BIMANUAL INTERFERENCE IN PARAMETRIC AND STRUCTURAL LEARNING

By

Alexander T. Brunfeldt

A DISSERTATION

Submitted to Michigan State University in partial fulfillment of the requirements for the degree of

Kinesiology—Doctor of Philosophy

PUBLIC ABSTRACT

BIMANUAL INTERFERENCE IN PARAMETRIC AND STRUCTURAL LEARNING

By

Alexander T. Brunfeldt

Humans have the unique ability to produce highly coordinated movements, especially while using both hands to achieve a shared goal. The purpose of this dissertation was to investigate the factors influencing a natural consequence of our motor system – bimanual interference. While the word 'interference' often has a negative connotation, interference in the motor system naturally arises from the complex interaction of brain circuitry and anatomical connections and allows motor researchers to explore these systems in detail to provide understanding of how motor information is shared across the brain. In a series of three aims, I investigate possible neural and anatomical mechanisms for interference and frame my interpretation in contemporary theories of volitional motor control.

Previous research has demonstrated that as the force demands for movement increases, interference between the upper extremities during movement increases. This interference likely occurs by neurons communicating across the hemispheres through a process called neural crosstalk. While this is a well-established understanding of how interference arises, it is currently not known whether and to what extent interference is affected by motor adaptation, or short-term learning of new movements. I designed two experiments to test the hypothesis that if interference is mediated by neural crosstalk, and that adaptation increases sensitivity to sensory information, interference will be more robust in participants engaging in an adaptation task in one hand while moving the other hand without visual feedback. I found that participants who adapted did indeed show more interference, and this increase is likely due to a shared representation of sensorymotor processes between hemispheres.

While the first aim shows adaptation can affect interference via sensory upregulation, my second and third aims attempted to directly test the role adaptation plays in this process. In Aim 2, I designed an experiment to test whether learning can transfer from one hand to the other. Specifically, half of participants performed a reaching task where visual feedback was randomly rotated so that what they saw no longer matched where they reached while the other participants reached normally. Following this, both groups made reaches to a target where visual feedback was rotated by a fixed amount, and I show that participants who previously experienced the random rotations adapted faster. Importantly, my results show that measures targeting feedback processing are transferred more robustly than measures targeting movement planning. Since results from Aim 1 suggest that interference is increased by an upregulation in sensitivity to sensory information, and Aim 2 shows it is mostly the feedback information processing that is shared between limbs, this led me to determine if learning random rotations prior to our interference task can increasing bimanual interference.

Aim 3 addressed this question by first having half of our participants engage in random rotation training, while the others reached normally. We then exposed both groups to the interference task used in Aim 1. We found that participants who learned the random rotation had more interference than those reaching with normal visual feedback during training, especially early in the adaptation process. Taken together, these experiments extend our understanding of bimanual coordination to highlight the importance of learning and adaptation in the communication of motor information between the hemispheres and may help to promote their use in future research and clinical applications.

ABSTRACT

BIMANUAL INTERFERENCE IN PARAMETRIC AND STRUCTURAL LEARNING By

Alexander T. Brunfeldt

The purpose of this dissertation was to investigate interference during bimanual coordination and to what extent adaptation to novel sensorimotor environments enhances this communication. Previously, motor interference has been investigated in continuous movements such as circle drawing or hand waving and isometric force production, but more recently it has been shown in discrete, goal-directed reaching. Early interpretations of motor interference have suggested it is the consequence of increased neural activity in the ipsilateral motor cortex (controlling the contralateral limb) through neural crosstalk. Neural crosstalk is evidenced by increased cortical excitability and decreased inhibition leading to activation of homologous muscles and this can be increased by imposing greater force demands on movement. However, it is not yet known what effect motor adaptation plays in this process, as adaptation has been shown to upregulate sensory feedback gains. Therefore, I designed a series of three aims.

In Aim 1, I conducted two experiments to investigate the role adaptation on motor interference and to determine if increasing the force demands for movement increases interference. Participants performed a bimanual center-out reaching task where one hand either adapted to a fixed rotation in visual feedback (experiment 1) or reached to targets rotated by the opposing amount (experiment 2). I found that as the force demands for reaching increased, so too did interference. Moreover, participants in experiment 1 showed more robust interference than those in experiment 2 suggesting that adaptation may upregulate sensitivity to feedback processing. I discuss the results in the context of the optimal feedback control theory, which

predicts that participants are tuning their sensorimotor system to rely more heavily on feedback information in the face of an unpredictable sensory environment. My next two aims sought to further investigate this possibility by training participants with random rotations to drive the motor system to be even more sensitive to feedback information.

In Aim 2, I had participants engage in structural training. This process confronts participants with random rotations in visual feedback, and previous research has shown they can learn the underlying structure leading to facilitated adaptation. Since these random perturbations should increase participants' reliance on feedback processes, I hypothesized this might increase interference in our task. But first, I needed to determine if structural learning transferred to the contralateral effector to inform how best to test this hypothesis. In this second aim, participants first learned either random rotations or reached under veridical visual feedback in their right hand. Then, both groups adapted to a fixed rotation in visual feedback in the left hand. I show facilitated adaptation in the structure group, particularly in feedback processes. These results suggest that structural learning generalizes to a contralateral effector, and most importantly sensory upregulation driven by one hand is accessed by the other.

Results for Aim 1 suggest motor adaptation increases interference due to a shared control strategy between limbs, likely due to the upregulation of sensory feedback gains. And in Aim 2, I show structural learning can transfer across effectors, especially feedback processing; therefore, I hypothesized that structural learning can increase bimanual interference. Aim 3 tested this by exposing one group to structural training, while the other received veridical feedback, followed by both groups engaging in the bimanual interference task. I show that structural learners showed more interference than controls. Taken together, this dissertation suggests that motor interference is mediated interhemispheric connections and that adaptation bolsters this communication.

Copyright by ALEXANDER T. BRUNFELDT 2020 To my parents For their unyielding support, and for always urging me to 'apply myself'

To my wife My best friend, Who inspires me grow in all ways And without whom this dissertation would not exist

ACKNOWLEDGEMENTS

My decision to pursue a PhD was not an easy one to make – I had rewarding job working at the University of Michigan – but it was something my boss Dr. Jepsen said under his breath in a meeting that tipped the scales. He said it was his job to *ask* the questions. At the time I was the person *answering* the questions, and I felt that if I were to grow as a researcher, I needed the training to understand what made a worthwhile and meaningful question. During my time at MSU, I feel I have made great strides in being able to this, and I owe much of this growth to the Motor Neuroscience Laboratory. Dr. Florian Kagerer has been instrumental in this process. His attention to detail, knowledge of the fundamental approach to science, and mentorship style has given me confidence to tackle new challenges – not only in science but in life. And to Dr. Phillip Desrochers, whom I cannot thank enough for his generosity, comity, scientific instinct, and companionship, I would not have been able to finish this chapter of my life without his friendship. I would be remiss to leave out the undergraduate members of the lab, who do much of the heavy lifting, but without whom we could not hope to finish our work and who made the MNL feel like a 'real' lab and a wonderful place to work.

I would also like to thank my committee, Drs. Ranganathan, Lee, and Altmann, for their support of my studies and research goals. I appreciate their guidance in tailoring a substantive course load and fine tuning of scientific thought needed for completion of my dissertation work.

During the leadup to by time at MSU, I spent nearly a decade in various labs and academic programs, and by far the MSU Kinesiology graduate program is the most close-knit and supportive. From the faculty, staff, and KGSO – all have made the challenge bearable and

V

enjoyable (at times). I would especially like to thank Dr. Lauren Walker, Phil Walker, and Tzu-Hsiang Lin for their friendship.

As my time at MSU came to an end, I spoke many times with my parents, David and Joan, expressing my gratitude for their support during my graduate studies. I have tried to view my journey through their perspective, and I am humbled by the sacrifices they have made to provide opportunities to achieve to me and my siblings, Adam and Angela.

I would like to thank my wife, Dr. Elaine Sinclair for her support and inspiration these past several years. She certainly got me into this mess, but she certainly helped me get out of it! Joking aside, she never gave up of me even when I wanted to give up on myself. I could not have finished my studies without her determined, self-possessed attitude and optimistic outlook.

Finally, I would like to thank the Graduate School of Michigan State University for funding support through the University Distinguished Fellowship and the Department of Education for the Summer Renewable Research Fellowship.

LIST OF TABLES	ix
LIST OF FIGURES	x
KEY TO SYMBOLS AND ABBREVIATIONS	xi
CHAPTER 1 – BIMANUAL COORDINATION AND INTERFERENCE: A REVIEW 1.1 Models for volitional movement control	
1.2 Structural learning and facilitated adaptation	
1.3 Interlimb transfer tasks	
1.4 Specific Aims	16
CHAPTER 2 – BIMANUAL INTERFERENCE INCREASES WITH FORCE DEMAN IS FACILITATED BY VISUOMOTOR ADAPTATION	DS AND 19 19
2.2 Methods	
2.2.1 Participants	
2.2.2 Procedures	
2.2.3 Data Analysis	
2.3 Results	
2.3.1 Experiment 1	
2.3.2 Experiment 2	
2.3.3 Interexperimental comparisons	40
2.4 Discussion	
CHAPTER 3 - STRUCTURAL LEARNING GENERALIZES TO A CONTRALATER	AL
EFFECTOR	
3.2 Methods	4 0 51
3.2 1 Derticipanta	
3.2.1 Faiticipants	
3.2.2 Procedures	
3.2.5 Data Analysis	
3.3.1 Replication Study	
3.3.2 Training	

TABLE OF CONTENTS

3.3.3 Testing
3.4 Discussion
CHAPTER 4 - STRUCTURAL LEARNING INCREASES BIMANUAL INTERFERENCE 68 4.1 Introduction
4.2.2 Procedures
4.2.3 Data Analysis
4.3 Results
4.3.1 Right, adapting hand
4.3.2 Left, interfered-with hand
4.4 Discussion
CHAPTER 5 – GENERAL DISCUSSION
5.2 Aim 2: Structural learning generalizes across effectors
5.3 Aim 3: To determine if facilitated adaptation increases interference
5.4 Broader implications for basic science and translational motor control
5.5 Summary
APPENDIX
REFERENCES

LIST OF TABLES

Table 3-1: Inferential statistics of feedback measures	61
Table 4-1: Omnibus ANOVAs for left hand interference	83

LIST OF FIGURES

Figure 1-1: Optimal feedback control theory	6
Figure 1-2: Structural Learning.	12
Figure 2-1: Experiment 1 initial directional error	27
Figure 2-2: Experiment 1 left hand interference	30
Figure 2-3: Experiment 1 lateral force against force channel	34
Figure 2-4: Experiment 2 left hand interference	37
Figure 2-5: Experiment 2 lateral force against force channel	39
Figure 2-6: Interexperiment interference comparison	41
Figure 3-1: Replication study adaptation	55
Figure 3-2: Transfer study adaptation	57
Figure 3-3: Transfer study transfer of feedback measures	60
Figure 4-1: Experimental procedures flowchart	75
Figure 4-2: Right hand Initial directional error (IDE) and root mean squared error (RMSE) – interference task	80
Figure 4-3 - Self-report aiming angle	82
Figure 4-4 - Left hand interference	85
Figure 4-5 - Lateral force during force channel trials - left hand	88

KEY TO SYMBOLS AND ABBREVIATIONS

^O – Degrees

- HKB-Haken-Kelso-Bunz
- UCM Uncontrolled Manifold Hypothesis
- OFCT Optimal Feedback Control Theory
- IDE Initial Directional Error
- EPX Lateral Endpoint Error
- LFPV Lateral Force at Peak Velocity
- LFOFF -- Lateral Force at Movement Offset
- Tukey HSD Tukey's Honest Significant Difference
- RMSE Root Mean Squared Error
- MT Movement Time
- ML Movement Length
- nJ Normalized Jerk Score
- TMS Transcranial Magnetic Stimulation
- EMG Electromyography
- EDE Endpoint Directional Error
- ANOVA Analysis of Variance
- ges Generalized eta-squared

CHAPTER 1 – BIMANUAL COORDINATION AND INTERFERENCE: A REVIEW

Imagine a simple task, such as cooking scrambled eggs. One hand must firmly hold the pan still, while the other whisks to prevent the eggs from sticking. The simplicity of this task belies the complexity of control needed to perform asymmetrical actions with the hands. The field of bimanual coordination research attempts to understand the conditions for which independent control of the hands is required to achieve a common goal. Under normal circumstances, humans are adept at producing actions which seem to allow for such independent control; however, certain tasks and conditions can cause a breakdown in tightly coordinated movements. Take for example the childhood game of 'rubbing your stomach and patting your head'. This is trivial when performed slowly, but as the frequency of each movement increases, performers often experience instability in their actions. More seriously, however, are neurological conditions such as Parkinson's disease which can produce unwanted movement in one limb, while the other produces volitional movement (Cox et al., 2012). This can make everyday activities laborious and preclude some from engaging in tasks he or she would normally require for daily life.

This phenomenon, unwanted movement of one limb while the other performs volitional action, is often called interference (Swinnen, 2002). While this term connotes a failure to properly control each limb, interference should rather be viewed as the behavioral limitations of the motor system to produce highly complex asymmetrical actions – often imposed by researchers in order to probe the underlying function of the motor system. The resulting motion often exhibits a coupling of the limbs mediated by connections between the hemispheres of the brain via the corpus callosum (Franz et al., 1996). There are several ways researchers can design

tasks to elicit interference ranging from simple isometric force contraction (Cunningham, 2017; Perez & Cohen, 2008) and finger tapping tasks (Wenderoth et al., 2003), to more complex movements such as bimanual circling (Kelso et al., 1979; Schöner & Kelso, 1988) and adaptation tasks (Diedrichsen, 2007; Kagerer, 2015). In the latter case, one possible mechanism underlying the phenomenon may be that an updated internal model of the sensorimotor consequences of movement are shared across effectors. An internal model is one element of popular models of the motor system which makes predictions of the current state of the effector by integrating prior motor commands with delayed feedback. The motor system can then make online corrections to minimize the difference between the expected and actual sensory feedback in order to optimally control the limb (Todorov & Jordan, 2002). In an adaptation task where visual information no longer matches the produced movement, corrections in motor output can correct for this discrepancy and the system can learn to apply a new control policy on subsequent trials. It is possible that interference in a task that requires one hand to adapt to a visuomotor perturbation, while the other reaches without visual feedback, results from applying this new control policy to both effectors which results in motor interference in the 'invisible' hand. A series of experiments were conducted, using the task described here, to investigate to what extent interference is due to a shared internal model.

1.1 Models for volitional movement control

One of the earliest and most influential descriptions of bimanual coordination comes from the dynamical systems theory, such that human coordination arises from the formation of stable attractor states. When performing a task where both hands must simultaneously trace circles continuously and repetitively, there exists a stable coordination pattern where the location of

each hand is at the same location as the other (both hands at 3 o'clock, moving clockwise), termed 'anti-phase'. When participants are required to match the circling frequency to a metronome, as the pacing frequency increases, the coordination pattern becomes unstable and there is a spontaneous switch to a more stable, in-phase pattern (one hand moving counter clockwise and the other clockwise) (Kelso, 1984). Therefore, interference may represent the coupling of homologous muscles during stable coordination. While the HKB model has strong explanatory power for continuous movements, far fewer studies have employed it for discrete center-out movements (Schöner, 1990). Alternative motor control theories have focused on discrete movements and may provide stronger internal validity to the experiments conducted here. The uncontrolled manifold (UCM) hypothesis attempts to separate variability into that which affects task performance from that which does not. The fundamental premise of the UCM hypothesis is that variability in the motor control system is not a problem but rather the manifestation of the central organization of the system itself (Latash et al., 2002). The often-cited example used to illustrate how variability can be partitioned is in a task where one must use two fingers to press with a combined force of 10 N. That is, $F_1 + F_2 = 10$. The solution to this task falls along a line for which an infinite number of solutions exist. This line represents the uncontrolled manifold because any control along this manifold is inconsequential to successful completion of the task. However, any combination of forces that fall outside of this manifold give rise to variability orthogonal to the UCM and must be accounted for. The UCM hypothesis has been applied to a variety of tasks from sit-to-stand (Scholz & Schöner, 1999), bimanual pointing (Domkin et al., 2001), and continuous movements (Latash et al., 2001). Applying the UCM hypothesis to my studies is attractive at first glance. It may be that interference in the kinesthetically controlled hand is the result of variability orthogonal to the UCM since it has no

bearing on the task completion. This prediction would imply that interference would vary in direction and magnitude, but this is not the case. My studies used a procedure that produce predictable interference patterns that are in the same direction and with a magnitude that is relatively constant (Kagerer, 2015, 2016b). Moreover, while the UCM hypothesis is supported in studies that employ discrete movements, its explanatory power is limited by the need to analyze 'postures' rather than movements (Domkin et al., 2001). That is, the UCM hypothesis has strong explanatory power for the product of movement but lacks in its ability to describe the processes by which movements are produced and learned. Therefore, I wished to use a theory or concept of motor control that had the ability to explain the consistent directionality of interference, allowed for its description over the time-course of individual movements, and described interference over the course adaptation tasks.

Considering the shortcomings of the theories and concepts explained above, I applied a theory that has strong explanatory power for discrete, goal directed movement, can describe the how interference is accumulated throughout movement, and can account for the directionality of interference observed in our laboratory's previous findings. Optimal feedback control theory (OFCT) has the potential to meet all of these criteria. According to OFCT, the goal of the motor system is to generate a control policy, which transforms the state estimate of the effector and environment into motor commands, that will minimize some cost function. This cost function consists of two parts. There is cost associated with the external goal of the movement, such as reaching out to grasp a cup and bringing it one's mouth. That is, the cost associated with task-relevant states leading to reward. The second cost penalizes effort associated with unnecessary motor commands, typically defined as the sum of the squared motor commands (Diedrichsen et al., 2010). The goal of determining the optimal control policy is therefore critically dependent on

an accurate state estimation. To do this, there must be an adaptive process that relies both on feedforward (predictive) and feedback processes.

Once a task is selected, for example reaching for a cup, a motor command is sent to the muscles controlling the arm to impart a state change of the effector. Additionally, an efferent copy of that command is sent to a forward model that creates a prediction of the state change that will occur from the motor command. Once the state of the arm has changed, actual sensory feedback of the movement, delayed by time and corrupted by noise, is integrated with the state prediction to obtain an accurate state estimate at all times throughout a movement. An important feature of OFCT is that there is no conceptual difference between these feedforward and feedback components - they constitute two ends of a continuum. At one end, the controller relies heavily on internal predictions such as early in movement or movements with large sensory noise or delays. At the other end of the spectrum are movements that are made in an unpredictable or novel environment, such as when faced with perturbations, or when movements are long enough in duration as to reliably use sensory feedback for online correction (Todorov, 2004). At the step of sensory integration, the state estimation is calculated by adjusting the Kalman filter gain (K, in Figure 1-1) to selectively emphasize one source of information over the other. In fact, the source of information (feedforward or feedback) is weighted according to the inverse of variance associated with that source (Vaziri et al., 2006). Taken as a whole, OFCT can be visualized as an integrative model, shown in Figure 1-1, which combines a forward internal model that predicts the sensory consequences of the prepared motor command and an inverse internal model that computes a motor command that best matches the desired sensory consequences of that movement (from (Diedrichsen et al., 2010)).



Figure 1-1: Optimal feedback control theory. Motor commands **u** are set to a set of effectors represented here by a plant containing the state vector **x**, the command, and the plant dynamics A,B. In addition to the motor command, an efference copy is sent to a forward model that generates a predicted state \mathbf{x}^* . Once the effector has changed state, the actual sensory information **y** is integrated with the predicted state, and a gain K is adjusted depending of the uncertainty in either the prediction or feedback to obtain an accurate state estimate $\hat{\mathbf{x}}$. An optimal control policy L is then generated such that the mapping between $\hat{\mathbf{x}}$ and \mathbf{u} minimizes the cost which depends on the external task constraints q and control effort r. Taken from (Diedrichsen et al., 2010).

