of proprioceptive recalibration, it would suggest hemispheric asymmetry for encoding visual and proprioceptive information.

Methods

Subjects

Forty-six right-handed young adults (mean age = 21.0 years, SD = 3.58, 29 women) were recruited from York University and volunteered to participate in the tasks described below. Data from three subjects were eliminated from analyses and hence not included in the results provided, as they were unable to consistently report the position of their hand in space (i.e. their uncertainty ranges (defined below) were greater than 3 times the average uncertainty range). Subjects were pre-screened verbally for self-reported handedness and any history of visual, neurological, and/or motor dysfunction. Following pre-screening, subjects were randomly assigned to either the right-hand training (n = 20) or left-hand training (n = 26; analysis with n = 23) groups. All subjects provided informed consent in
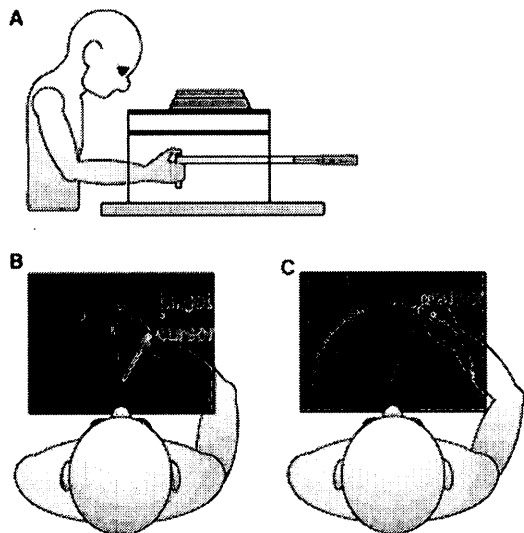
Fig. 1 Experimental set-up and design. a Side view of the experimental set-up. b–c Top view of the experimental surface visible to subjects. b Visuomotor distortion introduced in the rotated Reach Training Task. The *cursor* representing the hand was rotated 30° clockwise with respect to the actual hand location (*circle*). Reach targets (*circles*) were located at 0° in line with body midline and 30° *left* and *right* of body midline. c Reference markers (*circles*) were located at 30° *left* and *right* of midline. The grooved path along which the subjects' unseen hand travelled is represented by the *rectangle*

accordance with the ethical guidelines set by the York Human Participants Review Subcommittee.

General experimental set-up

A side view of the set-up is provided in Fig. 1a and is similar to the set-up used in Cressman and Henriques (2010) and Cressman et al. (2010). Subjects were seated in a

height-adjustable chair so that they could comfortably see and reach to all target and marker locations presented on an opaque, reflective surface. Subjects grasped the vertical handle of a two-joint robot manipulandum mounted in the horizontal plane (Interactive Motion Technologies). Visual stimuli were projected from a monitor (Samsung 510N, refresh rate 72 Hz) installed 17 cm above the robot onto a reflective surface aligned in the same horizontal plane as the robot. The room lights were dimmed, and subjects' view of their hand was blocked by the reflective surface and a black cloth draped between the experimental set-up and subjects' shoulders.

General procedure

Similar to our previous study (Cressman and Henriques 2009), the experiment consisted of two separate testing sessions completed on two separate days. Each testing session involved two tasks. On the first testing day, subjects completed the reaching trials outlined below while seeing a green cursor disc 1 cm in size that was aligned with their unseen hand. On the second testing day, subjects completed the reaching trials while viewing a cursor that was misaligned from the actual location of their unseen hand (Fig. 1b). The misaligned cursor was rotated 30° clockwise (CW) relative to actual hand position, with the origin of the rotation at the starting hand position. The cursor was represented by a green disc 1 cm in diameter (Fig. 1b). The descriptions and order of tasks are outlined below and in Fig. 2.

Training and adaptation

While grasping the robot manipulandum with either the right or left hand, subjects were instructed to reach to a yellow visual target disc, 1 cm in size, as quickly and accurately as possible while viewing either an aligned (first
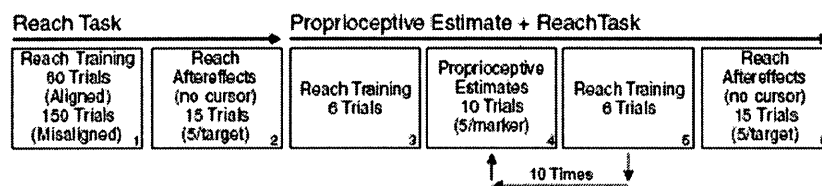
Fig. 2 Breakdown of the testing sessions within the experiment. In the first testing session, subjects reached with an aligned cursor that accurately represented the position of their hand in the reach training trials. In the second testing session, subjects reached with a misaligned cursor that was rotated 30° clockwise with respect to the actual hand location during the reach training trials. Using their *right* or *left* hand, subjects began a testing session by reaching to visual targets with a *green* cursor that provided visual feedback of hand position (*Box 1*). After completing either 60 (*aligned* cursor) or 150 (*misaligned* cursor) reach training

trials, subjects next reached to each of the three targets 5 times without a cursor in order to assess visuomotor adaptation (reach aftereffects trials, *Box 2*). Subjects then completed 6 reaches to the reach targets with the cursor present (*Box 3*). This was followed by 10 sets of 10 proprioceptive estimate trials (*Box 4*) and 6 visually guided reaches (*Box 5*) for a total of 100 proprioceptive estimate and 60 reach training trials. Following this, subjects again reached to each of the three targets 5 times without a cursor in order to assess maintenance of visuomotor adaptation (*Box 6*)

testing session) or misaligned (second testing session) cursor that moved with their hand. The reach targets were located radially 10 cm from the home position at 0° (centre), 30° left (CCW) and 30° right (CW) of centre (circles in Fig. 1b). The home position was located approximately 40 cm in front of the subjects along their body midline (indicated by the black circle in Fig. 1b). This position was not illuminated, and visual feedback was provided only when the hand had travelled 4 cm outwards from the home position. The reach was considered complete once the centre of the cursor had moved to within 0.5 cm of the target's centre. At this point, both the cursor and target discs disappeared and subjects moved their hands back to the home position in the absence of visual feedback along a linear route. If subjects attempted to move outside of the established path, a 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 path wall (Henriques and Soechting 2003; Cressman and Henriques 2009; Jones et al. 2010).

Each session began with subjects completing either 60 reaches with an aligned cursor (1st session) or 150 reaches with the misaligned cursor (2nd session) (box 1 in Fig. 2). Afterwards, subjects reached to the same targets 5 times each without cursor feedback for a total of 15 trials (box 2 in Fig. 2) to assess visuomotor adaptation (i.e. aftereffects in the second testing session). Subjects then reached again with the aligned or misaligned cursor for an additional 6 trials (box 3 in Fig. 2). Following these reaching trials, we began to assess subjects' estimates of hand position (box 4 in Fig. 2) as described below.

Proprioceptive estimate trials + reach trials

A proprioceptive estimate trial began with the subject grasping the robot manipulandum at the home position, which was indicated by a 1-cm green disc. After 500 ms, this disc disappeared and the subject was instructed to push his or her hand outward along a constrained robot-generated linear path (as described previously and shown by the rectangle in Fig. 1c). On all trials, once the hand reached the end of the path, a reference marker located 30° left (CCW) or 30° right (CW) of centre represented by a circle 1 cm in diameter appeared (circles, Fig. 1c) and subjects made a two-alternative forced-choice judgment about the position of their hand (left or right) relative to the reference marker. There was no time constraint for giving a response. After responding, the reference marker disappeared and the subject moved the robot directly back to the home position along a linear route to begin the next trial.

The position of the hand with respect to each reference marker was adjusted over trials using an adaptive staircase algorithm (Kesten 1958; Treutwein 1995) as described by

Cressman and Henriques (2009). Subjects alternated between 10 proprioceptive estimate trials and 6 reach trials with cursor feedback for a total of 100 proprioceptive estimate trials and 60 reaching trials (boxes 3–5 in Fig. 2). Subjects then reached 15 more times without the cursor (box 6 in Fig. 2) as a final measure of reach adaptation.

Data analysis

Visuomotor adaptation

Directional deviations of the hand made during reaching trials without visual feedback were analysed to assess motor adaptation. Reach endpoint errors were defined as the angular difference between a movement vector (from the home position to reach endpoint) and a reference vector (from the home position to the target). Reach errors at peak velocity were defined as the angular difference between a movement vector joining the home position and the position of the hand at peak velocity and the reference vector. Both errors at reach endpoint and at peak velocity were analysed to determine whether subjects adapted their reaches to the targets after aiming with a rotated cursor, and whether there was any change in reach adaptation following the proprioceptive estimate trials. Analyses were conducted using separate 2 Group (right-hand group vs. left-hand group) × 2 Feedback condition (aligned vs. misaligned cursor) × 2 Epoch (preceding proprioceptive estimate trials vs. following proprioceptive estimate trials) × 3 Target (30° CW vs. 0° vs. 30° CCW) mixed repeated measures analysis of variance (RM-ANOVA). Group was treated as a between-subjects factor, while all others were treated as within-group factors. A Bonferroni correction was applied to post hoc pairwise comparisons.

Proprioceptive estimates of hand position

A logistic function was fitted to each subject's responses for each reference marker in each testing session in order to determine the location at which subjects perceived their hand to be aligned with a reference marker. From this logistic function, we calculated the bias (the point at which the probability of responding left was 50%) and uncertainty (the difference between the values at which the probability of responding left was 25 and 75%). The bias value is a measure of subjects' accuracy of proprioceptive sense of hand position, while the magnitude of the uncertainty range defines its precision (Cressman and Henriques 2009, 2010). A 2 Group (right-hand group vs. left-hand group) × 2 Feedback condition (aligned vs. misaligned cursor) × 2 Marker location (30° CW vs. 30° CCW) mixed RM-ANOVA was used to compare bias and uncertainty values following reach training with the right and left hands. Group was

treated as a between-subjects factor, while all others were treated as within-group factors. Proprioceptive recalibration was examined by comparing the bias values after training with a misaligned cursor with those following an aligned cursor (baseline). A Bonferroni correction was applied to all post hoc pairwise comparisons.

Results

Visuomotor adaptation

Directional endpoint reach errors made following reach training (i.e. before the proprioceptive estimation trials) are presented in Fig. 3a. After training with an aligned cursor, subjects in the left-hand group (open squares) had reach errors that were on average 2° leftwards of the targets and subjects in the right-hand group (open triangles) made reach errors that were on average 1° to the right of the targets. This is consistent with estimates of hand position (see Fig. 4a for bias results) and previous work suggesting that an inherent systematic bias exists in the two hands when reaching to targets (Jones et al. 2010; Wilson et al. 2010). After training with a rotated cursor (filled symbols), subjects in both groups had reach errors that deviated more leftwards than after training with an aligned cursor (filled symbols). Figure 3b depicts the mean changes in endpoint errors for the left- and right-hand groups preceding proprioceptive estimates trials (empty bars) and following the proprioceptive estimate trials (filled bars) relative to baseline performance (i.e. errors achieved on the first day of testing after training with an aligned cursor were subtracted from

errors achieved after reaching with a rotated cursor), along with endpoint errors from Cressman and Henriques (2009). A significant change in average reach aftereffects from aligned to misaligned training was observed ($F(1, 41) = 244.5$, $P < .001$). Aftereffects observed in the left-hand group did not differ from those observed in the right-hand group ($F(1, 41) = 1.63$, $P = .21$). In addition, these aftereffects are consistent with previous results following a gradually introduced misaligned reach cursor (Cressman and Henriques 2009). Analysis of the epoch factor revealed greater reach aftereffects following the proprioceptive estimate trials (14° and 17° for the left- and right-hand groups, respectively) compared to those preceding the proprioceptive estimate trials (12° and 13° for the left- and right-hand groups, respectively; $F(1, 41) = 12.76$, $P = .001$). This pattern was consistent for both groups ($F(1, 41) < 1$, $P = .35$). While larger aftereffects were also observed in Cressman and Henriques (2009) following proprioceptive estimate trials compared to those preceding proprioceptive estimates trials, this difference did not achieve statistical significance. Lastly, there was a significant effect of target ($F(2, 82) = 19.32$, $P < .001$) such that reaching errors around the lateral targets were slightly compressed towards the central workspace (i.e. reaching errors tended to be to the left of the CW target and right of the CCW target), although this effect did not differ between aligned and rotated conditions ($F(2, 82) = 2.63$, $P = .07$).

Reach aftereffects at peak velocity were analysed and revealed a similar pattern of results (Fig. 3b, circles). After training with a rotated cursor, subjects reached significantly more leftwards of the target than after training with an aligned cursor ($F(1, 41) = 154.71$, $P < .001$).

Fig. 3 Reaching errors for the *left-* and *right-*hand groups. a Mean 2-D representation of movement endpoint errors for the *left-(squares)* and *right-(triangles)* hand groups after training with aligned (*empty symbols*) and misaligned (*filled symbols*) visual feedback of the hand. The target locations are represented as *filled grey circles*. b Mean change in directional reach endpoint errors (*bars*) and errors at peak velocity (*circles*) after reaching with misaligned visual feedback of the

hand for the *left-* and *right-*hand groups and data from Cressman and Henriques (2009). Values reflect baseline-subtracted aftereffect errors preceding proprioceptive estimate trials (*empty bars* and *black outlined circles*) and following proprioceptive estimate trials (*filled bars* and *white outlined circles*). Aftereffects of 30° would reflect 100% adaptation. *Error bars* reflect standard error of the mean

Fig. 4 Proprioceptive estimates for the *left-* and *right-*hand groups. **a** Mean angular biases in the proprioceptive estimate trials for the *left* (*squares*) and *right* (*triangles*) hand groups following training with aligned (*empty symbols*) and misaligned (*filled symbols*) visual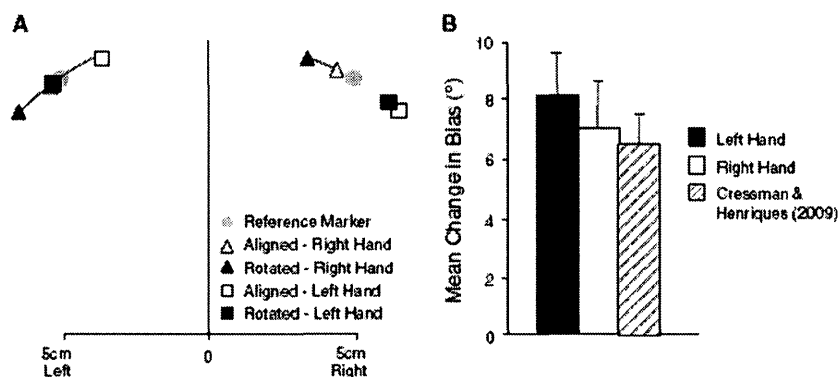 feedback of the hand. The actual reference marker positions are represented as *filled grey circles* and a line connects each proprioceptive estimate of hand position after training with an aligned and rotated cursor for either the *left* or *right* hand with its corresponding reference marker. **b** Mean changes in bias for the *left-* and *right-*hand groups, as well as from subjects from Cressman and Henriques (2009), averaged across reference marker positions and subjects. *Error bars* reflect standard error of the mean

These aftereffects were comparable across groups ($F(1, 41) = 3.07$, $P = .08$). As with endpoint aftereffects, aftereffects at peak velocity following proprioceptive estimates ($11.8°$ and $16.8°$ for the left- and right-hand groups, respectively) were greater than those preceding proprioceptive estimates trials ($9.1°$ and $11.0°$ for the left- and right-hand groups, respectively; $F(1, 41) = 6.89$, $P = .01$). This pattern was again consistent for both groups ($F(1, 41) < 1$, $P = .35$), although the compression of reaching errors around the targets towards the centre was only observed for reaches made following aligned training ($F(2, 28) = 18.94$, $P < .001$). The similarity between directional reach errors at peak velocity and reach endpoint suggests that subjects did not make online corrections to their reach trajectories in the absence of visual feedback of hand position.

Proprioceptive estimates of hand position

Bias

Figure 4a depicts the positions at which subjects in the left- and right-hand groups perceived their hands to be aligned with the reference markers after training with an aligned (empty symbols) and misaligned cursor (filled symbols). Estimates of hand position following training with aligned cursor feedback significantly differed between left- and right-hand groups ($F(1, 41) = 70.12$, $P < .001$). Specifically, subjects in the left-hand group judged their hand to be in line with the reference marker when it was $9°$ to the right of it, while subjects in the right-hand group estimated their hand to be in line with the reference marker when it was $3°$ to the left of it. These results

are in agreement with previous hand biases observed when subjects were asked to judge the position of their hand prior to any reach training: subjects estimated their right hand was more rightwards than it actually was and their left hand was more leftwards than it actually was (Jones et al. 2010). Figure 4b depicts the mean change in bias for the left (filled bar) and right (empty bar) hand groups. On average, the position at which subjects' felt their hand coincided with the reference marker was shifted leftwards by $7.6°$ after training with a misaligned cursor compared to after reaching with an aligned cursor ($F(1, 37) = 69.56$, $P < .001$). This shift is consistent with changes observed by Cressman and Henriques (2009; Fig. 4b, patterned bar), in which subjects estimated the position of their right hand following reach training trials in which the visuomotor distortion was gradually introduced. In the present study, post hoc tests revealed that subjects in both groups recalibrated their proprioceptive estimates of hand position around the $30°$ CW and $30°$ CCW reference markers ($P < .005$ for all contrasts). No differences in estimates between the left and right reference marker locations were observed between conditions for the right-hand group, suggesting that recalibration was comparable across the locations; however, estimates following rotated training were different between the two reference marker locations for the left-hand group, suggesting that subjects experienced greater recalibration around the CCW marker ($11°$) than the CW marker ($4°$; $P = .01$). This effect does not appear to be dependent on initial proprioceptive estimates as there was no difference in biases following reaches with the aligned cursor between the two reference markers for the left-hand group (CCW marker $= 8.9°$, CW marker $= 9.0°$; $P = .95$).
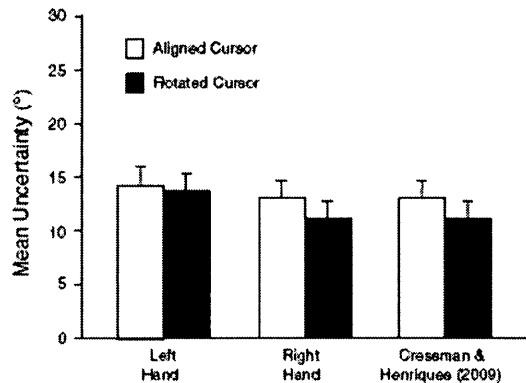
Fig. 5 Magnitude of the uncertainty ranges in the proprioceptive estimate trials for the *left*- and *right*-hand groups and data from Cressman and Henriques (2009) averaged across reference marker positions and subjects after reaching with an aligned cursor (*empty bars*) or misaligned cursor (*filled bars*). *Error bars* reflect standard error of the mean

Fig. 6 Mean changes in proprioceptive biases and aftereffects after reach training with a misaligned cursor compared to an aligned cursor. The mean change in bias (*bars*) is plotted along with the mean change in aftereffects (*diamonds*) for the *left*- and *right*-hand groups. Results are shown in degrees and as a percentage of the distortion introduced during reach training trials. *Error bars* reflect standard error of the mean

Uncertainty

Figure 5 depicts the magnitude of the uncertainty ranges for the left- and right-hand groups following reaches made with aligned (empty bars) and misaligned (filled bars) cursor feedback. Subjects' levels of precision in estimating the location of their unseen hands were comparable after reach training with an aligned and misaligned cursor ($F(1, 41) = <1$, $P = .40$), at all reference markers ($F(1, 41) = <1$, $P = .93$). Precision of estimates did not differ between the two groups ($F(1, 41) < 1$, $P = .24$). These results are in accordance with previous results following adaptation to a gradually introduced distortion (Cressman and Henriques 2009).

