THE SENSORIMOTOR CONTROL OF SEQUENTIAL FORCES

THE SENSORIMOTOR CONTROL OF SEUQENTIAL FORCES: INVESTIGATIONS INTO VISUAL-SOMATOSENSORY FEEDBACK MODALITIES AND MODELS OF FORCE-TIMING INTERACTIONS

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ABSTRACT

Many daily motor tasks involve the precise control of both force level and motor timing. The neural mechanisms concurrently managing these movement parameters remain unclear, as the dominant focus of previous literature has been to examine each in isolation. As a result, little is understood regarding the contribution of various sensory modalities to force output and interval production in sequential motor tasks. This thesis uses a sequential force production task to investigate the roles of visual and somatosensory feedback modalities in the timed control of force.

In Chapter 2 we found that removal of visual feedback information does not affect motor timing behavior according to the predictions of the two-level timing model by Wing and Kristofferson (1973). In addition, our results revealed that, without a visual reference, errors in force output are exhibited, which are related to the processing for reafferent somatosensation from self-generated force pulses (Chapters 2 and 3). Following this, we used extensions of our experimental paradigm to further examine the processing of reafferent somatosensory feedback in the control of force.

First, we investigated performance of the sequential force production task when target force magnitudes continuously changed between iterations. We found that the pattern of errors exhibited following visual feedback removal are consistent with a shift in the perceived magnitude of force output and that the direction of error may be determined by prior task constraints (Chapter 4).

Secondly, we examined force output in two bimanual extensions of the sequential force production task: one that required the combined effort of both hands and a second that involved simultaneous, but independent action. Our results revealed evidence of effector-specificity in the processing of and compensation for reafferent somatosensation (Chapter 5).

Lastly, we devised a vocal analog to the sequential force production task to investigate a long-standing problem in vocal intensity control, termed the Lombard effect. We found that the interplay between audition and somatosensation in the control of sound level by the vocal effectors mirrored that observed between vision and somatosensation in the control of force by the distal effectors (Chapter 6). These results lead us to conclude that the calibration of attenuation reafferent feedback by other sensory modalities may occur for multiple effector systems beyond manual control.

Overall the studies presented in this thesis have provided a thorough investigation into the mechanisms through which vision, audition and somatosensation contribute to the control of sequential force output. Our data contribute to current knowledge regarding the processing of reafferent sensory feedback, how it may be integrated with other sensory signals in the estimation and control of motor output and how these mechanisms influence the periodic production of sequential forces.

AUTHOR CONTRIBUTIONS

This thesis contains seven chapters of original research conducted by the author except for contributions made by the thesis supervisor, Dr. James Lyons, and member of the advisory committee, Dr. Ramesh Balasubramaniam, as well as specified contributions by co-author, Brian Richardson (PhD Candidate, McMaster Integrative Neuroscience Discovery and Study). As the first author of each chapter, I was heavily involved in all aspects of the research program described here, from experimental conception and design to data collection, analysis and subsequent writing of each manuscript. Dr. James Lyons contributed to the conception, design, interpretation of the results as well as editing and approving the final version of the manuscript for the experiments included in Chapters 4, 5 and 6. Dr. Ramesh Balasubramaniam was involved with conception, design, interpretation of results as well as editing and approval of the manuscript for all studies included. Finally, Brian Richardson helped with TMS instruction as well as participant supervision during the stimulation sessions of the experiment included in Chapter 3. All work presented in this thesis has been published in peer-reviewed scholarly journals. The publications associated with each chapter are listed below.

Chapter 2:

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Chapter 3:

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Chapter 4:

Therrien A.S., Lyons J., Balasubramaniam R. (2010). Repetitive finger force production in predictable environments. *Neuroscience Letters*, *479*, 69-73.

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Chapter 5:

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Chapter 6:

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LIST OF ABBREVIATIONS AND ACRONYMS

A	Auditory voice feedback present
Ag/AgCl	Silver/Silver Chloride
AMT	Active motor threshold
ANOVA	Analysis of variance
Bi	Bimanual
BiL	Bimanual – left hand
BiR	Bimanual – right hand
BL	Baseline
CE	Constant error
CNS	Central nervous system
cTBS	Continuous theta burst stimulation
CV	Coefficient of variation
DAQ	Data acquisition device
dB SPL	Decibel sound pressure level, unit of sound intensity
dPMC	Dorsal premotor cortex
EMG	Electromyography
FDI	First dorsal interosseous muscle
Hz	Hertz, unit of frequency
IRI	Inter-response interval
M1	Primary motor cortex
ms	Milisecond, unit of time

MVC	Maximum voluntary contraction
N	Newton, unit of force
NA	Auditory voice feedback removed
NV or NVF	Visual feedback of force output removed
Pa	Pascal, unit of pressure
PC	Personal computer
PF	Peak force
RMT	Resting motor threshold
rTMS	Repetitive transcranial magnetic stimulation
s	Second, unit of time
S1	Primary somatosensory cortex
SD	Standard deviation
Sh	Sham stimulation
SMA	Supplementary motor area
TMS	Transcranial magnetic stimulation
Tukey’s HSD	Tukey’s honestly significant difference test
UL	Unimanual – left hand
UR	Unimanual – right hand
μV	Microvolt, unit of electromotive force
V or VF	Visual feedback of force output present
VE	Variable error

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CHAPTER 1: GENERAL INTRODUCTION

1.1 – MOTIVATION

Many gross motor skills can be broken down to the sequential ordering of series of discrete motor acts. For example, playing the piano involves repetitive key presses, performed with varying degrees of force and at varying time intervals, which are ordered together to form the series of notes that make up a piece of music. Gross motor actions have been studied at the macro level, using the concept of a generalized motor program containing a representation of the task goal (Schmidt 1975), as well as at a more microscopic level, through careful examination of the individual actions that are combined to attain that goal (Schmidt & Lee 2005). These sequential actions require precise control of both force output and motor timing. This involves a combination of feedforward and feedback mechanisms wherein feedforward commands specify the required temporal interval and force level (Wing 2002), while feedback information is obtained from the integration of sensory signals about the timing of executed movement and current level of force output (Wolpert and Ghahramani 2000). Little is known about the neural strategies used to simultaneously manage these mechanisms in sequential motor tasks because the principal focus of literature in this area has been to investigate force and timing parameters separately. Consequently, it remains unclear how feedback from different sensory modalities (e.g. vision and somatosensation) mutually contributes to performance in sequential motor tasks and whether manipulation of these stimuli differentially affects the concurrent control of force and timing. This thesis examines performance of a sequential force production task to study the roles of visual and somatosensory feedback in the sensorimotor control of force and timing.

1.2 - VISUOMOTOR CONTROL OF FORCE

Force production tasks have long been used to probe mechanisms of visuomotor control. While the majority of this work has focused on the production of continuous isometric forces, a small proportion of literature has studied the performance of sequential force production tasks. Isometric force output typically varies around a mean and the amplitude of force variability, both of which are influenced by the availability of visual feedback (Baweja et al. 2009; Jones 2000; Hong et al. 2008; Slifkin et al. 2000; Sosnoff and Newell 2005a,b, 2006; Kuznetsov and Riley 2010; Vaillancourt et al. 2006; Vaillancourt and Russell 2002). Vision is considered to aid the regulation of force output through intermittent feedback control mechanisms (Slifkin et al. 2000). The visual system samples feedback information at a consistent rate to assess force output errors, which are then stored until the motor system can compute corrective commands scaled to the size of accumulated visual information (Slifkin et al. 2000). The rate at which these motor corrections can be made depends on the temporal (Slifkin et al. 2000; Sosnoff and Newell 2005a; Hong et al. 2008) and spatial reliability (Kuznetsov and Riley 2010; Hong et al. 2008; Sosnoff and Newell 2006; Vaillancourt et al. 2006) of visual information as well as the nature of the force production task itself (Sosnoff and Newell 2005a,b).