Optimal feedback control theory is an attractive concept for investigating interference during a bimanual reaching task. As mentioned earlier, I employed a theory capable of describing discrete, goal-directed movement. OFCT has been use for exactly these types of tasks such as eye and head movement during foveation (Saglam et al., 2011), skilled forelimb reaching in non-primates (Azim et al., 2014) and non-human primates (Archambault et al., 2015) and adaptation to both dynamic (Crevecoeur et al., 2016) and visuomotor (Honda et al., 2012) perturbations in sensory feedback. The internal model approach also allows researchers to accurately model kinematics throughout movement even though the trajectory itself does not need to be explicitly formed during movement planning, but rather it is a consequence of the optimal solution (Liu & Todorov, 2007). This suggest OFCT is capable of describing how feedback is used to make online corrections in the face of perturbations or due to unpredictable obstacles. Moreover, OFCT has been used to describe interactions between the limbs during bimanual reaching tasks. Diedrichsen in 2007 showed that when participants controlled two cursors reaching to two targets, perturbing one hand did not cause the other to deviate from a straight-line path to the target. However, when both hands controlled a shared cursor, the optimal solution was one where the perturbation was countered using both effectors (Diedrichsen, 2007). This elegant experiment has bearing on the current proposed study such that the optimal control strategy during the shared cursor condition was one where control effort was minimized by an interaction between limbs in the inverse internal model (L). Therefore, interference in our task may be a result of one limb updating an internal model for the new visuomotor mapping between output and perturbed feedback, and that internal model is shared with the contralateral limb. However, in Diedrichsen's study, the task constraints were such that both effectors had shared control over a single cursor. In Chapter 2 of this dissertation, I describe our task which has only

the right, perturbed hand controlling a single cursor, while the contralateral limb controls no visual stimulus at all. Therefore, the shared control task constraint is not present in the current studies and the control policy may not be optimized to induce interference in the kinesthetically controlled limb. Alternatively, there may be an explanation that is predicted from the OFCT's postulation that feedback gains are re-weighted based on the fidelity of either feedforward or feedback information. Franklin et al. had participants adapt to a dynamic perturbation that applied a force perpendicular to movement velocity during a reach to a peripheral target (Franklin et al., 2012). On probe trials that employed a force channel which constrained movement to a straight-line path to the target, the cursor jumped 2cm to the side. Participants pressed significantly harder against the force channel during exposure to the dynamic perturbation than during trials in a null-field. The authors conclude that sensorimotor integration down-regulated the state prediction due to the uncertainty introduced by the dynamic perturbation while upregulating visual feedback gains and this resulted in a larger visuomotor response to a visual jump in cursor location.

While not a fully formed theory of motor control, neural cross talk has been proposed as a potential mechanism of interference by observations that homologous regions of the primary motor cortex of each hemisphere share information via the corpus callosum. For example, when drawing two different shapes, one with each hand, typically developing people tend to draw similar shapes in each hand that assimilate features of both templates. However, in patients who have undergone a callosotomy, they are able to draw each shape with relative ease (Franz et al., 1996). This communication between hemispheres is important for volitional motor control because there are direct and indirect neural pathways supplying motor information to the periphery. Most of the neurons innervating motor units in the spinal cord decussate at the level of

the medulla in the brain stem. These fibers terminate in the lateral portion of the ventral horn and are responsible for fine movement of distal effectors such as arm, hand, and finger motor units. A ventral tract passes uncrossed through the brain stem and innervates ipsilateral neurons in the medial portions of the spinal cord responsible for more proximal motor units such as trunk and arm (Brinkman & Kuypers, 1972; Swinnen, 2002). Therefore, neurons in both primary motor cortices may send conflicting motor information to a limb, especially while the other limb is engaged in action. This observation has been demonstrated in tasks where participants producing isometric contractions with one finger will interference with control of the contralateral finger (Hu & Newell, 2010). It has been shown that during these tasks, inhibitory projections from the hemisphere controlling volitional action have reduced effect on the contralateral hemisphere (Perez & Cohen, 2008). Mirrored EMG activity has also been seen in rhythmic movements where homologous muscle synchronize firing in a purely unimanual task (McDonnell & Ridding, 2006), and many movement disorders exhibit mirrored movements (Cincotta et al., 2006; Sitburana et al., 2009). However, this would suggest that interference in my task would be mostly, if not completely mirror symmetric. However, the task used in this dissertation has demonstrated that approximately 2/3 of participants exhibit an interference pattern where both hands move in the same direction, while 1/3 show mirror interference (Kagerer, 2015). Taken together, it may be that when both effectors access a shared internal model, leading to interference between the limbs, it is done so through neural crosstalk.

As I will describe in my first aim, I sought to extend the work our lab has previously done to determine whether and to what extent interference is due to a shared internal model, akin to Diedrichsen's shared cursor experiment, and furthered the work by Franklin et. al. to see if visuomotor perturbations can upregulate dynamic feedback gains to visuomotor perturbations.

Finally, I discuss these results in the context of findings from neural crosstalk literature which suggests interhemispheric communication is scaled by the force demands for reaching.

1.2 Structural learning and facilitated adaptation

In our interference task, participants are required to adapt to a fixed perturbation in one hand, while the other operates under kinesthetic control – making it susceptible to interference. Aim 1 attempted to shed light on whether and to what extent a shared internal model is responsible for this and considered the possibility sensory re-weighting is an underlying mechanism for interference. To further the experiments in aim 1, I more fully explored the latter possibility by manipulating the rate at which participants adapted to determine if facilitating adaptation increases interference. Adaptation and learning tasks often use perturbations to disrupt the relationship between the predicted and actual sensory feedback to investigate how participants update their internal models to parsimoniously resolve any discrepancies between them. Researchers overwhelmingly design tasks that introduce an abrupt perturbation, such as a rotation in visual feedback, to disrupt this relationship. Such tasks require participants to learn a fixed perturbation and in the adaptive control literature is known as *parametric* learning. The adaptive process therefore amounts to a search through parameter space that converges on the most optimal set of fixed parameters necessary to complete the task. The following equation illustrates the example of a fixed perturbation of 60° in cursor position, rotated around some origin.

$$\begin{bmatrix} x \\ y \end{bmatrix}^{cursor} = \begin{bmatrix} \cos 60 & \sin 60 \\ -\sin 60 & \cos 60 \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix}^{hand}$$

To solve this parametric problem, the motor system must learn the mapping between cursor and hand position, $U = f(X(t), \mu(t), t)$, where U is the cursor [x,y] position, X is the hand [x,y] position and μ represents the unknown parameters to be learned. The solution to this relationship

would be to produce a movement with the same structure, but whose values are opposite (e.g. - 60°). Recently, Braun and colleagues have introduced a version of this task that requires participants not to adapt to a fixed perturbation but rather to a fixed *structure* of perturbations. In this scenario, participants are exposed to many different perturbations all belonging to the same structure. Using the equation above, the rotation amount would not necessarily be 60° but could vary trial-to-trial. Instead of learning the fixed rotation matrix described above, they would be learning the correlation between all elements of the matrix. That is, they would be learning the structure of the transformation matrix, *f* (Braun et al., 2009a).

Take the example of learning to shoot an arrow on a windy day, illustrated by Figure 1-2. Panel **a** represents a chaotic wind pattern such that aiming has not impact on success (indicated by warmer colors). On a day where wind can only blow left or right, but with any magnitude, (panel **b**) the search through parameter space is constrained along the azimuth with zero adjustment of altitude. That is, due to a structure to the perturbations, the solution to this problem still has an infinite number of solutions, but the archer is capable of learning this reduced solution space. Panel **c** represents a structure constrained by rotations is visual feedback about the origin and represents the solution space for the example outlined in above equation. The search through parameter space then becomes exploration of the off-diagonal terms in the rotation matrix, and a successful reach will be constrained to a ring about the origin (Bond & Taylor, 2017).



Figure 1-2: Structural Learning. Description of figure is supplied in text. Image taken from (Bond & Taylor, 2017)

Structural learning has three benefits (Braun et al., 2009a). First, by constraining the parameter space to a lower-dimensional one, learning will progress faster – termed structurespecific facilitation. Second, when two tasks require participants to learn opposing perturbations (e.g. $+60^{\circ}$ followed by -60°) learning in the second task is impaired by the first, and re-test on the first task is impaired by the second – termed structure-specific interference reduction (note: this refers to anterograde and retrograde interference, respectively. Not to be confused with interference in bimanual coordination). Finally, when participants engage in a new task that belongs to the same structure, adaptation will be facilitated by the participant's exploration along the previously learned structure – structure-specific exploration. Braun et. al. designed a series of experiments that tested each of these concepts. They had participants perform center out reaches to eight radially arranged targets. Cursor feedback was provided on a screen that covered vision of the hands and midway through the task, exposed three groups of participants to one of three conditions. In the control group, veridical feedback was provided throughout, while in the two experimental groups participants either experienced a new random rotation for eight consecutive trials, or participants experienced a random linear transformation that consisted of combined rotations, shearing, and scaling. After learning their respective structures, all participants adapted to a fixed 60° rotation, followed by a fixed -60° rotation. They found the group who had previous experienced the random rotation structure adapted faster than the other two groups on both fixed perturbations. In a subsequent experiment, they had participants perform reaches in 3-D space and applied a force perturbation either in the horizontal or vertical plane. Upon testing both groups with both perturbations, participants' initial reaches countered the previously learned structure (either horizontal or vertical) before converging on the appropriate solution (Braun et al., 2009a). The results supported their three predictions about the benefits to structural learning,

but most importantly, they found improvements in both the feedforward and feedback components of movement. They conclude that structural learning assists in the optimization problem central to OFCT by reducing the parameter space through a mechanism of providing the motor system prior knowledge of the underlying structure to improve state estimation of the effector. In the context of my studies, I employed structural learning to facilitate adaptation, using the finding that state estimation is improved by faster gain modulation. That is, structural learning allows the state estimator to adjust gain more quickly to preferentially weight either feedforward or feedback components of the internal model. In our interference task, facilitated adaptation should give rise to a faster onset in interference by the participants' faster updating of their internal model. Additionally, I expected the improved feedback gain adjustment to enhance interference through better use of proprioceptive and visual information. However, before I tackled this experiment, I needed to establish that a previously learned structure can be accessed by the contralateral limb. Specifically, this informed me which hand should undergo structural training. I explore this topic more fully in the Chapter 3, but this decision will be informed by the design of an interlimb transfer task.

1.3 Interlimb transfer tasks

A key feature of our motor control system is its ability to perform similar movements in a vast array of scenarios. A right-handed person can easily write in a notebook located on the right side of the body, but she could just as easily perform this task with the notebook on her left side. This ability for humans to perform the same task in different circumstances is known as generalization (Shadmehr & Mussa-Ivaldi, 1994). In the example above, this is referred to as spatial generalization because the writer can perform in two workspaces separated spatially. Generalization also extends to the idea that our writer could (perhaps not as easily) write a

simple passage with her left hand. The importance of determining the underlying mechanisms of transfer, or generalization to a contralateral effector, is an attractive field of study, particularly in rehabilitation settings were one half of the body may have impaired movement such as in lateralized stroke.

Interlimb transfer tasks are designed to test whether and to what extent learning a new movement in one limb transfers to another. This can be done using visuomotor perturbations (Sainburg & Wang, 2002; Wang & Lei, 2015), dynamic perturbations (Joiner et al., 2013; Wang & Sainburg, 2004), and even complex sequence learning (Panzer et al., 2018). In addition to perturbation tasks and more cognitive tasks such as sequence learning, use-dependent learning transfers and can even improve transfer in error-based learning (Wang & Lei, 2015). Recently, the most common tasks used to investigate transfer have employed either dynamic or visuomotor perturbations. When participants adapted to novel arm dynamic produced by hanging a weight off of the dominant arm, subsequent adaptation in the contralateral arm was dramatically improved. However, initial training on the non-dominant arm did not transfer to the dominant limb (Wang & Sainburg, 2004). Adaptation to curl-field perturbations have also been shown to transfer from dominant to non-dominant limbs, but not vice-versa, and transfer only occurred in intrinsic coordinate frames (Criscimagna-Hemminger et al., 2003). Moreover, the amount of transfer does not depend on the length or onset (gradual vs. abrupt) of training, but longer training periods result in a more sustained transfer (Joiner et al., 2013).

In my experiments, I asked the question whether structural adaptation to visuomotor perturbations transfers to a contralateral limb. Several studies have looked at the important features and mechanisms underlying visuomotor transfer. Wang and Sainburg had participants adapt to a rotation in hand feedback with either the left or right arm, and subsequently exposed

the participants to the same perturbation with the contralateral limb. Both groups showed substantial improvements in adaptation compared to a previous adaptation session (Sainburg & Wang, 2002). Moreover, they found that performance differed, whether the transfer occurred from dominant to non-dominant hand or vice versa. The initial direction of reaches in the dominant hand were more accurate when the non-dominant hand had previously trained to the perturbation. However, opposite arm training improved final position and accuracy of the non-dominant arm. This suggests that training either the dominant or non-dominant arm transfers different aspects of control information and is not a result of a general cognitive strategy. The authors explain this result in context of the dynamic dominant limb is better able to specify and control the trajectory of movement, whereas the non-dominant limb is more well suited for stability and effector end-point control (Sainburg, 2002). Therefore, there exists asymmetrical transfer during visuomotor tasks – the information transferred is specialized to the control advantage of that limb receiving that information.

1.4 Specific Aims

In this dissertation, I explored the hypothesis that interference in a bimanual adaptation task results from a shared internal model of the relationship between motor action and sensory feedback. To do this, I aimed to investigate how updating an internal model can influence sensitivity to feedback signals providing information about limb dynamics. I also manipulated the adaption process to determine what effect this will have on bimanual interference. This work extends our knowledge of the basic control properties of bimanual movements and coordination through execution of the following specific aims.

Aim 1: To determine the effect of manipulating dynamic feedback on a visuomotor interference task.

It has been shown that when participants are required to adapt to moving in a novel force environment, thus requiring the formation of a new internal model of task dynamics, feedback gain for visual information is upregulated (Franklin et al., 2012). Therefore, I designed a study which tested the hypothesis that if participants are exposed to a visuomotor perturbation, they would upregulate feedback gain to dynamic information. The effect of upregulating dynamic feedback gain showed two distinct features. First, interference was proportional to the force requirements for movement in a dose-response fashion. Second, when the adaptation component was removed, interference was not proportional to task dynamics. This is consistent idea that the interfered with hand shares features of the newly updated internal model used to control the perturbed hand by increasing feedback gains while decreasing predictive processes (Crevecoeur et al., 2010).

Aim 2: To determine whether structural learning generalizes across effectors

I examined if learning the underlying structure of random visuomotor perturbations in one limb transfers to the other. This would provide more support for the possibility that learning a new internal model in one limb is accessible to the contralateral limb. Interlimb transfer of fixed perturbations has been studied extensively in the past (Joiner & Smith, 2008; Sainburg & Wang, 2002; Wang & Sainburg, 2003, 2004), but to my knowledge no studies have determined if the learning of an underlying structure (via random rotations) transfers across effectors. Additionally, this information will be necessary to design the testing procedures used in Aim 3. *Aim 3: To determine if facilitated adaptation increases interference*

Participants underwent the interference task defined in aim 1 following the exposure to a training phase where one group is provided veridical feedback, while a second group engages in structural learning. This measured the effect facilitated adaptation will have on interference, with the expectation that improved adaptation will increase subsequent interference.

CHAPTER 2 – BIMANUAL INTERFERENCE INCREASES WITH FORCE DEMANDS AND IS FACILITATED BY VISUOMOTOR ADAPTATION

2.1 Introduction

Bimanual coordination is a hallmark of human movement where task constraints dictate whether the hands should operate tightly coupled or independently. For example, when using both hands to put on eyeglasses, the hands must produce symmetrical, synchronous actions to ensure proper execution and reduce risk of injury. Many activities require the hands to produce simultaneous yet independent movement such as tying one's shoes or cutting with scissors. Limitations to independent control of the limbs can be observed behaviorally by assimilation of movement characteristics of the contralateral limb, or motor interference – one of the most common demonstrations being 'rub your belly and pat your head'.

In the past several decades, research had mainly focused on two types of tasks to observe interference – those relying on temporal or spatial constraints (see Swinnen, 2002 for review). Finger tapping tasks that require participants to produce simple integer ratio rhythms (such as 1:1, 2:1, or 3:1) are easily produced, even at high frequencies, whereas complex polyrhythms (3:2, or 5:3) are more difficult and usually exhibit greater variability (Peper et al., 1995; Summers et al., 1993). Temporal coupling between fingers producing cyclic movements can maintain stable, discrete phase relationships, but can become unstable as movement frequencies increase. The motor system responds to this instability by transitioning to a more stable pattern – one which requires simultaneous, homologous muscle activation (Kelso et al., 1979; Schöner & Kelso, 1988). Spatiotemporal interference has been shown to rely heavily on communication between the hemispheres via the corpus callosum. When drawing different shapes, one with each

hand, healthy individuals produce shapes that assimilate characteristics of the contralateral hand's template. Patients who had their corpus callosum surgically severed perform remarkably well at drawing each shape independently, especially when the callosotomy involves the posterior corpus callosum (Eliassen et al., 1999; Franz et al., 1996).

One concept developed to help explain the nature of communication between the hemispheres is neural crosstalk. It is based on the anatomical fact that axons controlling distal effectors (fingers, hands) decussate in the medulla, whereas axons controlling axial and proximal muscles (trunk, arm) project both ipsilaterally and contralaterally. Therefore, hands and fingers are largely controlled by the contralateral hemisphere, whereas for arm control, both hemispheres are thought to contribute (Brinkman & Kuypers, 1972). Therefore, when sending motor commands to one limb, unwanted activation of the contralateral limb may occur. Coactivation of contralateral muscles in a resting limb has been observed in isometric force production such that increasing levels of force production induces greater coactivation and is suggested to be mediated by interhemispheric projections between primary motor cortices resulting in decreased inhibition of neurons in the primary motor cortex (Cunningham, 2017; Perez & Cohen, 2008). Walter and Swinnen showed interlimb interference in dynamic tasks where each limb must produce a different trajectory profile (Walter & Swinnen, 1990). Interestingly, their work showed that increasing the torque required to produce these movements increased the amount of interlimb interference.

Among different theoretical frameworks applied to bimanual coordination, optimal feedback control theory has had some success in explaining the coordination of bimanual movements from a control perspective (Schwartz, 2016; Scott, 2004; Todorov & Jordan, 2002). This theory posits that the nervous system optimizes a control policy that minimizes a task-

dependent cost function by maximizing reward and minimizing effort. To counter delays in sensory feedback, a prediction is made using prior knowledge, gained through learning, of the relationship between the expected and actual sensory feedback and is referred to as the 'internal model'. When executing a movement, an efferent copy of the motor command allows a forward internal model to predict the state of the body resulting from the command. Actual sensory feedback is compared to the prediction and any discrepancy is recognized as error. The goal is to minimize the error between the expected and actual feedback relevant to performance characteristics required for task completion. To understand how the internal model is updated to minimize this error, researchers have employed tasks which require participants to adapt to perturbations in both visual (Krakauer et al., 2000) and dynamic feedback (Shadmehr & Mussa-Ivaldi, 1994). Optimal control theory has been studied in bimanual tasks when both hands control a single cursor displayed at the midpoint between the two hands. When a perturbation is applied to one hand, the optimal solution distributes the correction between the hands in order to minimize the control effort (Diedrichsen, 2007). Franklin et al. have shown that when adapting to a force perturbation orthogonal to movement direction (curl-field adaptation), the sensorimotor system upregulates feedback gains to visual information (Franklin et al., 2012). Recently, tasks where one hand is perturbed while the other hand is controlled without visual feedback has been used to induce interference in the kinesthetically controlled hand (Kagerer, 2015, 2016a). In this context, it is suggested the interference is due in part to the updated internal model being shared between effectors. In the context of optimal feedback control theory, this would suggest that while adapting to a visual perturbation in one hand, the strategy that minimizes control effort is one where the relationship between expected and actual sensory feedback is applied to both effectors. Since the kinesthetically controlled hand cannot access

visual feedback, the error signal associated with vision is minimal, even when a motor command is sent which rotates movement trajectories. This result may also be explained within the neural crosstalk framework, such that producing asymmetrical movements induces interference via coactivation of homologous muscles. These two explanations are not necessarily mutually exclusive, but we wished to describe the contribution of each to interference.