Visuomotor adaptation vs. proprioceptive recalibration

Figure 6 shows a summary of the changes in proprioceptive recalibration (bias) and reach adaptation (aftereffects) following training with a misaligned cursor as a percentage of the visuomotor distortion introduced and with respect to the overall magnitude of the distortion introduced (i.e. 30°). Specifically, Fig. 6 depicts the mean changes in proprioceptive biases (bars) and reach endpoint aftereffects (diamonds) following training with a misaligned cursor compared to training with an aligned cursor for each group. From this figure, we see that on average, subjects recalibrated proprioception by approximately 25% of the distortion introduced. In addition, after training with the misaligned cursor, subjects showed aftereffects equal to approximately 50% of the distortion introduced. We subsequently examined the relationship between the motor
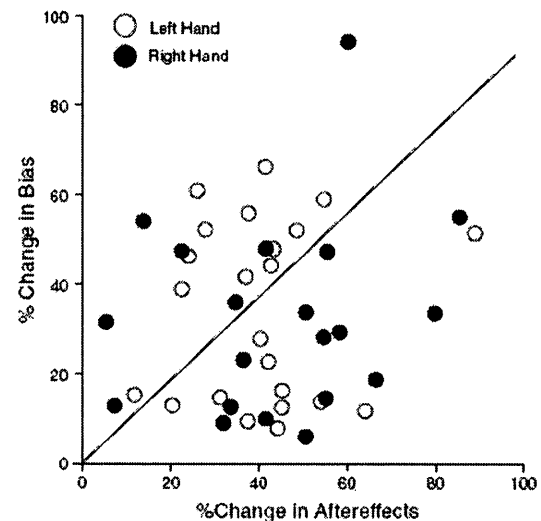
Fig. 7 Changes in proprioceptive biases and aftereffects are expressed as a percentage of the visuomotor distortion introduced for the *left*- (*empty circles*) and *right*-hand groups (*filled circles*). The *solid line* is a unit slope and so indicates equivalent levels of proprioceptive recalibration and visuomotor adaptation

changes (aftereffects) and sensory changes (proprioceptive recalibration) expressed as a percentage of the visuomotor distortion introduced using a bivariate correlation (Fig. 7). Consistent with previous works (Cressman and Henriques 2009; Salomonczyk et al. 2011), results revealed that all subjects adapted their movements and recalibrated proprioception, though a significant relationship between these changes was not observed ($r = .052$, $P = .74$).

Discussion

The present study examined whether proprioceptive recalibration occurs following visuomotor adaptation to an abrupt distortion and whether this recalibration is comparable across the left and right hands of right-handed individuals. On average, subjects adapted their reaches by 14° and recalibrated the position at which they felt their hand was aligned with a reference marker by 7.6° after training with a rotated cursor compared to reach training with an aligned cursor. This change in felt hand position was in the same direction that subjects' adapted their reaches during reach training and was approximately 25% of the magnitude of the visuomotor distortion introduced. These results address our first question of interest and suggest that proprioceptive recalibration does occur following visuomotor adaptation to an abrupt distortion. Given that subjects in both groups adapted their reaches and recalibrated, proprioception around all targets and reference markers indicates that proprioceptive recalibration occurs comparably in the left and right hands, which addresses our second question of interest. Furthermore, our findings for our right-hand group replicate those of Cressman and colleagues (Cressman and Henriques 2009, 2010) wherein proprioceptive recalibration was observed following adaptation to a visuomotor distortion that was introduced gradually. In fact, recalibration was comparable in magnitude across these studies (approximately 7° leftwards), regardless of both the hand used and whether the perturbation was introduced gradually or abruptly.

Effect of initial error on recalibration

We found similar changes in hand proprioceptive estimates and no-cursor (open-loop) reaches as we did in our previous studies where the cursor was gradually rotated during training. These findings are consistent with previous results that suggest adaptation is comparable between abrupt and gradual perturbations (Klassen et al. 2005). For example, Klassen and colleagues introduced a 30° visuomotor rotation either abruptly or gradually (in 0.125° increments) and found no difference in motor learning retention when subjects were tested 24 h later. However, Kagerer et al. (1997) introduced a 90° visuomotor rotation either at once or in 10° increments and observed increased retention (aftereffects) in subjects who reached with a gradually introduced 90° visuomotor perturbation compared to those in which the perturbation was abruptly introduced (43.1° and 28.22°, respectively). In contrast to these findings, Buch et al. (2003) reported *decreased* aftereffects following gradual exposure to a 90° visuomotor rotation compared with abrupt exposure; however, this trend was only described for older adults. The differences in motor adaptation following

reaches with an abruptly versus gradually introduced distortion appear to depend on the initial error signals experienced, such that differences in aftereffects following gradual or abrupt learning seem to occur only for visuomotor rotations greater than the 30° rotation used in our current study. According to Abeele and Bock (2001), different mechanisms are engaged when learning large (over 90°) versus small rotations, and these separate mechanisms, which may further be differentially engaged when learning abrupt versus gradual rotations, lead to the inconsistency between findings of increased or decreased adaptation depending on the magnitude of the initial error signal. It could also be that adapting to a very large and thus difficult or less relevant perturbation may be easier to do when the error signals and overall difficulty increase gradually: for instance, correct credit assignment for reaching error in the case when the cursor is suddenly deviated from the hand movement by a rotation of 90° or more may be quite different than that for smaller or gradual deviations (Wei and Kording 2009).

In instances when the distortion is introduced abruptly and large reach errors are initially experienced, it has been suggested that explicit, strategic control processes are engaged early in the learning process in order to produce rapid corrections in motor performance (Redding and Wallace 1996). In contrast, when the distortion is introduced gradually and small reach errors are experienced, reach adaptation is proposed to arise through implicit processes that reduce the discrepancies between vision and proprioception. The fact that we found similar changes in movements and sensory recalibration following abrupt-cursor adaptation compared to gradual-cursor adaptation suggests that these changes are not cognitively or strategically driven as proposed by previous research using prism adaptation paradigms (Redding and Wallace 1996). In fact, given the results of Mazzoni and Krakauer (2006), the sensory and motor changes observed in the present study most likely arise implicitly rather than explicitly.

Arm symmetry

It has been suggested that the two arms may be better at using different types of sensory information for localizing a target. For instance, Goble and Brown (2008) have suggested that the left limb is better at matching proprioceptive targets and the right limb for matching visual targets. In the current study, biases measured following reach training with an aligned cursor did produce a small asymmetry across the two hands, where larger rightward biases were present in the left-hand group and smaller leftward biases were present in the right-hand group. These results are consistent with Goble and Brown's (2008) proposal, in that subjects were able to more accurately localize their right

hand relative to a visual reference marker compared to the left hand. Yet in our previous study, we found the same magnitude of proprioceptive biases when subjects judged the position of the right hand with respect to body midline (i.e. proprioceptive reference) and a visual reference. Likewise, we found no differences in the magnitude of reaching errors to a visual target made without any cursor feedback following either right or left-hand training with an aligned or rotated cursor: absolute reach endpoint errors were 1.5° on average following aligned-cursor training and were not different between the two groups. Differences in findings between our work and Goble's may arise due to the nature of the task. Goble and Brown's findings were observed during a task that involved moving the arm around the elbow joint in order to match the angle of the opposite arm in a bimanual task or to match a visual reference. In contrast, our task was a unimanual task and we did not find similar asymmetries between the two arms in either our sensory or motor tasks. In the current study, and in our previous work (Jones et al. 2010), the extent of the misestimates of proprioceptive biases of the unseen hand position of the two arms was similar. Moreover, we have shown that proprioceptive biases and uncertainty ranges, measured without a preceding reach-training task, do not differ at all in magnitude (just in direction) across the two hands (Jones et al. 2010; Rincon-Gonzalez et al. 2011; Wilson et al. 2010). Thus, perhaps arm asymmetry is only observable when the two arms are working together to complete the same task.

While sense of felt hand position was shifted at all reference markers and movements adapted at all targets examined, proprioceptive recalibration was significantly less at the rightwards (CCW) marker than at the leftwards (CW) marker for the left-hand group: this asymmetry was not observed in the right-hand group. Previous results suggest that motor adaptation asymmetries may arise following reaches with prism goggles due to asymmetries in underlying attentional biases (Goedert et al. 2010). However, given that we found that movement aftereffects were comparable in magnitude across all targets suggests that the asymmetric proprioceptive recalibration we observed may not have arisen due to attentional biases. Moreover, no differences in bias between the two reference markers following aligned reach training were observed in the left-hand group, further weakening the argument for an attentional bias underlying asymmetrical recalibration. An alternative explanation may involve asymmetries in encoding limb position and interactions with workspace locations. As discussed previously, Goble and Brown (2010) suggest that the left hand is more accurate at matching proprioceptive targets than the right hand. Moreover, Goble (2010) recently demonstrated that joint matching is better when the tested joint is in the far-left workspace. That proprioceptive estimates of hand position were shifted following rotated training more so for a

reference marker in the left workspace than the right may be a result of an inherent workspace bias for the left limb, which only becomes evident when information from proprioceptive and visual modalities are incongruent. More research is required in order to address this question specifically.

Proprioceptive recalibration

While the precise relationship between sensory and motor changes arising from reaching with altered visual feedback of the hand remains to be determined, results from the current study (i.e. Fig. 7) and previous studies from the Henriques' laboratory (Cressman and Henriques 2009; Salomonczyk et al. 2011) and recent work by de Grave et al. (2011) suggest that these processes may occur simultaneously, yet independently of each other. Specifically, we find that proprioceptive recalibration is uncorrelated with motor changes (aftereffects) following visuomotor adaptation paradigms (Cressman and Henriques 2009; Salomonczyk et al. 2011). Moreover, de Grave et al. (2011) recently demonstrated that visuomotor adaptation in response to a cursor perturbation that was shifted in depth relative to the body was not related to changes in the perceived "reachability" of a target (i.e. changes in subjects reaches were not correlated with their perceptions regarding their ability to successfully reach a target). In accordance with these findings, recent work from Block and Bastian (2011) suggests that sensory realignment (i.e. proprioceptive recalibration) also arises independently of sensory weighting.

Recalibration of proprioception may arise because the central nervous system performs motor tasks optimally when a unified estimate of hand position is available. When sensory estimates of hand position are incongruent, the brain may seek to resolve this sensory discrepancy by recalibrating a less salient sense (proprioception) to match the more reliable visual input. In the current study, we only asked subjects to estimate the position of their hand with respect to visual reference markers. Thus, it could be argued that our results demonstrate sensory (visual-proprioceptive) realignment without providing evidence that proprioception was recalibrated, such that subjects experienced an overall shift of sense of felt hand position that was independent of having to align one's hand with a visual cue. Based on our previous results, in which we demonstrate similar shifts in proprioceptive biases regardless of whether subjects are required to judge the position of their hand relative to a visual or proprioceptive reference marker at the same location (Cressman and Henriques 2009), we are confident that the changes in felt hand position we observe at visual reference markers reflect a more global shift in felt hand position, as opposed to intersensory realignment. In

addition, we have recently not only repeated these results using proprioceptive and visual reference markers, but also have shown similar shifts in proprioceptive biases when subjects were required to indicate the position of their right (adapted) hand with their left hand [i.e. a proprioceptive–proprioceptive alignment task (Clayton et al. 2011)]. Similar to the results we have reported previously, we again find a shift in proprioceptive biases that are reflective of proprioceptive recalibration.

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Proprioceptive recalibration following prolonged training and increasing distortions in visuomotor adaptation

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ABSTRACT

Reaching with misaligned visual feedback of the hand leads to reach adaptation (motor recalibration) and also results in partial sensory recalibration, where proprioceptive estimates of hand position are changed in a way that is consistent with the visual distortion. The goal of the present study was to explore the relationship between changes in sensory and motor systems by examining these processes following (1) prolonged reach training and (2) training with increasing visuomotor distortions. To examine proprioceptive recalibration, we determined the position at which subjects felt their hand was aligned with a reference marker after completing three blocks of reach training trials with a cursor that was rotated 30° clockwise (CW) for all blocks, or with a visuomotor distortion that was increased incrementally across the training blocks up to 70° CW relative to actual hand motion. On average, subjects adapted their reaches by 16° and recalibrated their sense of felt hand position by 7° leftwards following the first block of reach training trials in which they reached with a cursor that was rotated 30° CW relative to the hand, compared to baseline values. There was no change in these values for the 30° training group across subsequent training blocks. However, subjects training with increasing levels of visuomotor distortion showed increased reach adaptation (up to 34° leftward movement aftereffects) and sensory recalibration (up to 15° leftwards). Analysis of motor and sensory changes following each training block did not reveal any significant correlations, suggesting that the processes underlying motor adaptation and proprioceptive recalibration occur simultaneously yet independently of each other.

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1. Introduction

When reaching to a target with misaligned visual feedback of the hand (i.e. reaching in a virtual reality environment or while wearing prism goggles), individuals adjust their movements in order for the visual representation of the hand to achieve the desired endpoint. Moreover, when the distortion is suddenly removed, reach errors referred to as aftereffects are observed, as subjects continue to make movements adapted to the distortion (Krakauer, Ghilardi, & Ghez, 1999; Krakauer, Pine, Ghilardi, & Ghez, 2000; Martin, Keating, Goodkin, Bastian, & Thach, 1996; Redding & Wallace, 2000; Simani, McGuire, & Sabes, 2007). It has been suggested that in addition to this motor adaptation, proprioception is also recalibrated following reaches made with altered visual feedback. This proposal is based on changes in reaches observed when subjects are required to reach

to visual and proprioceptive targets with their adapted hand following prism exposure (Harris, 1963; Hay & Pick, 1966; Redding & Wallace, 2000) and visuomotor adaptation, in which visual feedback of the hand position was displaced (Simani et al., 2007; van Beers, Wolpert, & Haggard, 2002). While subjects' reaches are altered after reaching with altered visual feedback of the hand, it is unclear whether these changes reflect proprioceptive recalibration per se. Given that subjects moved their adapted arm, errors may better reflect motor adaptation than cross-sensory recalibration (i.e. changes to the motor system rather than sensory changes). To avoid this potential motor confound, Henriques and colleagues (Cressman & Henriques, 2009, 2010; Cressman, Salomonczyk, & Henriques, 2010) and Ostry, Darainy, Mattar, Wong, and Gribble (2010) have recently designed novel perceptual tasks to examine proprioceptive recalibration. In these tasks subjects estimate the position of their hand with respect to a visual or proprioceptive (i.e. body midline) reference marker and hence do not perform any goal-directed movements with the adapted hand.

Results using this proprioceptive estimation task reveal that proprioceptive estimates of hand position are significantly shifted

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in the direction of motor adaptation after subjects reach with visual or force perturbations applied to the hand. Moreover, these changes in felt hand position do not differ in magnitude when estimates of hand position following visuomotor adaptation are made relative to visual or proprioceptive references (Cressman & Henriques, 2009), suggesting that these misestimates are due to recalibration of proprioception rather than any change in the visual percept. As additional support for the recalibration of proprioception, we have shown that changes in felt hand position do not transfer between limbs following visuomotor adaptation (Salomonczyk, Henriques, & Cressman, 2010). Specifically, if the visual representation of space had been recalibrated, we expect that changes in sensory alignment would have been present in both the trained and untrained hand, which we did not observe.

We have found that proprioceptive recalibration is a robust process that occurs along with motor changes under a variety of contexts, including when the hand is passively or actively displaced, when the visuomotor distortion is gradually or abruptly introduced, following training with a rotated or translated cursor, using either the left or right hand, and in both young and older adults (Cressman & Henriques, 2009; Cressman et al., 2010; Salomonczyk et al., 2010). While sensory changes are also observed in conjunction with motor changes following dynamic learning (Ostry et al., 2010) these changes are slightly smaller than those observed following visuomotor rotation training (11% vs. 33% of the deviation of the accompanying movement aftereffects). Surprisingly, we also found similar changes in felt hand position even in the absence of visuomotor adaptation training trials. In this task, subjects were merely exposed to a sensory discrepancy between visual and proprioceptive signals while their hand was passively moved by a robot and they viewed a cursor that simultaneously travelled directly to the target (Cressman & Henriques, 2010). Because no goal-directed reach training was involved and no motor commands were generated, the sensorimotor error signal was eliminated and subjects experienced only a cross-sensory error signal derived from the discrepancy between visual and proprioceptive feedback. In addition to recalibrating proprioception, this cross-sensory error signal was sufficient to produce significant movement aftereffects when subjects were asked to reach to targets with no visual feedback. While these aftereffects were only one third of the magnitude reported in previous studies where subjects could use the additional sensorimotor error signal to adapt their reaches (i.e. 20% vs. 60% of the 30° visuomotor distortion; Cressman & Henriques, 2009), they were similar in magnitude to and correlated with the changes in proprioception. Given that movement aftereffects produced following cross-sensory discrepancy exposure were almost two thirds smaller than those produced following visuomotor adaptation learning trials, the larger aftereffects following visuomotor adaptation may be due to additional changes exclusive to the motor system derived from the sensorimotor error signal.

Based on these previous results, it is possible that motor and sensory recalibration following sensorimotor learning rely on different training signals. As with visual processing (Goodale & Milner, 1992; Milner & Goodale, 1995), separate cortical areas have been suggested to be involved in action-oriented proprioceptive processing (the posterior parietal cortex) vs. perception oriented proprioceptive processing (the insula; Dijkerman & de Haan, 2007). Thus, perhaps the separate streams may be differentially involved in realigning proprioceptive and visual feedback of the hand and for providing a unified estimate of hand position for feedforward motor control. To study the relationship between motor and sensory changes, we sought to examine these processes following (1) prolonged reach training and (2) training with increasing levels of visuomotor distortion. While proprioceptive recalibration occurs under a variety of contexts following motor learning, it is unclear

if proprioceptive recalibration saturates in the same manner as movement aftereffects (as found by Krakauer, Ghez, and Ghilardi (2005) and Wong and Henriques (2009)) or whether prolonged training would lead to increased proprioceptive recalibration. For example, although we found proprioceptive recalibration to be much smaller than movement aftereffects following over 200 visuomotor adaptation trials (Cressman & Henriques, 2009), it is possible that proprioceptive recalibration requires more training in order to attain levels equivalent to those for motor adaptation. Based on previous findings demonstrating that the magnitude of the distortion affects motor learning (Abeele & Bock, 2001; Kagerer, Contreras-Vidal, & Stelmach, 1997), we also examined whether adaptation to increasing distortions (and thus exposure to increasing sensorimotor error signals) would result in sensory changes consistent with those of the motor system. To address these questions, we used the same technique for measuring hand proprioception following visuomotor adaptation to a rotated cursor as described by Henriques and colleagues (Cressman & Henriques, 2009, 2010; Cressman et al., 2010; Salomonczyk et al., 2010).

2. Methods

2.1. Subjects

Twenty-three right-handed young adults (mean age = 22.58, SD = 4.09, 14 female) were recruited from York University and volunteered to participate in the experiments described below. Subjects were pre-screened verbally for self-reported handedness and any history of visual, neurological, and/or motor dysfunction. Following pre-screening, subjects were randomly assigned to either the 30° (n = 10) or 70° (n = 13) training groups. All subjects provided informed consent in accordance with the ethical guidelines set by the York University Human Participants Review Sub-Committee.

2.2. General experimental setup

A side view of the set up is provided in Fig. 1A. Subjects were seated in a height adjustable chair so that they could comfortably see and reach to all target and reference marker locations presented on an opaque, reflective surface. Subjects grasped the vertical handle of a two-joint robot manipulandum mounted in the horizontal plane (Interactive Motion Technologies). Visual stimuli were projected from a monitor (Samsung 510 N, refresh rate 72 Hz) installed 17 cm above the robot onto a reflective surface. The reflective surface was opaque and positioned so that images displayed on the monitor appeared to lie in the same horizontal plane as that of the robot handle. The room lights were dimmed and subjects' view of their hand was blocked by the reflective surface and a black cloth draped between the experimental set up and subjects' shoulders.

2.3. General procedure

The experiment consisted of two separate testing sessions completed on two testing days. Each testing session involved two tasks (comprising one block) and on the second day of testing these tasks were repeated three times (Fig. 2). On the first testing day subjects completed the reaching trials outlined below while seeing a cursor that was veridical, or aligned, with their hand. On the second testing day subjects completed the reaching trials while viewing a cursor that was misaligned from the actual location of their unseen hand. The misaligned cursor was rotated 30°, 50° or 70° clockwise (CW) relative to the actual hand position and was represented by a green disc 1 cm in diameter (white circle, Fig. 1B). The 30° training group completed all three blocks of the second session with a 30° rotated cursor, while the 70° training group completed the first block of the second session with a 30° rotated cursor, the second block with a 50° rotated cursor, and the third block with a 70° rotated cursor. For both groups, the 30° rotation was introduced gradually such that on the first trial the cursor was rotated 0.75° clockwise (CW) with respect to the hand. The rotation then increased by 0.75° each trial, until the full distortion was achieved. For the 70° training group, the cursor distortion in the 50° and 70° blocks was again introduced gradually by 0.75°/trial, starting from the rotation of the previous block (i.e. in block two the distortion was introduced at 30.75°, and increased by 0.75° per trial up to 50°; in block three the distortion was introduced at 50.75°, and increased by 0.75° per trial up to 70°).