In continuous isometric force production, increased temporal regularity of visual feedback facilitates performance (via decreased variability) and results in increased complexity of the force signal, indicating less intermittent control and more rapid feedback corrections (Slifkin et al. 2000; Sosnoff and Newell 2005a). These changes in behavior follow a hyperbolic function typically reaching asymptote at visual feedback frequencies between 6.4-25.6 Hz, suggests limits on the rate at which visual information can be processed in the temporal domain (Slifkin et al. 2000; Sosnoff and Newell 2005a). Similarly, augmenting the spatial resolution (pixels/N) of visual feedback reduces the intermittency of error corrections and produces more complex force output (Kuznetsov and Riley 2010), but does so only for a preferred range of visual gain levels (Sosnoff and Newell 2006; Hong et al. 2008). Interestingly, Hong et al. (2008) showed that when combined the effects of spatial and temporal properties of visual feedback are compensatory in nature. In conditions of low spatial precision, force output can be improved by increasing the temporal frequency at which visual feedback is provided, and vice versa; although, there is a lack of perfect symmetry in the effect with spatial resolution unable to compensate for high levels of temporal uncertainty.

While the results highlighted above have been found in studies of continuous isometric force at fixed magnitudes, the visuomotor control of force output changes with differing force production tasks. Sosnoff and Newell (2005a) found that processing of intermittent visual feedback was mediated nonlinearly by isometric force level, such that mid-range forces (~25% MVC) were associated with enhanced utilization of both high-frequency feedback corrections and feedforward control processes. In sequential force production tasks, the use of intermittent visual information is also dependent on task frequency. Force signals produced at slower movement rates have shown deterministic properties, while higher frequency force pulses have been found to be more stochastic in nature (Sosnoff and Newell 2005b). These signal tendencies are indicative of task specific control mechanisms, where task frequency demands influence whether feedback or feedforward processes dominate force output (Pew 1974; Sosnoff and Newell 2005b).

Overall, visual feedback reduces the uncertainty of produced forces, but only when provided with sufficient temporal and spatial precision. Interestingly, highly intermittent visual information has been shown to be more detrimental to force performance compared to conditions where visual feedback is removed entirely (Sosnoff and Newell 2005b). Indeed, while errors in force magnitude have been observed (Sosnoff and Newell 2005b; Vaillancourt and Russell 2002), the variability of force output has been shown to decrease following visual feedback withdrawal in both constant isometric (Baweja et al. 2009) and rhythmic force production tasks (Sosnoff and Newell 2005b). Reduced variability despite persistent errors in these conditions is thought to represent an absence of visuomotor corrections and a transition to other processes of motor control (Baweja et al. 2009; Sosnoff and Newell 2005b). In constant isometric force production tasks, changes in motor output seen following removal of visual feedback have been interpreted as a function of changes to visuomotor memory representations of the target force (Baweja et al. 2009; Vaillancourt and Russell 2002); however, it remains unclear whether the same mechanisms are at work in sequential force production tasks performed without vision.

1.3 – SOMATOSENSORY FEEDBACK IN THE CONTROL OF FORCE

In the absence of a visual reference, predictive control processes are thought to drive motor output, relying upon somatosensory feedback to estimate performance (Jones 2000). Continuous isometric forces produced using only somatosensation exhibit high variability compared to conditions where both somatosensory and visual feedback modalities are available (Jones 2000). One reason for this variable performance could be that somatosensory feedback from self-generated action, or reafferent somatosensory feedback, is perceived less saliently than that originating from an external source (Blakemore et al. 1998; Blakemore et al. 1999). The mechanism thought to underlie this sensory attenuation has its origin in computational theories of motor control and is centered on the concept of an internal model – a neural representation of the motor system (Kawato 1999; Wolpert et al. 1998; Wolpert and Ghahramani 2000). Specifically, reafference mechanisms make use of a forward internal model, which generates predictions of future sensory states using an efference copy of descending motor commands (Kawato 1999; Wolpert et al. 1998; Wolpert and Ghahramani 2000). These predictions can then be compared to incoming afferent information to assess the accuracy of motor execution as well as distinguish self-generated from externally generated sensory feedback (Wolpert and Ghahramani 2000). In the case of reafferent somatosensory feedback there is a match between predicted and actual sensory signals. The comparison of these signals is argued to result in attenuation of the predicted component of incoming afferent information, resulting in reduced perception of self-generated ‘tickle’ sensations (Blakemore et al. 1998; Blakemore et al. 1999).

In force production tasks, sensory attenuation leads to self-generated forces that are perceived as being weaker than they actually are and this phenomenon has been shown to induce a compensatory overproduction of force (Shergill et al. 2003; Bays et al. 2005; Bays et al. 2006; Voss et al. 2007). Participants asked to reproduce previously experienced forces, applied by either another participant or a robotic arm, consistently underestimated their own output, producing forces in excess of target magnitudes (Shergill et al. 2003). Attenuation effects were reduced when temporal asynchronies were inserted between produced and experiences forces (Bays et al. 2005). Moreover, no sensory attenuation was reported when participants were instructed to tap away from the load cell (Bays et al. 2005; Bays et al., 2006). If the finger unexpectedly failed to make contact however, attenuated perception of the experienced force was still observed, so long as it was delivered at the same time as if contact had been made (Bays et al. 2006). Thus, while precise temporal and spatial correspondence between the perceived stimulus and its causal movement is required, mechanisms of sensory attenuation function predictively to affect perceptions of self-generated force.

1.4 – THE CONTROL OF MOTOR TIMING

In addition to the control of force level, performance in sequential force production tasks is also dependent on mechanisms of motor timing. Broadly speaking, neural timing has been studied from two principal frameworks. According to information processing accounts, central timekeeping arises from a dedicated mechanism representing the temporal relationship between successive events (Wing 2002). This ‘internal clock’ is considered to serve time perception as well as motor production and function independently of both the effector and sensory modality of event stimuli (Hazeltine et al. 1997; Ivry and Schlerf 2008). Conversely, connectionist accounts of central timing attribute timing function to the dynamic properties of non-dedicated neural mechanisms, which necessarily entails both effector and sensory modality specific processing (Ivry and Schlerf 2008; Sternad et al. 2000).

Much research into mechanisms of neural timing has been motivated by the scalar property exhibited by judgments of temporal duration in interval timing tasks. This property is described by Weber's Law, which states that the threshold for a perceptible change in a stimulus is a constant ratio of the original stimulus magnitude (Bhusi and Meck 2005). For neural timing, this translates to the assertion that response variability in temporal discrimination varies proportionately with duration (Bhusi and Mech 2005). In line with information processing accounts, it has been shown that this relationship remains constant in both perception and action tasks (Ivry and Hazeltine 1995; Keele et al. 1985). Taken together with findings of crossmodal (Grondin and McAuley 2009, Ulrich et al. 2006) and cross-effector timing ability (Franz et al. 1992; Keele et al. 1985) as well as specific timekeeping deficits associated with lesions to selective brain regions (for review see Ivry and Spencer 2004), a large body of evidence has been accumulated in support of a specialized central timekeeping mechanism. As such, this thesis takes an information processing approach to studying motor timing in the context of simultaneous force control.

Motor timing is typically studied using the interval production task introduced by Stevens (1886). In this task, participants begin by synchronizing their movement (e.g. finger taps or force pulses) to an external pacing stimulus (e.g. an auditory metronome). After a period of time, the pacing stimulus is removed and participants are required to continue producing the desired movement frequency for the remainder of an experimental trial. Intervals produced in this continuation phase show a characteristic negative covariation, such that longer-than-average intervals alternate with shorter-than-average ones. Additionally, individual interval variability exhibits the scalar property.

Under the information-processing framework, Wing and Kristofferson (1973) proposed a model accounting for these observations as reflecting the cumulative variance from two levels of motor timing function. The model includes a central clock, which generates periodic, open loop signals that are subject to random variability. Each clock signal triggers the initiation of a behavioral response, which is in turn subject to variable delays in motor implementation. Both clock and motor components of the model form distinct neural processes and thus are assumed to accumulate variance independently of one another. Due to the open loop nature of the central clock, errors induced by variability in either level go uncorrected in subsequent responses. As a result, variability in the motor implementation phase is predicted to negatively covary between successive intervals. Timer variability however, will scale only with the duration of the target interval. Through calculation of the covariance between consecutive inter-response-intervals (IRIs), one can estimate the proportion of variance associated with motor processing. Variance attributable to central timer function can then be determined by subtracting motor variance from the total variance observed in behavioral data.