The purpose of this study is therefore to (1) determine if increasing the force required to move both effectors in a bimanual reaching task will increase the amount of interference in the kinesthetically controlled arm contralateral to the arm exposed to a visual perturbation; and (2) to determine if adding an adaptation component to the production of asymmetrical movements increases interference by upregulating sensory feedback. In our first experiment, participants adapted to a visual rotation in hand feedback for the right hand while the left hand moved without visual feedback. Three groups received one of three resisting forces exerted through a virtual spring. We hypothesized that if interlimb interference is modulated by the amount of force required to move, then increasing the virtual spring constant will increase the observed interference. In a second experiment, we repeated the design of the first experiment, but instead of having participants adapt to a visual perturbation, we rotated the target locations in the right hand. This removed the adaptation component while maintaining the asymmetry of movement. We hypothesized that if updating the internal model upregulates sensory feedback, then interference in the first experiment would be greater than the interference observed in the second experiment.
2.2 Methods

2.2.1 Participants

Forty-five healthy, right handed individuals (age: 20.9 +/- 0.8 years, 31 female) participated in the first experiment and 36 participated in the second (age: 20.9 +/- 1.1 years , 28 female); each participant scored at least +70 on the Edinburgh Handedness Inventory – Short Form (Oldfield, 1971; Veale, 2013). All participants gave informed consent, and the study was approved by Michigan State University's Institutional Review Board.

2.2.2 Procedures

2.2.2.1 Experiment 1

Participants were seated comfortably in front of a bimanual Kinarm End-point robot (Kinarm End-point Lab, BKIN Technologies, Kingston, ON). They were instructed to use two manipulanda to control two virtual cursors projected on a screen occluding vision of the hands. The task was to reach two targets positioned either 90° or 270° with respect to the home position (distance 10cm), and participants were instructed to move both hands simultaneously fast and straight. Order of the target positions was pseudorandomized, such that no more than two consecutive target locations were in the same direction. Also, the number of 'forward' trials (90°) matched the number of 'backward' trials (270°). Movements of the two hands were always in the same direction, either forward or backward.

Each participant completed a total of 220 trials. During the first 20 trials (visual baseline) cursor feedback for both hands was veridical. During the next 20 trials (kinesthetic baseline) the cursor representing the right hand was visible, but no visual feedback was provided for the left hand. Participants were instructed to continue moving both hands simultaneously to the targets, and to stop their nonvisible left hand when they estimated it to be in the target. Following this

second baseline, a 140-trial exposure phase introduced an abrupt clockwise 40° rotation of visual feedback for the right hand, requiring participants to compensate counterclockwise; the left hand remained without visual feedback. Participants were instructed to continue moving the left hand straight toward the targets. During a post-exposure phase of 40 trials the visual perturbation was removed; the left hand's visual feedback remained off in this phase. The post-exposure phase was used to measure aftereffects of adaptation.

Participants were randomly assigned to one of three groups, each with a different force applied to the hands at the manipulanda. Two groups received a spring restoring force directed from handle position to the home position, with a magnitude of either 30 N/m or 60 N/m, while a control group received no force (0 N/m). Our primary dependent variable for the right hand was initial directional error (IDE), calculated as the angle between target vector and movement vector at peak velocity; IDE is used as a measure for movement planning. In the left hand, we calculated both IDE and lateral endpoint error (EPX), defined as the lateral distance between target location and endpoint of the hand. In addition, we introduced a 2 mm wide force channel in the left hand on approximately 20% of trials, which restricted movement to a straight line to the targets. For these force channel trials, we measured the lateral force exerted on the channel wall throughout the movement.

Due to using a restoring force in each hand, one potential confound on IDE and EPX is that there is a component of force directed toward the midline of movement. This would constrain the left hand from deviating from a straight-line path to the target in the two groups which received the restoring force. To control for this, we also measured the lateral force applied against the virtual spring at peak hand velocity (LFPV) and movement offset (LFOFF) in the left manipulandum. We chose these two timepoints to coincide with IDE and EPX, respectively.

2.2.2.2 Experiment 2

We hypothesized in the first experiment that increasing the force demands for movement would increase the amount of interference in the left hand while the right hand adapted to a rotation in hand feedback. Interference in this condition could be due to neural crosstalk, without adaptation playing a major role. To address this possibility, we devised a second experiment that removed the adaptation component and asked participants to move their right hands to targets rotated by 40° (counterclockwise) about the home position. This would allow us to determine the contribution of producing asymmetrical movements to interference without the need for participants to change their established internal models. We therefore had participants perform a set of trials identical to experiment 1, the only differences being that during the exposure phase, they reached under veridical feedback to rotated targets. Therefore, in both experiments, the 'ideal' movement direction would be exactly the same for the right hand. In the first experiment, however, participants would be updating their internal model of the relationship between expected and actual sensory feedback, but not in the second. Experimental design, data analysis, and the calculation of all outcome variables were identical between the two experiments.

2.2.3 Data Analysis

We took the absolute values for IDE, EPX, LFPV, LFOFF, and force channel data to correct for sign differences in forward vs. backward trials. To correct for baseline differences, we subtracted the mean baseline performance from all exposure and post-exposure trials for each of the outcome variables. We then averaged 10 consecutive trials for a total of 22 blocks throughout the experiment. For analysis of the force channel trials, we resampled the force time-series to 1000 samples and averaged 6 consecutive force channel trials during the first 28 trials ('early'), middle 28 trials ('middle') and last 28 trials ('late') of the exposure phase. This allowed us to compare

force profiles between trials of differing movement length. For IDE, EPX, LFPV, LFOFF, and the force channel trials we performed separate 3 (group: 0-30-60N/m) x 3 (time: early-middlelate) mixed model repeated measures ANOVAs. We additionally performed a 3 (group: 0-30-60N/m) x 2 (time: early-late) ANOVA for each outcome variable during the post-exposure phase. Significant group effects were followed up with Tukey HSD post-hoc multiple comparisons. All statistical procedures were performed in R 3.3.2, with the *ezANOVA* package; violations of sphericity were accounted for by using the Greenhouse-Geisser correction.

2.3 Results

2.3.1 Experiment 1

2.3.1.1 Visually guided hand

To verify all group performed similarly during baseline trials, we performed one-way ANOVAs on the average of the 20 trials during each baseline. There were no differences between groups for IDE during either of the two baselines [VB: F(2) = 0.121, p > 0.05; KB: F(2) = 0.789, p > 0.05]. During exposure, there was a main effect for time [F(2,84) = 820.36, p < 0.0001], indicating that IDE decreased from early to late exposure. There was no group main effect or Group x Time interaction, indicating that all three groups adapted similarly to the visual feedback perturbation. In the 10-trial block immediately following the exposure phase, where veridical feedback was restored, groups did not significantly differ in the magnitude of their aftereffects [F(2,42) = 0.14, p = 0.87]. Taken together, these results suggest that all groups reduced their IDE in a similar way during exposure and attained comparable levels of adaptation as shown by the similar aftereffects early in post-exposure (see Figure 2-1).



Figure 2-1: Experiment 1 initial directional error. IDE was calculated as the angle between target vector and movement vector at peak velocity. Data are shown for the exposure phase (blocks 5-18) in response to a clockwise 40° rotation in hand feedback and post-exposure phase with veridical feedback (blocks 19-22). Open circles represent IDE for the right, adapting hand, and filled circles for the interfered-with, left hand.

2.3.1.2 Kinesthetically guided hand

2.3.1.2.1 Kinematics

Both IDE and EPX were not significantly different between groups during both baseline phases (all p > 0.05). For IDE, there was a group difference during exposure [F(2,42) = 4.87, p < 0.05], and a Group x Time interaction [F(4,84) = 5.62, p < 0.01]. Post-hoc analysis showed no group differences at the beginning or middle of exposure, but significantly higher IDE for the 60 N/m group at the end of exposure [60 N/m – 0 N/m difference: 4.57° , CI: (2.06, 7.08), p < 0.01; 60 N/m – 30 N/m: 3.69° , CI: (1.17, 6.20), p < 0.01]. Figure 2-2A illustrates these comparisons, suggesting IDE increases in the 60 N/m group throughout the exposure phase, while it remains at or near zero degrees for the other two groups. During the post-exposure phase, when veridical feedback was restored, there was a main effect for group [F(2,42)=5.89, p < 0.01] and a main effect for time [F(1,42) = 5.85, p < 0.05]. Post-hoc analysis revealed the 60 N/m group had greater IDE than the 30 N/m group at the beginning of post-exposure [difference: 2.42° , CI: (0.41, 4.44), p < 0.05] and at the end of post-exposure [difference: 1.8° , CI: (0.21, 3.40), p < 0.05].

For EPX, there was a main effect for group during exposure [F(2,42) = 5.22, p < 0.05], but no other effects or interactions. Post-hoc analysis did not show a difference between groups at the beginning of exposure, but EPX was significantly larger in the 60 N/m group than in the 0 N/m group at the middle and end of exposure [60 N/m – 0 N/m difference at middle: 0.37 cm, CI: (0.008, 0.73), p < 0.05; at end: 0.52 cm, CI: (0.19, 0.84), p < 0.05]. Similar to IDE, EPX in the 60 N/m group increased throughout exposure but remained relatively constant in the 0- and 30 N/m groups. (Figure 2-2C). During post-exposure, there were no main effects or interactions. Taken together, the left hand performance was deviated from a straight-line path to the target by introducing a visual perturbation in the right hand. This interference was most pronounced in the group receiving the 60 N/m restoring force in both hands. Overall, interference remained relatively constant for the 0- and 30 N/m groups but increased throughout exposure for the 60 N/m group.



Figure 2-2: Experiment 1 left hand interference. Interference measures are shown for the exposure and post-exposure phases for each of the three groups in response to a clockwise rotation in cursor feedback in the right hand. IDE (A) and LFPV (B) were calculated at peak velocity, and EPX (C) and LFOFF (D) were calculated at movement offset in blocks of 10 trials. The dashed vertical lines denote the blocks time points used for computing the ANOVAs (see section 2.2).

2.3.1.2.2 Kinetics

By applying a spring force in two of the groups, there is a component of force directed toward the midline of movement. Since this force is different based on group assignment and could confound our kinematic measurements, we measured the lateral force applied to the handle at peak velocity (LFPV) and at the endpoint of movement (LFOFF) as an additional measure of interference. LFPV during exposure showed a main effect for group [F(2,42) = 14.12, p < 0.01]and a main effect for time [F(2,84) = 6.58, p < 0.01]. At the beginning and middle of exposure, the 60 N/m group had greater LFPV than the 0 N/m group [60 N/m-0 N/m difference at beginning 0.11 N, CI: (0.02, 0.2), p < 0.05; at middle: 0.21 N, CI: (0.08, 0.34), p < 0.01]. In the 30 N/m group there was a trend for greater LFPV compared to the 0 N/m group at the midpoint of exposure [difference: 0.129 N, CI: (0, 0.25), p = 0.051], and at the end of exposure both groups receiving a restoring force showed greater LFPV than the 0 N/m group [30 N/m - 0 N/m]difference: 0.148 N, CI: (0.03, 0.265), p < 0.05; 60 N/m – 0 N/m difference: 0.191 N, CI: (0.07, (0.31), p < 0.01). In the post-exposure phase, LFPV was different among groups [F(2,42) = 9.67, p < 0.01)], but there was no significant change over time (p = 0.4). Similar to the end of the exposure phase, the two groups moving against a virtual spring produced greater LFPV than the no spring group (Figure 2-2B).

For LFOFF, groups differed during exposure [F(2,42) = 38.41, p < 0.01), with both a main effect for time [F(2,84) = 3.66, p < 0.05] and Group x Time interaction [F(4,84) = 2.85, p < 0.05]. The 60 N/m group had greater LFOFF than the 0 N/m group at the beginning of exposure [difference: 0.214 N, CI: (0.074, 0.352), p < 0.01], and at the middle of exposure, the 60 N/m group produced greater LFOFF than the other two [60 N/m – 30 N/m difference: 0.297 N, CI: (0.148, 0.446), p < 0.01; 60 N/m – 0 N/m difference: 0.427 N, CI: (0.278, 0.576), p < 0.01].

Multiple comparisons at the end of exposure revealed significant differences for all comparisons, suggesting LFOFF systematically increased with an increase in the restoring force magnitude [30 N/m – 0 N/m difference: 0.136 N, CI: (0.017, 0.255), p < 0.05; 60 N/m – 30 N/m difference: 0.238 N, CI: (0.119, 0.357) p < 0.01; 60 N/m – 0 N/m difference: 0.374 N, CI: (0.255, 0.493), p < 0.01], as illustrated in Figure 2-2D. During post-exposure, there was a main effect for group [F(2,42) = 11.4, p < 0.01], a main effect for time [F(1,42) = 19.9, p < 0.01], and a Group x Time interaction [F(2,42) = 4.31, p < 0.05]. LFOFF decreased over the post-exposure phase in the 60-and 30 N/m groups (t = 3.52, p < 0.01 and t = 2.84, p < 0.05, respectively), but did not change in the 0 N/m group (p = 0.48).

Interference, measured by the lateral force applied to left manipulandum at peak velocity and movement offset, increased as the force demands for reaching also increased in a doseresponse fashion. Additionally, interference increased for the left hand as the right hand was producing more asymmetrical movements in response to adaptation to a visual rotation in hand feedback.

To further assess the influence of task kinetics on interference, we analyzed the movements using a force channel in approximately 20% of trials. This allowed us to analyze the development of interference within a target-directed movement, where movement onset is defined as 0% and movement offset is 100% of movement extent. Results from the 3 group x 3 time ANOVA showed a main effect for group [F(2,42) = 15.62, p < 0.01], but no time main effect or Group x Time interaction. Figure 2-3 illustrates that as the movement progresses toward endpoint, the lateral force increases monotonically for all groups, but the groups receiving the restoring force generate more lateral force. The lateral force exerted on the channel wall reinforces the finding in LFOFF that there may be a proportional increase in interference with an

increase in the force demands of movement. Multiple comparisons at 95% of movement extent reported the 60 N/m group exerted significantly more force than the 0 N/m and 30 N/m groups at all three time points throughout the exposure phase [60 N/m – 30 N/m difference: 1.2 N, CI: (0.49, 1.91), p < 0.01; 60 N/m – 0 N/m difference: 1.55 N, CI: (0.84, 2.26), p < 0.01]; the 30 N/m and 0 N/m groups did not differ from each other (p = 0.45). Here we show interference in the left hand appears to increase linearly with movement extent. This is consistent with the magnitude of the lateral component of restoring force in the 30- and 60 N/m groups. Near movement offset, interference increases as the force demands for movement increase, especially at the end of the exposure phase.



Figure 2-3: Experiment 1 lateral force against force channel. The force applied against the channel wall was resampled to 1000 samples and averaged (solid lines) across participants in each group. The cloud around the average represents the standard error of the mean. The dashed vertical lines indicate 95% of the movement extent where 0% represents movement onset and 100% represents movement offset. Force data are shown for the early (top), middle (center), and late (bottom) time points during exposure.

2.3.2 Experiment 2

We conducted a second experiment to determine the amount of interference due to neural crosstalk alone, without the addition of an adaptation component. To test this, we performed a nearly identical experiment with the only difference occurring during the exposure phase whereby the target locations for the right hand were rotated by 40° rather than rotating the visual feedback. Therefore, the ideal hand trajectory for both experiments was matched, but in this second experiment there was no need for participants to update their internal model.

2.3.2.1 Visually guided hand

In the visually guided right hand, there was no difference between groups in IDE (p = 0.20), but there was a main effect for time [F(1.16, 38.36) = 61.42, p < 0.01]. Since this experiment did not introduce a visual feedback perturbation, and participants moved to the rotated targets with veridical visual feedback, the main effect for time here likely reflects initial reaching error due to a shift in task procedures (i.e.: reaching to rotated targets). It is important to note that there was no difference between groups, a similar finding to experiment 1, supporting the notion that any group differences in interference measures in the left, kinesthetically guided hand were not due to differences in initial reaching direction in the visually guided hand.

2.3.2.2 Kinesthetically guided hand

2.3.2.2.1 Kinematics

Initial directional error (IDE), the angle between the movement vector and target vector, was not different between groups, nor did it change over the course of the exposure phase (all p > 0.05). Similarly, there were no differences during post-exposure (all p > 0.05). Lateral endpoint error (EPX), the cartesian distance between target location and hand location at movement offset in

the x-direction, showed a main effect for group [F(2,33) = 5.42, p < 0.01)]. Post-hoc analysis showed the 30 N/m group having greater EPX than the 0 N/m during the middle 10 trial block [difference: 0.477cm, CI: (0.06, 0.90), p < 0.05)] and last 10 trial block [difference: 0.607cm, CI: (0.21, 1.00), p < 0.01] of exposure. There were no other group differences during exposure, nor was there a main effect for time (p = 0.7). In post-exposure, there was a main effect for group [F(2,33) = 3.47, p < 0.05], but no main effect for time or Group x Time interaction.



Figure 2-4: Experiment 2 left hand interference. Interference measures are shown for the exposure and post-exposure phases for each of the three groups in response to a counterclockwise rotation in target location for the right hand. For description of axes and analysis see Figure 2-2 caption.

2.3.2.2.2 Kinetics

Lateral force at peak velocity (LFPV) remained constant over the course of exposure (p = 0.9), and there was no difference between groups (p = 0.08). Similar results were found in post-exposure (all p > 0.05). Lateral force at offset (LFOFF) also remained constant throughout the exposure phase (p = 0.7), but there was a main effect for group [F(2,33) = 14.73, p < 0.01]. Post-hoc analysis revealed the 60 N/m group had greater LFOFF than the 0 N/m group throughout exposure [beginning difference: 0.288N, CI: (0.09, 0.49), p < 0.01), middle difference: 0.258N, CI: (0.12, 0.43), p < 0.01, end difference: 0.273, CI: (0.11, 0.41), p < 0.01). There was a trend towards the 60 N/m group having greater LFOFF than the 30 N/m group at the end of exposure [difference: 0.146N, CI: (0.0,0.30), p = 0.065). During post-exposure, only a main effect for time was detected [F(1,33) = 5.44, p < 0.05].

Results from the ANOVA on the force channel data revealed no group difference in lateral force applied against the channel wall, nor was there a Group x Time interaction (all p > 0.1), but there was a main effect for time [F(1.25,41.14) = 7.02, p < 0.01)]. Post-hoc pairwise t-tests revealed a significant decrease in applied lateral force from the first block of 6 channel trials (mean = 1.26N) to the last block of force channel trials (mean = 0.42N) [p < 0.05, Bonferroni corrected].



Figure 2-5: Experiment 2 lateral force against force channel. See caption for Figure 2-3

2.3.3 Interexperimental comparisons

Although these were separate experiments, we wanted to quantify the performance difference using a common measure. Therefore, we compared the lateral force during force channel trials between experiments during the last block of 6 force channel trials. In the final block of exposure in experiment 1 participants experiencing the -40° visual feedback rotation were producing movements that most closely match those produced by participants in the second experiment reaching to 40° rotated targets. We also chose the force channel trials for this analysis because there is no confound in the relationship between position and force due to different spring constants between groups. Since the force channel constrains movement to a straight path to the target, the lateral forces applied by the spring force are negligible in all groups. Therefore, we performed a 3 group x 2 experiment ANOVA on the final 6 trial block at 95% of movement extent. Results showed a main effect for group [F(2,75) = 10.34, p < 0.01] and a Group x Experiment interaction [F(2,75) = 4.92, p < 0.05]. Post-hoc analysis showed that lateral force in the 60 N/m group in experiment 1 was significantly greater than the 60 N/m group in experiment 2 [difference 0.94N; p < 0.05]. This suggests that in our task, interference can be elicited by producing asymmetrical movements and is increased by adding an adaptation component.