2.3.1. Task 1: reach training and motor adaptation

While grasping the robot manipulandum with the right hand, subjects were instructed to reach to a visual target (yellow circle, 1 cm in diameter) as quickly and accurately as possible while viewing either an aligned (first testing day) or misaligned (second testing day) cursor that moved with their hand. The reach targets were located radially 10 cm from the home position at 5 and 30° left (CCW) and right
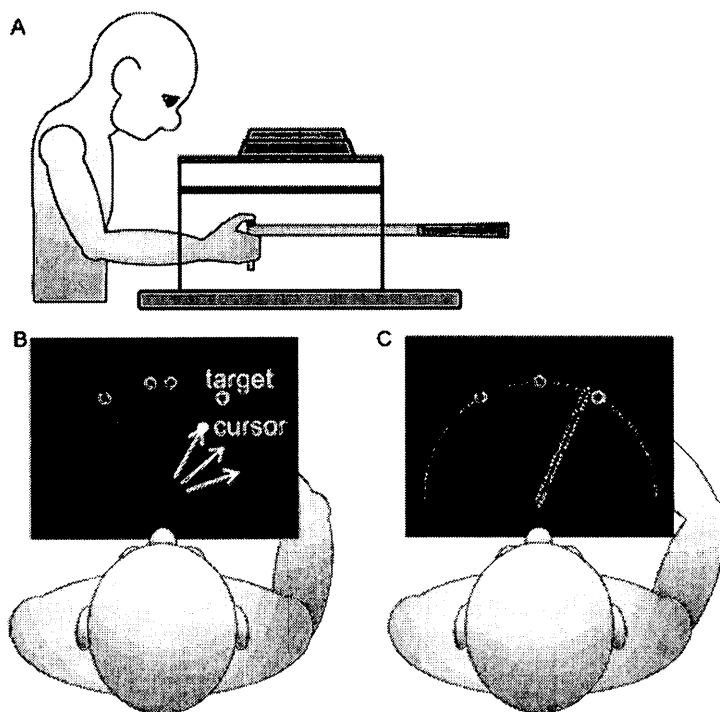
Fig. 1. Experimental setup and design. (A) Side view of the experimental setup. (B and C) Top view of the experimental surface visible to subjects. (B) Visuomotor distortion introduced in the rotated Reach Training Task. The 1 cm green cursor (representing the hand) was rotated 30° clockwise with respect to the actual hand location (white disk) during the first rotation training block and increased to 50° and 70° for the second and third rotation training blocks, respectively for the 70° training group. Reach targets (white rings) 1 cm in size were located 10 cm from the home position (black circle) at 5° and 30° left and right of body midline. (C) In the proprioceptive estimate task, subjects actively pushed their hand out 10 cm along a constrained linear path (depicted by the rectangle) from the home position and judged the position of their hand with respect to a reference marker. Reference markers (white rings) were located at 0° and 30° left and right of midline.

(CW) of centre (white rings in Fig. 1B). The home position was located approximately 40 cm in front of subjects, in line with their body midline (indicated by the black circle in Fig. 1B). This position was not illuminated and visual feedback was provided only when the hand had travelled 4 cm outwards from the home position. The reach was considered complete once the centre of the cursor had moved to within 0.5 cm of the target's centre. At this point, both the cursor and target disappeared and subjects moved their hands back to the home position along a linear route in the absence of visual feedback. If subjects attempted to move outside of the established linear path, a 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 (Cressman & Henriques, 2009, 2010; Cressman et al., 2010; Henriques & Soechting, 2003; Jones, Cressman, & Henriques, 2010). The order of the reach trials was pseudo-randomized such that subjects reached once to 3 of the reach targets, specifically the two peripheral targets and one of the pair of peri-central (5°) targets, before any target was repeated. Subjects completed 99 reach trials (box 1, Fig. 2).

After completing the 99 reach training trials, subjects immediately completed 12 aiming movements, 3 reaches to each of 4 reach targets (i.e. both outer targets and the two peri-central targets), without the cursor (box 2, Fig. 2). These trials were included to measure aftereffect reach errors to ensure that subjects had adapted their reaches in response to the misaligned cursor on the second testing day. On these trials subjects were instructed to aim to a target and hold their end position. Once this end position had been maintained for 500 ms, the visual target disappeared and the trial was considered complete. Subjects were guided back to the home position by a linear grooved path. The position of the robot manipulandum was recorded throughout all reaching trials at a sampling rate of 50 Hz and a spatial accuracy of 0.1 mm.

2.3.2. Task 2: proprioceptive estimate trials + reach trials

In this task, proprioceptive estimates and reach trials (boxes 3–5 in Fig. 2) were systematically interleaved. Subjects began by completing an additional 12 reaching trials with an aligned (first testing day) or misaligned (second testing day) cursor (box 3). Subjects reached once to 3 of the reach targets, specifically the two peripheral targets and one of the pair of peri-central (5°) targets, before any target was repeated. These reaches were then immediately followed by interleaving sets of 15 proprioceptive estimate trials (box 4) and 6 reaching trials (box 5). A proprioceptive estimate trial began with the subject grasping the robot manipulandum at the home position. The position of the hand at the home position was indicated by a 1 cm green disc. After 500 ms this disc disappeared and the subject was instructed to push his or her hand outward along a constrained robot-generated linear path 10 cm in length (as described previously, rectangle in Fig. 1C). On all trials, once the hand reached the end of the path (along the dotted arc in Fig. 1C) a reference marker located at 0°, 30° left (CCW) or 30° right (CW) of centre (white rings, Fig. 1C) appeared and subjects made a two-alternative forced choice judgment about the position of their hand (left or right) relative to the reference marker. There was no time constraint for giving a response. After responding, the reference marker disappeared and the subject moved the robot directly back to the home position along the same linear route to begin the next trial. The position of the hand with respect to each reference marker was adjusted over trials using an adaptive staircase algorithm (Kesten, 1958; Treutwein, 1996) as described by Cressman and Henriques (2009, 2010) and Jones et al. (2010). In particular, for each reference marker there were 2 staircases, one starting 20° to the left (CCW) of the reference marker and one starting 20° to the right (CW). The 2 staircases were adjusted independently and randomly interleaved as outlined by Cressman and Henriques (2009). The test sequence of 15 proprioceptive estimates followed by 6 reaches was completed 10 times, for a total of 222 trials (150 proprioceptive estimate trials (50 at each reference marker) + 72 reach trials).

Subjects completed 15 final no cursor reaches (box 6, Fig. 2) immediately after completing the proprioceptive estimate + reach task in order to ensure that they were still reaching in a similar manner as before the proprioceptive estimate trials. These reaches were carried out like the previous 12 no cursor reach trials (box 2 in Fig. 2) but now all 5 reach targets and reference marker positions were presented.

2.4. Data analysis

2.4.1. Motor adaptation

We analyzed reaching errors (i.e. aftereffects) made in the no-cursor reach trials to (1) determine if subjects adapted their reaches after aiming with a misaligned
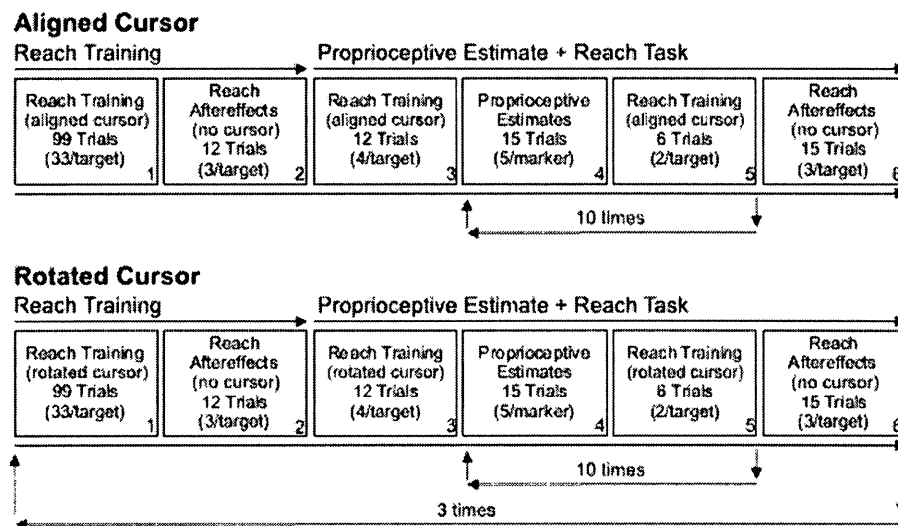
Aligned Cursor

Rotated Cursor

Fig. 2. Breakdown of the testing sessions within the experiment. In the first testing session (top row) subjects reached with an aligned cursor that accurately represented the position of their hand in the reach training trials. In the second testing session (bottom row), subjects first reached with a misaligned cursor that was rotated 30° clockwise with respect to the actual hand location during the reach training trials (first rotated block). Subjects then completed two more training blocks during which time the cursor was rotated 30° or 50° (second rotated block) and 30° or 70° (third rotated block). After completing 99 reach training trials with an aligned (top row) or misaligned cursor (bottom row), subjects next reached to each of four reach targets (the two outer targets and the two inner targets), 3 times each without a cursor in order to assess motor adaptation (reach aftereffects trials, Box 2 in top and bottom rows). Subjects then completed 12 reaches to the reach targets with the cursor present (Box 3). This was followed by 10 sets of 15 proprioceptive estimate trials (Box 4) and 6 visually guided reaches (Box 5) for a total of 150 proprioceptive estimate and 60 reach trials. Following this, subjects reached to all targets and reference markers 3 times without a cursor in order to assess maintenance of reach aftereffects (Box 6). In the first testing session, subjects only completed one block of training trials with aligned visual feedback of the hand. In the second testing session, subjects completed three training blocks with misaligned visual feedback of the hand.

cursor and (2) ensure that subjects maintained adaptation across the proprioceptive estimate and reach trials. Reach endpoint errors were defined as the angular difference between a movement vector (from the home position to reach endpoint) and a reference vector (joining the home position and the target). Reach errors at peak velocity (PV) were defined in a similar manner. In particular, reach errors at PV were defined as the angular difference between a movement vector at peak velocity and a reference vector. To determine if subjects had indeed adapted their reaches, we analyzed mean endpoint aftereffects and aftereffects at peak velocity separately using a RM-ANOVA with 2 Training Group (30° group vs. 70° group) × 4 Visual Feedback Block (aligned feedback vs. first block of rotated feedback (30°) vs. second block of rotated feedback (30° or 50°) vs. third block of rotated feedback (30° or 70°)) × 2 Time (trials completed following reach training vs. trials completed following the proprioceptive estimate and reach trials) factors. Training Group was a between-group factor while Visual Feedback Block and Time were within-group factors. Tukey's Honestly Significant Difference (HSD) post hoc tests were administered to determine the locus of these differences (alpha = .05). In addition to revealing if subjects adapted their reaches in response to the visuomotor distortion and maintained this level of adaptation across the testing session, this analysis allowed us to determine if reach adaptation increased with increasing practice and/or distortion following visuomotor learning.

2.4.2. Proprioceptive estimates of hand position

To examine the influence of prolonged reach training and the magnitude of visuomotor distortion on changes in proprioceptive recalibration, we determined the locations at which subjects felt their hands were aligned with the reference markers. This location was determined by fitting a logistic function (solid black line, Fig. 3B) to each subject's responses (Fig. 3A) for each reference marker in each testing session. The point of responding "left" 50% of the time (i.e. responding "left" and "right" equally often) represents bias (Cressman & Henriques, 2009, 2010; Jones et al., 2010). In addition to calculating bias, we also determined subjects' uncertainty (or precision) by finding the difference between the values at which the point of responding "left" was 25% and 75% (dashed grey lines, Fig. 3B). Bias and uncertainty related to a particular reference marker were excluded if the associated uncertainty was greater than the mean uncertainty across all reference markers + 2 standard deviations. Based on this analysis, only two proprioceptive estimates (less than 1% of total estimates) were excluded.

Biases and uncertainty ranges were analyzed in a 2 Training Group (30° group vs. 70° group) × 4 Block (aligned feedback vs. first block of rotated feedback (30°) vs. second block of rotated feedback (30° or 50°) vs. third block of rotated feedback

(30° or 70°)) × Marker Location (0° vs. 30° CW vs. 30° CCW) RM-ANOVA. Differences with a probability of less than .05 were considered to be significant. Tukey's Honestly Significant Difference (HSD) post hoc tests were administered to determine the locus of these differences (alpha = .05).

3. Results

3.1. Motor adaptation

Across groups, subjects reached to the targets with an average movement time of $1.95\,s \pm .93\,s$ (SD) and an average peak velocity of $16.4\,cm/s \pm 5.9\,cm/s$ (SD) when no visual feedback of the hand was provided. Mean reach endpoint errors (i.e. aftereffects) for these no-cursor trials following training with an aligned cursor were on average 0.75° to the right of the target. These small reaching errors suggest that all subjects were able to accurately reach to a target even without any visual feedback of their hand position. Mean aftereffects following training with misaligned visual feedback of the hand are displayed in Fig. 4. In this figure we see that after training with a rotated cursor, endpoint errors deviated significantly more leftwards of the target ($F(3,63) = 78.104$, $p < .001$) for both training groups. Following the first block of 30° rotated cursor feedback training, reaching movements deviated on average 16° leftwards for all subjects compared to aftereffects following aligned training. The training groups then differed on subsequent training blocks ($F(3,63) = 10.445$, $p < .001$). Specifically, aftereffects for those subjects that trained with a 30° cursor rotation (white bars in Fig. 4) remained constant and did not differ significantly with successive blocks of training ($p > .05$ for all contrasts). In contrast, aftereffects for subjects that trained with a 50° and 70° rotation in rotated training Blocks 2 and 3 respectively (filled bars), increased to 27.6° and 33.8° respectively compared to training with an aligned cursor ($p < .001$). For the 70° training group, aftereffects follow-
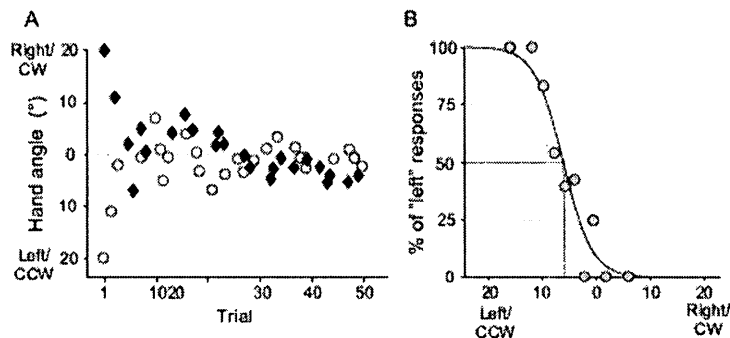
Fig. 3. Angular position of the hand during proprioceptive estimate trials and percentage of left responses for a single subject when the 0° visual reference marker was displayed. (A) The left (white circles) and right (black diamonds) staircases began with the subject's hand deviated by 20° from the reference marker (dashed line) and gradually converged over trials. (B) A logistic function was fitted to the response data to define bias and uncertainty, where bias is the probability of responding left 50% of the time (dashed black line) and uncertainty is the difference between the values at which the probability of responding left was 25 and 75% (dashed grey lines).
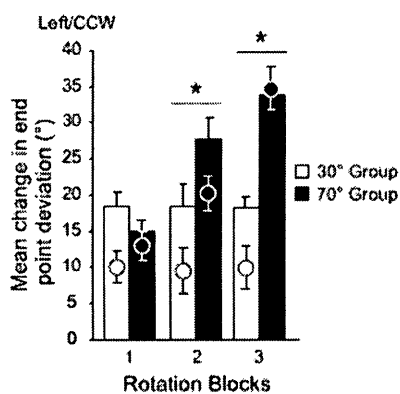

Fig. 4. Aftereffects following training with misaligned visual feedback of the hand. Endpoint errors were calculated by subtracting angular reach endpoint errors in the no cursor reach trials after training with an aligned cursor from errors completed in the no cursor reach trials after training with a rotated cursor. Errors at peak velocity were calculated by subtracting angular reach errors at peak velocity in the no cursor reach trials after training with an aligned cursor from errors completed in the no cursor reach trials after training with a rotated cursor. Errors at reach endpoint (bars) and at peak velocity (circles) averaged across targets and subjects for the 30° training group (open symbols) and the 70° training group (filled symbols) are shown for the no cursor reaches completed after the three consecutive rotated training blocks of trials. Asterisks indicate significant group differences (p < .05). Error bars reflect standard error of the mean.

ing each training block differed significantly from the previous block (aligned block 1 vs. rotated block 1, p < .001; rotated block 1 vs. rotated block 2, p < .001, rotated block 2 vs. rotated block 3, p = .006). For both groups, aftereffects following reach training trials did not differ from aftereffects following proprioceptive estimates ($F(1,21) < 1$). Thus, results from the 70° training group indicate that as the magnitude of the distortion of the visual cursor feedback became greater, so too did motor adaptation. However, the relative proportion of aftereffects was consistent for each training block and on average represented 51% of the visuomotor distortion: a one-way ANOVA revealed no differences between blocks ($F(2,38) < 1$, p = .654; 70° group: first rotated block, $\bar{x}$ = 49%, SD = 19.38; second rotated block, $\bar{x}$ = 55%, SD = 22.82; third rotated block, $\bar{x}$ = 48%, SD = 21.41). As well, subjects in the 30° training group maintained a reach adaptation level of 61% of the visuomotor distortion across all training blocks, similar to that of the 70° training group (30°

group: first rotated block $\bar{x}$ = 60%, SD = 24.78; second rotated block, $\bar{x}$ = 63%, SD = 23.47; third rotated block, $\bar{x}$ = 60%, SD = 17.04). Reach errors at peak velocity followed the same pattern of results as the reach endpoints described above, consistent with previous work from our lab suggesting that deviations at end point and peak velocity are comparable (Wong & Henriques, 2009).