The Wing-Kristofferson timing model follows a hierarchical control scheme with the central clock governing motor implementation mechanisms (Wing 2002). Literature has examined the characteristics of an internally driven timekeeper in the context of behavioral observations during rhythm production (Vorberg and Hambuch 1984) and bimanual timing (Helmuth and Ivry 1996; Ivry and Richardson 2001). Proportionately less work however, has studied the motor execution of timed movements in conjunction with other aspects of behavioral control. This is important, as motor execution must often be timed relative to external events or task goals. Accordingly, results of patient lesion studies (Ivry et al. 2002; Spencer et al. 2003) as well as behavioral results in healthy controls (Billon and Semjen 1995; Billon et al. 1996) have supported the proposal of an alternate hierarchy where temporal intervals are specified in terms of critical sensorimotor events, such as the achievement of a target force level. Although information processing frameworks of motor timing assume independence between timekeeper and motor implementation systems, they do not account for potential interactions between force and time at the level of parameter specification, which may function upstream of motor implementation mechanisms (Ivry 1986; Wing 2002).

1.5 – SIMULTANEOUS CONTROL OF FORCE AND MOTOR TIMING

Evidence for interaction between force control and motor timing processes comes from the observation of systematic dependencies between the rise-time to peak force and the variability of that peak force in unimanual isometric force production (Carlton et al. 1993; Kim et al. 1999; Newell and Carlton 1988; Poston et al. 2010). Similar interactions between temporal and force variability have also been shown in unimanual sequential force production tasks (Keele et al. 1987; Sternad et al. 2000). Perhaps more compelling however, are the results of Billon and colleagues (1996) and Billon and Semjen (1995) who found that accentuating one finger tap, by increasing force level, in a series of taps induces temporal irregularities in the sequence. Variation of temporal intervals surrounding the forceful movement may reflect transient modulation of the internal timekeeper in order to account for dynamic perturbations induced by changes in motor output.

Conversely, the notion of independence between force control and motor timing is in broad agreement with early theories of motor control, which specify that force and time make up independent parameters scaling the execution of a generalized motor program (Schmidt 1975; Schmidt and Lee 2005). Evidence in support of distinct force and time control processes comes from both neurophysiological and behavioral data. Single unit recordings in non-human primates have shown that while most cortico-motor neuron activity correlates with force output, some units discharge with the rate of change of force implying a role in temporal regulation (Smith et al. 1975). In humans, Freund and Büdingen (1978) found the duration of initial EMG bursts in quick isometric force pulses by several hand and forearm muscles remained fixed, despite changes in target force magnitude. Furthermore, that both simple and choice reaction times in a unimanual isometric force production task remained invariant to changes in force level, but not pulse duration, lead Ivry (1986) to propose a model where motor planning of force activation and deactivation occurs separately from motor timing instructions and remains independent in a holding buffer to await a response stimulus.

Evidence in support of force-time independence also comes from studies of sequential force production tasks, which have demonstrated that participants show greater accuracy and less variability in reproducing series of temporal intervals compared to series of force targets (Inui et al. 1998; Inui and Ichihara 2001; Pope et al. 2005; Sternad et al. 2000). Neuroimaging data has uncovered differential brain activity in response to changes in the temporal and force constraints of a rhythmic grip force task (Pope et al. 2005). Furthermore, it has been shown that accuracy in the production of periodic forces is not correlated with accuracy in motor timing (Keele et al. 1987); although, some dependence between force and time precision has been found at high movement frequencies (Inui et al. 1998) as well as after extensive training (Inui and Ichihara 2001).

1.6 – THE CONTROL OF BIMANUAL FORCES

Another context in which force and time show independent control is in the production of bimanual forces. These can involve the achievement of distinct effector-specific goals, or the realization of a single target force through the shared effort of both limbs. Tasks such as the former allow for examination of potential interference between control processes for each hand, whereas the latter type permit assessment of inter-limb coupling strategies. When compared with bimanual motor timing, the bimanual control of sequential forces displays a greater capacity for asymmetry between limbs (Inui and Hatta 2002, Rinkenauer et al. 2001). This asymmetry seems to follow handedness and extend to utilization of visual feedback. In both singular and periodic bimanual force pulses, the dominant hand produces greater force levels, regardless of its MVC (Henningsen et al. 1995; Inui and Hatta 2002). In addition, unilateral visual feedback provided of the non-dominant limb results in a significant increase in force variability for both hands compared to feedback of the dominant limb (Henningsen et al. 1995; Inui and Hatta 2002). Furthermore, in rhythmic shared-goal tasks, discrepancies in coupling strength between the hands in force and time have been attributed to differences in the bimanual control strategies employed for changes in these task parameters (Masumoto and Inui 2012, 2013).

Although tighter coupling may exist in relative phasing of the two hands, coordination in bimanual force output has been shown in both brief isometric and repetitive force production tasks. Brief bimanual force pulses exhibit strong interference effects when tasks involve asymmetric targets between the hands (Hu and Newell 2011, 2012; Rinkenauer et al. 2002); however, the degree of bimanual interference is reduced when sufficient time is allotted for motor planning (Masumoto and Inui 2013; Steglich et al. 1999). This effect of time on asymmetric bimanual performance may reflect a period of transient interhemispheric cross talk that occurs during motor programming while limb movements are being actively decoupled (Steglich et al. 1999).

Asymmetric force output constraints are also present in tasks requiring the achievement of a common goal between the hands. Coupling strength in these conditions seems to be modulated by parameters such as available sensory feedback and the force level being produced. In the presence of visual feedback, between-hand correlations of force output are negative suggesting coordinative error compensation behavior, but switch to become positive once feedback is removed (Masumoto and Inui 2012; Ranganathan and Newell 2008). Interestingly, even with a visual reference, correlations become more positive as target force magnitudes increase indicating between-hand enslaving that may result from reductions in available degrees of freedom as force output nears maximal capacity (Hu and Newell 2011; Masumoto and Inui 2012; Morrrison and Newell 1998).

1.7 – SEQUENTIAL FORCE PRODUCTION BY THE VOCAL EFFECTORS: AN APPLICATION OF THE LOMBARD EFFECT

The use of sensory feedback to improve accuracy and minimize the variability of forces is not restricted to the distal effectors. Indeed, human speech production is one of the most complex examples of multisensory integration in the coordination of multiple muscle groups (Smotherman 2007). A distinguishing factor of vocalization however, is that the primary motor output is auditory, rather than the visual consequences of manual control (Rosenbaum 2009). Human oral effectors include the respiratory muscles, the larynx, oral and nasal cavities of the vocal tract and orofacial muscles, collectively referred to as the articulators (Ghanzafar and Rendall 2008, Rosenbaum 2010; Smotherman 2007). These effectors produce sound when expired air from the lungs undergoes patterned vibrations through contractions of the laryngeal vocal folds (Rosenbaum 2010). The resulting sound waves are then filtered by the vocal tract before movements of the jaw, lips and tongue shape the flow of air into the phonetic features of language (Rosenbaum 2010; Smotherman 2007). Aside from the linguisitic components of human speech, the major perceptual elements of vocal output are pitch, timbre and loudness (Ghazafar and Rendall 2008). While voice pitch and timbre are products of resonance in the larynx and vocal tract, loudness, or vocal intensity, is mediated by changes in subglottic pressure and achieved by adjustments to expiratory force output by the respirators (Smotherman 2007).

Literature comparing isometric force production between the vocal and manual effectors has shown that orofacial muscles produce less accurate and less stable (more variable) force output when compared to index finger flexors (Gentil and Tournier 1998; Ofori et al. 2012; Van Steenberghe et al. 1991). Rate of force development however, is much faster in the articulators (Gentil and Tournier 1998). Motor performance of these two effector systems is further mediated by the sensory modality of feedback provided. Visual feedback results in reduced error and variability in isometric force performance by the manual, compared to oral, effectors (Gentil and Tournier 1998; Jacobs et al. 1992; Jacobs and Van Steenberghe 1995; Van Steenberghe et al. 1991). Auditory feedback meanwhile, has been shown to enhance isometric force output in the orofacial muscles (Sussman et al. 1974); although it has been shown to be sufficient in guiding fingertip force production as well (Proedhl et al. 2008; Tachibana et al. 2010).