Figure 2-6: Interexperiment interference comparison. Interexperiment comparison of force channel trials, assessed during the last 6 force channel trials of the exposure phase at 95% of movement extent. Bar color corresponds to the magnitude of the spring constant, applied to both hands, of a virtual spring directed towards the home position.

2.4 Discussion

In two experiments we showed that in a center-out reaching task where both hands are required to concurrently produce discrete asymmetrical movements, visible and perturbed (Experiment 1) or visible and directionally shifted (Experiment 2) hand movements interfered with the control of the other, non-visible, kinesthetically controlled hand in specific ways: (1) when the force demands for movement were increased, interference increased, and (2) when asymmetrical movements were elicited via adaptation in one hand, interference in the kinesthetically controlled contralateral hand was more pronounced. This was shown by a dose-response in interference due to increasing resistive forces and a sustained amount of interference when participants were exposed to a visuomotor perturbation to which they adapted over time.

In the first experiment, when participants were required to adapt to a 40° visual feedback rotation in the right hand, we observed an increase in interference as the force demands for reaching increased in a dose-response fashion (LFOFF). Additionally, over the course of adaptation, interference increased over time in both kinematic and kinetic measures. This result extends previous work (Kagerer, 2015, 2016a), which showed interference in the kinesthetically controlled left hand in both the feedforward and feedback components of movement, by showing interference can be increased by applying resistive forces. In our second experiment, interference quickly reached its maximum level within the first few trials and remained elevated for the duration of the exposure phase. However, when interference was measured using a force channel in the left hand, interference decreased over time.

Interference has been described as a process mediated by neural crosstalk allowing for the co-contraction of homologous muscles. For example, interference observed in asymmetric continuous tasks such as circling has been proposed to be a consequence of neural crosstalk

which acts to couple the actions of the two limbs (Heuer et al., 2001; Spijkers & Heuer, 2007). In discrete tasks, amplitude coupling may indicate that bimanual reaching is programmed not independently for each limb, but through a functional grouping of muscles acting as a single unit (Kelso et al., 1979). Interference observed in our experiments could represent the assimilation of spatial or dynamic information in the interfered-with left hand from the right hand. With respect to modulation of interference through force, previous studies have shown that interference increased with force demands during asymmetrical reaching (Walter & Swinnen, 1990), polyrhythm tasks (Kennedy et al., 2017), and isometric force production (Cunningham, 2017). A potential mechanism contributing to neural crosstalk is, e.g., modulations in inhibitory cortical circuitry. Interhemispheric inhibition from the more engaged to the less engaged hemisphere is inversely correlated with muscle activation, such that greater isometric force production releases inhibition in the less engaged hemisphere (Perez & Cohen, 2008). Therefore, it is possible that the interference observed in our experiment is the result of decreased inhibition of the hemisphere controlling the kinesthetically guided hand. The reduced inhibition may lead to increased muscle activity in the hand that is being interfered with in response to motor commands being conferred by the adapting hand/hemisphere system. Additionally, in our experiments, we see that when participants are required to adapt to a visuomotor perturbation in one hand in order to produce asymmetrical reaches, the interference is more pronounced and sustained compared to simply reaching to rotated targets. This observation is supported by our kinetic measures, such that LFOFF in the first experiment exhibits a dose-response to an increasing resistive force, but not in the second experiment. Also, the lateral force applied against the force channel in the left hand was sustained for participants in the first experiment, but that force decreased across exposure for participants in the second experiment. Therefore,

interference may reflect a communication of kinetic information across the hemispheres via neural crosstalk, but it can be enhanced by adding an adaptive component to the task.

We propose here that interference via neural crosstalk is bolstered by a shared internal model, where both controllers are accessing a sensorimotor map that is updated for the right, perturbed hand and is shared with the left, kinesthetically controlled hand. Previous research has shown that when two hands control a shared cursor, and one hand is perturbed by a force-field, both hands counter the perturbation. However, when each hand controls its own cursor, adaptation was only seen in the hand receiving the perturbation (Diedrichsen, 2007). Therefore, the control policy appears to be optimized for the task constraints. Our task differs from Diedrichsen's in two important ways: First, we use a visuomotor perturbation instead of a dynamic perturbation. Adaptation to dynamic perturbations shows limited interlimb transfer (Tcheang et al., 2007), and is thought to be represented in an intrinsic, joint-centered coordinate frame whereas adaptation to visuomotor perturbations are represented in extrinsic, head-centered coordinate frames (Krakauer et al., 1999). Second, participants in our experiments did not receive visual feedback about the left hand, and left hand trajectories did not influence control of the visible cursor. This effectively removes the task constraint that led to spatial coupling in Diedrichsen's experiment. Therefore, the deviated movements in our experiments are the result of motor information from one hand interfering with the control of the other.

It is plausible that interference during bimanual reaching is the behavioral consequence of sharing a common control policy communicated by neural populations between hemispheres. When participants are required to produce these asymmetrical movements via adaptation, neural populations that rely heavily on visual processing may have been more engaged compared to those in participants who reached to rotated targets. One possible explanation for the more robust

and sustained interference in the first experiment may be predicted by optimal control theory (see Scott, 2004 for review) such that neuronal activity in the primary motor cortex is modulated by behavioral context. It has been shown that distinct neuronal populations represent different hierarchical levels of sensory feedback processing during movement. Namely, there are populations that respond to the direction of movement, while other populations respond to which muscles are needed to produce a movement (Georgopoulos et al., 1986; Kakei et al., 1999). Therefore, if the motor system optimizes control at each level independently, the overall system will converge to an optimal solution (Herter et al., 2007). Further, this increased recruitment of neuronal populations is thought to result in upregulation of sensory feedback gain, leading to an increased reliance on sensory feedback. This, in turn, could then result in the more robust interference seen in our first experiment where there was a dose-response in interference as the force demands increased, a result not found in the second experiment. Franklin et al. showed similar multimodal sensory feedback upregulation in an experiment in which participants became more sensitive to shifts in cursor position as they adapted to a force-field perturbation (Franklin et al., 2012). According to optimal feedback control theory, producing movements in an unfamiliar environment down-regulates the importance of feedforward predictions of the sensory consequences of movement in favor of upregulating sensitivity to actual sensory feedback. Therefore, participants making reaches under visual feedback perturbation in our first experiment may be more sensitive to proprioceptive and tactile feedback resulting in an interference pattern in the left hand that coincides with the resistive spring constant.

It has been proposed that sensorimotor adaptation tasks like the one employed here may not be entirely driven by an implicit learning process, but that participants supplement with an explicit strategy (Mazzoni & Krakauer, 2006; Taylor et al., 2014). In our experiments, we did not

have a direct measure for determining the contribution of an explicit component in the adaptation. However, our second experiment is a strictly explicit task – participants are reaching to rotated targets under veridical feedback, with no adaptation required in the right hand. It is plausible to assume that interference in our tasks is due in part to competing explicit strategies, but when comparing to experiment 1, one can argue the sharing of an implicit internal model contributes to more robust interference in our task. A potential avenue for future study would be to systematically test the contributions of each process to the interference phenomenon. One challenge facing this prospect is the lack of empirical data regarding implicit vs. explicit contributions during bimanual tasks. We propose that interference in our experiments may reflect the contribution of both processes. Interference in our second experiment may result from a breakdown in participants' ability to execute two different explicit strategies. Participants were instructed to continue moving straight toward the targets with the nonvisible left hand while performing reaches to a different set of targets in the visible right hand. In this context, one could argue that participants were required to engage in two different explicit tasks. The breakdown in coordination may result from neural crosstalk communicating the spatial and dynamic information of the explicit strategy in the right hand to the left hand. If one adopted this reasoning, it could be argued that in the first experiment, the addition of a more implicit component enhanced the interference through a sensorimotor representation update in the right hand and shared with the left hand.

This study is one of few to have looked at the influence on adaptation on interference, and to the best of our knowledge, one of only a handful studies to show that adaptation upregulates gain for sensory information not present in the perturbation (see Franklin et al., 2012; Franklin, Wolpert, & Franklin, 2017). This informs our understanding of adaptation from the

optimal feedback control theory perspective to suggest that sensorimotor integration, comparing expected and actual sensory feedback, may have cross-modal interactions. We also found that interference in discrete movement tasks induced by imposing spatial constraints is enhanced by motor adaptation in one hand. This work contributes to our understanding of the complex coordinative actions that resembling naturalistic movement and suggests adaptation increases the communication between hemispheres. Further research investigating the factors influencing the transfer of motor information from one hemisphere/hand to the other should consider the adaptive process as an important factor in task development.

CHAPTER 3 - STRUCTURAL LEARNING GENERALIZES TO A CONTRALATERAL EFFECTOR

3.1 Introduction

The ability for humans to adapt to seemingly random environments belies the fact that there often exists some underlying structure to the relationship between sensory input and motor output. The neuromotor system can extract invariant properties of the environment and apply the necessary actions in order to produce highly reliable movements in the face of this uncertainty. The ability to sip coffee from a mug while seated in your kitchen requires countering the acceleration due to gravity – a compensation many of us find trivial. However, accomplishing this feat on a moving subway train that is jostling side-to-side may be a challenge for the novice rider. Through years of practice, we have adapted to our environment by generating some internal knowledge of the relationship between our movements and the corresponding sensory information we should expect in such an environment. That is, we have developed an internal model used to predict the sensory consequences of movement, and we generate an optimized output to counter the perturbation (Todorov & Jordan, 2002). Motor control researchers investigate the updating of this internal model by manipulating feedback participants receive about the environment and measure the change in motor behavior. Typically, motor adaptation is investigated using abrupt perturbations to sensory feedback such as rotations in visual feedback (Krakauer, Pine, Ghilardi, & Ghez, 2000) or velocity dependent force fields (Diedrichsen, 2007; Shadmehr & Mussa-Ivaldi, 1994) and improvement in performance is measured over time. In these tasks, the perturbation is fixed – that is, the magnitude and direction does not change trial to trial. The motor control system 'solves' for the perturbation by countering its specific effects,

and in control systems literature, this is known as *parametric* system identification (Tutunji, 2016). If we now extend our coffee example to sipping on a subway car jostling along the track, we can consider how the neuromotor system confronts a more complex environment. There are accelerations that vary in magnitude and direction, such that solving for one parameter leads to an underdefined solution. In order to counter the jostling of the train, the set of corrective actions one could take would span three-dimensional space. However, in our example, let us say the perturbations can only occur side-to-side, or forward and backward with any magnitude. That is, there is structure to the perturbations. This structure would constrain the possible solutions to a lower dimensional space existing on the transverse plane. It is important to note that the perturbations are still random, in both magnitude and direction, but the rider is capable of learning the underlying structure to the perturbations. Braun and colleagues refer to this learning-to-learn phenomenon as structural learning (Braun et al., 2009a).

According to Braun et al., structural learning confers three advantages that lead to facilitated adaptation. First, when learning to counter a fixed perturbation, adaptation will occur faster if this perturbation lies within the previously learned structure, termed structure-specific facilitation. Second, it has been shown that consolidation of motor memories is interfered with when participants are instructed to learn two consecutive tasks with competing control strategies – i.e. learning a 30° visuomotor rotation followed immediately by a -30° rotation (Krakauer, 2005). Since both rotations lie within the same structure, structure-specific interference reduction protects against both retrograde- and anterograde interference in motor memory consolidation. Finally, when switching to a new task that belongs to the same structure, for example training on perturbations oriented in the sagittal plane followed by testing on perturbations in the transverse plane, participants favor initial reaches in the sagittal plane, termed structure-specific

exploration. This final benefit suggests that structural training should generalize to broader contexts as long as the new task lies within the previously learned structure.

A remarkable feature of our motor system is the ability to apply motor skills to new contexts, even if we have not encountered them before. A right-handed person would surely write her name with a notepad located on the right side, but she could just as easily write her name with the paper on her left. This ability to perform a motor task to another workspace location is known as generalization. Generalization has been shown in complex adaptation tasks, where participants learned to overcome novel task dynamics with one limb in an ipsilateral workspace and showed this learning transferred to the contralateral workspace with the same limb (Shadmehr & Mussa-Ivaldi, 1994). Generalization literature has primarily focused on the extent to which motor adaptation in one limb transfers to a contralateral limb. Interlimb transfer has been shown for visuomotor perturbations (Sainburg & Wang, 2002; Wang & Lei, 2015), dynamic perturbations (Joiner et al., 2013), and complex sequence learning tasks (Laszlo et al., 1970; Panzer et al., 2018). During such tasks, participants learn to counter novel perturbations or new complex movements in one limb and are subsequently tested using the other limb. To test interlimb savings, the contralateral limb is exposed to the same perturbation adapted to in the training limb (Stockinger et al., 2015), whereas interlimb transfer of after-effects can be assayed by training one limb to counter a perturbation and subsequently testing the contralateral limb on a null-field (Wang & Lei, 2015). However, it has not yet been shown whether and to what extent structural learning can generalize to a contralateral effector. One potential issue is in determining what constitutes transfer or what constitutes savings in such a task. Participants engaging in structural training are not exposed to the fixed perturbation experienced during the testing phase (savings), nor will they learn to introduce movement bias due to the mean distribution of

perturbations being zero (transfer) (see Supplement of Braun et al., 2009). However, structural learning should generalize to a contralateral effector because participants will engage in structure-specific exploration of a previously learned structure in the other limb. Therefore, the purpose of this study is to determine what, if any control characteristics of structural learning generalizes to a contralateral effector. We exposed participants to random visuomotor perturbations in one hand, followed by a testing session with a fixed rotation in hand feedback in the other hand. If structural learning generalizes to a contralateral effector, through structurespecific exploration, participants would show facilitated adaptation to a fixed perturbation lying in the same structure compared to participants who trained under veridical feedback alone.

3.2 Methods

3.2.1 Participants

Twenty six, right handed individuals (age: 20.5 +/- 1 years, 21 female) participated in our experiment; each scored at least +70 of the Edinburgh Handedness Inventory – Short Form (Oldfield, 1971; Veale, 2013). Each participant gave informed consent, and the study procedures were approved by the Michigan State University Institutional Review Board.

3.2.2 Procedures

Following the assessment of handedness, participants were seated at a bimanual Kinarm endpoint lab (BKIN Technologies, Kingston, ON). They interacted with one of two manipulanda at a time that controlled a virtual cursor projected on a screen occluding vision of the hands. The task consisted of a training session in the right hand, immediately followed by a testing session in the left hand. During the training session, participants were instructed to move a virtual cursor representing the location of the hand from a home position to a target position located 10cm either straight ahead (90°) or straight backwards (270°) from the home position. Participants were

instructed to move as straight, fast, and accurately as possible to the target position, wait in the target until the home position reappeared, and move back to the home position. Data were recorded only for the center-out reach. Following a baseline period of 16 trials with veridical visual feedback, participants either continued with veridical feedback (control group) or experienced pseudorandom rotations in visual feedback (structure group) for 240 trials. The perturbation schedule was derived from Braun et al. (Braun et al., 2009a), such that participants were exposed to the same rotation for 4 consecutive trials (2 to 90° target, 2 to 270° target), but then experienced a new randomly generated rotation for the next block of 4 trials resulting in 60 unique rotations per participant. Rotation amounts ranged from $+/-90^{\circ}$ and excluded a $+/-10^{\circ}$ range around both $+60^{\circ}$ and -60° . The training session ended with a washout period of 16 trials of veridical feedback for both groups. The reason for excluding rotation amounts around $\pm -60^{\circ}$ was that following the training session in the right hand, participants performed a testing session in the left hand. Following 16 trials of veridical feedback, both groups adapted to a fixed rotation of 60° in cursor feedback. Finally, veridical feedback was restored for another 16 trials to measure the aftereffects of adaptation.

In the study by Braun et al., participants reached to 8 radially arranged targets, with a new randomly generated rotation amount applied once for each target (Braun et al., 2009a). In our experiment, we had participants make only 4 consecutive reaches under the same rotation amount; since this could have limited the participants' ability to learn the structure of the perturbations, we performed an additional study ('replication study') with 10 participants (5 control, 5 structure) who performed both the training and testing sessions in the right hand only. This way, we verified that the changes we made to our perturbation schedule did not prevent acquisition of the structure.

3.2.3 Data Analysis

Our primary outcome measure for the adaptation of feedforward processes was initial directional error (IDE), defined as the angle between a vector pointing from the home to target positions and a second vector pointing from the home position and the location of the hand at peak velocity. For measures of adaptation involving both feedforward and feedback processes, we also calculated root mean square error (RMSE) as the square root of the sum of squares of the lateral distance between the hand position and a line between the target and home positions, normalized to movement length. In addition, we calculated movement time (MT), movement length (ML), and normalized jerk (nJ) (see (Teulings et al., 1997) for calculation).

Each outcome measure was normalized by subtracting each participant's mean value during baseline from all trials, and data were reduced by binning into 4 trials blocks. Unpaired ttests were performed during the washout period in the right hand to verify the perturbation schedule experienced by the structure group did not introduce movement bias that may be transferred to the training session. In the training session, we performed a 2 (group) x 2 (time) mixed design ANOVA for each measure where time refers to the first and last 4 trial block during exposure to the fixed perturbation in the left hand. Significant Group x Time interactions were further analyzed by performing unpaired t-tests at both the first and last 4-trials blocks of exposure with Bonferroni correction. Heteroscedasticity was controlled for using Welch two sample t-tests where necessary. Statistical analyses were performed in R (R-project) using the afex statistical package.

3.3 Results

3.3.1 Replication Study

Similar to the findings of Braun et al. (Braun et al., 2009a), participants in the structural training group in our replication study showed facilitated adaptation compared to controls. This result was seen both in feedforward (IDE: Figure 3-1, left panel) and feedback processes (RMSE: Figure 3-1, right panel). Interestingly, the difference between groups in IDE did not emerge until the second 4 trial block of the exposure phase. This may be due to the smaller block size (4 trials) used for data reduction in our experiment compared to 8 trial blocks used by Braun et al.. Since the fixed perturbation was abruptly applied, participants likely reached straight towards the targets in accordance with their established internal model, but after only 4 trials, the structure group quickly searched the previously learned structure for an appropriate response. These results confirm that the changes we made to the perturbation schedule experienced by the structure group in training allowed for structural learning in both feedforward and feedback measures. The remainder of the Results section will focus on the outcome of our main experiment to determine if structural training can generalize to a contralateral effector.

3.3.2 Training

We performed an unpaired Welch two sample t-test comparing IDE in the right hand between groups during the post-training period to ensure no bias was introduced in the structure group. Results show there was no difference in IDE between groups (p = 0.27) indicating that, although participants in the structure group are learning the underlying structure of visuomotor rotations, there is no systematic bias in the feedforward component of reaching.



Figure 3-1: Replication study adaptation. Initial directional error (IDE), left panel, and root mean squared error (RMSE), right panel, for the testing session in the right hand. Following training to either veridical reaching (control) or random rotations in hand feedback (structure), participants were exposed to a fixed 60° rotation in hand feedback. Facilitated adaptation was seen in both feedforward (IDE) and feedback processes (RMSE) when testing was performed in the same hand that trained, replicating the findings of (Bond & Taylor, 2017; Braun et al., 2009b).

3.3.3 Testing

Following training in the right hand, participants in both groups were instructed to adapt to a fixed 60° rotation in visual feedback in the left hand. For IDE, while there was no main effect for group (p = 0.38), there was a main effect for time [F(1,24) = 146.5, p < 0.0001] and a Group x Time interaction [F(1,24) = 5.38, p = 0.03]. Post-hoc analysis revealed that participants in the structure group adapted faster to the initial exposure [first exposure block: t(23.1) = 2.52, p = 0.038)] but that both groups attained the same level of overall adaptation near the end of exposure (p > 0.05 at last exposure block). This suggests that participants in both groups significantly reduced their initial reaching error over the course of the exposure phase. And while participants in both groups attained the same level of adaptation by the end of the exposure phase, participants in the structure group adapted their feedforward processes faster. These results are shown in Figure 3-2.