3.2. Proprioceptive recalibration

3.2.1. Bias

Fig. 5A displays mean proprioceptive biases at all three reference marker locations (circles) for both the 30° (top panel) and 70° training groups (bottom panel). The diamonds indicate biases following training with an aligned cursor, while the three sets of triangles indicate biases following the three training blocks with a rotated cursor (white= 1st block, grey= 2nd block, black= 3rd block). For both groups of subjects we see that, on average, estimates of unseen hand location were slightly biased to the left after reaching with an aligned cursor. In fact, the mean bias collapsed across all subjects and reference markers was 5.1° left of the reference marker (previous studies in our lab have shown that this is merely a hand bias, Jones et al., 2010). More importantly however, following reach training with misaligned cursor feedback of the hand, biases were shifted further left for both training groups. Fig. 5B displays the mean changes in bias following visuomotor adaptation training. Following training with a 30° rotated cursor, biases were shifted on average 7.3° more leftwards for all subjects compared to estimates following training with an aligned cursor ($F(3,63)= 42.39$, p < .001). However, the training groups differed on subsequent blocks ($F(3,63)= 4.771$, p = .005). Similar to the aftereffects errors discussed above, biases for the 30° training group did not change across successive blocks of reach training trials with a cursor rotated 30° CW with respect to the hand (p > .05 for all contrasts). Moreover, the average biases for the 70° training group following training with a 50° and 70° rotated cursor increased leftwards by 12.2° and 14.7° respectively, relative to performance following training with an aligned cursor. For the 70° training group, changes in bias following each rotated training block were different from the previous block (rotated block 1 vs. 2, p = .001; block 2 vs. 3, p = .048). Changes in bias were similar across all reference marker locations ($F(2,42) < 1$ for both groups). Thus, as the magnitude of the visuomotor distortion became greater, so too did proprioceptive recalibration. However, the relative proportion of changes in bias for the 70° training group were consistent for each training block and on average represented 24% of the visuomotor
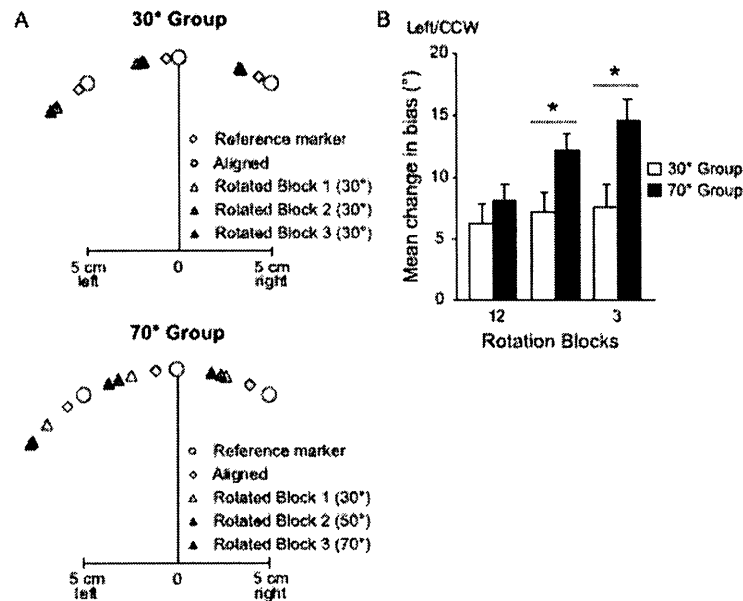
Fig. 5. Proprioceptive biases following training with aligned and misaligned visual feedback of the hand. (A) Mean 2-D proprioceptive biases following training with an aligned (diamonds) or misaligned (after the first rotated block: white triangles; second rotated block; grey triangles; third rotated block: black triangles) cursor for subjects in the 30° (upper panel) and 70° (lower panel) training groups. The actual reference marker positions are represented as circles. (B) Mean changes in biases after training with a misaligned cursor compared to an aligned cursor were averaged across reference markers for the 30° (open bars) and 70° (filled bars) training groups. Asterisks indicate significant group differences ($p < .05$). Error bars reflect standard error of the mean.

distortion (first rotated block, $\bar{x} = 26\%$, SD = 18.04; second rotated block, $\bar{x} = 24\%$, SD = 10.10; third rotated block, $\bar{x} = 21\%$, SD = 9.32). Subjects in the 30° training group also maintained a change in bias equivalent to 28% of the visuomotor distortion across all training blocks consistent with that of 70° training group (first rotated block $\bar{x} = 29\%$, SD = 20.22; second rotated block, $\bar{x} = 29\%$, SD = 19.18; third rotated block, $\bar{x} = 26\%$, SD = 15.93).

3.2.2. Uncertainty

Fig. 6 depicts the magnitude of the uncertainty ranges for both the 30° (white bars) and 70° (filled bars) training groups follow-
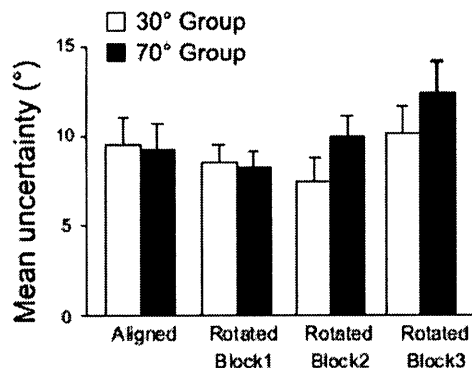

Fig. 6. Magnitude of the uncertainty ranges in the proprioceptive estimate trials were averaged across subjects and reference marker positions following reach training with an aligned cursor or with a misaligned cursor (after rotated training block 1, 2 and 3) for subjects in the 30° (open bars) and 70° (filled bars) training groups. Error bars reflect standard error of the mean.

ing reaches with an aligned and misaligned cursor. Uncertainty levels were on average 9.5° for each reference marker. Subjects' levels of precision in estimating the location of their unseen hand were comparable after reach training with aligned and misaligned cursor feedback ($F(3,63) = 2.455$, $p = .071$). While no overall differences were observed between groups ($F(1,21) < 1$) or reference marker locations ($F(2,42) = 2.26$, $p = .117$), a significant interaction was observed, wherein subjects in the 70° training group demonstrated greater precision (7.8°) when estimating hand position relative to the centre reference marker compared with the markers located 30° left and right of centre (12° and 10.2°, respectively; $F(2,42) = 4.423$, $p = .018$). No other differences were observed.

3.3. Motor adaptation vs. proprioceptive recalibration

Fig. 7A displays mean changes in bias and aftereffects following training with a misaligned cursor compared to an aligned cursor. From this figure we see that subjects adapted their reaches and recalibrated proprioception, and that proprioceptive recalibration was less than reach adaptation for both groups of subjects across all training blocks. In fact, on average, both groups of subjects recalibrated proprioception by roughly 45% of the movement aftereffects achieved on all training blocks. Furthermore, from Fig. 7A we see that the 70° training group demonstrated a continual increase in changes in bias and aftereffects following training with an increasing visuomotor distortion, while the 30° training group did not show any changes in either bias or aftereffects following repeated training with a 30° cursor rotation.

From Fig. 7A it appears that the magnitude of proprioceptive recalibration increased coincidentally with increasing aftereffects. In Fig. 7B and C we plot the changes in proprioceptive recalibration and reach adaptation as a percentage of the visuomotor distortion for the 30° training group and 70° group, respectively. We found no
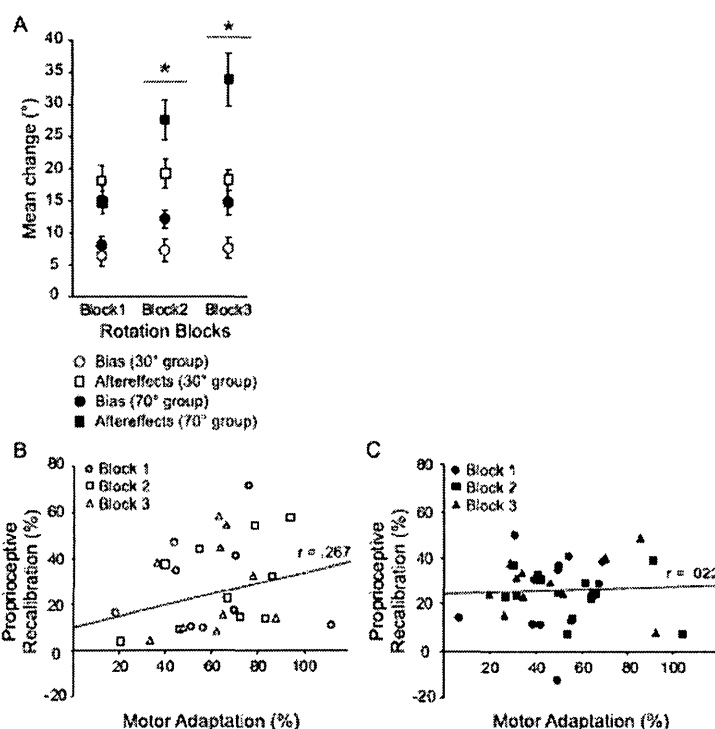
Fig. 7. Comparison between changes in bias and aftereffects across the two training groups. (A) Angular changes in bias (circles) and aftereffects (squares), averaged across subjects and locations, following reach training with misaligned visual feedback of the hand in the three training blocks are shown for subjects in the 30° (open symbols) and 70° (filled symbols) training groups. Asterisks indicate significant group differences (p < .05). Error bars reflect standard error of the mean. (B and C) Changes in sensory and motor recalibration as a percentage of the visuomotor distortion introduced during each training block for subjects in the 30° training group (B) and 70° training group (C) following rotated blocks 1 (circles), 2 (squares) and 3 (triangles). Each symbol represents the percentage change in bias and %change in aftereffects averaged across marker and target locations for each subject. Solid line indicates the line of best fit for all data points.

significant relationship between the magnitude of proprioceptive recalibration and the extent of aftereffects (when expressed as a percentage of the visuomotor distortion) for either the 30° training group, Fig. 7B: $\beta 1 = .225$, $p = .154$, or for the 70° training group, Fig. 7C: $\beta 1 = .026$, $p = .896$; or when values from all subjects and all blocks of trials were included in the analysis ($\beta 1 = .123$, $p = .154$). Likewise, individual analyses of each training block for both groups of subjects did not reveal any significant relationships between the percentage of proprioceptive recalibration and reach adaptation achieved (30° training group: first rotated block, $\beta 1 = .026$, $p = .931$; second rotated block, $\beta 1 = .397$, $p = .155$; third rotated block, $\beta 1 = .313$, $p = .344$; 70° training group: first rotated block, $\beta 1 = .306$, $p = .272$; second rotated block, $\beta 1 = -.118$, $p = .378$; third rotated block, $\beta 1 = -.087$, $p = .514$). Given that these coincident sensory and motor changes were not correlated, we hypothesized that the trend of increasing proprioceptive recalibration with increasing reach adaptation in the 70° training group, as shown in Fig. 7A, was due to the size of the error signal. To determine if the magnitude of the visuomotor distortion was driving these changes, we analyzed the actual mean changes in bias (in degrees) of the 70° training group (as these subjects experienced an increase in the visuomotor distortion) in a regression in which actual changes in aftereffects (in degrees) and magnitude of the visuomotor distortion were used as predictor variables. While the overall correlation was significant ($F(2,36) = 4.67$, $p = .019$), it was only the magnitude of the visuomotor distortion that was a significant predictor of the changes in bias ($\beta 1 = .193$, $p = .007$). Changes in aftereffects did not significantly

predict changes in bias for this training group ($\beta 2 = -.057$, $p = .494$) or when all subjects were included in analyses ($\beta 2 = .021$, $p = .499$).

Finally, to compare the relationship between sensory and motor recalibration across the 2 groups of subjects and training blocks, we divided the actual change in bias by the change in aftereffects for each subject following all three rotated feedback training blocks to derive a ratio of sensory to motor recalibration. We then subjected these values to a 2 Group (30° training group vs. 70° training group) × 3 Block (first block of rotated feedback (30°) vs. second block of rotated feedback (30° or 50°) vs. third block of rotated feedback (30° or 70°)) RM-ANOVA to determine if these ratios remained consistent across training blocks. No significant differences between blocks ($F(2,42) = 1.92$, $p = .174$) or groups ($F(1,21) < 1$) were observed. Thus, the proportion of sensory to motor recalibration remained consistent across blocks for both groups. Altogether these findings indicate that while the relationship between sensory and motor recalibration remains constant following prolonged training or reaching with a greater visuomotor distortion, results suggest that these two processes may be independent and due to two separate adaptation processes.

4. Discussion

The goal of the present study was to examine the relationship between changes in sensory and motor systems following visuomotor adaptation. To do so we asked if prolonged reach training with distorted visual feedback of the hand or training with an increas-

ing visuomotor distortion leads to increased motor adaptation and proprioceptive recalibration. Subjects completed one block of reach training trials with an aligned cursor and three blocks of reach training with a misaligned cursor that (a) was rotated 30° clockwise relative to the subject's unseen hand for all three blocks, or (b) was incrementally rotated 30°, 50° and 70° clockwise across three subsequent training blocks. After each training block we assessed reach adaptation and sense of felt hand position. We found that following initial training to a cursor rotated 30° CW with respect to the hand, subjects adapted their reaches by 16° or approximately 55% of the distortion compared to when they reached with aligned visual feedback of the hand. Subjects also shifted the position at which they felt their hand was aligned with a reference marker leftwards by 7° or roughly one quarter of the visuomotor distortion. Prolonged reach training with a 30° rotation did not lead to any further motor adaptation or proprioceptive recalibration, suggesting that both motor recalibration and sensory recalibration saturated within the first 100 trials of reach training. Conversely, reach adaptation increased to 28° and 34° following training with a 50° and 70° cursor rotation, respectively, while changes in bias increased to 12° and 15° following the same rotations. Overall, the magnitude of proprioceptive recalibration was approximately 45% of the observed reach adaptation across all conditions for both groups.

The magnitude of the visuomotor distortion was correlated with both changes in proprioceptive bias and movement aftereffects; however, no relationship between these sensory and motor changes was observed overall or within training blocks. In contrast to changes in proprioceptive biases and movement aftereffects, the precision of subjects' estimates of hand position did not change across training blocks. Thus subjects responded in a similar manner regardless of the magnitude of the distortion or the number of reach training trials completed. In accordance with these findings, Cressman et al. (2010) also found that uncertainty in felt hand position remained consistent across training sessions and hence was not related to changes in proprioceptive bias and reach aftereffects in both young and older adults. Taken together, these findings suggest that the size of the distortion has a similar effect on both sensory and motor changes but does not affect the precision of subjects' estimates of hand position.

Following the first block of learning trials and throughout subsequent blocks, subjects in both groups began to feel their hand near the position that it was visually represented by a cursor. In the current study, this was demonstrated by asking subjects to estimate the location of their unseen hand with respect to a visual reference marker. Previous work has also shown recalibration of felt sense of hand position with respect to an internal reference as defined by the subjects' body midline (Cressman & Henriques, 2009). Moreover, this recalibration was not different from recalibration observed when a visual reference marker was displayed at the same location. These results strongly suggest that proprioception is recalibrated following visuomotor adaptation such that proprioceptive estimates of hand position are shifted to match the visual percept of hand position. Furthermore, given that proprioceptive recalibration failed to transfer from the trained hand to the untrained hand following visuomotor adaptation training (Salomonczyk et al., 2010) provides additional evidence that our method assesses proprioceptive recalibration rather than a visual shift, or combination of the two.

4.1. The influence of reach training

While more extensive training has been hypothesized to contribute to greater perceptual changes (Ostry et al., 2010), we found that this was not the case. Changes in bias and aftereffects after subsequent training trials with the same distortion were no larger than those following the first block of training with misaligned

visual feedback of the hand. This is consistent with reach adaptation findings from Krakauer et al. (2005), who showed that prolonged training with a cursor that was rotated with respect to the hand did not result in an increase in the magnitude of motor adaptation. Based on their findings, Krakauer et al. suggested that motor learning saturates within the first block of reach training. Results from our lab (Wong & Henriques, 2009) also indicate that prolonged training over subsequent testing days does not result in increased motor learning as we found no differences between aftereffects following an initial day of reach training (250 trials) and subsequent testing days in which 750 additional trials were performed.

Several authors have suggested a multi-rate model of motor learning wherein one system is highly sensitive to error but learning is rapidly forgotten, while the other system is less sensitive to error but retains learning much more robustly (Kording, Tenenbaum, & Shadmehr, 2007; Shadmehr, Smith, & Krakauer, 2010; Smith, Ghazizadeh, & Shadmehr, 2006). The latter slow-learning process is associated with long-term stable motor changes in the effector (Criscimagna-Hemminger & Shadmehr, 2008), likely because errors that drive this long-term slow learning may be attributed to more long-lasting changes in the plant or effector, like those resulting from fatigue, damage or development. For example, errors due to growth of the arm during childhood would require a more enduring change in estimating the state of the plant than those errors produced when using a new tool. Since sensory information like proprioception are critical for state estimates, it may be that changes in proprioceptive estimates or proprioceptive recalibration may be associated more with a slower learning process than those that lead to changes in movements (aftereffects) which tend to be greater in magnitude. However, further studies are necessary to properly test this possibility. So far, the multi-rate model of motor learning has not been explored for visuomotor adaptation, only for saccade adaptation and force-field learning.

4.2. Mechanisms contributing to motor adaptation and proprioceptive recalibration

Results from our lab do indicate that learning rates during closed loop reaches are dependent on the magnitude of the visuomotor distortion (Balitsky-Thompson & Henriques, 2010; Dionne & Henriques, 2008). The increase in aftereffects or deviations in open loop reaches and the increase in bias observed in the present study were systematically shown to be related to the magnitude of the visuomotor distortion, suggesting that changes in the sensory and motor systems are tied directly to the magnitude of the distortion rather than practice. Consistent with previous work from our lab (Cressman & Henriques, 2009; Cressman et al., 2010; Salomonczyk et al., 2010), sensory and motor changes were not significantly correlated, suggesting that these changes arose via coincident yet separate mechanisms. Differences in changes in sensory and motor systems could arise due to the source of error signals used to generate adaptive responses in the two systems. Sensory prediction errors, or the difference between the actual sensory feedback and expected sensory feedback for a given motor command, are considered to be the predominant error signal driving motor adaptation (Miall & Wolpert, 1996; Tseng, Diedrichsen, Krakauer, Shadmehr, & Bastian, 2007). While previous studies suggest that this error signal also contributes to changes in proprioception (Simani et al., 2007; van Beers et al., 2002), studies from our lab have shown that a cross-sensory error signal (visual-proprioceptive discrepancy) is sufficient and more likely to be responsible for updating proprioceptive estimates of hand position (Cressman & Henriques, 2010). As well, this cross-sensory error signal may even be partially responsible for changes in movements following visuomotor adaptation. To investigate the role of cross-sensory error signals in both sensory and motor recalibration, Cressman and Henriques

(2010) eliminated sensory prediction errors by having a robot manipulandum passively guide subjects' hands while they viewed a cursor rotated 30° CW with respect to their hand move directly to a target (i.e. the cursor moved to target so there was no discrepancy in desired/predicted and actual movement). Following exposure to this cross-sensory discrepancy between seen and felt hand movement, proprioceptive estimates of the hand were shifted in the direction of the distortion and by the same magnitude as that produced following adaptation to a visuomotor rotation of 30° CW when subjects actively and voluntarily directed their reaches toward the target (Cressman & Henriques, 2009). Moreover, when subjects reached to the same targets following exposure to this cross-sensory discrepancy, their open-loop reaches were also significantly deviated. However, these aftereffects were only about a third of the size of aftereffects typically following adaptation. Indeed, the aftereffects in this study were about the same size as, and were significantly correlated with, proprioceptive misestimates of hand position. This is in contrast to the lack of correlation between aftereffects and proprioceptive recalibration following visuomotor adaptation reported previously (Cressman & Henriques, 2009) and in the present study. Thus, aftereffects following mere exposure to cross-sensory discrepancy may be due to a change in felt hand position rather than any real motor recalibration and sensory prediction errors may not be the only training signal responsible for motor recalibration (i.e., movement aftereffects) produced during visuomotor adaptation. In the present study we explored how the magnitude of the distortion would affect proprioceptive recalibration and motor adaptation. In previous research, the magnitude of the distortion (and thus the sensory prediction error signal) has been shown to affect motor learning (Abeele & Bock, 2001; Kagerer et al., 1997). Here, we observed that an increase in the magnitude of a visuomotor distortion resulted in proportional increases to both proprioceptive and motor recalibration. These results suggest that the magnitude of the cross-sensory error signal gives rise to changes in proprioception directly.

Like in our previous studies, a visual cue indicated the initial start position of the hand for the proprioceptive estimation trials so that we could ensure that our observed changes in proprioceptive estimates were not due to a drift in proprioception (Brown, Rosenbaum, & Sainburg, 2003). Given that subjects were provided with a visual representation of their hand position at the beginning of these estimation trials, it is possible that this cue may also have been used to recalibrate proprioceptive estimates of hand position (this time to a visually aligned location) and minimize the proprioceptive bias which was measured at the endpoint of the movement trajectory located 10 cm away, thus reducing the overall changes in felt hand position following visuomotor adaptation. Nonetheless, we did find a significant change in proprioceptive estimate of hand position. While the role of this initial visual hand feedback on proprioceptive recalibration remains to be determined, the results of the present study provide valuable insight into how the size of the visuomotor distortion and the length of training affect both sensory and motor changes.

4.3. Vision and proprioception

Both vision and proprioception have been shown to play integral roles in sensorimotor adaptation (Simani et al., 2007; van Beers et al., 2002). Sensory information from these modalities may be processed in a similar manner within the brain as it has been suggested that both visual (Goodale & Milner, 1992; Milner & Goodale, 1995) and proprioceptive signals (Dijkerman & de Haan, 2007) are processed within two distinct streams – dependent on whether the information is to be used to guide action or for perception. Furthermore, Dijkerman and de Haan suggest that the two proprioceptive processing streams may even be represented in different areas of the brain such that action-oriented processing occurs in the posterior parietal cortex (PPC) and perception-oriented processing occurs in the insula as well as the PPC. The processing of proprioception necessary for re-aligning proprioceptive and visual feedback of the hand (i.e. resolving the cross-sensory error signal) may therefore be separate from the processing of proprioception necessary for providing a unified estimate of hand position for feed-forward motor control (i.e. resolving the sensory prediction error signal). This segregated processing could explain how sensory and motor recalibration could arise as two related yet distinct processes in the brain. Further evidence for the possibility of distinct processes comes from findings of visuomotor adaptation in deafferented individuals who have been shown to adapt their reaches following reaching with misaligned visual feedback of the hand (Bernier, Chua, Bard, & Franks, 2006; Ingram et al., 2000).