That the articulators may be specialized for audiomotor control is in agreement with the finding that auditory feedback is crucial to the development of speech in children (Goldstein and Schwade 2008; Waldstein 1990) and the continual monitoring of vocalization in adults (Corey and Cuddapah 2008; Houde and Jordan 1998; Liu et al. 2009; Schenk et al. 2003). When auditory feedback of self-generated vocalization is delayed, either artificially or through post-lingual hearing loss, speech fluency is severely disrupted (Corey and Cuddapha 2008; Schenk 2003). In addition, pitch-shifted auditory feedback of one's speech alters pronunciation, such that speakers will modify vocal pitch in the direction opposite of the perceived shift (Houde and Jordan 1998; Liu et al. 2009). With respect to force production during vocalization, another way in which vocal output changes with altered sensory feedback is demonstrated in the Lombard effect, wherein speakers exhibit immediate, involuntary increases in vocal intensity in response to high levels of ambient noise or when auditory voice feedback is removed entirely (Lane & Tranel 1971; Lombard 1911; Patel and Schell 2008; Pick et al. 1989; Tonkinson 1994; Zollinger and Brumm 2011).

While the current mechanism underlying the Lombard effect remains unclear, literature studying the phenomenon has emphasized the role of auditory feedback in its expression. This is likely due to the observation that central control of vocal intensity seems to rely heavily on audition. Even after prolonged periods, hearing-impaired individuals exhibit significant difficulty in controlling the intensity of vocal output, showing large changes in voice amplitude in response to gain manipulations of their hearing-aid device (Laugesen et al. 2009). Expression of the Lombard effect is also enhanced in communicative situations (Garnier et al. 2010; Patel and Schell 2008). Moreover, Lombard speech has been shown to be more intelligible and possess different spectral qualities than loud speech produced in quiet (Letowski et al. 1993; Pittman and Wiley 2001). Collectively, these findings have lead to the hypothesis that the Lombard effect is the result of an enhanced need for auditory self-monitoring in order to optimize vocal information transfer.

It is important to note however, that distortions in vocal output occurring with altered auditory information arise from adaptive changes to vocal effector activity, which indicates that the central nervous system monitors somatosensory error signals from the speech effectors in addition to auditory feedback (Houde and Jordan 1998). Indeed, somatosensory feedback from the articulators is known to play an important role in controlling the pitch and timing of overt speech as well as manage simultaneous speaking and breathing (Smotherman 2007). That individuals are able to maintain intelligible speech for long periods following hearing loss suggests that, in the absence of auditory input, somatosensation may even become the dominant source of sensory feedback in vocal monitoring (Cowie et al. 1982; Ghanzafar and Turesson 2008; Perkell et al. 2007). Furthermore, mechanical perturbation-adaptation paradigms applied during vocal production have shown that somatosensation alone is sufficient to initiate speech motor learning (Lametti et al. 2012; Nasir and Ostry 2006, 2008; Tremblay et al. 2003).

Despite ample evidence that somatosensory feedback from the oral effectors is integrated along with auditory information in vocal control, the interplay between these sensory modalities in the Lombard effect has only been studied indirectly. Experienced singers can learn to consciously resist changes in vocal intensity when performing in chorus (Tonkinson 1994). While simple instructions to maintain steady voice amplitude are insufficient, provision of a visual reference of vocal intensity has allowed individuals to inhibit the Lombard effect when auditory feedback is masked (Pick et al. 1989). Together, these findings point to the involvement of non-auditory mechanisms that must either be improved with time or calibrated with other sources of external feedback; however the precise contribution of somatosensation to expression of the Lombard effect remains unclear.

1.8 – SUMMARY, THESIS OBJECTIVES AND HYPOTHESES

Everyday actions often involve the simultaneous control of muscle force and motor timing. The preceding sections of this chapter have reviewed the dominant factors involved in the modulation of these two motor parameters as well as current theories regarding their underlying control mechanisms. The central regulation of force level involves a combination of feedback and feedforward processes that rely on both visual and somatosensory information. An extensive literature has studied the visuomotor control of continuous forces, but proportionately less work has considered the role of visual information in the production of sequential forces. In addition, while the processing of somatosensory feedback from self-generated forces has been examined, it remains unclear how this information is integrated with visual feedback in sequential force production. Thus, **the first objective of this thesis is to investigate the mechanisms through which vision and somatosensation reciprocally contribute to performance in sequential force production by the manual effectors**.

Visual feedback is thought to stabilize force output through intermittent control mechanisms (Slifkin et al. 2000) and, upon its removal, force errors are exhibited along with signal structure changes that reflect a switch to more predictive mechanisms of force control (Vaillancourt and Russell 2002; Sosnoff and Newell 2005a,b). These feedforward processes use somatosensory information to estimate body state, but perception of reafferent somatosensory feedback is predictively attenuated inducing errant force output (Bays et al. 2006; Wolpert and Ghahramani 2000). Taken together, these findings lead to the compelling hypothesis that force output errors exhibited in the absence of visual feedback may be related to the attenuation of perceptions of self-generated forces. Furthermore, that these errors are not exhibited continuously, despite the continuous evaluation of self-generated feedback during movement, suggests that reafference effects must be compensated through other mechanisms of motor control. Given the stabilizing effects of vision on force output, a secondary hypothesis is that mechanisms of visuomotor control may serve to compensate and correct for attenuated perceptions of reafferent sensory feedback. These hypotheses are investigated in Chapters 2, 3 and 4 of this thesis.

Apart from force magnitude, sequential tasks also involve simultaneous timing constraints, which have typically been studied in isolation of other properties of motor output. Current literature remains divided on the question of whether coincident force and timing control processes are mutually exclusive. Accordingly, whether the manipulation of visual and somatosensory feedback modalities in a sequential force production task influences the concurrent control of force level and motor timing has yet to be resolved; therefore, **the second objective of this thesis is to determine whether manipulation of these feedback stimuli differentially affects the simultaneous control of force level and motor timing**.

The Wing- Kristofferson (1973) model of motor timing contends that a behavioral time series of inter-response intervals will show characteristic variance such that the durations of adjacent intervals will negatively covary and the variability of individual intervals will be proportional only to their duration (Wing 2002). These predictions stem from the notion that a neural clock triggers periodic motor responses based on an internally represented interval that is specified independently of other motor parameters, like force level (Hazeltine et al. 1997). Modulation of timing behavior as a result of added force constraints on one of a series of periodic responses suggest that interval specification by the central timekeeper may interact with motor implementation in order to account for the dynamic properties of action execution (Billon and Semjen 1995; Billon et al. 1996). The instinctive hypothesis is that if control mechanisms for the force and timing parameters of periodic movements involving dual constraints in both domains are interdependent, the series of IRIs produced would fail to demonstrate the characteristic negative autocovariance predicted by the Wing-Kristofferson model. Alternatively, the persistence of negatively covarying IRIs in such a task would add support to the notion that the control of force and motor timing remain independent at the level of parameter specification (Ivry 1986). These issues are examined in Chapter 2 of this dissertation.

Furthered understanding of the mechanisms through which vision and somatosensation are integrated in the control of periodic unimanual forces can be applied to enhance our knowledge of other motor contexts in which sequential forces are produced, such as the repetitive production of bimanual forces and the production of periodic forces by other effector systems. It is known that the control of bimanual forces as well as bimanual motor timing differ from tasks involving the production of either by a single hand; however, whether bimanual differences also extend to the roles of visual and somatosensory feedback in those control mechanisms remains to be elucidated. Additionally, the effects of visual feedback removal on the coupling behavior of individual bimanual force pulses has been investigated, but the influence of vision in the control of sequential bimanual forces has not. Beyond the manual effectors, the use of multiple sources of sensory feedback in the specification and stabilization of force output can be seen in the control of vocal intensity by the speech effector system, where the primary output is auditory rather than visual. A principal focus of literature studying loudness in human speech has been the integration of auditory information. Much less is known about the role of somatosensory feedback from the speech effectors in the online control of vocal intensity level. Consequently, **the third objective of this thesis is to investigate how multiple sources of sensory feedback mutually contribute to the control of sequential forces by bimanual effectors as well as how they may be applied to the vocal effector system**.