Figure 3-2: Transfer study adaptation: IDE (left panel) and RMSE (right panel) in the left hand testing session following right hand training to either veridical reaching (control) or random rotations in hand feedback (structure). Facilitated adaptation transferred to the non-dominant hand, suggesting structural training generalizes to a contralateral effector.

For RMSE, our measure for the linearity of movement which contains both feedforward and feedback processes, there was a trend for the main effect for group [F(1,24) = 3.64, p = 0.07] and a main effect for time [F(1,24) = 304.4, p < 0.0001]. We also found a significant Group x Time interaction [F(1,24) = 9.74, p < 0.01]. Post-hoc analysis showed that during the first 4 trials of exposure, participants in the structure group moved straighter than those in the control group [t(17.7) = 3.05, p < 0.05], but there was no significant difference at the end of exposure (p > 0.05). These results indicate that both groups are producing straighter movements as exposure to the perturbation persists, but that participants in the structure group reach straighter initially, but the two groups attain the same level of movement straightness by the end of exposure. Figure 3-2 illustrates these findings, and differences between the groups is limited to the first 4 reaches during the exposure phase. Finally, we show clear aftereffects in both IDE and RMSE, but two-sample t-tests at the first block of post-exposure shows no difference between groups (both p > 0.05). This suggests that both groups have achieved the same level of adaptation by the end of the exposure phase.

To further assess how participants adapted both the feedforward and feedback components of movement, we assessed MT, ML, and nJ. In all three outcome measures, we found significant main effects for group and time, as well as significant Group x Time interactions. We also found that for each variable, post-hoc analysis reported a significant difference between the two groups during the first block of exposure, but that both groups performed similarly at the last block of exposure. Additionally, in each of these measures, two sample t-tests at the first block of post-exposure show no difference between groups, further supporting the notion that both groups reached the same level of adaptation (all p > 0.05). The inferential statistics are summarized in Table 3-1 and results are illustrated in Figure 3-3. Taken
together, our results suggest that participants in the structure group are moving faster, shorter, and smoother than those in the control group at the beginning, but not at the end of the exposure phase.



Figure 3-3: Transfer study transfer of feedback measures: Movement time (MT), change in movement length (ML) and normalized jerk score (nJ) for the left hand in response to a 60° rotation in hand feedback. Participants who previously trained in the right hand to random rotations moved faster, shorter, and smoother than those who trained with veridical visual feedback. Facilitated adaptation generalized to the contralateral effector, especially in these feedback measures.

Line	Dependent	Test	Test Statistic	Confidence
	Variable			
а	Movement	Mixed method ANOVA	Group: F(1,24) = 8.66	Group: p < 0.01
	Time (MT)		Time: $F(1,24) = 76.9$	Time: p < 0.0001
			interaction: $F(1,24) = 22.1$	interaction: p < 0.0001
b	Movement	Mixed method ANOVA	Group: F(1,24) = 14.4	Group: p < 0.001
	Length (ML)		Time: $F(1,24) = 216.7$	Time: p < 0.0001
			interaction: $F(1,24) = 25.4$	interaction: p < 0.0001
с	Normalized	Mixed method ANOVA	Group: F(1,24) = 8.4	Group: p < 0.01
	Jerk Score (nJ)		Time: $F(1,24) = 31.1$	Time: p < 0.0001
			interaction: F(1,24) =12.53	interaction: p < 0.0001
d	Movement	Welch Two-Sample	Early: $t(18.3) = 4.05$	Early: p* < 0.01
	Time (MT)		Late: $t(21.5) = 0.51$	Late: $p^* = 0.62$
e	Movement	Welch Two-Sample	Early: $t(23.7) = 4.59$	Early: p* < 0.001
	Length (ML)		Late: $t(23.6) = 0.34$	Late: $p^* = 0.73$
f	Normalized	Welch Two-Sample	Early: $t(13.3) = 3.28$	Early: p* < 0.05
	Jerk Score (nJ)	-	Late: $t(20.9) = 0.84$	Late: $p^* = 0.41$

Table 3-1: Inferential statistics of feedback measures. Summary of inferential statistics for movement time, movement length, and normalized jerk score. Mixed-method ANOVAs (lines a-c) were conducted with between-subjects factor group (control/structure) and within-subjects factor time (first 4 and last 4 trials of exposure). For post-hoc analyses, two Welch Two-sample t-tests (lines d-f) were conducted for each outcome variable, one for the first 4 trials and one for the last 4 trials during the exposure phase. * indicates the Bonferroni adjusted p-values for each test.

3.4 Discussion

Structural learning is described as a 'learning-to-learn' phenomenon that allows us to extract invariant features from our environment to aid learning on related tasks. This feature has been explored at length in cognitive tasks (Griffiths & Tenenbaum, 2005). In motor tasks, structural learning has been shown to provide three structure-specific benefits to the learner: (1) facilitation on similar tasks, (2) interference reduction when exposed to conditions requiring opposite control strategies, and (3) exploration of a previously learned structure when confronted with a new task (Braun et al., 2009a). The purpose of this study was to determine if structural learning in one effector leads to facilitated adaptation in the contralateral effector. We show that, when participants trained to counter random rotations in visual feedback in the right hand (which, of course, could not be learned due to the randomness of the rotations), adaptation to a fixed rotation in the left hand was faster compared to participants who trained with veridical feedback alone. Reminiscent of early work in variable practice and motor schema formation (Schmidt, 1975; Wulf & Schmidt, 1988), Braun et al. were among the first to apply structural learning to visuomotor perturbation tasks, where they devised a series of three experiments, each showing one of the three benefits described above. Importantly, they describe learning from a Bayesian perspective such that the learner establishes a probability distribution that best describes the relationship between their prediction of the sensory consequences of movement with the actual feedback received during training (Braun et al., 2009, in Supplement). Therefore, in parametric learning, the prior probabilities update this mapping until a solution in achieved that minimizes the error between prediction and reality. That is, there must exist one point in parameter space that represents the solution to a given control problem, and in order to learn such a solution, one must map all causal dependencies in the input-output response of the system. However, in

structural learning, not all cause and effect relationships must be learned. Instead, one can learn an intermediary 'meta-parameter' that constrains the parameter space to a lower dimensionality. In the current experiment, this meta-parameter would represent the internal variables specific to rotations. Therefore, when exposed to a perturbation consisting of a fixed rotation in hand feedback, the participants who previously trained on a series of random rotations, will explore preferentially along this reduced dimensionality space. What we have shown here is that this constrained space is accessible to the contralateral effector. Moreover, the facilitated adaptation occurred in both the feedforward (IDE) and feedback (RMSE, MT, ML, nJ) components, hallmarks of an adaptive controller.

Adaptive control is most widely described for human motor control in the context of optimal feedback control theory (OFCT). Optimal control is achieved by the motor system by adjusting feedback gain in order to minimize the costs associated with the task specific goals and costs associated with muscle activation (Diedrichsen et al., 2010). One requirement for this process to be effective in the presence of delayed feedback and signal dependent noise is for the motor system to integrate actual sensory feedback with the predicted sensory consequences of movement. This sensory integration is then used to make a more accurate evaluation of the state of the effector which is then used to for optimal control (Todorov, 2004; Todorov & Jordan, 2002). Computational models of the OFCT employ a Kalman filter at this sensory integration step which modulates a parameter K in response to how much importance we place on our predictions or the actual sensory feedback (Shadmehr & Krakauer, 2008). When our belief in the predicted sensory consequences of movement is high K becomes large and we place more importance on feedforward control. Conversely, when our prediction is considered corrupted by noise, or in the case of adaptation experiments, perturbed by manipulations to sensory feedback,

K is reduced so that we place more importance on the feedback processes to assess the status of the effector (Schwartz, 2016). It has been proposed that this Kalman filter operates as a Bayesian estimator in which control is implemented on the basis of prior experience and predictions about the future (Vaziri et al., 2006). Therefore, in structural learning, the prior experience of being exposed to random rotations will make predictions about the optimal aiming direction ineffective in countering the perturbation. However, since there is structure to the perturbations, that is they always come in the form of rotations and not some other perturbation like gain manipulation, the prior experience allows one to make predictions about the form of feedback responses necessary to counter the perturbation. This would suggest that the motor system can adapt to such perturbations and it is possible the adaptation processes conforms to OFCT. In fact, Braun and colleagues found that exposure to random perturbations can be modelled by a simple optimal controller such that the observed mismatch between actual and predicted sensory information can be used for both adaptation of the state of the effector and the parameter estimation to drive optimal control (Braun et al., 2009b). Additionally, it has been shown that both the feedforward and feedback components of control are adapted during structural learning and that these processes are controlled independently (Yousif & Diedrichsen, 2012). In our current experiment, we replicate these findings to show that adaptation to both feedforward and feedback processes are facilitated by structural learning and extend previous work by shown both processes transfer to a contralateral effector. However, we show that transfer primarily occurs in the feedback processes, illustrated by Figures 3-2, 3-3 whereby group differences in IDE appear much smaller than in other measures. This may be due to the unpredictability of movements, thereby reducing the emphasis on feedforward predictions, or it may be a consequence of our transfer task only testing the non-dominant to dominant direction.

It has been shown that in transfer tasks, there is an asymmetry of transfer when training occurs first the in dominant hand and testing then occurs in the non-dominant hand, and viceversa. Since our experiment first trained the dominant hand, followed by testing in the nondominant hand, different control parameters may have selectively transferred. It has been shown that transfer from the non-dominant to dominant hand in both visuomotor (Wang & Sainburg, 2004) and curl-field adaptation (Criscimagna-Hemminger et al., 2003) is limited compared to transfer in the other direction. For this reason, we chose to limit our experiment to investigate the non-dominant to dominant direction. One avenue for future study would be to test transfer in the non-dominant to dominant direction to test the hypothesis that each arm has access to specialized motor information based on its propensity for either feedforward (dominant arm) or feedback (non-dominant arm) information in accordance with the dynamic dominance hypothesis (Sainburg & Kalakanis, 2000). Sainburg and Wang show that opposite arm training during visuomotor transfer improves the initial direction of subsequent testing of the dominant arm, while opposite arm training improves final endpoint accuracy during subsequent testing of the non-dominant arm (Sainburg & Wang, 2002). Our results support the latter finding, whereby outcome measures relying heavily on feedback processes (MT, ML, nJ) show greater transfer than initial directional error (IDE). Interestingly, it has recently been shown that during an interference task like the one used here, the right adapting hand imposed its control strength trajectory control – onto the left kinesthetically controlled hand (Kagerer, 2014). Perhaps interference in our experiment is the result of both prior training transferring positional control and concurrent coordination imposing trajectory control onto the left hand. One other possibility is that the unpredictability of the training schedule led participants in the structure group to upregulate their sensitivity to feedback information. Then on subsequent testing in the

contralateral limb, they applied this optimal control strategy which led to the greatest improvements being observed in these feedback measures. Finally, we show that the facilitated transfer in the structure group is ephemeral. By approximately the 9th block (within first 20 trials of exposure to fixed perturbation), the two groups appear to converge to the same adaptation level. It has also been shown that the amount of transfer observed does not depend on the length or onset (gradual vs. abrupt) of the training period, but that extended training periods result in more sustained transfer (Joiner et al., 2013). This would suggest that longer training periods could extend the duration of the facilitated adaptation, but previous results within the same limb also show this ephemeral nature (Bond & Taylor, 2017; Braun et al., 2009a).

There exists a potential limitation in escribing facilitated adaptation to structure learning rather than the variable practice of parametric learning. In the current study, and similarly those previously exploring structural learning, the perturbation schedule allows for small bouts of parametric learning. During the training session in the current study, participants were allowed to adapt to the same perturbation for 4 consecutive trials. That is, they engaged in 60 bouts of adaptation to a fixed perturbation. Previous work on purely random force-field perturbations has shown that participants are capable of adapting to the mean direction and magnitude of the perturbation ensemble (Takahashi et al., 2001). Interestingly, they showed that compared to participants adapting to a fixed perturbation with the same value as the mean during random training, aftereffects were 42% smaller during null-field trials for those learning random rotation. Therefore, one may consider the null-field condition representing a unique solution on the belonging to the previously learned structure. Systematically investigating the role of perturbation 'block' width remains an open avenue for further study.

Structural learning is described as a 'learning-to-learn' phenomenon such that invariant properties of seemingly random relationships lead to faster learning, protection against conflicting tasks, and generalization to related tasks. Here we show that structural learning facilitates adaptation to a fixed rotation in hand feedback for the contralateral hand. Generalization to the contralateral hand was seen in both feedforward and feedback processes, but the largest effects were seen in feedback processes. This may be due to the unpredictability of motor training, leading to an upregulation in sensory feedback gains, or may reflect independence of feedforward and feedback processes in transfer tasks. Further research should investigate these avenues to better inform the processes of structural learning and motor transfer.

CHAPTER 4 - STRUCTURAL LEARNING INCREASES BIMANUAL INTERFERENCE

4.1 Introduction

The ability to coordinate the hands during bimanual reaching is a critical component of many activities of daily living. Often, the two hands are required to operate in unison, such as removing a hot pan from the oven, but other times the hands must produce coupled, yet independent actions, such as hammering a nail. However, there are circumstances where the independent control of effectors is limited by task difficulty. This can manifest behaviorally as an assimilation of movement characteristics of one effector by volitional control of the other. This motor interference is a natural feature of the motor control system. Mirrored interference, or mirrored movements, are common in children, but are considered pathologic if they persist beyond 10 years of age (Cox et al., 2012). Motor interference has also been shown in healthy adults, and is thought to involve the communication of motor information between the hemispheres via the corpus callosum (Franz et al., 1996). Swinnen suggests that interference is the result of spatiotemporal task constraints that, when a task becomes sufficiently difficult or asymmetric, produce new coordination patterns resembling interference (Swinnen, 2002). For example, when participants try to draw a circle with one hand while simultaneously drawing a line with the other, they produce shapes resembling a mixture of the two (Franz, 1997). In addition to directional interference, amplitude coupling is observed when participants attempt to produce center-out movements of different length (Sherwood, 1991). Moreover, when reaching to two targets with different spatial characteristics, people tend to match the velocity and acceleration profiles of each hand (Kelso et al., 1979). Taken together, it is understood that fully

independent control of the limbs depends on task constraints, and certain tasks can elicit motor interference.

One potential mechanism for motor interference is neural crosstalk. This is often described as activation of a resting limb by projections that originate in the ipsilateral hemisphere which controls an actively engaged limb, or by interhemispheric projections from the contralateral hemisphere (Li et al., 2007). Neural crosstalk is typically measured using transcranial magnetic stimulation (TMS) and electromyography (EMG) in tasks involving isometric contractions of the hands. Participants are instructed to produce increasing amounts of force in one hand while the other hand rests quietly at their side. Both increases in muscle activity in the resting limb and changes to cortical excitability have been observed in these tasks (Cunningham, 2017; Perez & Cohen, 2008). TMS data show that with increasing voluntary contraction in one hand, there is a systematic release of both interhemispheric inhibition from the active-to-resting motor cortex and intrahemispheric inhibition in the resting motor cortex (Perez & Cohen, 2008, 2009). This dose-response in changes to motor cortex excitability follows with behavioral tasks showing a dose-response in interference when the force demands for reaching increase (Walter & Swinnen, 1990; Brunfeldt, et al., in review). Therefore, it is possible that interference in discrete reaching tasks is mediated by a release of interhemispheric inhibition and a systematic increase in cortical excitability observed in isometric force tasks. In addition to showing a dose-response in interference with the force demands for movement, Brunfeldt et al. show that when asymmetrical movements are induced by one hand having to adapt to a visuomotor perturbation, the interference is more robust (Brunfeldt, et al., in review). Their interpretation is that the adaptation process enhances interference by the sharing of an updated

internal model generated by the adapting hand to bolster the underlying interhemispheric communication via neural crosstalk.

The concept of an internal model comes from optimal feedback control theory (OFCT), and has been suggested as an explanation of interference in bimanual reaching tasks (Kagerer, 2015, 2016a). Briefly, this theory posits that in order to control movements with delayed and noisy feedback, the motor system must generate (via an internal model) a prediction about the sensory consequences of movement. This prediction is integrated with the actual sensory feedback in order to more accurately define that state of the effector and feedback gains are regulated to form an optimal control law governing movement (Todorov, 2004; Todorov & Jordan, 2002). Interference, when viewed as an assimilation of movement characteristics, then may be described as a coordination pattern that attempts to minimize the control effort associated with bimanual movements. In fact, Diedrichsen has shown that when controlling a shared cursor, where one hand must adapt to a force perturbation, the optimal control strategy is one where both hands counter the perturbation. However, when each hand controls its own cursor, only the hand receiving the perturbation corrects for it. (Diedrichsen, 2007). In the shared cursor scenario, it may be that participants are cued to share the updated internal model by sharing the cursor, resulting in motor interference. From the OFCT perspective, adaptation drives the motor system to up- or down-regulate its sensitivity to actual sensory feedback based on the veracity of the predicted sensory consequences of movement (Franklin et al., 2012), and if this representation is shared among effectors, interference may be affected by manipulating the adaptation process. Moreover, interference is dose-dependent on the force demands for reaching and adaptation serves to bolster this response by making participants more sensitive to proprioceptive feedback (Brunfeldt et al., in review). Therefore, the purpose of this study is to determine if manipulating

the way in which participants adapt to a visuomotor perturbation influences interference during a bimanual reaching task. To do this, we designed a task that would manipulate the rate at which participants adapted to a visuomotor perturbation in one hand, while the other hand operated under kinesthetic control. One way to manipulate adaptation is to gradually introduce the perturbation (Kagerer et al., 1997; Turnham et al., 2012). However, this would result in the difference between the predicted and actual sensory feedback (error signal) remaining small throughout adaptation, giving high veracity to the predicted sensory feedback. Alternatively, having participants learn random rotations should deemphasize this prediction in favor of feedback information, which may lead to greater interference via an upregulation in feedback gain. Fortunately, learning random rotations leads to facilitated adaptation through a processes called structural learning (Bond & Taylor, 2017; Braun et al., 2009b, 2009a).

Structural learning is described as a 'learning-to-learn' phenomenon where invariant features of the environment are extracted to facilitate learning and adaptation (Griffiths & Tenenbaum, 2005). Structural learning has its origins in the variability of practice literature, and is similar to both Schmidt's motor schema theory (Schmidt, 1975) and contextual interference (see Magill & Hall, 1990 for review). In the context of visuomotor learning, participants who train to counter random rotations in visual feedback cannot learn a fixed solution to this control problem, but rather they learn how to counter rotations 'in general'. Structural training therefore provides three benefits to the learner: (1) they will learn any perturbation belonging to a previously learned structure faster than a novice learner, (2) they will be less susceptible to perturbations that require opposite control strategies, and (3) they will learn new tasks faster, if those belong to the previously learned structure (Braun et al., 2009a). Importantly, structural learning affects both the feedforward and feedback learning processes independently (Yousif &

Diedrichsen, 2012), and feedback processes are more affected due to the unpredictability of the training schedule (Brunfeldt et al. (b), *in prep*). Therefore, if participants first engage in structural training to upregulate their sensitivity to primarily feedback processes, and are then exposed to an interference task which requires them to produce asymmetrical movements via adaptation in one hand, we hypothesize interference will be greater in structural learners compared to those not previously exposed to random rotations in hand feedback.