Proprioceptive recalibration may arise because the central nervous system requires a unified estimate of hand position for motor control. Previous research has shown that motor performance is better when one has access to information from multiple sensory modalities compared to a single one, even though vision and proprioception sometimes provide naturally conflicting information (van Beers et al., 2002). Thus, one way for the brain to resolve conflicting information in order to provide a unified estimate is to recalibrate one sense so it better matches the other. In the present case, proprioception is recalibrated to match visual estimates of hand position.

4.4. Conclusions

While the precise relationship between cross-sensory error and sensory prediction error signals on reach adaptation and proprioceptive recalibration remains to be determined, our results provide further evidence of sensory plasticity after learning to reach with misaligned visual feedback of the hand. Our method of assessing proprioceptive recalibration allows us to examine the influence of cross-sensory recalibration processes directly, independent of motor adaptation. With our method, proprioceptive recalibration has been observed in a variety of contexts, including following learning with translated and rotated cursor distortions (Cressman & Henriques, 2009, 2010) and force field perturbation (Ostry et al., 2010) when estimating the position of the hand relative to both proprioceptive and visual stimuli (Cressman & Henriques, 2009), following adaptation of both the left and right hands (Salomonczyk et al., 2010), across the lifespan (Cressman et al., 2010), and following prolonged reach training and training to increased distortions. With our method, we possess the requisite tools to investigate the role of distinct error signals in motor and sensory plasticity and with further studies we hope to gain insight into the contribution of these signals to recalibration processes. At present, results indicate that the magnitude of the visuomotor rotation predicts the magnitude of sensory and motor changes following adaptation.

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The role of the cross-sensory error signal in visuomotor adaptation

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Abstract Reaching to targets with misaligned visual feedback of the hand leads to changes in proprioceptive estimates of hand position and reach aftereffects. In such tasks, subjects are able to make use of two error signals: the discrepancy between the desired and actual movement, known as the sensorimotor error signal, and the discrepancy between visual and proprioceptive estimates of hand position, which we refer to as the cross-sensory error signal. We have recently shown that mere exposure to a sensory discrepancy in the absence of goal-directed movement (i.e. no sensorimotor error signal) is sufficient to produce similar changes in felt hand position and reach aftereffects. Here, we sought to determine the extent that this cross-sensory error signal can contribute to proprioceptive recalibration and movement aftereffects by manipulating the magnitude of this signal in the absence of volitional aiming movements. Subjects pushed their hand out along a robot-generated linear path that was gradually rotated clockwise relative to the path of a cursor. On all trials, subjects viewed a cursor that headed directly towards a remembered target while their hand moved out synchronously. After exposure to a 30° rotated hand-cursor distortion, subjects recalibrated their sense of felt hand position and adapted their reaches. However, no additional increases in recalibration or aftereffects were observed following further increases in the cross-sensory error signal (e.g. up to 70°). This is in contrast to our previous study where subjects freely reached to targets with misaligned visual hand position feedback, hence experiencing both sensorimotor and cross-sensory errors, and the distortion magnitude systematically predicted increases in proprioceptive recalibration and reach aftereffects. Given these findings, we suggest that the cross-sensory error signal results in changes to felt hand position which drive partial reach aftereffects, while larger aftereffects that are produced after visuomotor adaptation (and that vary with the size of distortion) are related to the sensorimotor error signal.

Keywords Visuomotor adaptation · Vision · Proprioception · Proprioceptive recalibration · Error-driven learning

Introduction

When reaching with a visuomotor distortion (i.e. when wearing prism goggles or in a virtual-reality environment), one adjusts his or her movements in order to bring the visual representation of the hand to the desired target (Martin et al. 1996b; Krakauer et al. 1999, 2000; Redding and Wallace 2000; Simani et al. 2007). In general, it is proposed that motor adaptation arises primarily due to error-based learning (Tseng et al. 2007; Berniker and Kording 2008; Wei and Kording 2009; Hinder et al. 2010; Shadmehr et al. 2010), where the difference between one's desired performance and actual performance, or between the predicted and actual sensory consequences of one's movements, is reduced. Specifically, if the "seen" hand movement does

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not reach the desired goal or differs from the predicted outcome, then the brain uses this *sensorimotor error signal* (Wong and Shelhamer 2011) to change one's motor performance on subsequent movements. Moreover, these movements continue to deviate even when (misaligned) visual feedback of hand position is removed (Martin et al. 1996a; Krakauer et al. 1999, 2000; Redding and Wallace 2000; Simani et al. 2007). These persistent movement deviations, known as aftereffects, are robust evidence that the central nervous system (CNS) has learned a new visuomotor mapping in response to the sensorimotor error signal.

Evidence suggests that in addition to motor changes observed following visuomotor adaptation, sensory changes occur as well. More specifically, one's sense of felt hand position shifts in the direction of the visual feedback provided. This has been demonstrated following adaptation to prism goggles, in which the entire visual field is displaced (Harris 1963; Hay and Pick 1966; Redding and Wallace 1996, 2004) and more recently following adaptation in a virtual setup, where only the visual feedback of hand position is displaced (van Beers et al. 2002; Simani et al. 2007). Using this second paradigm, we have shown that this shift is approximately 20 % of the visuomotor distortion introduced, or roughly one-half to one-third of the extent of reach adaptation achieved (Cressman and Henriques 2009; Salomonczyk et al. 2011, 2012). While this shift in felt hand position, which we term proprioceptive recalibration, is small, it is robust and occurs coincidentally with motor changes under a variety of contexts. For example, we have observed this shift in felt hand position following motor adaptation to rotated and translated cursor distortions (Cressman and Henriques 2009), during active and passive hand placement (Cressman and Henriques 2009), in both the left and right hands (Salomonczyk et al. 2012) and in healthy young and older adults (Cressman et al. 2010).

Recently, we have suggested that a second error signal arising from the discrepancy between seen and felt positions of the reaching hand (what we term the *cross-sensory error signal*) may contribute to sensory and motor adaptation (Cressman and Henriques 2010; Henriques and Cressman 2012). In particular, we have proposed that this cross-sensory error signal leads to the observed changes in perceived hand position, such that sensory signals are recalibrated to provide a unified state estimate of the hand/ effector. To investigate the role of this cross-sensory error signal in motor learning, we devised a novel learning paradigm that isolated the visual-proprioceptive discrepancy (and thus this cross-sensory error signal) from the usual visuomotor discrepancy (Cressman and Henriques 2010). In particular, we employed a paradigm where subject did not make free, goal-directed reaches to the target during training, but instead moved their hand (active movement

condition), or had their hand passively moved by the manipulandum (passive movement condition), along a robot-constrained pathway while they viewed a cursor that moved directly towards a remembered target. The pathway that the unseen hand travelled was gradually rotated with respect to the cursor-target pathway over trials, creating a discrepancy between the seen and felt motion of the hand. Since the actual direction of the hand motion was not under the control of the subject, and the hand-cursor always headed towards the target, subjects did not experience any reaching errors or sensory consequences of a goal-directed action and hence any sensorimotor error. Furthermore, those in the passive exposure training condition experienced no volitional movement as their hand was passively moved for them. However, like previous adaptation paradigms, subjects in both active and passive movement conditions experienced a cross-sensory error signal as their felt sense of hand position was gradually misaligned from the cursor representation of their hand. Following active or passive exposure to this cross-sensory error signal, we found that all subjects still recalibrated proprioception, and the magnitude of this proprioceptive shift was comparable to that achieved following typical learning paradigms in which subjects were able to reach freely to targets with the visuomotor distortion (and utilize both the cross-sensory and sensorimotor error signals). Additionally, we found that following active and passive exposure training, subjects adapted their movements such that reaches made without visual feedback of their hand position were deviated in the direction opposite the cursor distortion. However, these movement aftereffects were two-thirds smaller than those observed following typical training with a visuomotor discrepancy. As well, unlike any of our previous studies, the observed proprioceptive recalibration and motor aftereffects were correlated with each other, suggesting that they may have been driven by the same mechanism (Cressman and Henriques 2010). Taken together, the findings of this study suggest that exposure to a sensory discrepancy alone is sufficient to form a new visuomotor mapping in the absence of a sensorimotor error signal. More importantly, results imply that the cross-sensory error signal alone may drive partial motor learning.

In the present study, we looked to investigate the extent that this cross-sensory error signal can contribute to motor learning by determining if induced changes in perceived hand position can be used in computing subsequent motor commands. To do so, we examined motor and sensory changes following exposure to a cross-sensory error signal that was systematically increased and compared these results to those from a previous study that examined motor and sensory changes following typical visuomotor adaptation (Salomonczyk et al. 2011). The influence of the size of

the sensorimotor error (and hence combination of increases in the sensorimotor error signal and cross-sensory error signal) on motor learning and sensory plasticity has been previously characterized (Marko et al. 2012; Abeele and Bock 2001; Wei and Kording 2009; Salomonczyk et al. 2012), yet the influence of the cross-sensory error signal on its own remains to be determined. Thus, we sought to determine the extent that proprioception can be recalibrated with an increasing cross-sensory error signal and further characterize its role in motor control.

Methods

Subjects

Twenty-three healthy, right-handed young adults (mean age = 20.58, SD = 3.08 years, 11 females) volunteered to participate in the experiment described below. All subjects were pre-screened verbally for self-reported handedness and a history of visual, neurological and/or motor dysfunction. Subjects were then randomly assigned to either the 50° or 70° training groups (50° group: $n = 12$; 70°: $n = 11$). All subjects provided informed consent, and the study was conducted in accordance with the ethical guidelines approved by the York University Human Participants Review Subcommittee.

General experimental setup

A side view of the setup is illustrated in Fig. 1a and is similar to that used by Cressman and Henriques (2009, 2010). Subjects were seated at a table such that the distance of the chair from the table and the height of the chair were adjusted in order to ensure that each subject could comfortably see and reach to all target positions. Once the chair was adjusted, it remained in the same position for the entire experiment. Subjects were instructed to grasp the vertical handle of a two-joint robot manipulandum (Interactive Motion Technologies) with their right hand such that their thumb was positioned on a top marker (1.4 cm in diameter). The position of the robot manipulandum was recorded throughout trials at a sampling rate of 50 Hz and a spatial accuracy of 0.1 mm. Visual stimuli were projected from a monitor (model: Samsung 510 N, refresh rate: 72 Hz) installed 17 cm above the robot and viewed by subjects as a reflected image. The reflective surface was opaque and positioned so that the imaged displayed on the monitor appeared to lie in the same horizontal plane as the robot handle. The room lights were dimmed, and subjects' view of their right hands were blocked by the reflective surface and a black cloth draped between the experimental setup and subjects' right shoulders.
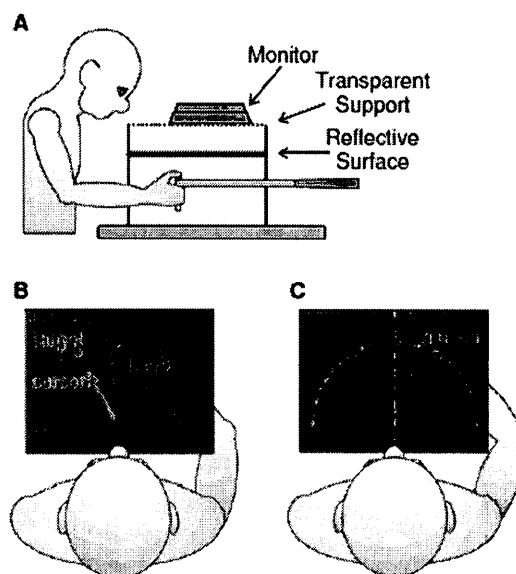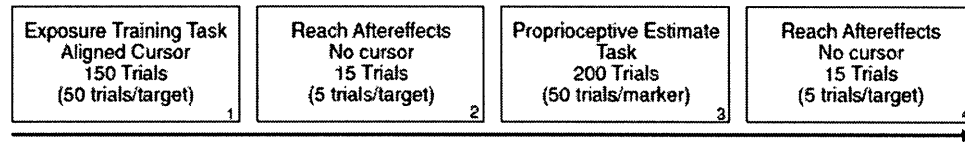

Fig. 1 Experimental set up and design. (a) Side view of the experimental set up. b and c top view of the experimental surface visible to subjects. b Cross-sensory discrepancy introduced in the rotation exposure training task and target locations. The unseen hand's constrained pathway was rotated 30° clockwise (CW) with respect to the cursor-target pathway during the first rotation exposure training block and increased to 50° or 70° CW for the second rotation exposure training block for the 50° training group and 70° training group, respectively. Targets (yellow rings) 1 cm in size were located 10 cm from the home position (black circle) at 0° and 30° left and right of midline. c In the proprioceptive estimate task, subjects actively pushed their hand out 10 cm along a constrained linear path (depicted by the red rectangle) from the home position and judged the position of their hand with respect to a reference marker. Reference markers (yellow rings) were located at 0° and 30° left and right of midline

General procedure

The experiment consisted of two separate testing sessions completed on two testing days. Each testing session involved four tasks (comprising one block), and on the second day of testing, these tasks were repeated two times (i.e. subjects completed two blocks, Fig. 2). On the first testing day, subjects completed the exposure training trials outlined below while viewing a cursor that was veridical, or aligned, with their unseen hand. On the second testing day, subjects completed the exposure training trials while viewing a cursor that was misaligned from the actual location of their unseen hand (grey circle, Fig. 1b). Specifically, a subject's unseen hand moved out along a path that was gradually rotated to 30°, 50° or 70° clockwise (CW) relative to the cursor position, which was represented by a green disc 1 cm in diameter (green circle, Fig. 1b). The 50° training

Part 1: Baseline

Exposure Training Task Aligned Cursor 150 Trials (50 trials/target) 1	Reach Aftereffects No cursor 15 Trials (5 trials/target) 2	Proprioceptive Estimate Task 200 Trials (50 trials/marker) 3	Reach Aftereffects No cursor 15 Trials (5 trials/target) 4

Part 2: Misaligned Cursor

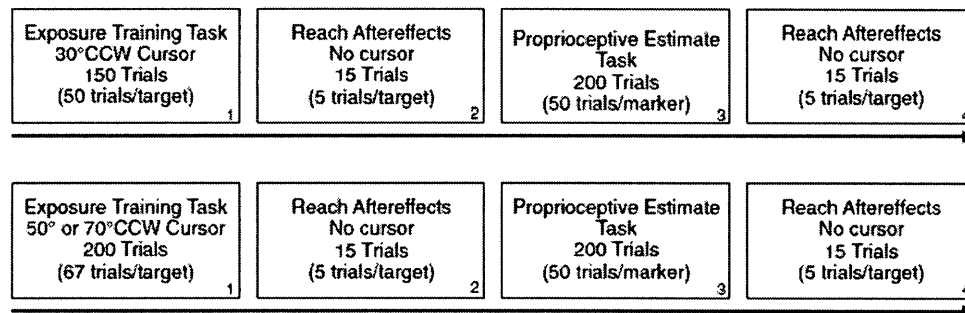| Exposure Training Task 30°CCW Cursor 150 Trials (50 trials/target) 1	Reach Aftereffects No cursor 15 Trials (5 trials/target) 2	Proprioceptive Estimate Task 200 Trials (50 trials/marker) 3	Reach Aftereffects No cursor 15 Trials (5 trials/target) 4
Exposure Training Task 50° or 70°CCW Cursor 200 Trials (67 trials/target) 1	Reach Aftereffects No cursor 15 Trials (5 trials/target) 2	Proprioceptive Estimate Task 200 Trials (50 trials/marker) 3	Reach Aftereffects No cursor 15 Trials (5 trials/target) 4

Fig. 2 Breakdown of the testing sessions within the experiment. In the first testing session (*top row*), subjects moved the robot arm with an aligned cursor that accurately represented the position of their hand during the exposure training trials. In the second testing sessions (*second* and *third rows*), subjects' unseen hand path was increasingly misaligned from the cursor-target pathway by 30° (*first rotated block*) up to 50° or 70° clockwise (*second rotated block*). After completing 150 exposure trials with an aligned or misaligned cursor, subjects next reached freely to each of three reach targets 5 times each without a cursor in order to assess motor adaptation (reach aftereffect trials, *Box 2* in each row). Subjects then completed 200 proprioceptive estimate trials (*Box 3* in each row) followed by another set of free, no cursor reaches (*Box 4* in each row) to examine the maintenance of reach aftereffects. In the first testing session, subjects only completed one block of exposure training trials with aligned visual feedback of the hand. In the second testing session, subjects completed two training blocks with misaligned visual feedback of the hand

group completed the first block of trials of the second testing session such that their hand moved out along a path that was rotated 30° CW relative to the cursor, and in the second block of trials, their hand was rotated 50° CW relative to the cursor motion. The 70° training group completed the first block of trials of the second testing session with the same 30° CW hand-cursor distortion as the 50° training group; however, they were exposed to a 70° CW hand-cursor discrepancy during the second block of training trials. For both groups, the 30° hand-cursor rotation was introduced gradually such that on the first trial, the path that the unseen hand moved out along was rotated 0.75° CW with respect to the cursor. The rotation then increased by 0.75° each trial, until the full 30° distortion was achieved. The distortions in the 50° and 70° blocks (i.e. second blocks of trials of the second testing session) were also introduced gradually by 0.75° per trial, starting from the rotation of the previous block (i.e. in the first trial of block two, the distortion was introduced at 30.75° and increased by 0.75° per trial up to 50° or 70°).

Task 1: exposure training

At the start of each trial, the robot manipulandum was positioned below the home position, which was indicated by a green circle 1 cm in diameter and located approximately 25 cm directly in front of subjects' midline. This circle then disappeared and a yellow target circle 1 cm in diameter (yellow circle in Fig. 1b) was presented for 500 ms. The targets were located radially 10 cm from the home position at 0° (in line with subjects' midline), 30° right (CW) and 30° left (CCW) from centre. Once the target disappeared, subjects were instructed to actively push the robot manipulandum out along a robot-generated constrained linear path (red rectangle, Fig. 1b) while viewing a cursor that represented their unseen hand position. On all trials, the cursor headed directly to the remembered target position. If subjects attempted to move outside of the established path, a 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 channel wall (Henriques and Soechting 2003). In each session, the trials

were pseudo-randomized such that each target was displayed at least once before any target was repeated.

To ensure that subjects paid attention to the cursor, we had them both (1) stop their movement when they felt their hand had reached the remembered target location, and (2) after stopping their movement, indicate via a key press if the cursor had "blinked" during the movement (for 50 % of trials, the cursor was extinguished (i.e. blinked) for 30 ms in the middle portion of its trajectory). Thus, subjects controlled the distance that their hand moved outwards away from their body, but not the lateral direction that the hand travelled.

Subjects completed 150 training trials with a cursor that was aligned with their hand (first testing session: Fig. 2, Part 1, Box 1), 150 training trials with a gradually introduced 30° hand-cursor path discrepancy (second testing session, block 1; Fig. 2, Part 2, Box 1), and 200 trials with a gradually introduced 50° or 70° hand-cursor path discrepancy (second testing session, block 2). Thus, subjects were exposed to the full 50° or 70° hand-cursor path discrepancy on 173 or 146 trials, respectively. This is a greater number of training trials at the full hand-cursor discrepancy than our previous paradigms (e.g. Cressman and Henriques 2010; Salomonczyk et al. 2011). Given this large number of trials we had subjects complete in the current experiment, and the fact that we have previously shown that there are no further changes in performance after training with misaligned visual hand feedback for 160 trials versus 60 trials (i.e. motor adaptation and proprioceptive recalibration do not increase after training for more than 60 trials), we are confident that the results discussed below are not due to the slightly different number of exposure trials at the full exposure completed by our 50° and 70° training groups.

Task 2: reach aftereffects to assess visuomotor adaptation

This task was performed twice in each block, immediately after the exposure training task and immediately after the proprioceptive estimate task (boxes labelled 2 and 4 in Fig. 2). During these trials, the robot-generated constrained pathway was removed and subjects could freely move the robot. A trial would start with the robot handle illuminated at the home position. One of three reach targets located at 0°, 30° right (CW) and 30° left (CCW) of centre (Fig. 1b) would then appear, and after 500 ms, the home position would disappear. This was the cue for subjects to reach to the visible target using the robot handle without any visual cursor feedback of their hand position. Once subjects believed they were at the target, they were to hold their final position. Once the final position was held for 250 ms, the reach movement was deemed complete. The target would then disappear, and subjects were to return their hand to the

home position guided by a robot-generated constrained linear path. Subjects completed 5 trials to each of the three targets for a total of 15 trials.