Of particular interest to the third objective of this thesis are the aforementioned hypotheses that errors in force output exhibited in the absence of vision may be related to the processing of reafferent somatosensory feedback and that the role of visual information, when it is present, may be to calibrate attenuated perceptions of self-generated forces. Bimanual forces exhibit effector-specific control in sequential tasks (Inui and Hatta 2002; Rinkenauer et al. 2001), but interference effects seen with asymmetric force targets suggest some between-hand coupling of force output (Rinkenauer et al. 2001). Furthermore, in the absence of vision, non-sequential force production is associated with between-hand enslaving (Hu and Newell 2011, 2012). An interesting hypothesis is that reafference mechanisms may also function in an effector-specific manner, which could differentially influence force output errors produced by each limb in bimanual tasks without vision. Conversely, it is also possible that removal of visual feedback in a sequential task could enhance bimanual coupling behavior and influence force output in these conditions. This thesis addresses these queries in Chapter 5.

Finally, with respect to vocalization, the exact mechanism underlying the Lombard effect has remained unknown since it's initial discovery (Lombard, 1911; Zollinger and Brumm 2011). Central control of vocal intensity shows a strong reliance on audition (Laugesen et al. 2009), but studies of singers and other trained individuals indicate that non-auditory mechanisms, which may be calibrated through other sources of sensory feedback, are also involved (Pick et al. 1989; Tonkinson 1994). The changes in vocal intensity associated with the Lombard effect parallel the changes seen in peripheral forces that are produced using only reafferent somatosensory feedback (Shergill et al. 2003). Given that vocal intensity is mediated through the force output of the respiratory muscles, it is possible that the interaction between auditory and somatosensory feedback in the control of this vocal parameter may function similarly to that, which is hypothesized, between vision and somatosensation in the control of force by the distal effectors. This possibility is investigated in Chapter 6 of this dissertation.

1.9 – THESIS OVERVIEW AND OUTLINE OF EXPERIMENTS

This thesis investigates the mechanisms of sensorimotor control of sequential force production. Using a behavioral approach, we examine the performance of a repetitive force production task performed to visually specified force targets and in synchrony with an external pacing stimulus. Chapters 2, 3 and 4 examine the production of unimanual pinch-grip forces by the right hand under varying conditions where visual feedback of force output, pacing stimuli and target force magnitude are manipulated. In Chapter 5, two bimanual extensions of the repetitive force production task are investigated and contrasted with performance in unimanual conditions. In Chapter 6, a vocal analog to the repetitive force production task is examined to assess parallels between mechanisms of sequential force control by the manual and vocal effector systems. Finally, Chapter 7 includes a general discussion, which outlines the conclusions drawn from the body of work contained in this thesis as well as how the findings of these basic studies contribute to our current understanding of the role of sensory feedback in the control of periodic forces. A brief summary of the studies included in Chapters 2 through 6 and their respective hypotheses is included below.

In Chapter 2, we designed an experimental task that allowed for the examination of the influence of withdrawal of visual feedback of force output on concurrent force level and motor timing performance. The task design was derived from literature studying the effects of visual feedback removal on the performance of continuous isometric force production (Vaillancourt and Russell 2002) and previous research studying periodic motor timing (Wing 2002). Force output decays in the absence of vision and the force signal structure changes to reflect a switch from feedback to feedforward control processes as a function of visual feedback withdrawal (Vaillancourt and Russell, 2002). While central timekeeping is considered to function independently of force level specification, some evidence exists of interactions between these motor parameters in tasks involving simultaneous control of both in one of a series of movements (Billon et al. 1996, Sternad et al. 2000). Our objective was to determine whether the removal of visual feedback in a sequential force production task would result in the same error pattern found in continuous force production and whether dual force and timing constraints for each movement in a sequence would yield evidence of systematic dependencies between these two facets of motor control. Results showed that force output increased, rather than decayed, following visual feedback removal and that simultaneous force level requirements did not differentially influence timing variability as determined by extrapolations of the Wing and Kristofferson (1973) timing model.

The finding of positive force errors following visual feedback removal in the results included in Chapter 2, motivated the study included in Chapter 3. In the absence of a visual reference, only somatosensory feedback is available to estimate current force output. Literature studying perceptions of force output generated using somatosensation found similar overproduction of force, attributing it to mechanisms of sensory reafference attenuating perceptions of self-generated sensory feedback (Shergill et al. 2003). That force overproduction errors were not exhibited when visual feedback was present in our previous work suggested that vision might serve to calibrate attenuated perceptions of reafferent somatosensation. Depression of motor cortical activity through application of continuous theta-burst stimulation (cTBS) was previously found to reduce the overestimation of reference forces by disrupting reafference processing (Voss et al. 2007). We hypothesized that if sensory reafference effects were responsible for the positive force output errors noted in our previous work, application of cTBS to the motor cortex should also reduce the overproduction of force following withdrawal of visual feedback. Performance of the repetitive force production task both in the presence of, and following the removal of visual feedback of force output was contrasted over three stimulation sessions: baseline (no cTBS), after receipt of cTBS to primary motor cortex and after a sham stimulation (placebo condition). Results showed that cTBS reduced the overproduction of force in the absence of visual feedback, but had no effect on forces produced with it. These findings were interpreted as adding support to the notion that force output errors exhibited following visual feedback removal may be related to the processing of reafferent somatosensory feedback and that vision may serve to calibrate the effects of reafference on self-generated somatosensation. With this added credence to the assertion that our repetitive force production task highlighted the interplay between vision and reafferent somatosensation in the regulation of force output, we could now use the experimental paradigm to further our understanding of these mechanisms force control more generally.

In Chapter 4, we questioned whether the overproduction of force in the absence of visual feedback reflected a shift in perceived magnitude of force output, or whether it represented a disrupted ability to scale the relative difference between successive force pulses. This is relevant as, in activities of daily living, it is rare that one would produce series of equal magnitude forces. Rather, it is more common for a task to require the scaling of sequential forces to changing target demands (e.g. hammering a nail into a piece of wood). Thus, our objective with this study was to investigate the effect of removing visual feedback in a sequential force production task with continuously changing target force magnitudes. Our repetitive force production task was modified so that target force magnitudes continuously increased or decreased over the course of experimental trials. Results revealed that, despite errors in force output in the absence of vision, reproduction of the relative difference between successive forces was accurate.

Additionally, the direction in which target forces changed prior to visual feedback removal, determined the direction of error following it.

In Chapter 5, a second extension of our repetitive force production task was designed to examine the interplay between vision and reafferent somatosensation in the control of bimanual forces. Bimanual forces are associated with asymmetric control mechanisms (Inui and Hatta 2002). We hypothesized that asymmetries in force overproduction errors following visual feedback removal might reflect equally asymmetric processing of reafferent sensory information. As a further probe we applied the cTBS protocol employed in Chapter 2 to assess unilateral perturbation to reafference mechanisms. Results revealed asymmetries the degree of force overproduction exhibited in the absence of vision and a lack of between-hand coupling. Moreover, application of cTBS reduced positive force errors following visual feedback withdrawal selectively for the hand contralateral to stimulation.

The objective of Chapter 6 was to apply the findings included in Chapters 2 and 3 to the interplay between reafferent somatosensory feedback and other sensory modalities in the control of force by effectors other than the hands. In particular, this study was motivated by a phenomenon termed the Lombard effect, where speakers involuntarily increase vocal intensity in the presence of high levels of ambient noise or when auditory feedback is prevented through other means (Lombard 1911). Vocal intensity is controlled through expiratory force (Smotherman, 2007). We hypothesized that the relationship between auditory and reafferent somatosensory feedback in the regulation of vocal intensity may parallel that found between vision and somatosensation in peripheral force production and that the Lombard effect may result from compensatory errors arising from attenuated perceptions of vocal output in the absence of auditory reference stimuli. Results showed that when audition was replaced with a secondary external reference (i.e. visual feedback), expression of the Lombard effect was reduced.