4.2 Methods

4.2.1 Participants

A total of 31 people volunteered to participate in our study. Following removal of one participant for a failure to comply with task instructions, thirty young adults (age: 19.1 +/- 0.5 years, 21 female) completed all testing procedures. Each participant scored at least +70 on the Edinburgh Handedness Inventory – Short Form (Oldfield, 1971; Veale, 2013) to verify only strongly right handed volunteers participated in our experiment. Study procedures were approved by the Michigan State University Institutional Review Board prior to participant recruitment, and participants consented to the following procedures.

4.2.2 Procedures

Participants were comfortably seated at a bimanual Kinarm endpoint robot (Kinarm, BKIN Technologies, Kingston ON). They completed two center-out reaching tasks, first with the right hand, and immediately followed by a bimanual task. In both tasks, vision of the hands was occluded by a mirror on which visual feedback of the hands was projected with a single cursor in the unimanual task and two cursors in the bimanual task. In the unimanual training task, participants were instructed to move the cursor with their right hand from a home position located in the right workspace to a target located 10cm either straight forward (90°) or straight

backward (270°). They were verbally instructed to move as straight, fast, and accurately as possible to the peripheral target. Following a baseline of 16 trials with veridical feedback, participants in the control group (n = 15) continued to reach with veridical visual feedback for 240 trials, but participants in the structure group (n = 15) were exposed to a random visuomotor rotations. The perturbation schedule was derived from Braun et al. (Braun et al., 2009a), whereby every 4 trials a newly generated random rotation was applied for 4 consecutive trials, for a total of 60 unique rotations throughout this exposure phase. The set of possible rotations ranged from -/+ 90° and excluded a +/- 10° range centered around both +40° and -40°. Both groups then completed 16 trials with veridical feedback.

Immediately following the training task, participants in both groups completed the same bimanual interference task to assess the sharing of motor information across hemispheres (Kagerer, 2015, 2016a). Participants were instructed to reach simultaneously with both hands as straight, fast, and accurately as possible from two home positions to two target positions located 10cm straight ahead (90°) or straight backward (270°) from their respective home positions. After 20 visual baseline trials with veridical feedback for both hands, vision of the left hand was removed, and participants were instructed to continue reaching with both hands for 20 more kinesthetic baseline trials. Since they did not receive visual feedback for the left hand, participants were instructed to stop moving when they estimated to be in the target location. The exposure phase consisted on 140 trials where an abrupt 40° rotation in visual feedback was introduced in the right hand, requiring participants to compensate in the counterclockwise direction. Visual feedback for the left hand remained off during the exposure phase, making that hand more susceptible to interference from the adapting right hand. Participants were told to continue moving straight with the left hand toward its respective target. The post-exposure

phase, of 40 trials under veridical feedback, was used to assess aftereffects of the adaptation.

Figure 4-1 shows a schematic of the experimental design.



Figure 4-1: Experimental procedures flowchart: The experiment consisted of two tasks. First in the training task, with only the right hand, participants trained either with veridical (control) or random rotations in visual feedback (structure). Next, they completed the interference task using both hands were both groups were exposed to a fixed 40° rotation in hand feedback in the right hand, while the left hand did not receive visual feedback making it susceptible to interference from the right.

Recently, it has been proposed that motor adaptation may not be entirely driven by implicit processes, and that adaptation may contain an explicit component (Mazzoni & Krakauer, 2006; Taylor et al., 2014). Therefore, it is possible interference in our task represents the application of an explicit strategy, formed to counter the perturbation in the right hand, and applied to the left hand. To assay the contribution of an explicit strategy to interference, we asked participants to take a short survey between the exposure and post-exposure phases. We chose this timepoint because it represents the moment when participants would have had the greatest exposure to the perturbation and the administration of the survey would not interfere with the adaptation process itself. The survey was conducted on two separate sheets of paper, one for 90° reaches and one for 270° reaches. This was done to limit participants' responses to one reaching direction at a time so to avoid repeated measures confounds. Each sheet of paper had the home and target locations marked with small circles. A large outer circle was centered at the 'home' location and extended to the 'target' location. Participants were instructed to place an "X" on the large outer circle at the location where they were aiming with their right hand. We measured the angle between the target vector and a vector starting at the 'home' location and the location of the "X" drawn by the participant for each forward/backward reach. Survey material are located in the Appendix.

4.2.3 Data Analysis

In the right, adapting hand, we calculated initial directional error (IDE), defined as the angle between the target vector and movement vector at peak hand velocity as our primary measure of feedforward adaptation. Our primary measure of feedback adaptation was root mean squared error (RMSE), calculated as the cumulative sum of lateral distance between the hand path and a straight-line path to the target, normalized to sample number.

In the left, interfered-with hand, our primary measure for assessing the feedforward component of interference was initial directional error (IDE), and as an additional measure of feedforward interference, we measured the lateral force at peak velocity (LFPV) participants applied to the manipulandum. Our primary measure of feedback interference was endpoint directional error (EDE), calculated as the angle between the target vector and movement vector at movement offset. Additionally, we measured the lateral force as offset (LFOFF). In roughly 20% of trials, we applied a force channel to the left hand that constrained movement to a straight path to the target. This allowed us to measure the lateral force applied throughout the movement to assess how interference develops as a function of movement extent.

For the training task, we performed a two sample t-test on IDE values in the post-training phase of 16 trials with veridical feedback to verify participants in the structure group did not develop a movement bias due to visuomotor savings (Zarahn et al., 2008). For the interference task, we took the absolute values for IDE, EDE, LFPV, LFOFF, and force channel data to correct for sign differences in forward vs. backward trials. We then subtracted the mean baseline performance from all exposure and post-exposure trials to correct for baseline differences in all outcome variables. Data were reduced into 10 trial blocks for a total of 22 blocks in the interference task. For force channel data, we resampled the force time-series data to 1000 samples and averaged 6 consecutive force channel trials at the beginning (first 30 trials), middle 30 trials and last 30 trials of the exposure phase. This allowed us to examine how interference in the left hand developed over the movement extent across the exposure phase. For IDE, RMSE, EDE, LFPV, and LFOFF we performed separate mixed model ANOVAs with between-subjects factor group (control/structure) and within-subjects factor time (early-middle-late exposure) where these timepoints correspond blocks 5, 12, and 18, respectively. We also performed 2 group x 2 time

ANOVAs during the post-exposure phase, where time referred to blocks 19 and 22, to assess aftereffects. Significant interactions were followed by two sample t-tests at each timepoint to determine where significant group differences were observed. All statistical procedures were conducted in R 3.6, with the *afex* package (ANOVAs) or base *t.test* function; violations to sphericity were corrected for using the Greenhouse-Geisser method (ANOVAs) or by performing Welch's Two Sample t-tests (t-tests); we used Bonferroni correction for multiple comparisons. Finally, we report generalized eta-squared (ges) effects sizes for ANOVAs (Olejnik & Algina, 2003) and 95% confidence intervals of the difference in means between the two groups for t-tests.

4.3 Results

4.3.1 Right, adapting hand

A critical internal check of testing procedures is to verify that exposing the structure group to random rotations in hand feedback did not introduce movement bias – that is, to make sure no 'covert' parametric learning occurred. Welch's Two Sample t-tests on IDE data in the post-training (washout) phase showed no difference between structural learners and those who had only been exposed to veridical visual feedback. [t(111.6) = 1.2, p = 0.23, CI: (-0.65,2.66)]. While these data support that no parametric learning can be detected in our task, significant differences in the right hand during the interference task, where the right hand adapted to a fixed 40° rotation, would suggest that participants in the structure group relied on a previously learned structure to facilitate adaptation. In IDE for the right hand, we found a main effects for group [F(1,28) = 7.26, p < 0.05, ges = 0.16] and time [F(1.3,35.9) = 303.8, p < 0.0001, ges = 0.75], and a Group x Time interaction [F(1.3,35.9) = 15.38, p < 0.01, ges = 0.13]. We found that the structure group had smaller IDE at the beginning of the exposure phase [t(27.8) = 5.26, p* <

0.0001, CI: (5.2,11.8)], but there was no difference at the midpoint or end of exposure (both p > 0.4). For RMSE in the right hand, we found main effects for group [F1,28) = 6.27, p < 0.05, ges = 0.14] and time [F(1.36,38.2) = 273.0, p < 0.0001, ges = 0.74], and a significant Group x Time interaction [F(1.36,38.2) = 19.54, ges = 0.17]. Post-hoc t-tests show that the structure group had smaller RMSE than the control group at the beginning [t(27.9) = -4.3, p < 0.01, CI: (-10.5,-3.7)], but the groups did not differ significantly at the middle or end of exposure (both p > 0.4). This suggests that structural learning facilitates adaptation to a fixed perturbation belonging to the same structure in both feedforward and feedback processes, as evidenced by IDE and RMSE, respectively, and that this result is ephemeral. Visual inspection of IDE and RMSE in the right hand during the interference task (Figure 4-2) shows that the facilitated adaptation only lasts for roughly 30-40 trials.



Figure 4-2: Right hand Initial directional error (IDE) and root mean squared error

(**RMSE**) – **interference task**. Data are shown for the exposure to a 40° rotation in hand feedback (blocks 5-18; each block contained 10 trials), followed by the post-exposure phase with veridical feedback. Control participants previously trained with veridical feedback, whereas the structure group previously trained with random rotations in hand feedback. Vertical dotted lines indicate timepoints for the mixed model ANOVA analysis. Participants in the structure group showed facilitated adaptation in both the feedforward (IDE) and feedback (RMSE) measures, and this result was localized to the first 30-40 trials of exposure.

Finally, we had participants take a short survey between the exposure and post-exposure phases to assay the extent to which they were using an explicit strategy to counter the perturbation in the right hand. The response that would indicate participants used an exclusively explicit strategy would be $+40^{\circ}$, as this would represent the aiming direction that would perfectly counter the perturbation for both forward and backward reaches. The mean response for all participants was 3.8° with range (-46, 52). Figure 4-3 shows a count histogram for all responses to our survey; the distribution appears bimodal, with many responses near both +/- 25° . Additionally, there are several responses at or near zero. Finally, there appears to be no effect of movement direction (forward/backward) on responses, as the mean response for forward trials was 0.6° (standard deviation = 25.1) and 7° (standard deviation = 21.5) for backward trials.



Figure 4-3 - Self-report aiming angle. Count histogram of self-reported aiming angle of the right hand. Participants responded to a survey asking where they were "aiming with their right hand to get the cursor in the target." The angle that would perfectly counter the perturbation would be $+40^{\circ}$. Mean responses for both groups was 3.8° with a range of $(-46^{\circ}, 52^{\circ})$. Bin width is 5° .

4.3.2 Left, interfered-with hand

While participants were adapting to a rotation in hand feedback in the right hand, they were instructed to reach simultaneously with their left hand without visual feedback provided. This made the left hand susceptible to interference from the right, and interference would be reflected as a deviation from a straight-line path to the target. To measure feedforward interference, we calculated IDE and LFPV. For IDE in the left hand, there were no main effects for group or time, nor was there an interaction between these factors (all p > 0.05). For LFPV, there was a main effect of time [F(1.6,45.4) = 9.0, p < 0.01, ges = 0.07], but neither the main effect for group, nor the Group x Time interaction was significant (both p > 0.05). Our analyses of feedback interference, EDE and LFOFF, did not show main effects or interactions (all p > 0.05). Data are illustrated in Figure 4-4, and all analyses are presented in Table 4-1 for reference. On its face, these results might suggest structural learning and subsequent adaptation in the right hand has no impact on interference in the left hand. However, previous work has shown that interference is closely tied to the asymmetry of movement (Brunfeldt et al., *in prep*).

Line	Dependent Variable	Test	Test Statistic	Confidence		
Left Hand Interference – Exposure Phase						
a	Initial Directional Error (IDE)	Mixed method ANOVA	Group: $F(1,28) = 1.82$ Time: $F(1.51,42.3) = 0.97$ Interaction: $F(1.51,42.3) = 0.03$	Group: p=0.19, ges=0.04 Time: p=0.37, ges=0.01 interaction: p=0.95, ges<0.01		
b	Lateral Force at Peak Velocity (LFPV)	Mixed method ANOVA	Group: $F(1,28) = 2.65$ Time: $F(1.62,45.4) = 9.0$ Interaction: $F(1.62,45.4) = 0.01$	Group: p=0.11, ges=0.07 Time: p = 0.001**, ges=0.07 interaction: p=0.98, ges<0.01		
с	Endpoint Directional Error (EDE)	Mixed method ANOVA	Group: F(1,28) = 1.61 Time: F(1.54,43.1) = 0.55 interaction: F(1.54,43.1) = 1.69	Group: p=0.21, ges=0.04 Time: p=0.54, ges<0.01 interaction: p=0.2, ges=0.01		
d	Lateral Force at Offset (LFOFF)	Mixed method ANOVA	Group: $F(1,28) = 1.69$ Time: $F(1.8,50.3) = 0.77$ Interaction: $F(1.8,50.3) = 2.18$	Group: p=0.2, ges=0.07 Time: p=0.46, ges<0.01 Interaction: p=0.13, ges=0.02		
Left Hand Interference – Post Exposure Phase						
e	Initial Directional Error (IDE)	Mixed method ANOVA	Group: $F(1,28) = 0.89$ Time: $F(1,28) = 9.56$ Interaction: $F(1,28) = 0.15$	Group: p=0.35, ges=0.03 Time: p=0.004**, ges=0.03 Interaction: p=0.7, ges<0.01		
f	Lateral Force at Peak Velocity (LFPV)	Mixed method ANOVA	Group: $F(1,28) = 2.43$ Time: $F(1,28) = 1.26$ Interaction: $F(1,28) = 0.44$	Group: p=0.13, ges=0.07 Time: p=0.27, ges<0.01 Interaction: p=0.51, ges<0.01		
g	Endpoint Directional Error (EDE)	Mixed method ANOVA	Group: F(1,28) = 1.56 Time: F(1,28) = 6.94 interaction: F(1,28) = 0.14	Group: p=0.22, ges=0.04 Time: p=0.01*, ges=0.05 Interaction: 0.71, ges<0.01		
h	Lateral Force at Offset (LFOFF)	Mixed method ANOVA	Group: $F(1,28) = 0.12$ Time: $F(1,28) = 4.51$ Interaction: $F(1,28) = 0.19$	Group: p=0.73, ges<0.01 Time: p=0.04*, ges=0.02 Interaction: p=0.67, ges<0.01		

Table 4-1: Omnibus ANOVAs for left hand interference. Mixed model ANOVAs for left hand interference during exposure and post-exposure phases of the interference task. The Group factor refers to either control participants, who received veridical feedback during the training task, or structure participants, who received structural training during the training task. The Time factor refers to early (block 5), middle (block 12), and late (block 18) exposure, and blocks 19 and 22 for the post-exposure phase. * represents p < 0.05 and ** p < 0.01



Figure 4-4 - Left hand interference. Interference measures are shown for both feedforward measures (IDE, LFPV; left column) and feedback measures (EDE, LFOFF; right column). Vertical dotted lines indicate the beginning, middle, and end of the exposure to a fixed 40° rotation in hand feedback for the right hand. While there was not a significant Group x Time interaction during exposure, analysis of the first 30 trials (blocks 5-7) show that participants in the structure group had greater interference than control participants.

Previous experiments investigating structural learning have shown that facilitated adaptation only briefly persists. That is, structurally trained participants will compensate for rotated movements more quickly than novice learners, but the two will produce similar movement after only 20-30 trials (Bond & Taylor, 2017; Braun et al., 2009a). In the current experiment, this would translate to the structure group producing more asymmetrical movements early, but not late during the exposure phase. It is possible that the two later timepoints (blocks 12 and 18), where we would not expect much difference between groups, may be washing out any group differences early in exposure. Additionally, in the right adapting hand, visual inspection of the learning curves presented in Figure 4-2 suggests facilitated adaptation only persists for roughly 30-40 trials. Therefore, we chose to perform two sample t-tests for the first 30 trials of the exposure phase for each outcome variable in the left hand. Participants in the structure group showed greater interference in both feedforward measures [IDE: t(67.4) = 2.52, p < 0.05, CI: (0.38,2.99); LFPV: t(67.3) = 2.86, p < 0.01, CI: (0.05,0.26)] and feedback measures [EDE: t(55.3) = 2.36, p < 0.05, CI: (0.34,4.14); LFOFF: t(58.3) = 2.46, p < 0.05, CI: (0.04,0.42)]. These results reinforce the finding that asymmetrical movements produce interference, and that the ephemeral nature of facilitated adaptation via structural learning produces greater interference early, but not late in adaptation.

To further investigate this result, and to see how interference develops over the extent of a reach, we introduced a force channel in approximately 20% of trials. This allowed us to measure the lateral force applied against the channel wall throughout each movement to obtain force time-series graphs. Figure 4-5 shows the lateral force time-series graphs for the first (top panel), middle (middle panel), and last (bottom panel) 30 trials during exposure. In the first half of the exposure phase, interference appears to be greater in the structure group in roughly the

first 50-60% of movement, but by the end of the reach, the two groups show similar levels of interference. By the end of the exposure phase, there is very little difference between groups. Additionally, the overall amount of interference appears to be smaller in both groups at the end of exposure compared to the earlier timepoints.



Figure 4-5 - Lateral force during force channel trials - left hand. In 20% of trials, there was a force channel applied to the left hand that constrained movement to a straight-line path to each target. Lateral force was measured at the robot manipulandum. Data were resampled and averaged for 6 consecutive channel trials for the first (top panel), middle (middle panel), and last (bottom panel) 30 trials of the exposure phase.

4.4 Discussion

The results of this study highlight two important features of adaptation and bimanual coordination. First, we lend support to previous findings that structural training facilitates adaptation both in feedforward and feedback processes. We extend this finding by showing that facilitated adaptation in the right hand during bimanual reaching, increases interference in the left, kinesthetically controlled hand. This greater interference in the left hand, due to the asymmetry of movement, is likely a function of neural crosstalk between the hemispheres, but the possibility that due to the unpredictability of sensory feedback during structural training, participants upregulate their sensitivity to feedback through optimal adaptive processes. Here we discuss the possible mechanistic and theoretical underpinnings of motor interference during bimanual coordination.

Facilitated adaptation via structural learning, indicated by reduced IDE and RMSE in the structure group in our experiment, suggests that previous exposure to random rotations in hand feedback improves both the feedforward and feedback processes. This result has been shown in previous work using structural training to both visuomotor and dynamic perturbation structures (Braun et al., 2009a), and extends these findings to show that this is true for bimanual tasks as well. This is perhaps not a surprise, as structural learning affords three main benefits as outlined by Braun et al. (Braun et al., 2009a). First, exposure to a fixed rotation belonging to the same structure as was trained previously, results in faster adaptation (structure-specific facilitation). In our experiment, participants in the structure group trained on random rotations in hand feedback ranging from -90° to $+90^{\circ}$ and were then exposed to a fixed 40° rotation. Since this fixed perturbation belongs to a class of visuomotor rotations, even though they had not experienced that specific rotation, they relied on a reduced parameter space to speed up adaptation. This

reduced parameter space constrains the search through all possible solutions to the perturbation along a structure learned in the training task. Second, structural learning protects against interference from tasks requiring conflicting control strategies, or structure-specific interference reduction. Please note, that 'interference' in this context refers to retro- and anterograde interference in memory consolidation, not motor interference during bimanual movements (Krakauer, 2005; Miall et al., 2004). Our results extend this finding by showing that during a bimanual task, where the two hands are required to perform two different reaches, we still show facilitated adaptation in the right hand. Finally, structural learning facilitates the learning of novel tasks belonging to the same structure by preferentially exploring along the previously learned structure, or structure-specific exploration. It has been shown that the planning and execution of bimanual tasks is not simply the application of two independent control policies, but rather bimanual actions are planned as a coordinative unit (Hughes & Franz, 2008). Therefore, one may consider our bimanual interference task employed here representing a new task belonging to the same structure experienced during training. We show that participants still show facilitated adaptation by exploring the same structure learned in the training task, despite the addition of a second effector.