Task 3: proprioceptive estimates to assess perceived hand position

To evaluate sensory changes resulting from motor adaptation, previous studies have typically employed tasks which required subjects to make goal-directed reaches using the adapted hand (Simani et al. 2007; van Beers et al. 2002). Reach errors arising in these paradigms could be due to changes in felt hand position resulting from proprioceptive recalibration, changes in motor commands resulting from an updated internal model, or a combination of sensory and motor changes. The present task was designed to isolate subjects' sense of felt hand position from goal-directed movement by removing any visual feedback during hand movement and having subjects make an estimate of their hand's static position with respect to a visual or proprioceptive (body midline) reference marker. We have previously shown that subjects' estimates are similar regardless of whether they actively guide their hand into position along a robot-generated constrained linear path, or their hand is moved along the same path into position by the robot (Cressman and Henriques 2009). Moreover, estimates appear to be similar regardless of the path taken by the hand to its final position (Jones et al. 2012), suggesting that subjects use final hand position information to estimate the location of their hands, independent of how the hand was moved into position and the path taken. Due to time constraints associated with passive movement and the number of trials completed by subjects in the current experiment, we employed the active version of the proprioceptive estimate paradigm described below.

A trial began with the subject grasping the robot manipulandum at the home position indicated by a green circle. After 500 ms, this circle disappeared, and subjects were instructed to push their hand outward along a robot-generated constrained linear path 10 cm in length (as described in task 1, red rectangle in Fig. 1c). Once the hand arrived at the end of the path (along the dotted arc shown in Fig. 1c), a visual reference marker located at 0°, 30° left (CCW) or 30° right (CW) of centre (yellow circles, Fig. 1c) appeared and subjects made a two-alternative forced-choice judgment about the position of their hand (left or right) relative to the visual reference marker. A visual reference marker appeared on 75 % of the proprioceptive estimate trials, while for the remaining 25 % of trials subjects were instructed to judge the location of their hand with respect to their body midline (indicated by the dashed vertical line in Fig. 1c); the midline trials were indicated with a sound cue (beep). There was no time constraint for giving a response.

After responding, the visual reference marker (for all non-body midline trials) disappeared, and subjects moved the robot directly back to the home position along the same linear route to begin the next trial. The position of the hand with respect to each reference marker was adjusted over trials using an adaptive staircase algorithm (Kesten 1958; Treutwein 1995) as described by Cressman and Henriques (2009, 2010) and Jones et al. (2010). In particular, for each reference marker, there were 2 staircases, one starting 20° to the left (CCW) of the reference marker and one starting 20° to the right (CW). The 2 staircases were adjusted independently and randomly interleaved as outlined by Cressman and Henriques (2009). Thus, if subjects responded consistently (i.e. associated a given felt hand position with a given reference marker), the two staircases converged.

Data analysis

Before examining motor adaptation and proprioceptive recalibration, we first wanted to ensure that subjects were (1) moving out smoothly with minimal lateral deviation from the force channel and (2) paying attention to the cursor during the aligned and misaligned exposure training trials. To ensure that subjects were moving smoothly with minimal lateral deviation from the force channel, we calculated the perpendicular deviations of the hand for all trials when the target was located at 0°. We observed a mean perpendicular deviation of 0.33 mm (with a mean SD across trials = .44 mm) which is within the 3 mm of the robot-generated channel. Averaged across all subjects, the maximum deviations were 1.3 mm left and 1.4 mm right of the home-target vector, which is again within the confines of the channel, suggesting that subjects stayed well within the confines of the force channel.

We found that, on average, the robot was stopped 10.08 cm (SD .70 cm) after movements were initiated, which is very close to the 10 cm movement target goal. In addition, subjects correctly reported whether the cursor had blinked or not on 90 % of all trials. A one-way ANOVA comparing the percentage of correctly reported blinks across training blocks revealed a non-significant block effect ($F(2,75) = 1.54$, $p = .22$), suggesting that subjects attended to the cursor in a similar manner across aligned and rotated training blocks.

Motor adaptation

We analysed reaching errors (i.e. aftereffects) made in the reach aftereffects trials in which no visual cursor was presented (Task 2) to (1) determine whether subjects adapted their reaches after exposure to misaligned visual-proprioceptive feedback of their hand position and (2) examine whether subjects maintained this adaptation across the

proprioceptive estimate trials. Reach endpoint errors were defined as the angular difference between a movement vector (from the home position to reach endpoint) and a reference vector (joining the home position and the target). To determine whether subjects had indeed adapted their reaches, we analysed mean endpoints in aftereffect trials using a 2 training group (50° group vs. 70° group) × 3 visual feedback block (aligned feedback vs. first block of rotated feedback (30°) vs. second block of rotated feedback (50° or 70°)) × 3 target (0° vs. 30° CW vs. 30° CCW) repeated-measures analysis of variance (RM-ANOVA). Training group was a between-group factor, while visual feedback block and target were within-group factors. Post-hoc pair-wise comparisons were used to explore the loci of these differences, and a Bonferonni correction was applied (alpha = .05). In addition to revealing if subjects adapted their reaches following exposure training, this analysis allowed us to determine whether reach adaptation increased with the increasing hand-cursor distortion.

To determine whether subjects maintained their reach adaptation following proprioceptive estimate trials, we compared aftereffects between reaches following exposure training and those following proprioceptive estimate trials. To do so, we subtracted the reach errors following aligned exposure training from the two rotated exposure training blocks. These baseline-subtracted aftereffects were compared using a 2 training group (50° group vs. 70° group) × 2 visual feedback block (30° rotated feedback vs. 50° or 70° rotated feedback) × 2 time (reach aftereffects following exposure trials vs. reach aftereffects following proprioceptive estimate trials) RM-ANOVA. Post-hoc pair-wise comparisons were used to explore the loci of these differences and a Bonferonni correction was applied (alpha = .05).

Proprioceptive estimates of hand position

To examine the influence of the magnitude of the cross-sensory error signal on changes in proprioceptive recalibration, we determined the location at which subjects felt their hands were aligned with each reference marker after each block of exposure training trials (Cressman and Henriques 2009, 2010; Cressman et al. 2010; Jones et al. 2010; Salomonczyk et al. 2011, 2012). This location was determined by fitting a logistic function to each subject's responses for each reference marker during each testing session. The position at which subjects responded "left" 50 % of the time (i.e. responded "left" and "right" equally often) represents their bias. In addition to calculating bias, we also determined subjects' uncertainty (or precision) by finding the difference between the values at which the point of responding "left" was 25 % and 75 %. Bias and uncertainty related to a particular reference marker were excluded if

the associated uncertainty was greater than the mean uncertainty across all reference markers +2 standard deviations. Based on this analysis, only 1 proprioceptive estimate (less than 0.01 % of total estimates) was excluded. Biases and uncertainty ranges were analysed in a 2 training group (50° group vs. 70° group) × 3 visual feedback during the exposure trials (aligned feedback vs. first block of rotated feedback (30°) vs. second block of rotated feedback (50° or 70°)) × 4 marker location (0° vs. 30° CW vs. 30° CCW vs. body midline) RM-ANOVA. Post-hoc pair-wise comparisons were used to explore the loci of these differences, and a Bonferonni correction was applied (alpha = .05). In addition to revealing if subjects recalibrated proprioception following exposure training, this analysis allowed us to determine whether recalibration increased with an increasing hand-cursor distortion (i.e. cross-sensory error signal).

Results

Motor adaptation

Following exposure training with an aligned cursor, mean reach endpoint errors were on average 1.0° to the left of the target. These small reaching errors suggest that subjects were able to accurately reach to a target without visual feedback of their hand position after having been forced to repeatedly move their hands to the targets along a constrained path. Mean baseline-subtracted aftereffects following exposure training with a rotated cursor are displayed in Fig. 3 alongside results from Salomonczyk et al. (2011; filled bars). Mean reach endpoint errors differed significantly between the exposure training conditions $(F(2,42) = 17.82, p < .001)$. Post-hoc analysis revealed that after exposure training with a hand-cursor discrepancy of 30° (empty bars, Fig. 3), all subjects on average made reaching errors significantly more rightwards of the targets compared to after training with a cursor that was aligned with their hand position (mean difference = 8.9°, $p < .001$). The magnitude of these errors is considerably less than those from 2011 results, in which subjects trained by making unconstrained reaching movements towards targets while visual feedback of the hand was rotated 30° CW with respect to the unseen hand. Following exposure training with either a 50° or 70° misaligned cursor, reaches were still more rightwards of the target compared to after training with an aligned cursor (mean difference = 9.9°, $p < .001$); however, they were not any greater than those following 30° misaligned exposure training (mean difference between first and second rotated blocks = 1.0°, $p > .99$). Furthermore, no difference in training group $(F(1,21) < 1, p = .42)$ or interaction between exposure condition and training group was observed $(F(2,42) < 1, p = .42)$. This is in
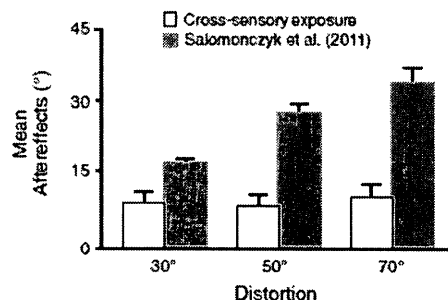

Fig. 3 Aftereffects following exposure training with misaligned visual feedback of the hand. *Endpoint errors* were calculated by subtracting angular reach endpoint errors in the no cursor reach aftereffect trials after training with an aligned cursor from errors completed in the no cursor reach aftereffect trials after training with a misaligned cursor. Errors at reach endpoints were averaged across targets and subjects, and are shown for the no cursor reaches completed after the two consecutive rotated training blocks. *Empty bars* reflect aftereffects following the exposure training paradigm while *filled bars* reflect aftereffects following visuomotor reaching from Salomonczyk et al. (2011). *Error bars* reflect SEM

contrast to our previous findings in which subjects showed increasing aftereffects after they reached voluntarily with a visuomotor distortion that increased in magnitude. These results suggest that reach adaptation following exposure to misaligned visual-proprioceptive feedback saturates, such that no further increase in aftereffects occurs with distortion magnitudes greater than 30°.

There was an overall main effect of target location, such that reaches tended to fall to the right of the 30° CW and 0° targets and slightly to the left of the 30° CCW target $(F(2,42) = 36.34, p < .001)$, indicating that subjects slightly expanded the workspace (consistent with previous work). Importantly, no interaction effects were observed between targets and training groups $(F(2,42) = 2.40, p = .12)$ or targets and visual feedback conditions $(F(4,84) < 1, p = .62)$, suggesting that reach adaptation occurred comparably between training groups and was not dependent on the location of the target in the workspace.

Analysis of baseline-subtracted endpoint errors using a RM-ANOVA revealed that the magnitude of these aftereffects decreased with time, such that those aftereffects measured following proprioceptive estimates were on average 5° smaller compared to those measured immediately following exposure training $(F(1,21) = 12.14, p < .01)$. However, previously described results revealed a significant difference between the aligned and both the first and second rotated blocks $(F(2,42) = 17.82, p < .001$, see above), suggesting that while aftereffects may have diminished following proprioceptive estimates compared to those following exposure training, they were still present. No interaction effects were observed between time and rotated

exposure training blocks ($F(1,24) < 1$, $p = .62$) or time and group ($F(1,21) = 1.32$, $p = .50$). Thus, aftereffects measured following proprioceptive estimates, while smaller, still showed a comparable pattern of effects as those aftereffects measured following exposure training.

Proprioceptive recalibration

Bias

Mean proprioceptive biases at each reference marker location (grey circles) for both training groups are displayed in Fig. 4a. The diamonds indicate bias values following exposure training with aligned visual feedback of hand position, while the triangles indicate biases following exposure training with a 30° misaligned cursor (empty triangles) or

a 50° or 70° misaligned cursor (grey filled triangles). Bias estimates for the proprioceptive midline marker (dashed line) are displayed above visual marker estimates as dashed symbols. For both training groups, we see that estimates of unseen hand position were biased following aligned cursor-hand exposure training slightly towards the left (6°). Previous studies in our lab have suggested that this directional bias arises due to a systematic hand bias (Jones et al. 2010; Salomonczyk et al. 2012) where subjects overestimate how far right their right hand is, resulting in a leftward bias. Mean bias estimates differed significantly between the exposure training conditions ($F(2,42) = 17.73$, $p < .001$). Post-hoc analysis revealed that after exposure training with a 30° misaligned cursor, biases were shifted significantly rightwards (mean difference across all subjects = 5.3°, $p < .001$), consistent with the direction of motor adaptation
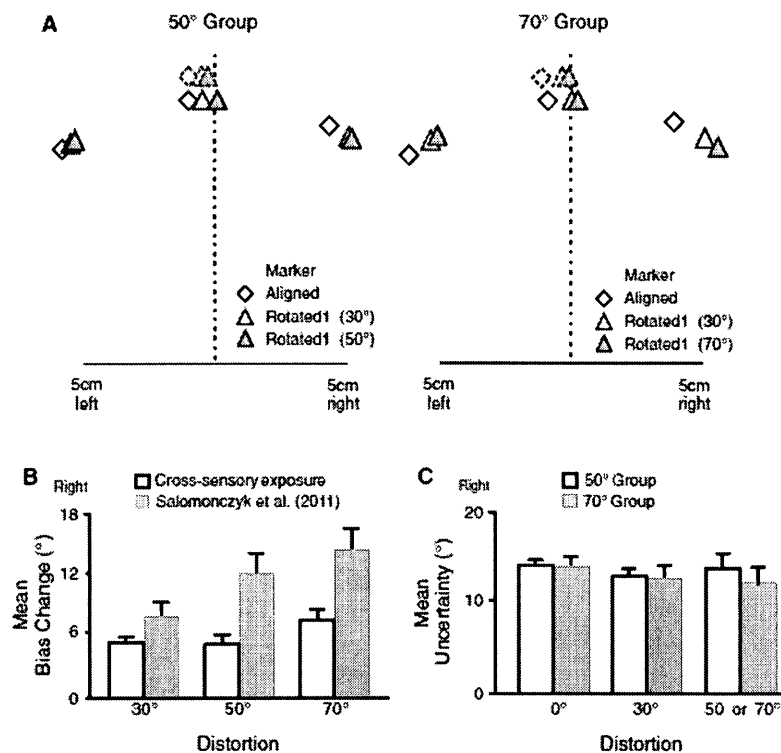

Fig. 4 Proprioceptive biases following training with aligned and misaligned visual feedback of the hand. a Mean 2-D proprioceptive biases following training with an aligned (empty diamonds) or misaligned (after the first 30° rotated block: empty triangles; after the second rotated block: filled triangles) cursor for subjects in the 50° training group (left panel) and 70° training group (right panel). The actual reference marker positions are represented as grey circles. Estimates around the midline (dashed line) are depicted on top of the estimates around the central visual marker and are outlined with

a dashed line. b Mean changes in biases after training with a misaligned cursor compared to an aligned cursor were averaged across reference markers and subjects. Empty bars reflect proprioceptive recalibration following the exposure training paradigm while filled bars reflect proprioceptive recalibration following visuomotor reaching from Salomonczyk et al. (2011). c Mean uncertainty of proprioceptive estimates following training with an aligned (0°) or misaligned (30°, 50° and 70°) cursor for the 50° training group (open bars) and 70° training group (filled bars). Error bars reflect SEM

(aftereffects, Fig. 3). These results are also consistent with the magnitude of proprioceptive recalibration observed in results from Salomonczyk et al. (2011), shown as filled bars in Fig. 4b. Following exposure training with either a 50° or 70° misaligned cursor, bias estimates were still more rightwards of the target compared to after training with an aligned cursor (mean difference = 6.4, $p < .001$); however, they were not any greater than those following 30° misaligned exposure training (mean difference between first and second rotated blocks = 1.1°, $p = .45$). Furthermore, no difference in group ($F(1,21) < 1$, $p = .76$) or interaction between exposure condition and training group was observed ($F(2,42) < 1$, $p = .47$). These results suggest that proprioceptive recalibration following exposure to misaligned visual-proprioceptive feedback saturates, such that no further increase in aftereffects occurs with distortion magnitudes greater than 30°.

Proprioceptive estimates of hand position were comparable across all visual reference and body midline (Fig. 4a, b, dashed insets) marker locations ($F(3,63) = 1.96$, $p = .13$), and no interaction between marker location and exposure block was observed ($F(3,63) = 1.21$, $p = .31$).

Altogether, these results suggest that proprioception is recalibrated around both visual and midline reference markers following exposure to misaligned visual-proprioceptive hand feedback, although this sensory change saturates within a 30° distortion. This then indicates that a cross-sensory error signal available during exposure training on its own is not enough to drive additional sensory recalibration when the error signal increases above 30° cursor-hand misalignment.

Uncertainty

Mean uncertainty is displayed in Fig. 4c. On average, the overall magnitude of the uncertainty range was 13.2° and is consistent with measures of precision reported in previous exposure training paradigms (Cressman and Henriques 2010) and results from Salomonczyk et al. (2011). Uncertainty was comparable across all training blocks ($F(2,42) < 1$, $p = .48$) and reference marker locations ($F(3,63) = 1.61$, $p = .20$). There were no differences in uncertainty between training groups ($F(1,21) < 1$, $p = .53$). No interaction effects were observed ($p > .34$). Thus, subjects' precision in estimating the location of their unseen hand relative to the markers was not affected by the magnitude of the cross-sensory error signal experienced or the marker location.

Relationship between aftereffects and recalibration

Taken together, results indicate that subjects adapted their reaches and mis-estimated the position of their hand after

viewing a rotated cursor that moved synchronously with their unseen hand. Both reach aftereffects and proprioceptive estimates were shifted clockwise by approximately 9° and 5°, respectively, regardless of the magnitude of the visuo-proprioceptive distortion experienced. A paired-samples t test did not reveal a significant difference between the magnitude of aftereffects and proprioceptive recalibration ($t(45) = .80$, $p = .43$). To examine the possibility that both aftereffects and bias rely on the cross-sensory error signal, we applied a step-wise regression procedure with the per cent change in bias and the size of the distortion as predictors of per cent change in aftereffects. Change in bias was selected as the predictor as we hypothesized that changes in felt hand position contributed to updates in the motor plan, resulting in adaptive reach movements (aftereffects). This relationship is displayed in Fig. 5. Results revealed that the change in bias significantly predicted the change in aftereffects ($\beta = .48$, $p = .001$, one-tailed), though the magnitude of the distortion did not ($\beta = -.193$, $p = .08$, one-tailed). We observed that change in bias was a significant predictor of change in aftereffects for both training groups (50° group: $\beta = .39$, $p = .02$, one-tailed; 70° group: $\beta = .71$, $p = .004$, one-tailed). This correlation was also present at each training block (first rotated block: $\beta = .42$, $p = .03$, one-tailed; second rotated block: $\beta = .50$, $p = .02$,
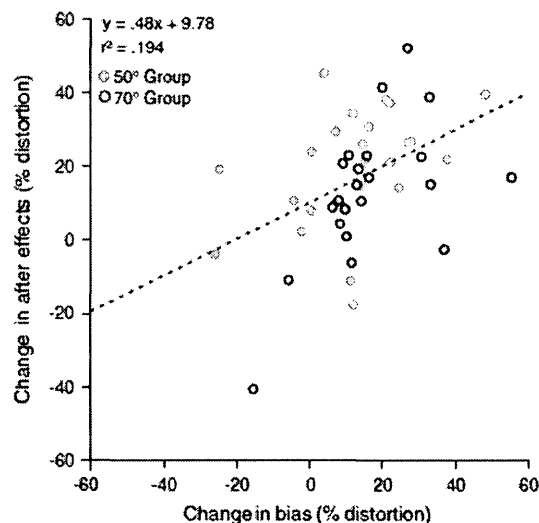

Fig. 5 Changes in sensory recalibration (bias) and motor adaptation (aftereffects) as a percentage of the visuomotor distortion introduced during each exposure training block for subjects in the 50° training group (*filled symbols*) and 70° training group (*empty symbols*) following rotated exposure training trials. Each symbol represents the percentage change in bias and percentage change in aftereffects averaged across marker and target locations (respectively) for each subject. The *solid line* indicates the line of best fit for all data points

one-tailed). These results, along with the observation that changes in bias and aftereffects were very similar, suggest that a similar error signal is underlying these processes. These findings are consistent with a previous study examining the relationship between changes in bias and aftereffects following exposure training (Cressman and Henriques 2010). However, these findings are in contrast to previous studies employing free reaching during visuomotor training (Cressman and Henriques 2009; Cressman et al. 2010; Salomonczyk et al. 2011; Salomonczyk et al. 2012), including our study investigating the role of the magnitude of the sensorimotor error signal (Salomonczyk et al. 2011). In these studies, bias and aftereffects were uncorrelated, and in our 2011 study, the magnitude of the error signal did predict changes in bias and aftereffects. These results suggest that the cross-sensory error signal, on its own, exerts an initial effect on sensory and motor changes (potentially up to when the distortion is 30°). Further changes in response to distortions greater than 30° appear to be driven by the sensorimotor error signal or a combination of the two.