In summary, the collective findings of the studies included in this thesis add to current understanding of the mechanisms through which sensory feedback contributes to sequential force control. Chapter 2 shows that humans exhibit errors when producing sequential forces in the absence of a visual reference; although, they maintain motor timing ability. Chapter 3 demonstrates that these force output errors may result from attenuated perception of reafferent somatosensory feedback and that visual information, when present, may serve to calibrate reafference effects. Chapter 4 reveals that reafferent attenuation consistent with a shift in the perceived magnitude of self-generated forces and that prior task constraints may influence the direction of compensatory error. Chapter 5 provides evidence of effector-specificity in the processing of reafferent feedback. Lastly, Chapter 6 suggests that the calibration of attenuated reafferent feedback by other sensory modalities may extend beyond the manual effectors.

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CHAPTER 2: TIMING AND VISUAL FEEDBACK CONSTRAINTS ON REPETITIVE FINGER FORCE PRODUCTION

2.1 – ABSTRACT

While much is known about sequential effects in motor timing, less is understood about whether movement parameters like force show sequential dependencies. In this study we examined the effect of timing constraints on repetitive unimanual force production sequences. Ten healthy participants produced a series of pinch grip forces in time to a metronome and to visually specified force amplitudes. Either visual feedback of force produced or the auditory metronome was removed 10s into the experimental trial, with participants performing continued reponses for the remaining 20s. In the continuation trials, a negative lag-1 autocovariance in the inter-response intervals (IRIs) was observed as is commonly seen in motor timing tasks. However, removal of visual feedback resulted in a systematic increase in mean force output through the course of the trial, resulting in positive lag-1 autocovariance values. An interaction was found between mean IRI and peak force magnitude, with greater force variability seen for the larger intervals. However, the imposition of dual force and timing constraints had no effect on the underlying variability of the peak force or the IRIs. The results are discussed in the context of force and time being independently specified components of a generalized motor program.

2.2 – INTRODUCTION

A common observation in rhythmic finger tapping is that interresponse intervals (IRIs) vary – longer-than-average intervals typically alternate with intervals that are shorter-than-average and vice versa. The seminal work by Wing and Kristofferson (1973) explained the variability of rhythmic sequence timing using a two-level timing model. The model proposed the idea of an internal clock that provides a stochastic timekeeping signal specifying each internally formulated interval, which is prone to statistical variation. Before an observable movement can be recorded however, the output of the clock is subject to delays in motor execution. Due to the theorized independence between clock and motor components, a series of consecutive IRIs shows variance that has been influenced by an additive effect of these two noise sources. The production of time intervals has long been studied through examination of serial rhythmic movement tasks across various subject populations, using an array of effectors and pacing conditions (see Wing 2002 for review). With the exception of a few studies, the timing of actions has been the primary focus of this research and there has been little investigation of the simultaneous production of force (Pope et al. 2005), although serial production of force has been studied to some extent (Wing et al. 2004). In this paper, we explore the question of whether such sequential dependencies might be seen in the repetitive production of pinch grip force.

A fundamental question we ask in this study is whether the control processes for force and time are autonomous or, conversely, if they are contingent upon one another. A prevailing view in the neuropsychological literature is that the control of timing is independent of force control. This view stems from evidence that participants consistently show diminished accuracy and greater variability in producing a series of peak forces, contrasting with the ease with which they are able to maintain relatively accurate series of IRIs (Pope et al. 2005; Sternad et al. 2000). Patient studies also support the argument that force and time are separately controlled entities in the brain. Pope and colleagues (2006) observed that the performance of patients with Parkinson's disease in a rhythmic force production task showed marked impairments in force production, but the ability to accurately produce IRIs remained relatively spared. Neuroimaging evidence from a similar experiment suggests a special role for the basal ganglia in force production (Pope et al. 2005). Patients with focal basal ganglia lesions seem to have minor problems with force control, but timing functions are intact (Aparicio et al, 2005). On the other hand, individuals with cerebellar disorders often exhibit impaired control in discrete timing tasks, but are spared in the ability to produce accurate force magnitudes (Schlerf et al. 2007; Spencer et al. 2003; Spencer et al. 2007; Spencer and Ivry 2005).

The conjecture that time and force are independently controlled, however, is in strong contrast to the anecdotal observation that in order to execute any movement correctly the relative timing of force generation and relaxation must be appropriately scaled. Billon et al. (1996) examined participants performing one accentuated tap in a series of five taps. It was noted that the interval prior to the accentuated tap was consistently shortened, while the one following it was lengthened, suggesting that preparing for a specific impact force affects timing variability. Sternad et al. (2000) examined timing, force and concomitant force and time constraints on performance of a sequential finger tapping task. In conditions with the dual task constraints, the variability in the peak forces increased for larger movement periods. Taken together, these results indicate that the presence of an explicit temporal goal can also influence force production and variability patterns.

While subjects are relatively good at producing target force levels with visual feedback (external specification of required force), there are some well-identified phenomena seen when visual feedback is removed. Recent studies have noted that isometric force output shows a sharp decay in the absence of feedback (Vaillancourt and Russell 2002; Davis 2007). This decay began between 620 and 1600 ms after the withdrawal of feedback, indicating the presence of "memory" processes for the required force level. While the role of feedback withdrawal has been shown for both uni- and bimanual force production, the question of how repetitive sequential force production is affected when visual feedback of the target force level is removed has not been addressed. Here we ask: what are the effects of timing and/or sequential constraints on force production in the presence and absence of visual feedback? How different is repetitive force production compared to isometric production after withdrawal of visual feedback of the target force level?

The goals of the present study were two-fold. First, we sought to determine whether repetitive, unimanual force production is different when the force target and timing sequence are internally or externally specified. Secondly, the aim was to further investigate whether the imposition of both force and timing constraints to the task produced systematic dependencies between these two movement facets. We predicted that the imposition of force constraints on rhythmic timing would not influence the underlying timing variability, i.e. the time series of IRIs would show the characteristic negative lag-1 autocorrelation as predicted by Wing-Kristofferson (WK) model. We also hypothesized that in the absence of visual feedback, force levels produced in adjacent timing intervals would alternate between large and small resulting in a negative lag-1 autocorrelation structure for the sequence of peak forces. We predicted that removal of visual feedback of force output would result in an overall decline in mean force output, as seen in isometric force production tasks.

2.3 – METHOD

2.3.1 – Participants

Ten participants (6 male, 4 female; mean age 24.5 years) volunteered for this experiment. All participants were students from McMaster University. Participants were right handed according to both self-report as well as the Edinburgh Handedness Inventory (Oldfield 1971). Participants were free of any known neurological impairment or musculoskeletal impairment to the upper extremities and had normal or corrected normal vision at collection. In keeping with the Declaration of Helsinki, prior to participation, volunteers gave their informed consent in accordance with McMaster Research Ethics Board regulations.

2.3.2 – Apparatus

Force data were collected using a 6-DOF load cell (ATI Nano 17) mounted on a stainless steel stand so that forces were applied on the horizontal (z-axis). The apparatus was fixed to a table with a computer monitor placed behind for subject's feedback. Force data were sampled at 1000 Hz with data acquisition hardware (National Instruments DAQcard-6024E) using custom software written with Labview (Labview 8.2, National Instruments). This software was customized to provide visual feedback to the subjects on a Viewsonic 19" flat panel display with a refresh rate of 60Hz. The force transducers were calibrated with a 6 x 6 matrix that describes the relation of voltage gain to resolved force. The calibration matrix was factory generated and allowed for correction of crosstalk between each measured force and moment axis. Furthermore, signals were amplified with the packaged AMTI amplifier, and signals digitized with the National Instruments PCI-6220 DAQ. This combination of voltage amplification and 16-bit resolution of a DAQ lead to an ultimate resolution of 1/320 N in the z-axis. There was no hysteresis in the zero-level of the resolved forces, which indicates no significant drift or offset in the force data due to ongoing use of the apparatus.