From a theoretical perspective, structural learning has been modelled as an optimal adaptive controller, where the computational problem faced by the motor system is one of system identification. In motor control, the goal of system identification is to build or update an internal model that predicts the sensory consequences of movement (Shadmehr & Krakauer, 2008). In tasks with a fixed perturbation to feedback, there exists an internal model that best matches this prediction with the actual sensory feedback. Through parametric learning, the motor system identifies the combination of parameters that best counters this fixed perturbation. In

structural learning, because there is no one solution in the face of random perturbations, there exists an infinite number of combinations. However, if there is some invariant structure to the perturbations, say strictly visuomotor rotations, the motor system solves for a class of solutions all belonging to that structure. This would suggest that adaptive control principles, like those posited by optimal feedback control theory, could explain behavioral results from structural learning. Braun and colleagues designed a clever experiment where participants performed several thousand reaches with veridical feedback. However, on 20% of randomly selected trials, hand feedback was rotated by one of eight specific rotations. This allowed participants to develop structural knowledge of the perturbations and allowed the researchers to model online adaptive processes. They found that participants engaging in structural learning not only adapted the state estimation of the limb, needed for optimal control, but they also adapted to parameter estimation online (Braun et al., 2009b).

The import of this result for the current experiment is that structural learning conforms to OFCT. This theory suggests that once actual sensory feedback about movement is integrated with the predicted sensory consequences, the motor control system adjusts its sensitivity to either the prediction (for predictable environments) or feedback (for unpredictable environments) (Schwartz, 2016; Scott, 2004; Todorov & Jordan, 2002). Therefore, by training the structure group with random perturbations, we expected to see more interference due to upregulation of sensory feedback gains (Franklin et al., 2012). When we analyzed interference across the entire exposure phase, we did not see a difference between structural learners and control participants. However, when analyzing the first 30 trials, we show that interference was greater for the structure group in both the feedforward (IDE, LFPV) and feedback (EDE, LFOFF) measures. We chose to perform this analysis, despite there not being significant interaction effects, because

of two important factors. First, facilitated adaptation is ephemeral. Previous research shows that improvements in both feedforward and feedback processes only last on the order of 20-30 trials (Bond & Taylor, 2017; Braun et al., 2009b; Brunfeldt et al., *in prep*); and in our right hand IDE data presented here, we see a similar result for the first 30-40 trials. Additionally, Franklin and colleagues have shown that upregulation to sensory feedback gains are most prominent during early exposure to perturbations in feedback and is part of the adaptation process itself (Franklin et al., 2012, 2017). This interpretation is supported by our force channel data (Figure 4-5). We show the lateral force applied against the channel wall is elevated early, but not late in exposure. We propose that early in adaptation to a fixed perturbation, having previously trained on a structure of random visuomotor upregulates the motor system's sensitivity to feedback gains. Since the participants in both groups are relying on primarily kinesthetic feedback to control the left hand, and perhaps structural learners are increasing this gain more than control participants, interference is increased because the two limbs share an internal model of state estimation. The second factor that led us to assay the early exposure period is that during this period, participants in the structure group are generating more asymmetrical movements than control participants. Literature on neural crosstalk suggests that voluntary contraction in one effector results in the involuntary contraction of the contralateral effector and is likely due to a release of interhemispheric inhibition (Cunningham, 2017; Meyer et al., 1995; Perez & Cohen, 2008; Stedman et al., 1998). Therefore, during roughly the first 30 trials of our experiment, participants in the structure group may be increasing the activation of muscles needed to adapt (and rotate) the right-hand trajectories, which in turn decreases inhibition of the contralateral muscles resulting in interference in the left hand. In fact, it has been previously shown that in bimanual interference tasks, participants systematically scaled interference in response to the force

demands for reaching (Walter & Swinnen, 1990; Brunfeldt et al., in review). The ephemeral nature of both facilitated adaptation (right hand) and increased interference (left hand) is predicted by the theoretical approached proffered by Braun et al. (Braun et al., 2009b, supplement). According to their interpretation, learning can be represented with a Bayesian network of input-output responses. In structural learning, the joint probability distribution reduces to a set of conditional probabilities linked by a meta-parameter. This reduces the dimensionality of parameter space by constraining input-output linkages to not to the full set of input-output pairings, but rather through the learning of the intermediary meta-parameter. Therefore, when participants are confronted with a novel perturbation belonging to the previously learned structure, they rely these prior probabilities, constrained to lowerdimensionality space, to speed up adaptation. However, this conceptual approach does not suggest improved overall adaptation, nor do empirical results shown in our experiments or by others (Bond & Taylor, 2017; Braun et al., 2009b; Brunfeldt et al., in prep). Taken together, our results suggest that interference is mediated by the asymmetry of movement, likely due to neural crosstalk, but is bolstered by the sharing of an internal representation of the sensorimotor mapping updated for an adapting hand and shared with the contralateral effector. Additionally, structure learning results in increased communication between the hemispheres in two main ways. First, facilitated adaptation increases the asymmetry of movement and secondly, it upregulates sensitivity to sensory feedback gains used for the adaptation to a novel environment.

Emerging research in motor control has suggested that participants adapt to perturbations by relying on both implicit and explicit learning processes (Mazzoni & Krakauer, 2006; Taylor et al., 2014). And in our experiment, interference may reflect the application of an explicit strategy learned for the right, adapting hand, and applied to the left, interfered with hand. To test

this possibility, we had participants indicate their aiming direction at the end of the exposure phase. We found that participants in both groups failed to reliably indicate the appropriate aiming direction that would counter the perturbation. The 'ideal' aiming direction would be $+40^{\circ}$, but we found the mean response was $+3.8^{\circ}$ with a clear bimodal distribution with peaks centered around $+/-25^{\circ}$ (see Figure 4-3). We expected to have participants report approximately $+20^{\circ}$ to $+25^{\circ}$, as this would match the aiming directions reported in a similar (45° rotation) task used by Taylor et al. (Taylor et al., 2014). While many participants did report in this region, the peak in responses near -20° to -25° gives rise to two possibilities. First, participants in either group may not have relied on an explicit strategy, and perhaps participants in the structure group were unable to access explicit learning processes due to the random nature of rotations. This is unlikely the case, as it has been shown that both parametric and structural learning employs an explicit strategy (Bond & Taylor, 2017). The other possibility is that our survey of aiming was unclear to participants. We instructed them to indicate where they were "aiming with your right hand to get the cursor in the target." Some participants may have misinterpreted this to mean where they thought the cursor was traveling when reaching towards a straight forward/backward target. This is more likely the case, as participants were only asked once to respond to aiming direction, whereas previous studies have responses for every rotated trial (Bond & Taylor, 2017; Taylor et al., 2014). Perhaps then, measuring the 'explicit-ness' of adaptation to a visuomotor rotation requires participants to be repeated exposed to, and most importantly learn, how to respond to a formally explicit task.

In this experiment, we show that structural learning leads to facilitated adaptation in a bimanual interference task. Following training to either veridical feedback or random rotations, participants who learned the structure of visuomotor perturbations adapted faster to a fixed
perturbation belonging to the same structure. Additionally, they had greater interference in the contralateral limb likely due to increased asymmetry of movement and an upregulation in sensory feedback gains. These two findings extend previous work in bimanual coordination to suggest that the communication of motor information between the hemispheres can be manipulated by the adaptation process. Future research should systematically explore the relationship between motor interference and sensory integration, particularly with respect to sensory reweighting, changes in cortical excitability and inhibition, and the sharing of explicit strategies for motor adaptation.

CHAPTER 5 – GENERAL DISCUSSION

Bimanual coordination is a hallmark of human motor control, and understanding the theoretical underpinnings of coordinative actions provides insights into natural human behavior. The overall objective of this dissertation was to examine motor interference in healthy volunteers to provide readers with a basic science approach and interpretation of one important aspect of motor control. I approached this through three aims. In Aim 1, and extended the research previously done in our lab to use a more sophisticated testing apparatus which allowed us to systematically test the influence of task dynamics and adaptive processes on motor interference. In Aim 2, I was able to show structural adaptation generalizes to a contralateral effector and used this information to inform my third aim. Aim 3 combined the procedures used in the first two aims to investigate how manipulating the adaptation process can lead to increased communication between the hemispheres behaviorally recognized as interference. Together, these aims are linked mechanistically through discussion of neural crosstalk and theoretically through optimal feedback control theory. While each study was discussed in depth previously, this chapter will summarize the results and discuss the implications in totality. Finally, I will pose new avenues for future research, particularly in translational clinical neuroscience.

5.1 Aim 1: To determine the effect of manipulating dynamic feedback on a visuomotor interference task

When performing asymmetrical movements, the action of one limb can interfere with control of the other. This motor interference has been described in detail as stemming from the spatiotemporal task constraints (Swinnen, 2002). Previously in our lab, we have shown that while one hand adapts to a visuomotor perturbation, the other kinesthetically controlled hand is

involuntarily rotated (Kagerer, 2015, 2016b). Interestingly, this motor interference can be increased by increasing the resistance to movement (Walter & Swinnen, 1990). Therefore, I hypothesized that by adding a spring restoring force to both hands, while engaging in the interference task described in Kagerer's work, there should be a systematic increase in interference with increasing spring loads. My results supported this hypothesis, and while our initial interpretation was that this is due to a shared sensorimotor representation between the limbs, it did not rule out the possibility that interference was increased due to neural crosstalk (Perez & Cohen, 2008). Therefore, I had a second experiment within Aim 1 that removed the adaptation component to the task. I found that interference was still present, and that greater force demands did increase interference; however, adaptation made this effect more robust. My interpretation is that interference is mediated by neural crosstalk, but that adaption serves to bolster the underlying communication of motor information across the hemispheres. I sought to extend these findings by attempting to manipulate the adaptation process to affect interference. To do this, I required a proof-of-concept study to inform how best to design my final aim. Therefore, I developed the second aim as follows.

5.2 Aim 2: Structural learning generalizes across effectors

In order to determine the best procedure for investigating the effect of adaptation on interference, I needed a way to manipulate the adaptation process to upregulate participants' sensitivity to sensory feedback. Previous studies showed that adaptation to dynamic perturbations upregulated sensitivity to visual information (Franklin et al., 2012). Additionally, my Aim 1 study showed that visuomotor adaptation upregulated sensitivity to dynamic information. This led me to develop a task which overemphasizes the motor system's sensitivity to feedback, and I used the concept of structural learning to do so. In practice, structural learning exposes participants to

random perturbations in feedback that all belong to the same 'class' or structure (Braun et al., 2009a). Participants are capable of learning the underlying structure to facilitate adaptation on tasks belonging to this structure. This would have the added benefit for my studies such that participants would be more reliant on feedback processes due to the random nature of perturbations, thus tuning the sensorimotor system to be more susceptible to interference, or so I hypothesized. But first, I had to determine if structural learning generalized to the contralateral effector. Intermanual transfer is the process of generalizing learning from one hand to the other (Joiner et al., 2013; Sainburg & Wang, 2002). I hypothesized that if participants who previously learned a structure of perturbations in one hand were given the opportunity to adapt to a fixed perturbation belonging to the same structure in the other hand, they would show facilitated adaptation in both the feedforward and feedback processes compared to novice learners. I showed that structural learning indeed transfers across the hands, and that this result was most prominent for feedback processes. This was an encouraging result in terms of our interference task. This informed us that structural learning was not only capable of facilitating adaptation but could be accessed by the other hand. I interpret interference arising from asymmetrical movements via neural crosstalk and that adaptation serves to bolster this communication. Therefore, by showing the contralateral effector can access facilitated adaptation by the contralateral hand, this led me to pursue structural learning as a potential mediating factor which could increase interference in my Aim 1 task.

5.3 Aim 3: To determine if facilitated adaptation increases interference

Given my interpretation of the first two aims, namely that interference is mediated by neural crosstalk, adaptation bolsters this effect, and that facilitated adaptation via structural learning is accessed by the contralateral effector, I chose to combine these two aims into a final experiment.

This experiment had participants first train either with veridical feedback or with structural training, immediately followed by our bimanual interference task. I hypothesized that structural training would serve to increase participants' sensory feedback gains, and this would increase interference by the sharing of a common sensorimotor map updated for the right adapting hand and shared with the left hand. I show that interference was greater in the structure group compared to controls, particularly early in adaptation. This result supports the notion that neural crosstalk mediates interference via activation of homologous muscles due to asymmetric action (Cunningham, 2017; Perez & Cohen, 2009). I also show that interference is most prominent early in adaptation when the uncertainty of movement upregulates feedback gains (Franklin et al., 2012). Recently, several researchers have proposed that motor adaptation arises from both implicit and explicit learning (Taylor et al., 2014), and interference in our task may reflect the application of an explicit strategy. I asked participants to take a survey to assess the extent to which they used an explicit strategy to counter the perturbation in the right hand. Our results did not show a clear explicit component, but it may have been due to the design of our instrument. In the following section, I will address possible remedies to this limitation as well as a general discussion of the implications of this work and future avenues for translational applications.

5.4 Broader implications for basic science and translational motor control

Together, these studies provide contribute to the broader field of neuromotor control in several ways. First, these findings support the notion that interference in bimanual tasks is task dependent and extends to more complex movements such as goal-directed reaching. Much of the work on interference and bimanual coordination previously has limited tasks to continuous, cyclical movements such as hand waving or circle drawing (Haken et al., 1985; Kelso, 1984; Schöner, 1990). Additionally, much of the work on the transfer of motor information between

hemispheres focuses on tasks in which participants produce simple isometric contraction (Cunningham, 2017; Perez & Cohen, 2008, 2009). We extend these findings to show some of the same processes thought responsible for interference in those tasks may also play a role in a more complex, goal-directed movement. Namely, the process of neural crosstalk is one mechanism thought to mediate coactivation of homologous effectors during volitional movement in only one. An important feature of neural crosstalk is force scaling (Perez & Cohen, 2009; Walter & Swinnen, 1990), and I show in both experiments in Aim 1 that as the force demands for reaching increases, so too does interference. While this dissertation did not directly measure neural crosstalk, with technologies such as transcranial magnetic stimulation or electromyography, the behavioral results strongly suggest this process may mediate interference in the current tasks. One potential avenue for future work is to investigate changes to cortical excitability and inhibition in response to visuomotor adaptation tasks as has been shown before (Cirillo et al., 2011). This was previously attempted by me and others in the laboratory, with limited success. One major issue with that experiment was likely methodological problems with muscle selection and stimulation parameters, as well as limited interference due to low force demands for reaching. Therefore, the results from Aim 1 lend support for revisiting the investigation of direct measures of neural crosstalk using force dosing as outlined in this dissertation.

An important clinical application to this work, particularly with respect to neural crosstalk as a mechanism for interference, is the issue of learned non-use in post-stroke patients. Learned non-use is described as a maladaptive response in bimanual coordination following hemiparetic impairment following unilateral stroke (Taub et al., 2006). Essentially, patients with limited use of one upper extremity following stroke will learn to perform activities of daily living, typically done with either or both hands, with the less affected side. Over many weeks,

patients adapt to this coordination change, and over many years this behavior is learned such that improves are observed in clinical settings but not in the home setting (Andrews & Stewart, 1979). In fact, animal models of hemiparetic stroke have shown learned non-use is a function of decreased neural activation of the perilesional site due to interhemispheric projections from the non-affected hemisphere (Allred & Jones, 2008; Jones, 2014). Interestingly, bimanual training protocols in humans shows a protective effect against learned non-use, and may provide increased benefits over unimanual training alone (Kantak et al., 2016, 2017). Therefore, bimanual training tasks like the one used in this dissertation may provide benefits for individuals rehabilitating during the acute post-stroke phase. Combining my force-dosing behavioral results with those indicating changes to motor cortex excitability scale with force, one could conceive of a training task that systematically varies the force demands for reaching in a bimanual rehabilitative strategy. Moreover, results from Aims 1 and 3 suggest that adding an adaptive component to at least one limb may improve this protective effect by increasing motor communication between hemispheres.

An important extension of previous research, supported by findings from Aims 2 and 3, is that structural learning generalizes to and influence the control of the contralateral limb. This is not too surprising as theoretical arguments for structural learning confers three major structurespecific benefits to the learner: facilitation, interference reduction (please note this 'interference' refers to conflicts of motor consolidation, not asymmetrical movement interference (Krakauer, 2005)), and exploration (Braun et al., 2009a). Results from this dissertation show structurespecific facilitation for bimanual movements where one might expect adaptation would be impeded by conflicting control strategies. Additionally, participants explore along a previously learned structure to counter a fixed perturbation in the contralateral limb. This extends previous

work that shows parametric motor adaptation generalizes across workspaces and limbs (Sainburg & Wang, 2002; Shadmehr & Mussa-Ivaldi, 1994; Wang & Sainburg, 2004). An important concern raised in Aim 2 and was addressed, with limited success, in Aim 3 is the possibility that a significant amount of the learning that occurred was explicitly strategized (Mazzoni & Krakauer, 2006; Taylor et al., 2014). In fact, Bond and Taylor show that during structural learning, participants use primarily an explicit strategy to learn the structure. To address this, in Aim 3 I asked participants to indicate where they were aiming with their right hands to get the cursor in the target. This was similar to the procedure used in previous work with a few major differences. First, the survey was only administered once per target direction at the end of the exposure phase. In the works cited above, participants are asked on every trial to indicate their reaching direction. This repeated exposure to the use of an explicit strategy may drive an explicit learning process not naturally used to counter a motor perturbation. Secondly, these previous studies used the same workspace as the motor task to administer the test, whereas here I used a separate sheet of paper. Although the pages were placed in the same general location as the motor task workspace, some participants may not have been able to respond accurately due to changing task constraints. For future use of the task developed in Aim 3, the latter fix is simple – one can make a digital version of the survey akin to previous work (Taylor et al., 2014). As for the former, one could devise a study to systematically test the extent to which reporting of an explicit strategy during motor adaptation is a function of exposure to an explicit task.

5.5 Summary

The experiments conducted for this dissertation aimed to extend our knowledge of bimanual coordination in the context of adaptive approaches to motor interference. In two experiments, Aim 1 showed that motor interference is likely mediated by neural crosstalk, but that adaptation

make this communication more robust through an optimization of sensory feedback gains shared between effectors. In Aim 2, I show that learning the structure of perturbations generalizes to the contralateral limb, and that while feedforward processes do transfer, feedback processes are primarily affected. This is likely a result of the unpredictability of the sensorimotor environment, and in response, the motor system down-regulates predictive control in favor of feedback control. Finally, in Aim 3, I show that structural learning can facilitate adaptation in a bimanual task, and motor interference is increased in response to this facilitated adaptation. These studies extend the current understanding of bimanual coordination by investigating potential mechanisms for bimanual coupling during goal-directed reaching and to more fully describe the effect of adaptation on motor interference in the context of well-established theories of neuromotor control. APPENDIX

Place an "X" <u>on the circle</u> at the location where you were aiming with your hand to get the cursor in the target for a <u>forward</u> movement.



Place an "X" <u>on the circle</u> at the location where you were aiming with your hand to get the cursor in the target for a <u>backward</u> movement.