Discussion

The goal of the present study was to examine the extent that a cross-sensory error signal can contribute to proprioceptive recalibration and motor adaptation. To do so, we exposed subjects to a cross-sensory error signal, such that subjects viewed a cursor that travelled towards a remembered target location while their hand travelled along a constrained, robot-generated channel that was increasingly misaligned from the cursor-target pathway. The robot-generated channel only allowed subjects to move volitionally in the forward direction and not in the lateral direction, where the discrepancy between the senses (and the error signal) was introduced. This ensured that subjects did not experience an error in their reaching direction as the visual representation of their hand was always in line with the target. We found that subjects adapted their reaches and recalibrated their sense of felt hand position after exposure to this visuo-proprioceptive discrepancy, which occurred in the absence of the typical sensorimotor error signal associated with error-dependent learning. Specifically, after viewing a cursor that misrepresented the location of their hand by 30° during a constrained movement, subjects misreached in the same direction that their hand had moved during exposure training trials (9° change) and began to feel that their hand had shifted in the direction opposite the cursor distortion (6° change). Furthermore, subjects in the present study demonstrated a proprioceptive shift at both the visual reference markers and around their body midline, suggesting that hand proprioception rather than vision (or a visuomotor mapping) was recalibrated. Interestingly, reach

aftereffects and proprioceptive recalibration achieved early saturation, such that no further motor or sensory changes were observed after subjects were exposed to distortions greater than 30°.

Subjects completed a greater number of training trials in the current experiment than in previous paradigms (i.e. Salomonczyk et al. 2011). Thus, in order to ensure that we minimized subjects' fatigue and in attempt to keep subjects engaged in the task, we chose to have subjects actively push their hand out along a constrained pathway during the exposure training trials [as opposed to the passive exposure training in our previous study (Cressman and Henriques, 2010)]. Our previous exposure study, which compared active (subject-generated) and passive (robot-generated) movement during training, showed no differences in subsequent motor adaptation or proprioceptive recalibration between the two types of training (Cressman and Henriques 2010). This suggests that subjects were exposed to the same cross-sensory error signal in both paradigms. We believe that present results obtained with an active paradigm continue to reflect a purely cross-sensory error based on the following findings: firstly, present results are consistent with those of our 2010 study in which small yet persistent aftereffects were observed following exposure training with either an actively or passively placed hand. Thus, while the motor commands generated to push the hand along the constrained path may be used by forward models to predict sensory consequences of these movements, this contribution appears to be minimal since the absence of such motor commands (when the hand is passively led by the robot) leads to similar results for both exposure training and proprioceptive estimation. Second, present findings reflect saturation of reach aftereffects and proprioceptive recalibration following exposure training with distortions greater than 30°, which is inconsistent with results from Salomonczyk et al. (2011) as discussed below. Lastly, subjects' movements during exposure training were constricted in the lateral direction by a robot-generated force channel, yet we observed persistent changes in movements in this direction following misaligned exposure training. Altogether, these findings suggest that the present results reflect subjects' change in performance after exposure to a cross-sensory error signal, rather than a change in the forward model resulting from a sensorimotor error signal.

Role of error signals in adaptation and recalibration

In the present study, we systematically increased the discrepancy between the hand path and the cursor path over trials. While subjects initially showed motor aftereffects and proprioceptive recalibration following exposure to a 30° visuo-proprioceptive discrepancy, subjects did not show any further motor aftereffects or proprioceptive

is also produced. The forward model compares the desired and actual limb position using sensory information which is then fed back to the CNS to generate motor commands that will meet the given conditions (i.e. update the inverse model). Updating of the forward model has recently been implicated in the sensory (perceptual) changes associated with motor learning (Synofzik et al. 2008; Izawa et al. 2012). For example, by examining the role of sensory prediction errors on motor learning in cerebellar patients, Synofzik et al. (2008) showed that damage to the cerebellum resulted in impairments in linking sensory prediction errors to movements. In their task, subjects made pointing movements in the absence of visual feedback with the right hand, and perceptual judgements of those movements were made with the left hand using a cursor manipulated by a joystick. Results indicated that while motor adaptation for patients and controls was comparable, the perceived pointing direction was recalibrated to a lesser extent in patients than controls. Based on these results, the authors suggested that updates to the internal predictions of motor commands (i.e. the forward model) were responsible for perceptual changes and that this process was impaired in cerebellar patients. Furthermore, Izawa et al. (2012) recently showed that cerebellar patients are unable to learn to predict the visual sensory consequences of their motor commands. Realignment of perceived hand position was estimated following adaptation in a task in which subjects moved their right hand to a position within a circle (no explicit target was given) and then had their hand guided back to a start position. With their left hand, subjects then pointed to the location at which they perceived their right hand had crossed the circle. While motor adaptation was comparable, patients showed less perceptual realignment than controls, further suggesting the role for a forward model in sensory changes.

Sensory plasticity in motor learning

While an update in the forward model has been implicated in the sensory changes observed during visuomotor adaptation (Synofzik et al. 2008; Izawa et al. 2012), our results suggest that this sensory recalibration involves a shift in proprioception, rather than a learned association between one's movements and sensory consequences. We have previously suggested that sensory recalibration may occur coincidentally, though separate from motor adaptation, as we have shown that changes in movements and sensory recalibration are uncorrelated (Cressman and Henriques 2009; Cressman et al. 2010; Salomonczyk et al. 2011, 2012). Indeed, Izawa et al. (2012) failed to observe a relationship between the perceptual and motor changes in their subjects. Moreover, in accordance with our suggestion, cerebellar patients have been shown to recalibrate proprioception

such that proprioceptive estimates are shifted to match visual estimates of target positions in the absence (or lack) of motor adaptation (Block and Bastian 2012). In this task, subjects made reaching movements to visual and proprioceptive targets when visual and proprioceptive information were gradually misaligned. The authors found that following reach training, when endpoint feedback was not available, patients and controls realigned proprioceptive endpoints to the same extent; again, this realignment was independent of motor adaptation. Altogether, these findings indicate that the forward model may not have a role in realigning visual and proprioception, and instead suggest that proprioceptive recalibration may be used to update the state estimate for motor commands and thus lead to partial motor adaptation in some contexts.

For accurate and effective motor control, the CNS must consider the properties of the environment and objects we interact with, as well as our own effectors. This information is derived from sensory afferents. When faced with incongruence in sensory information (i.e. vision and proprioception), we have shown that the CNS recalibrates one sense to better match the other; in our case, proprioception is recalibrated to better align with visual estimates of hand position. Conversely, when an error in motor performance is experienced, the CNS may attribute these errors to internal misestimates (e.g. of effector location), but also to external or environmental causes. The CNS will then take into consideration both the updated body or effector percept and the adapted environmental percept when planning subsequent movements (Berniker and Kording 2012). In our present paradigm, subjects did not experience a performance error, and thus, we would not expect the environment percept to have been adapted. In other words, subsequent open-loop reach errors therefore reflected only an update in the body percept that did not increase with increasingly discrepant visuo-proprioceptive feedback. In contrast, subjects in our previous paradigms experienced both a cross-sensory discrepancy and motor performance errors, and subsequent open-loop reach errors could therefore have reflected a combination of the updated body and environment percepts that increased linearly with increasingly misaligned visual hand feedback. Thus, present findings suggest that proprioceptive recalibration may be used to update the state estimate for motor commands, resulting in motor adaptation in the absence of error-based learning. However, results suggest that the body percept or state estimate can only be updated to a certain extent, reflected by the saturation of proprioceptive recalibration and motor commands observed following exposure training with increasingly discrepant visuo-proprioceptive feedback.

In summary, these and other recent results suggest the need for a more comprehensive model of visuomotor learning that accounts for the role of visually driven

6 Motor adaptation and proprioceptive recalibration

Danielle Salomonczyk, Erin K. Cressman and Denise Y. P. Henriques

6.1 Introduction

The central nervous system (CNS) integrates information from multiple sensory modalities, including visual and proprioceptive information, when planning a reaching movement (Jeannerod, 1988). While visual and proprioceptive information regarding hand (or end-point effector) position are not always consistent, performance is typically better under reaching conditions in which both sources of information are available. Under certain task conditions visual signals tend to dominate, such that one relies more on visual information than proprioception to guide movement. For example, individuals reaching to a target with misaligned visual feedback of the hand, as experienced when reaching in a virtual reality environment or while wearing prism displacement goggles, adjust their movements in order for the visual representation of the hand to achieve the desired endpoint even when their actual hand is elsewhere in the workspace (Krakauer, Ghilardi and Ghez, 1999; Krakauer et al., 2000; Redding and Wallace, 1996; Simani, McGuire and Sabes, 2007). This motor adaptation typically occurs rapidly, reaching baseline levels within 20 trials per target, and without participants awareness (Krakauer et al., 2000). Furthermore, participants reach with these adapted movement patterns following removal of the distortion, and hence show aftereffects (Baraduc and Wolpert, 2002; Buch, Young and Contreras-Vidal, 2003; Krakauer et al., 1999; Krakauer et al., 2000; Martin et al., 1996). These aftereffects provide a measure of motor learning referred to as visuomotor adaptation and result from the CNS learning a new visuomotor mapping to guide movement.

In general, it is assumed that visuomotor adaptation relies mainly on error-based learning (Berniker and Kording, 2008; Shadmehr, Smith and Krakauer, 2010; Tseng et al., 2007; Wei and Kording, 2009). That is, the CNS compares the movement vector derived from ones actual performance (i.e. a vector from the start location to the end position achieved by the hand or end-effector) with a target vector (i.e., a vector from the start location to the target location). The resulting difference vector, which is derived from the sensory feedback of the movement, is then used to compute a new motor plan with the goal of bringing the end-effector to the target on the subsequent trial. Specifically, if the "seen" hand movement or visual representation of the hand does not achieve the target or differs from the predicted outcome, then the brain uses these errors to update sensorimotor mappings (i.e., adapt an internal model based on the differences between predicted and actual sensory feedback, (Miall and Wolpert, 1996; Wolpert, Ghahramani and Jordan, 1995). This error signal can be referred to as the *sensorimotor error signal* (Wong and Shelhamer, 2011) and is believed to result in implicit adaptation and movement aftereffects.

6.2   Sensory recalibration with prism displacement

In addition to movement aftereffects, it has been suggested that reaching with mis-aligned visual feedback of the hand results in sensory recalibration. In particular, in the case of visuomotor adaptation paradigms, proprioception is thought to be recalibrated or realigned to match the visual representation of the hand – an effect that we refer to as *proprioceptive recalibration*. Furthermore, it has been proposed that proprioceptive recalibration gives rise to motor adaptation (Craske and Gregg, 1966; Harris, 1963, 1965; Hay and Pick, 1966; Redding and Wallace, 1978, 1988, 1996, 1997, 2001, 2002, 2003, 2006; Templeton, Howard and Wilkinson, 1974). This proposed sensory recalibration was initially based on changes in reaching movements observed when participants were required to reach to proprioceptive targets with their adapted hand after training to reach to visual targets while wearing prism goggles that displaced the entire visual field (Harris, 1963; Hay and Pick 1966; Hay, Pick, and Ikeda, 1965; Redding and Wallace, 2000). The proprioceptive targets were usually a position in space perceived to be aligned with body midline (Harris, 1963; Hay and Pick, 1966; Hay et al., 1965) or the participants opposite, unadapted hand (Harris, 1965).

However, deviated reaches to proprioceptive targets do not provide direct evidence of sensory recalibration, or evidence that sensory recalibration is responsible for motor adaptation, based on the following three reasons. To start, the first reason involves the nature of the visual feedback displayed in prism adaptation paradigms. These paradigms often only provide visual feedback of the hand or end-effector to the participant at the end of a movement. This is because visual feedback of initial hand and target positions, even if displaced, would allow participants the opportunity to compute a correct movement vector and bring the hand or end-effector to the desired target location. Under these conditions there would be no discrepancy between expected movement outcomes and actual movement outcomes. Thus the CNS would not adapt to the sensory perturbation and no motor aftereffects or sensory recalibration would be expected to arise (Redding and Wallace, 1996), indicating that sensory recalibration does not

occur under all task constraints when reaching with displacing prisms. Second, prism displacing goggles displace not only the visual representation of the hand in space but also that of the target and the entire workspace. Thus, it is unclear whether changes in movements to visual or proprioceptive targets after training to reach to visual targets while wearing prism goggles arise due to the brain assigning the source of such movement errors to the workspace and/or to the effector (as opposed to sensory recalibration), which has been shown to affect motor learning (Berniker and Kording, 2008; Clower and Boussaoud, 2000). Lastly, changes in reaching movements made to proprioceptive targets following prism adaptation could reflect adapted motor commands (Hatada, Rossetti and Miall, 2006). Thus, some of the proposed sensory changes observed following reaches with prisms could arise due to motor adaptation or a spatial realignment of the workspace, rather than because of any recalibration in the sensory system(s).

6.3   Sensory recalibration with virtual reality

Recently, sensory recalibration has been examined following reaches made in a virtual reality environment (Simani, McGuire and Sabes, 2007; van Beers, Wolpert and Haggard, 2002). In contrast to the prism literature discussed above, reaching in a virtual reality environment has the advantage of allowing the experimenter to shift only the visual feedback or visual representation of the participants hand, as opposed to the entire workspace, which avoids the possibility of spatial (or visual) realignment of the workspace contributing to any motor (and/or sensory) changes. Initial work in this area by Simani and colleagues (2007) had participants adapt their reaching movements to visual targets in response to a virtually-shifted view of the hand (a cursor) and experimenters then measured their subsequent reaches to both visual and proprioceptive targets with both the adapted and non-adapted hands. Similar to the results discussed above with respect to the prism literature, following adaptation participants adapted their open-loop reaches (in which no visual feedback of the hand was provided). Moreover, these changes in reaches to visual and proprioceptive targets were additive. The authors interpreted these linearly related reaching aftereffects as evidence that motor adaptation had occurred due to cross-sensory recalibration. However, it is unclear if these results reflect cross-sensory recalibration per se as opposed to motor recalibration given that Simani and colleagues (2007) required participants to make voluntary goal-directed reaching movements to visual and proprioceptive targets using the adapted hand.

In order to examine the extent that sensory (and motor changes) contribute to visuomotor adaptation, we (and others) have developed novel perceptual tasks to assess proprioceptive recalibration. Specifically, Henriques and colleagues have designed perceptual tasks in which participants provide estimates regarding the path their hand has travelled or the position of their hand in the absence of any goal-directed movement. These proprioceptive estimates provide insight into sensory changes that are independent of any possible motor changes (or changes in the motor representation). The results of these studies suggest that proprioception, specifically felt hand position, is recalibrated following visuomotor adaptation (Cressman and Henriques, 2009, 2010; Cressman,

Salomonczyk and Henriques, 2010; Salomonczyk, Cressman and Henriques, 2011; Salomonczyk, Henriques and Cressman, in press) and following force-field adaptation (Ostry et al., 2010). As well, results provide further insight into the sensory plasticity observed in conjunction with changes to the motor system.

6.4   Recalibrating hand path

The first of these proprioceptive tasks examined shifts in participants perceived hand paths (Malfait, Henriques and Gribble, 2008). Participants manually tracked a target as it moved along an invisible square path. Visual feedback of unseen hand position was provided in the form of a cursor that was displayed only at the end of each trial. Cursor feedback was either aligned (baseline) or translated 5cm left with respect to participants' actual hand position. Following this tracking task, participants made perceptual estimates regarding the width of a square ("wide" vs. "narrow"). In particular, during these estimate trials, participants viewed a white cursor that moved along an invisible square trajectory (similar to what was observed when completing the adaptation training trials) while their hand was passively moved by a robot manipulandum in a rectangular pathway that was either wider or narrower than the square path that the cursor travelled. The authors observed that following visuomotor adaptation, participants' proprioceptive sense of hand path shape was distorted in the direction that they had adapted their movements: that is, participants perceived their felt hand path as wider than the target hand path following motor adaptation. To determine what other aspects related to felt hand path are influenced by visuomotor adaptation, Wong and Henriques (2009) examined participants' perceptions of hand path curvature following adaptation to a visuomotor rotation. In this study, participants reached to visual targets while cursor feedback of their unseen hand position was gradually deviated 30° clockwise with respect to the hand's actual location. Participants were then asked to judge the curvature ("convex" or "concave") of their hand path during estimation trials. The authors observed that visuomotor adaptation did not influence participants' perception of hand path curvature: that is, no differences in curvature thresholds between baseline and adaptation sessions were reported despite the fact that participants had adapted their movements.

6.5   Recalibrating hand position

Given the discrepancy in findings related to recalibration of sense of felt hand path, Henriques and colleagues next sought to examine shifts in sense of unseen felt hand position following adaptation to a visuomotor rotation. In a series of tasks, a two-joint robotic manipulandum (Figure 6.1A) was used to place or guide the participant's hand to specific locations in the workspace. Upon reaching the required position, participants were asked to judge whether their unseen hand was located to the left or the right of a visual reference marker, represented by a 1 cm yellow circle, or their body midline, which served as a proprioceptive marker (Figure 6.1B) These reference markers appeared only after the hand arrived at its final location, which prevented the markers

from serving as a "target". The position of the hand with respect to each reference marker was adjusted over trials using an adaptive staircase logarithm (Figure 6.1C; Cressman and Henriques, 2009; Jones et al., 2010; Salomonczyk et al., 2011) based on participants' responses. Participant's responses were then fitted to a logistic function like that shown in Figure 6.1D from which we determined the probability of responding "left" 50% of the time. This value, which we refer to as proprioceptive bias, provides a measure of participants' accuracy in aligning their felt hand position with that of the visual or proprioceptive markers. From the logistic function we also determined the difference between the probability of responding "left" 25% versus 75% of the time. This value, which we refer to as proprioceptive uncertainty, provides a measure of participants precision of their estimates. We determined these bias and uncertainty values following reach training trials in which participants make goal-directed reaches to visual targets with visual feedback of their hand provided by a 1 cm green cursor that was either aligned with their hand, or rotated with respect to the participants unseen hand position. By comparing proprioceptive biases between these conditions, we could establish whether proprioceptive recalibration arises following visuomotor adaptation.

6.5.1 Hand proprioception is recalibrated following visuomotor adaptation

We have observed significant shifts in proprioceptive estimates of hand position (proprioceptive recalibration) in the direction of movement adaptation following visuomotor adaptation training (Cressman and Henriques, 2009, 2010; Cressman et al., 2010; Salomonczyk et al., 2011). On average, healthy participants recalibrate their felt sense of hand position by roughly 6°, representing approximately 20% of the 30° visuomotor distortion. This shift has been observed at both visual and proprioceptive reference markers located in different positions of the workspace, which suggests that visual recalibration is not responsible for the observed shifts in felt hand position. Moreover, this proprioceptive shift has been observed in both the left and right hands of right-handed participants and is of similar magnitude in the two limbs (Salomonczyk et al., in press). Given that proprioceptive recalibration around visual markers occurs in both the left and right hands, and that the extent of recalibration is comparable across reference marker modalities (i.e., visual and proprioceptive markers), suggests that proprioceptive recalibration is not subject to limb-modality specialization, which has been observed in localization tasks (Goble and Brown, 2008).