2.3.3 – Task

Subjects were seated in a comfortable non-rotating chair with their right forearm resting on a table. They were positioned so they could reach the force transducer without strain to the forearm and successfully perform a pinch grip (between the right thumb and index finger) motion on it. During the experiment, subjects were presented with a target force and asked to match a visually specified target force by pinching the force transducer between the right thumb and index finger. The target force was presented as a column in a bar graph on a 19" flat panel display placed at a comfortable distance in front of the participant. A second column adjacent to the target bar represented the current force output of the subject. Changing amplitudes with each press on the load cell indicated the force levels of the subject. Each 5 N of force produced by the subject corresponded to a 1 cm increase in amplitude. Subjects were instructed to match the second column level to meet the target force level by modulating the pinch grip force. The goal of the task was to consistently match force output to the target amplitude. Subjects were given up to 5 practice trials to familiarize themselves with the experimental apparatus. Two target forces were used in the experiment: 8 N and 16 N. Each trial lasted 30s. The movement rate was specified by a metronome (1 or 2 Hz), which corresponded to time intervals of 1000ms or 500ms. In certain experimental conditions subjects were instructed to continue the repetitive force production after either the visual feedback of the target force or the metronome (or both) was removed after the first 10s of the trial. Thus there were two timing conditions (synchronization and continuation) and two visual feedback conditions (feedback vs no feedback). All the trials were presented in a randomized manner. There were six repetitions of each trial that yielded a total of 96 trials per subject.

2.3.4 - Data Analysis

Force data were stored for offline analysis on a customized PC workstation. A custom-written program in MATLAB^{TM} extracted the peak force (PF) for each pinch on the transducer as well as the iteration and time at which they occurred in the continuous force-time series. The program was also used to quantify the IRIs: the time between the measured peak force responses. Trial means were then computed from the series of PF and IRI values. Variability in performance was determined through calculation of standard deviation and coefficients of variation. As subjects were not informed of the experimental condition prior to the beginning of the trial, the first 2 s of data were not used in order to avoid contamination from transient behaviour as subjects adjusted their performance to the visual display and metronome frequency. Only the continuation phase data from each trial was used for analysis. Means were calculated across 6 repetitions per condition as well as across participants. Autocorrelations at lag-1 for all trials were performed using methods specified in Wing (2002).

2.3.5 - Statistical analysis

SPSS statistical software (SPSS 16.0, Chicago, Illinois) was used to conduct separate analysis of variance (ANOVA) with repeated measures for all dependent variables (2 metronome frequency conditions: 1 Hz, 2 Hz; 2 timing conditions: Synchronization, Continuation; 2 force target levels: 8 N, 16 N; and 2 visual feedback conditions: full visual feedback, no visual feedback) to assess statistical differences between conditions.

2.4 – RESULTS

2.4.1 - IRIs and their variability

A main effect of metronome frequency confirmed that participants successfully produced two different movement frequencies corresponding to the two frequency conditions ($F\ (1, 9) = 3583, p < .001, \eta^2 = 0.10$). There was also a frequency x timing interaction found for mean IRI ($F\ (1, 9) = 14.79, p < .01, \eta^2 = 0.62$). Mean IRI in continuation timing condition was shorter than that in synchronization timing (0.94 s and 0.48 s in continuation, vs. 0.99 s and 0.5 s in synchronization), which indicates that participants had a tendency to increase their movement frequency in the absence of a pacing metronome.

The influence of force constraints was seen in the significant interactions obtained for mean IRI between visual feedback condition, timing condition and metronome frequency. Figure 2.1a illustrates the interaction found for mean IRI between visual feedback and timing conditions (F (1, 9) = 10.22, $p < .05$, $\eta^2 = 0.53$). Figure 2.1b shows the interaction found for mean IRI between visual feedback condition and metronome frequency (F (1, 9) = 7.24, $p < .05$, $\eta^2 = 0.45$). The aforementioned influences of timing condition and metronome frequency were again reflected here. IRI decreased with continuation timing as well as with the faster movement frequency. However, mean IRI increased in the absence of visual feedback of force output in the continuation timing and 1 Hz movement frequency conditions. Further evidence for the influence of force constraints on timing ability is shown in Figure 2.1c. A significant interaction was found for mean IRI between movement frequency and force target (F (1, 9) = 5.79, $p < .05$, $\eta^2 = 0.39$). Once again, the drop in mean IRI with the faster movement frequency reflected the difference between the two prescribed rates. However, it can be seen that timing ability was influenced idiosyncratically depending on force and movement frequency. In the 1 Hz condition, mean IRI was greater with the lower, 8N, force target. In the 2 Hz condition though, mean IRI increased with the larger, 16 N, force target.

Significant interactions were obtained for both IRI SD (F (1, 9) = 56.48, $p < .001$, $\eta^2 = 0.86$) and IRI CV (F (1, 9) = 69.12, $p < .001$, $\eta^2 = 0.89$, Figure 2.1d) between movement frequency and timing condition. Across both factors, IRI variability was larger in the 1 Hz condition and increased for both movement frequencies in the continuation timing condition. More importantly, we observed that timing variability was not dependent on either force target magnitude or visual feedback condition.

As another assessment of the variation in the IRI series, autocorrelations were performed at lag-1. A significant main effect of timing condition was observed (F (1, 9) = 9.27, $p < .05$, $\eta^2 = 0.51$). For both timing conditions, negative mean lag-1 r values were obtained. The mean lag-1 r for synchronization timing was very close to zero (-0.00029) indicating almost complete synchronization with the pacing metronome. The mean lag-1 r value for continuation timing was significantly more negative (-0.06729, at $p < .05$), falling between zero and negative one half (the boundaries specified by the WK model).

2.4.2 - Peak forces and their variability

A main effect of force target indicated that participants successfully produced two different force levels corresponding to the 8 and 16 N force target conditions (F (1, 9) = 810.37, $p < .001$, $\eta^2 = 0.99$). Mean PF was larger in the absence of visual feedback (8.93 N and 16.47 N when feedback was present and 11.33 N and 18.05 N when feedback was removed). A significant interaction was also obtained for mean PF between visual feedback condition and movement frequency (F (1, 9) = 10.15, $p < .05$, $\eta^2 = 0.53$, Figure 2.2a-b). For both movement frequencies, mean PF increased in the absence of visual feedback of force output. In the absence of visual feedback however, mean PF decreased with the higher 2 Hz movement frequency.

Figure 2.2c illustrates the significant interaction observed for PF SD between force target and visual feedback condition (F (1, 9) = 13.87, $p < .01$. $\eta^2 = 0.61$). Inspections of Figure 3c reveals that irrespective of target force magnitude, PF variability increased in the absence of visual feedback. Examination of PF CV revealed a main effect for visual feedback condition (F (1, 9) = 70.42, $p < .001$, $\eta^2 = 0.89$), showing an increasing CV in the absence of visual feedback. Unlike the SD results, however, no significant effects of target force magnitude were seen in the CV values.

Lastly, to examine the effects of simultaneous time interval constraints on the variability of the force production sequence, the PF series were analyzed using an autocorrelation at lag-1. Figure 2.2d illustrates the significant interaction for mean PF lag-1 r between visual feedback condition and movement frequency (F (1, 9) = 5.14, $p < .05$, $\eta^2 = 0.36$). For both movement frequencies, contrary to our predictions, PF lag-1 r becomes more positive in the absence of visual feedback, suggesting a systematic increase in force magnitude over the course of the trial once the visual feedback is removed, as illustrated in the sample time series in Figure 2.3. For both visual feedback conditions, mean PF lag-1 r also becomes more positive for the faster, 2 Hz, movement frequency. Taken together, these results suggest that error accumulated to a greater extent in the absence of force feedback and as movement frequency increased.

2.5 – DISCUSSION

There were two principal objectives in conducting the present experiment. Firstly, we examined whether repetitive unimanual force production differed from isometric/brief impulse tasks when the force target and timing sequence were internally or externally specified. Secondly, we investigated whether the imposition of dual force and timing constraints to a rhythmic task produced any systematic dependencies between these two movement parameters.

Participants were highly successful in producing the two desired movement frequencies, although movement frequency increased in the absence of a pacing metronome. More importantly, interactions between force and timing were found in the mean IRI data. Intervals produced systematically increased in the absence of visual feedback. In previous work by Sternad et al. (2000) it was not until both force output and time interval constraints were simultaneously imposed in a task that a significant interaction was found between target period and target force. The interaction obtained for mean IRI between peak force and movement frequency in the present study is in general agreement with the postulation by Sternad at al. (2000) that something unique occurs when both force and time constraints are present in a task, something which does not occur in the presence of only one.