REFERENCES

REFERENCES

- Allred, R. P., & Jones, T. A. (2008). Maladaptive effects of learning with the less-affected forelimb after focal cortical infarcts in rats. *Experimental Neurology*, *210*(1), 172–181.
- Andrews, K., & Stewart, J. (1979). Stroke Recover: He can but does he? 1, 6.
- Archambault, P. S., Ferrari-Toniolo, S., Caminiti, R., & Battaglia-Mayer, A. (2015). Visuallyguided correction of hand reaching movements: The neurophysiological bases in the cerebral cortex. *Vision Research*, 110(PB), 244–256.
- Azim, E., Jiang, J., Alstermark, B., & Jessell, T. M. (2014). Skilled reaching relies on a V2a propriospinal internal copy circuit. *Nature*, *508*(7496), 357–363.
- Bond, K. M., & Taylor, J. A. (2017). Structural Learning in a Visuomotor Adaptation Task Is Explicitly Accessible. *Eneuro*, 4(4), ENEURO.0122–17.2017.
- Braun, D. A., Aertsen, A., Wolpert, D. M., & Mehring, C. (2009a). Motor task variation induces structural learning. *Current Biology* : *CB*, *19*(4), 352–357.
- Braun, D. A., Aertsen, A., Wolpert, D. M., & Mehring, C. (2009b). Learning optimal adaptation strategies in unpredictable motor tasks. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 29(20), 6472–6478.
- Brinkman, J., & Kuypers, H. (1972). Splitbrain Monkeys—Cerebral Control of Ipsilateral and Contralateral Arm, Hand, and Finger Movements. *Science (New York, N.Y.)*, *176*(4034), 536–.
- Cincotta, M., Borgheresi, A., Balestrieri, F., Giovannelli, F., Ragazzoni, A., Vanni, P., Benvenuti, F., Zaccara, G., & Ziemann, U. (2006). Mechanisms underlying mirror movements in Parkinson's disease: A transcranial magnetic stimulation study. *Movement Disorders*, 21(7), 1019–1025.
- Cirillo, J., Todd, G., & Semmler, J. G. (2011). Corticomotor excitability and plasticity following complex visuomotor training in young and old adults. *The European Journal of Neuroscience*, 34(11), 1847–1856.
- Cox, B., Cincotta, M., & Espay, A. (2012). Mirror Movements in Movement Disorders: A Review. *Tremor and Other Hyperkinetic Movements*, 2.
- Crevecoeur, F, McIntyre, J., Thonnard, J. L., & Lefèvre, P. (2010). Movement Stability Under Uncertain Internal Models of Dynamics. *J Neurophysiol*, *104*(3), 1301–1313.
- Crevecoeur, Frédéric, Munoz, D. P., & Scott, S. H. (2016). Dynamic Multisensory Integration: Somatosensory Speed Trumps Visual Accuracy during Feedback Control. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *36*(33), 8598–8611.

- Criscimagna-Hemminger, S. E., Donchin, O., Gazzaniga, M. S., & Shadmehr, R. (2003). Learned Dynamics of Reaching Movements Generalize From Dominant to Nondominant Arm. J Neurophysiol, 89(1), 168–176.
- Cunningham, D. A. (2017). The effect of motor overflow on bimanual asymmetric force coordination. *Experimental Brain Research*, *0*(0), 0–0.
- Diedrichsen, J. (2007). Optimal task-dependent changes of bimanual feedback control and adaptation. *Current Biology* : *CB*, *17*(19), 1675–1679.
- Diedrichsen, J., Shadmehr, R., & Ivry, R. B. (2010). The coordination of movement: Optimal feedback control and beyond. *Trends in Cognitive Sciences*, *14*(1), 31–39.
- Domkin, D., Laczko, J., Jaric, S., Johansson, H., & Latash, M. L. (2001). Structure of joint variability in bimanual pointing tasks. *Experimental Brain Research*, 143(1), 11–23.
- Eliassen, J. C., Baynes, K., & Gazzaniga, M. S. (1999). Direction information coordinated via the posterior third of the corpus callosum during bimanual movements. *Experimental Brain Research*, *128*(4), 573–577.
- Franklin, S., Wolpert, D. M., & Franklin, D. W. (2012). Visuomotor feedback gains upregulate during the learning of novel dynamics. J Neurophysiol, 108(2), 467–478.
- Franklin, S., Wolpert, D. M., & Franklin, D. W. (2017). Rapid visuomotor feedback gains are tuned to the task dynamics. J Neurophysiol, 118(5), 2711–2726.
- Franz, E. A. (1997). Spatial Coupling in the Coordination of Complex Actions. *The Quarterly Journal of Experimental Psychology Section A*, 50(3), 684–704. https://doi.org/10.1080/713755726
- Franz, E. A., Eliassen, J. C., Ivry, R. B., & Gazzaniga, M. S. (1996). Dissociation of spatial and temporal coupling in the bimanual movements of callosotomy patients. *Psychological Science*, 7(5), 306–310.
- Georgopoulos, A. P., Schwartz, A. B., & Kettner, R. E. (1986). Neuronal population coding of movement direction. *Science (New York, N.Y.)*, 233(4771), 1416–1419.
- Griffiths, T. L., & Tenenbaum, J. B. (2005). Structure and strength in causal induction. *Cognitive Psychology*, 51.
- Haken, H., Kelso, J., & Bunz, H. (1985). A Theoretical-Model of Phase-Transitions in Human Hand Movements. *Biological Cybernetics*, *51*(5), 347–356.
- Herter, T. M., Kurtzer, I., Cabel, D. W., Haunts, K. A., & Scott, S. H. (2007). Characterization of Torque-Related Activity in Primary Motor Cortex During a Multijoint Postural Task. J *Neurophysiol*, 97(4), 2887–2899.

- Heuer, H., Kleinsorge, T., Spijkers, W., & Steglich, W. (2001). Static and phasic cross-talk effects in discrete bimanual reversal movements. *Journal of Motor Behavior*, *33*(1), 67–85.
- Honda, T., Hirashima, M., & Nozaki, D. (2012). Adaptation to visual feedback delay influences visuomotor learning. *PLoS ONE*, 7(5), e37900.
- Hu, X., & Newell, K. M. (2010). Dependence of asymmetrical interference on task demands and hand dominance in bimanual isometric force tasks. *Experimental Brain Research*, 208(4), 533–541.
- Hughes, C. M. L., & Franz, E. A. (2008). Goal-related planning constraints in bimanual grasping and placing of objects. *Experimental Brain Research*, 188(4), 541–550. https://doi.org/10.1007/s00221-008-1387-8
- Joiner, W. M., Brayanov, J. B., & Smith, M. A. (2013). The training schedule affects the stability, not the magnitude, of the interlimb transfer of learned dynamics. J *Neurophysiol*, 110(4), 984–998.
- Joiner, W. M., & Smith, M. A. (2008). Long-Term Retention Explained by a Model of Short-Term Learning in the Adaptive Control of Reaching. *Journal of Neurophysiology*, 100(5), 2948–2955.
- Jones, T. A. (2014). Use it and/or lose it—Experience effects on brain remodeling across time after stroke. 1–8.
- Kagerer, F. A. (2014). Control of discrete bimanual movements: How each hand benefits from the other. *Neuroscience Letters*, 584, 33–38.
- Kagerer, F. A. (2015). Crossmodal interference in bimanual movements: Effects of abrupt visuomotor perturbation of one hand on the other. *Experimental Brain Research*, 233(3), 839– 849.
- Kagerer, F. A. (2016a). Nondominant-to-dominant hand interference in bimanual movements is facilitated by gradual visuomotor perturbation. *Neuroscience*, *318*(C), 94–103.
- Kagerer, F. A. (2016b). Asymmetric interference in left-handers during bimanual movements reflects switch in lateralized control characteristics. *Experimental Brain Research*, 234(6), 1545–1553.
- Kagerer, F. A., Contreras-Vidal, J. L., Bo, J., & Clark, J. E. (2006). Abrupt, but not gradual visuomotor distortion facilitates adaptation in children with developmental coordination disorder. *Human Movement Science*, 25(4), 622–633.
- Kagerer, F. A., Contreras-Vidal, J. L., & Stelmach, G. E. (1997). Adaptation to gradual as compared with sudden visuo-motor distortions. *Experimental Brain Research*, 115(3), 557–561.

- Kakei, S., Hoffman, D. S., & Strick, P. L. (1999). Muscle and movement representations in the primary motor cortex. *Science (New York, N.Y.)*, 285(5436), 2136–2139.
- Kantak, S., Jax, S., & Wittenberg, G. (2017). Bimanual coordination: A missing piece of arm rehabilitation after stroke. *Restorative Neurology and Neuroscience*, *35*(4), 347–364.
- Kantak, S., McGrath, R., & Zahedi, N. (2016). Goal conceptualization and symmetry of arm movements affect bimanual coordination in individuals after stroke. *Neuroscience Letters*, 626, 86–93.
- Kelso, J. A. (1984). Phase transitions and critical behavior in human bimanual coordination. *The American Journal of Physiology*, 246(6 Pt 2), R1000–4.
- Kelso, J. A., Southard, D. L., & Goodman, D. (1979). On the nature of human interlimb coordination. *Science (New York, N.Y.)*, 203(4384), 1029–1031.
- Kennedy, D. M., Rhee, J., Jimenez, J., & Shea, C. H. (2017). The influence of asymmetric force requirements on a multi-frequency bimanual coordination task. *Human Movement Science*, 51, 125–137.
- Krakauer, J. W. (2005). Adaptation to Visuomotor Transformations: Consolidation, Interference, and Forgetting. *Journal of Neuroscience*, 25(2), 473–478.
- Krakauer, J. W., Ghilardi, M. F., & Ghez, C. (1999). Independent learning of internal models for kinematic and dynamic control of reaching. *Nature Neuroscience*, 2(11), 1026–1031.
- Krakauer, J. W., Pine, Z. M., Ghilardi, M. F., & Ghez, C. (2000). Learning of visuomotor transformations for vectorial planning of reaching trajectories. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 20(23), 8916–8924.
- Laszlo, J. I., Baguley, R. A., & Bairstow, P. J. (1970). Bilateral Transfer in Tapping Skill in the Absence of Peripheral Information. *Journal of Motor Behavior*, 2(4), 261–271.
- Latash, M. L., Scholz, J. P., & Schöner, G. (2002). Motor control strategies revealed in the structure of motor variability. *Exercise and Sport Sciences Reviews*, *30*(1), 26–31.
- Latash, M., Scholz, J., Danion, F., & Schöner, G. (2001). Structure of motor variability in marginally redundant multifinger force production tasks. *Experimental Brain Research*, 141(2), 153–165.
- Li, J.-Y., Espay, A. J., Gunraj, C. A., Pal, P. K., Cunic, D. I., Lang, A. E., & Chen, R. (2007). Interhemispheric and ipsilateral connections in Parkinson's disease: Relation to mirror movements. *Movement Disorders*, 22(6), 813–821. https://doi.org/10.1002/mds.21386
- Liu, D., & Todorov, E. (2007). Evidence for the Flexible Sensorimotor Strategies Predicted by Optimal Feedback Control. *Journal of Neuroscience*, 27(35), 9354–9368.

- Magill, R., & Hall, K. (1990). A review of the contextual interference effect in motor skill acquisition. *Human Movement Science*, *9*(3–5), 241–289.
- Mazzoni, P., & Krakauer, J. W. (2006). An implicit plan overrides an explicit strategy during visuomotor adaptation. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 26(14), 3642–3645.
- McDonnell, M. N., & Ridding, M. C. (2006). Transient motor evoked potential suppression following a complex sensorimotor task. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology, 117*(6), 1266–1272.
- Meyer, B.-U., Röricht, S., von Einsiedel, H. G., Kruggel, F., & Weindl, A. (1995). Inhibitory and excitatory interhemispheric transfers between motor cortical areas in normal humans and patients with abnormalities of the corpus callosum. *Brain*, *118*(2), 429–440. https://doi.org/10.1093/brain/118.2.429
- Miall, R. C., Jenkinson, N., & Kulkarni, K. (2004). Adaptation to rotated visual feedback: A reexamination of motor interference. *Experimental Brain Research*, 154(2), 201–210. https://doi.org/10.1007/s00221-003-1630-2
- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*, 9(1), 97–113.
- Olejnik, S., & Algina, J. (2003). Generalized Eta and Omega Squared Statistics: Measures of Effect Size for Some Common Research Designs. *Psychological Methods*, 8(4), 434–447. https://doi.org/10.1037/1082-989X.8.4.434
- Panzer, S., Muehlbauer, T., Krueger, M., Buesch, D., Naundorf, F., & Shea, C. H. (2018). Short article: Effects of interlimb practice on coding and learning of movement sequences. *Quarterly Journal of Experimental Psychology*, 62(7), 1265–1276.
- Peper, C. E., Beek, P. J., & van Wieringen, P. (1995). Multifrequency Coordination in Bimanual Tapping—Asymmetrical Coupling and Signs of Supercriticality. *Journal of Experimental Psychology. Human Perception and Performance*, 21(5), 1117–1138.
- Perez, M. A., & Cohen, L. G. (2008). Mechanisms underlying functional changes in the primary motor cortex ipsilateral to an active hand. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 28(22), 5631–5640.
- Perez, M. A., & Cohen, L. G. (2009). Scaling of motor cortical excitability during unimanual force generation. *Cortex*, 45(9), 1065–1071. https://doi.org/10.1016/j.cortex.2008.12.006
- Saglam, M., Lehnen, N., & Glasauer, S. (2011). Optimal control of natural eye-head movements minimizes the impact of noise. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 31(45), 16185–16193.
- Sainburg, R. (2002). Evidence for a dynamic-dominance hypothesis of handedness. *Experimental Brain Research*, 142(2), 241–258.

- Sainburg, R. L., & Kalakanis, D. (2000). Differences in Control of Limb Dynamics During Dominant and Nondominant Arm Reaching. *Journal of Neurophysiology*, 83(5), 2661– 2675. https://doi.org/10.1152/jn.2000.83.5.2661
- Sainburg, Robert L, & Wang, J. (2002). Interlimb transfer of visuomotor rotations: Independence of direction and final position information. *Experimental Brain Research*, 145(4), 437– 447.
- Schmidt, R. A. (1975). A schema theory of discrete motor skill learning. *Psychological Review*, 82(4), 225–260. https://doi.org/10.1037/h0076770
- Scholz, J. P., & Schöner, G. (1999). The uncontrolled manifold concept: Identifying control variables for a functional task. *Experimental Brain Research*, *126*(3), 289–306.
- Schöner, G. (1990). A Dynamic Theory of Coordination of Discrete Movement. *Biological Cybernetics*, 63(4), 257–270.
- Schöner, G., & Kelso, J. A. (1988). Dynamic pattern generation in behavioral and neural systems. *Science (New York, N.Y.)*, 239(4847), 1513–1520.
- Schwartz, A. B. (2016). Movement: How the Brain Communicates with the World. *Cell*, *164*(6), 1122–1135.
- Scott, S. H. (2004). Optimal feedback control and the neural basis of volitional motor control. *Nature Reviews Neuroscience*, *5*(7), 532–546.
- Shadmehr, R, & Mussa-Ivaldi, F. A. (1994). Adaptive representation of dynamics during learning of a motor task. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 14(5 Pt 2), 3208–3224.
- Shadmehr, Reza, & Krakauer, J. W. (2008). A computational neuroanatomy for motor control. *Experimental Brain Research*, 185(3), 359–381. https://doi.org/10.1007/s00221-008-1280-5
- Sherwood, D. E. (1991). Distance and Location Assimilation Effects in Rapid Bimanual Movement. *Research Quarterly for Exercise and Sport*, 62(3), 302–308. https://doi.org/10.1080/02701367.1991.10608727
- Sitburana, O., Wu, L. J. C., Sheffield, J. K., Davidson, A., & Jankovic, J. (2009). Motor overflow and mirror dystonia. *Parkinsonism and Related Disorders*, 15(10), 758–761.
- Spijkers, W., & Heuer, H. (2007). Structural Constraints on the Performance of Symmetrical Bimanual Movements with Different Amplitudes. *The Quarterly Journal of Experimental Psychology*.
- Stedman, A., Davey, N. J., & Ellaway, P. H. (1998). Facilitation of human first dorsal interosseous muscle responses to transcranial magnetic stimulation during voluntary contraction of the contralateral homonymous muscle. 7.

- Stockinger, C., Thürer, B., Focke, A., & Stein, T. (2015). Intermanual transfer characteristics of dynamic learning: Direction, coordinate frame, and consolidation of interlimb generalization. *J Neurophysiol*, 114(6), 3166–3176.
- Summers, J. J., Rosenbaum, D. A., Burns, B. D., & Ford, S. K. (1993). Production of polyrhythms. *Journal of Experimental Psychology. Human Perception and Performance*, 19(2), 416–428.
- Swinnen, S. P. (2002). Intermanual coordination: From behavioural principles to neural-network interactions. *Nature Reviews Neuroscience*, *3*(5), 348–359.
- Takahashi, C. D., Scheidt, R. A., & Reinkensmeyer, D. J. (2001). Impedance Control and Internal Model Formation When Reaching in a Randomly Varying Dynamical Environment. *Journal of Neurophysiology*, 86(2), 1047–1051. https://doi.org/10.1152/jn.2001.86.2.1047
- Taub, E., Uswatte, G., Mark, V. W., & Morris, D. M. (2006). The learned nonuse phenomenon: Implications for rehabilitation. *EUROPA MEDICOPHYSICA*, 42, 15.
- Taylor, J. A., Krakauer, J. W., & Ivry, R. B. (2014). Explicit and implicit contributions to learning in a sensorimotor adaptation task. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 34(8), 3023–3032.
- Tcheang, L., Bays, P. M., Ingram, J. N., & Wolpert, D. M. (2007). Simultaneous bimanual dynamics are learned without interference. *Experimental Brain Research*, 183(1), 17–25.
- Teulings, H. L., Contreras-Vidal, J. L., Stelmach, G. E., & Adler, C. H. (1997). Parkinsonism reduces coordination of fingers, wrist, and arm in fine motor control. *Experimental Neurology*, 146(1), 159–170.
- Todorov, E. (2004). Optimality principles in sensorimotor control. *Nature Neuroscience*, 7(9), 907–915.
- Todorov, E., & Jordan, M. I. (2002). Optimal feedback control as a theory of motor coordination. *Nature Neuroscience*, *5*(11), 1226–1235.
- Turnham, E. J. A., Braun, D. A., & Wolpert, D. M. (2012). Facilitation of learning induced by both random and gradual visuomotor task variation. *Journal of Neurophysiology*, *107*(4), 1111–1122.
- Tutunji, T. A. (2016). Parametric system identification using neural networks. *Applied Soft Computing*, 47, 251–261. https://doi.org/10.1016/j.asoc.2016.05.012
- Vaziri, S., Diedrichsen, J., & Shadmehr, R. (2006). Why Does the Brain Predict Sensory Consequences of Oculomotor Commands? Optimal Integration of the Predicted and the Actual Sensory Feedback. *Journal of Neuroscience*, 26(16), 4188–4197.

- Veale, J. F. (2013). Edinburgh Handedness Inventory Short Form: A revised version based on confirmatory factor analysis. *Laterality: Asymmetries of Body, Brain and Cognition*.
- Walter, C. B., & Swinnen, S. P. (1990). Asymmetric interlimb interference during the performance of a dynamic bimanual task. *Brain and Cognition*, *14*(2), 185–200.
- Wang, J., & Lei, Y. (2015). Direct-effects and after-effects of visuomotor adaptation with one arm on subsequent performance with the other arm. *Journal of Neurophysiology*, 114(1), 468–473.
- Wang, J., & Sainburg, R. L. (2003). Mechanisms underlying interlimb transfer of visuomotor rotations. *Experimental Brain Research*, 149(4), 520–526.
- Wang, J., & Sainburg, R. L. (2004). Interlimb Transfer of Novel Inertial Dynamics Is Asymmetrical. J Neurophysiol, 92(1), 349–360.
- Wenderoth, N., Puttemans, V., Vangheluwe, S., & Swinnen, S. P. (2003). Bimanual Training Reduces Spatial Interference. *Journal of Motor Behavior*, *35*(3), 296–308.
- Wulf, G., & Schmidt, R. A. (1988). Variability in Practice: Facilitation in Retention and Transfer Through Schema Formation or Context Effects? *Journal of Motor Behavior*, 20(2), 133– 149. https://doi.org/10.1080/00222895.1988.10735438
- Yousif, N., & Diedrichsen, J. (2012). Structural learning in feedforward and feedback control. *Journal of Neurophysiology*, 108(9), 2373–2382.
- Zarahn, E., Weston, G. D., Liang, J., Mazzoni, P., & Krakauer, J. W. (2008). Explaining Savings for Visuomotor Adaptation: Linear Time-Invariant State-Space Models Are Not Sufficient. *Journal of Neurophysiology*, 100(5), 2537–2548. https://doi.org/10.1152/jn.90529.2008