The shift in proprioceptive bias following visuomotor adaptation training has also been observed in proprioceptive estimate trials in which participants actively moved the robot manipulandum into position, and when the robot manipulandum passively positioned their hand for them (Cressman and Henriques, 2009). Previous work suggests that individuals are typically better at localizing their limb following active placement compared with passive placement (Coslett, Buxbaum and Schwoebel, 2008; Laufer, Hocherman and Dickstein, 2001), perhaps due in part to the changes in the firing rates of sensory receptors (al-Falahe, Nagaoka and Vallbo, 1990) and/or centrally generated neuronal events, such as efference copies produced with self-generated move-
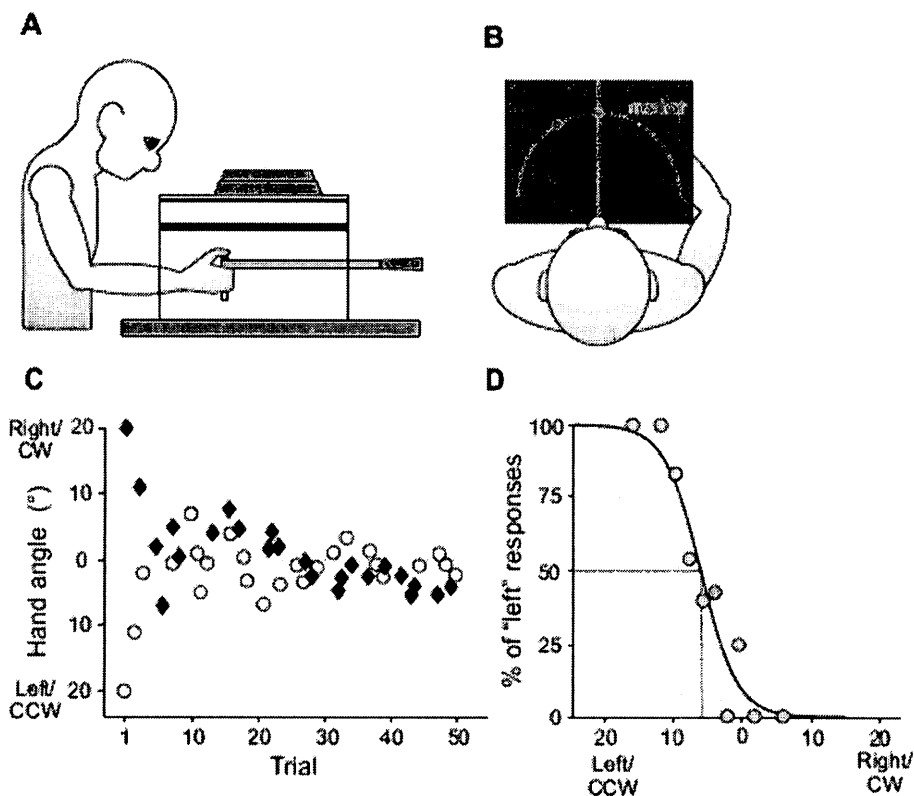
Figure 6.1. Experimental setup and design. A: Side view of the experimental setup. Images were projected onto a reflective surface such that stimuli appeared to lie in the same horizontal plane as the unseen hand. B-C: Top view of the experimental surface visible to participants. B: During proprioceptive estimates, participants either actively pushed their hand out along an invisible, constrained linear path (shaded rectangle) originating from the home position or the robot passively moved their hand along the same path. At the end of the path, participants were required to judge the position of their unseen hand with respect to a visual (circles) or proprioceptive (body midline, dashed line) reference marker. C: During reach training trials, participants were required to reach to visual targets with a cursor that was either aligned or rotated with respect to their unseen hand position (adapted from Salomonczyk, Cressman and Henriques, 2011).

ment (McCloskey, 1980). The results of Cressman and Henriques (2009) however, suggest that sensory recalibration (and localization of hand-marker alignment following aligned reach training) occurs to the same extent regardless of the origin of the movement during estimate trials, and instead appears to depend on the sensorimotor discrepancy experienced during visually-guided reach training.

6.5.2 The size of the distortion predicts the magnitude of recalibration

Previous work in visuomotor adaptation indicates that the initial magnitude of the sensorimotor discrepancy affects the extent of motor learning (i.e., aftereffects). Aftereffects are greater following reach training with a distortion that is introduced gradually, compared to when it is introduced abruptly and in full. This has been observed following adaptation to prism displacing goggles (Michel et al., 2007), visuomotor rotations introduced in a virtual reality paradigm (Abeele and Bock, 2001; Kagerer, Contreras-Vidal and Stelmach, 1997) and force field perturbations (Criscimagna-Hemminger, Bastian and Shadmehr, 2010). Furthermore, retention of motor learning has been reported to be greater when participants adapt to an incrementally introduced distortion compared to an abruptly introduced one (Klassen, Tong and Flanagan, 2005). The differences in learning reported between gradually and abruptly introduced distortions suggest that different learning processes are engaged depending on how the initial errors are experienced. When the distortion is introduced abruptly and large reach errors are initially experienced, explicit, strategic control processes may be engaged early in the learning process in order to correct for the perceived large errors in motor performance (Redding and Wallace, 1996). In contrast, when the distortion is introduced gradually and small reach errors are experienced, reach adaptation is proposed to arise through implicit processes that include an updating of the internal model, leading to better motor performance on subsequent trials. Recently, Salomonczyk et al. (In Press) evaluated proprioceptive recalibration following reach training with an abruptly introduced distortion and observed similar proprioceptive recalibration to that observed by Cressman and Henriques (2009) and Salomonczyk et al. (2011) when a gradually introduced distortion was introduced with the same final 30° clockwise hand-cursor error discrepancy (Figures 6.2A and B). This suggests that learning processes engaged during gradual and abrupt adaptation of small (< 90°) visuomotor rotations do not affect the sensory consequences of such learning, suggesting further that motor adaptation is separate from proprioceptive recalibration.

To further investigate sensory plasticity, we have also examined the relationship between proprioceptive recalibration and the magnitude of the sensorimotor discrepancy (i.e. the difference between the desired or expected movement outcome and the actual movement outcome), experienced during visuomotor adaptation. In a first experiment, we systematically manipulated the magnitude of the cursor distortion presented during reach training trials. Specifically, we examined if an increase in the size of the distortion would result in a consistent increase in the extent of proprioceptive recalibration (Salomonczyk et al., 2011). Participants completed three blocks of reach training trials with a rotated cursor that was displaced 30°, 50° and 70° clockwise with respect to the hand. Participants estimated the location of their unseen hand with respect to visual reference markers as described previously after each reach training block. We found that participants' estimates of hand position were deviated more leftwards following reach training with an increasingly distorted cursor, such that after training with a 70° distortion, participants' sense of felt hand position had shifted 15° leftwards in the direction of movement adaptation (which represents approximately 20% of the magnitude of the hand-cursor distortion; Figure 6.3A). Moreover, the motor aftereffects

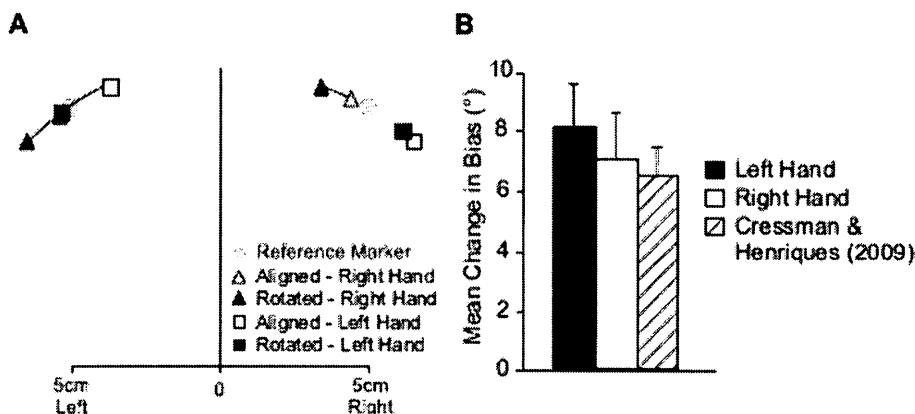*D. Salomonczyk, E. K. Cressman and D. Y. P. Henriques*

Figure 6.2. A: Mean 2-D biases in the proprioceptive estimate tasks for participants who completed the task with their right (triangles) or left (squares) hand with aligned (empty symbols) and misaligned (filled symbols) visual feedback of the hand. The actual reference marker positions are represented as filled grey circles and a line connects each estimate of hand position following reach training with an aligned and rotated cursor for a particular hand with its corresponding reference marker. B: Mean change in bias is depicted for participants who trained with the left or right hand alongside those who had trained with a gradually introduced visuomotor distortion (adapted from Salomonczyk, Henriques and Cressman, in press).

observed following each training block were consistent with those observed by Cressman and Henriques (2009) and Salomonczyk et al. (in press) and represented approximately 50% of the magnitude of the hand-cursor distortion (Figure 6.3B). While the magnitude of the distortion predicted the relative changes in proprioceptive recalibration and movement aftereffects, no correlation between the two effects was observed (Figure 6.3C). This was also the case in other work (Cressman and Henriques, 2009; Salomonczyk et al., in press). Thus, while both sensory and motor changes occur following visuomotor adaptation and these changes are directly related to the magnitude of the visuomotor distortion, evidence strongly indicates separate, yet simultaneous, mechanisms underlying proprioceptive recalibration and movement adaptation.

6.5.3 Proprioception is recalibrated across the lifespan

With respect to visuomotor adaptation, it has been suggested that explicit strategic processes deteriorate with age (Bock and Girgenrath, 2006). Indeed, older adults show less evidence of motor learning than young adults when a visuomotor distortion is introduced abruptly. In contrast to strategic processes, proprioceptive recalibration is thought to be maintained with advancing age. While it is proposed that one's ability to adapt to novel visuomotor environments is preserved with aging due to proprioceptive recalibration (Buch, Young and Contreras-Vidal, 2003), most research with older adults has focussed on evaluating proprioceptive acuity by having older adults perform joint
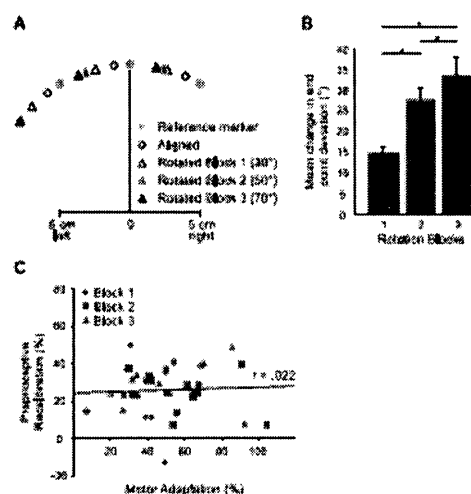
Figure 6.3. Proprioceptive recalibration and motor adaptation arising from an increasing visuomotor distortion. A: Mean 2-D proprioceptive biases following training with an aligned (diamonds) or misaligned (after the first rotated block (30°): white triangles; second rotated block (50°): grey triangles; third rotated block (70°): black triangles) cursor. B: Reaching errors at reach endpoint averaged across targets and participants are shown for the no cursor reaches completed after each of the three rotated reach training blocks. C: Changes in proprioceptive and motor recalibration are plotted as a percentage of the visuomotor distortion introduced during each training block (following rotated block 1 (30°): circles; second rotated block (50°): squares; and third rotated block (70°): triangles). Each symbol represents the percentage change in bias and percentage change in reach aftereffects averaged across marker and target locations for each participant. The solid line indicates the line of best fit for all data points (adapted from Salomonczyk, Cressman and Henriques, 2011).

matching tasks as opposed to examining proprioceptive sense of hand position directly. Results from these studies demonstrate marked deterioration in ones ability to match the position of one limb with that of the other, or to reproduce a final limb position from memory (Adamo, Alexander and Brown, 2009; Adamo, Martin and Brown, 2007; Goble et al., 2009; Kaplan et al., 1985).

We (Cressman et al., 2010) recently sought to evaluate proprioceptive acuity and recalibration directly following reach training with an aligned and misaligned cursor (Figure 6.4). While proprioceptive acuity has been reported to deteriorate with age as assessed by joint angle matching tasks, we did not observe any differences in the accuracy of hand-marker alignment estimates between young and older adults. This lack of observed difference in estimates following aligned training could be due to estimates of end-effector position being typically more precise than estimates of joint angle (Fuentes and Bastian, 2010). Results from the same study, also indicated that older adults recalibrate proprioception by approximately 20% of the magnitude of the distortion, which does not differ from the recalibration observed in young adults. How-
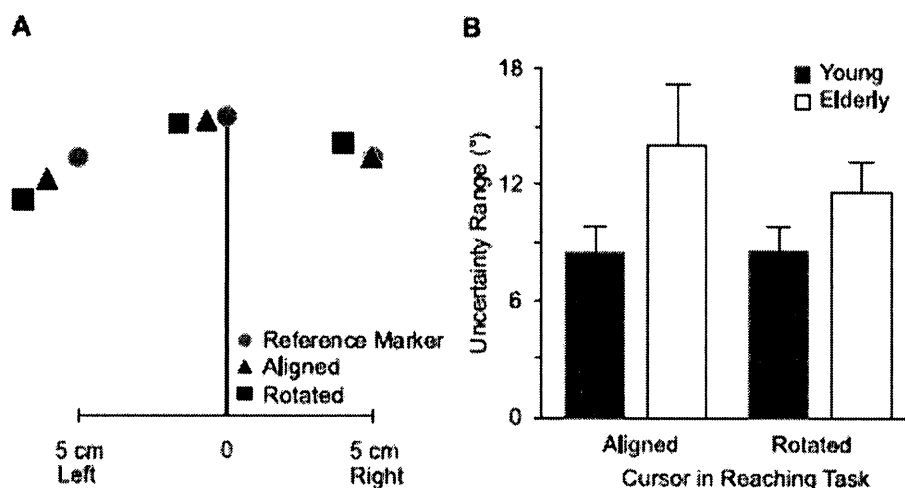
Figure 6.4. Proprioceptive recalibration in older adults. A: Mean 2-D biases in the proprioceptive estimate tasks following training with aligned (triangles) and misaligned (squares) visual feedback of the hand. B: Magnitude of the uncertainty ranges in the proprioceptive estimation tasks averaged across reference markers and participants following reach training with an aligned (right bars) or misaligned cursor (left bars) for both younger (black bars) and older participants (white bars) (adapted from Cressman, Salomonczyk and Henriques, 2010).

ever, while no differences in constant errors (bias) or recalibration were observed, older adults were more variable in their estimates of hand position than younger adults, reflected in the higher uncertainty values found in this group (Figure 6.4B). These results suggest that the extent of proprioceptive recalibration of the hand does not depend on the precision by which people are able to estimate hand position. Finally, similar to our previous findings discussed above (Cressman and Henriques, 2009; Salomonczyk et al., 2011, in press) the extent of proprioceptive recalibration was not correlated with the extent of visuomotor adaptation (aftereffects) which again supports the hypothesis that these two processes are mediated by separate mechanisms.

6.5.4 Proprioception is recalibrated without visuomotor adaptation

All of the findings discussed thus far suggest that proprioceptive recalibration arises independently of motor adaptation. Moreover, this independence holds true when the distortion consists of a cursor that is rotated or laterally displaced, both during active and passive hand displacements and across a wide variety of other parameters (Cressman and Henriques, 2009). Thus, differences between proprioceptive and motor recalibration may arise due to different error signals that each drive distinct changes in the CNS's representation of the body and world. To better investigate the differences in sensory recalibration and motor aftereffects following adaptation to altered

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visual feedback of the hand, Cressman and Henriques employed a "learning" paradigm that isolated the discrepancy between vision and proprioception (what we refer to as the cross-sensory error signal) from the sensorimotor error signal that is thought to drive visuomotor adaptation (Cressman and Henriques, 2010). In particular, participants movements were constricted during reach training trials, such that the motor component and resulting sensorimotor error signal were removed. This was achieved by either passively moving (passive task) or simply guiding (active task) participants unseen hands towards a briefly presented target while they were exposed to discrepant visual and proprioceptive information regarding their hand position. Specifically, participants always saw the cursor move in the direction of the target but the position of the unseen hand was gradually deviated such that the path the hand actually travelled was eventually rotated 30° counter-clockwise from the cursor. Given that there was no goal-directed movement, participants did not experience a sensorimotor error signal as they never experienced a discrepancy between their intended and actual movement outcomes. Thus, with this paradigm, the authors could effectively explore whether mere exposure to a cross-sensory error signal is sufficient to induce changes to sensory and motor systems.

Following exposure to the cross-sensory discrepancy, proprioceptive estimates of hand position were shifted in the direction of the distortion to the same extent as that observed following visuomotor adaptation training with the same hand-cursor distortion magnitude (Cressman and Henriques, 2010). When participants performed open-loop reaching trials (reaches made to targets without visual feedback of the hand), these reach aftereffects were also deviated like those observed following visuomotor adaptation training, however they were approximately one-third of the size of reach aftereffects achieved following visuomotor adaptation (Cressman and Henriques, 2009, 2010). In fact, these aftereffects were the same magnitude as the changes in proprioceptive bias (Figure 6.5A), and for the first time were correlated with them (Figure 6.5B). Thus, it is possible that these aftereffects observed following exposure to a cross-sensory discrepancy may be due to a change in felt hand position as originally suggested by early prism work, rather than attributable to any motor recalibration, (Harris, 1963, 1965; Hay and Pick, 1966; Hay et al., 1965).

6.6 The relationship between recalibration and adaptation

Together, the results of Henriques and colleagues (Cressman and Henriques, 2009, 2010; Cressman et al., 2010; Salomonczyk et al., 2011) and Ostry and colleagues (2010) suggest that one recalibrates proprioception in the trained hand following learning of a new visuomotor mapping. This recalibration is a robust phenomena that occurs under a variety of contexts, including active and passive placement of the hand during estimation trials, following adaptation to gradual and abrupt perturbations, following adaptation to increasing visuomotor distortions, following adaptation to cursor rotations and lateral translations, following adaptation to a force-field, in the left and right hands, and at different stages of the lifespan. These proprioceptive changes in the esti-
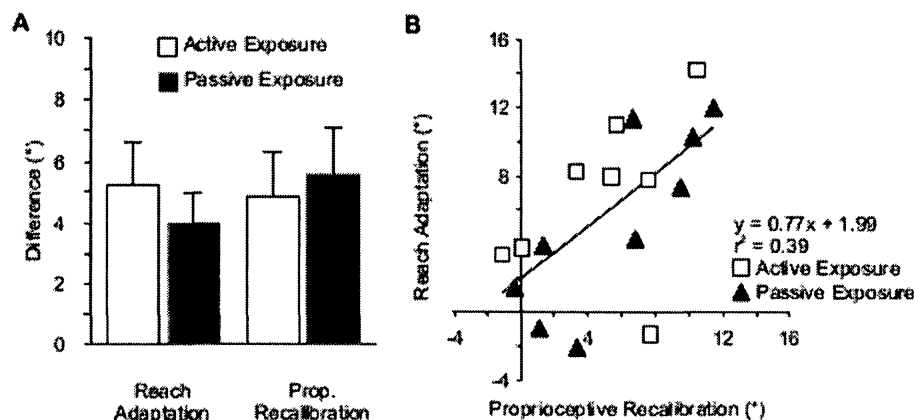
Figure 6.5. Proprioceptive and motor effects of exposure to misaligned visual and proprioceptive feedback of unseen hand position. A: Mean changes in reach aftereffects and proprioceptive biases following active (left) or passive (right) exposure training. B: Relationship between changes in reach aftereffects and proprioceptive biases following active (empty symbols) and passive (filled symbols) exposure training (adapted from Cressman and Henriques, 2010).

mates of hand position are only a fraction of the motor changes observed in the adapted hand. In fact, it is only when the sensorimotor error signal is removed during training trials, that we observe a correlation between sensory and motor plasticity. This suggests that the cross-sensory error signal gives rise to sensory changes and is able to influence motor adaptation (i.e., aftereffect reaches) to a certain extent. That motor adaptation can occur without corresponding recalibration of hand path geometry and even in individuals with no proprioceptive afferents (Bernier, Chua and Franks, 2005; Ingram et al., 2000) further suggests that mechanisms underlying the two processes are distinct and that proprioceptive recalibration of hand path and hand position may themselves be mediated by distinct mechanisms (Malfait, Henriques and Gribble, 2008; Wong and Henriques, 2009). However, further research is necessary to better characterize these processes and determine how they contribute to sensorimotor adaptation and proprioceptive recalibration.

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