Our data also revealed that variability was greater for the slower, 1 Hz, movement frequency. The autocorrelation at lag-1 revealed only a main effect for timing condition, with a negative lag-1 value for all continuation trials. This result is in broad agreement with several studies on continuation timing, such as those for finger, eye and speech movements (Wing 2002). It is important to note that we did not find any systematic dependencies between IRI variability on either the force target or feedback condition, which is also consistent with the results of Sternad et al (2000). Given that we did not find any large differences in IRI variability as a function of the force and feedback manipulation, we did not partition the variance into clock and motor components. Taken together, these findings attest to the robustness of central timing mechanisms and suggest that the imposition of force constraints to a rhythmic task does not differentially affect timing variability.

As was the case for movement frequency, participants were found to be successful in producing the two target force magnitudes prescribed by the task. Peak force variability also increased with increasing peak force magnitude fell in agreement with other work on sequential force production (Inui et al. 1998). Previous research on isometric force production has noted one consistent finding -- without visual feedback, force output declines exponentially (Baweja et al. 2009; Davis 2007; Vaillancourt and Russell 2002). In the present experiment, we observed a systematic increase in force output in the absence of visual feedback. Our results show that when visual feedback is not present to regulate the force levels, the errors tend to be positive and accumulate in the course of the trial (as seen in Figure 2.3).

There are important differences between continuous force production, which is under the realm of intermittent control mechanisms (Slifkin et al. 2000), and the task presented here. Visual feedback stabilizes the intermittent fluctuations, but removal of this information results in a decline in mean force output, which has been attributed to a "memory" process (Davis 2007). The present results show that a different mechanism might be at work in repetitive force production akin to the force escalation effect reported by Shergill et al. (2003). When participants were asked to press on a force transducer in an attempt to reproduce a magnitude of force applied to them, Shergill and colleagues discovered that participants continuously underestimated their produced force levels, thus leading to an escalation effect. This was attributed to central predictive mechanisms involving reafference (Blakemore et al. 2000) that reduce the salience of self-generated forces by causing them to be perceived as weaker (in the absence of feedback from any other modality). The perception of self-generated forces is especially attenuated during during self-generated movement. Our present results suggest that a similar mechanism might be involved when visual feedback is removed during repetitive force production. The force levels produced in the previous interval may be perceived to be weaker, resulting in an accrual of positive errors (more force) over the course of the trial. Perceptual judgment studies or a between-person force production tasks may be used to test this experimentally.

In order to discern the effects of the simultaneous force and time constraints on the correlational structure of the force production sequence, the peak force series was analyzed using an autocorrelation at lag-1. The mean lag-1 r became more positive in the absence of visual feedback as well as with the shorter target period suggesting that in these conditions there was a greater accumulation of errors. These results suggest that the presence or absence of the visual target information may have a larger effect than the absence of a metronomic timing stimulus on the accumulation of errors in the force series.

As seen in the results of timing variability, no systematic relationships were found between peak force variability and the timing goals of the task in contrast to those of Sternad et al. (2000), who reported increasing peak force variability with longer IRIs when the dual task constraints were in place. However, in the study by Sternad et al.

(2000), participants received continuous visual feedback of their force output relative to the prescribed target magnitude. Thus a direct comparison of our results is not possible.

In summary, there were two main findings from this experiment. First, the nature of visual feedback in the regulation of force production is different for isometric and repetitive tasks. While withdrawal of visual feedback results in a decline of force output in isometric production tasks, in a sequential task the same condition results in a gradual increase in force output. This was seen in the positive lag-1 autocorrelation values seen in the force values suggesting an accumulation of positive error over the course of the trial. Secondly, while an interaction was found between mean interval and peak force magnitude, no other relationships were found between target period and force in the task presently examined. More importantly, the imposition of force level constraints to the rhythmic timing task did not alter the underlying structure of timing variability. Taken together with the lack of interaction between variability in the forces produced and the temporal demands of the task, the results speak to the robustness of central timing processes and suggest that the imposition of dual force and time constraints did not differentially affect performance.

The idea of the independent modulation of force and time has been suggested in the concept of a Generalized Motor Program (Ivry 1986). The first level of this model involves program construction with separate subcomponents outlining force activation and deactivation as well as timing instructions. These components remain separate from one another until the second stage when the motor program is actually implemented. The lack of interaction seen between the force and time constraints on the variability of either is in general agreement with the idea that these two components of movement are specified separately in the motor program. This is not to say that they do not interact with each other at a lower level of movement organization. It is also not clear if the dependence between the two components might change as a function of movement rate. Further research might be needed to investigate the neurophysiological basis of this distinction, using patients with known deficits in either discrete timing tasks or force production. The positive lag-1 effect and the escalation in force levels in the absence of visual feedback also need considerable attention in future studies, especially in the context of long term correlations in sequential data (Wing et al. 2004). The question of what the upper bound is for the force escalation effect is also likely to be an important topic of research in the future.

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2.7 – FIGURE APPENDIX

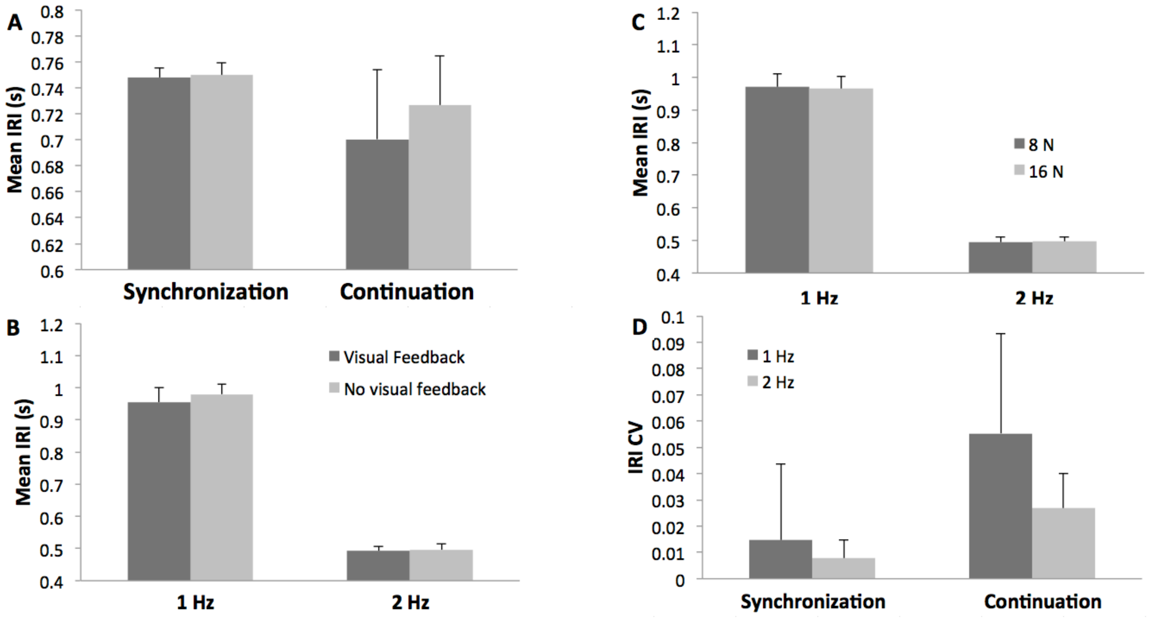

Figure 2.1. (**A**) Mean IRIs for synchronization and continuation timing conditions are plotted for both visual feedback conditions. (**B**) Mean IRIs for both movement frequencies (1 and 2 Hz) for the two visual feedback conditions. IRI decreased with continuation timing as well as with the faster movement frequency. However, mean IRI increased in the absence of visual feedback of force output only in continuation timing and 1 Hz movement frequency conditions. (**C**) Mean IRIs for both movement frequencies for the 8 N and 12 N force targets. Timing ability was influenced idiosyncratically depending on force and movement frequency. (**D**) IRI CVs for synchronization and continuation timing conditions the slow and fast movement frequencies. IRI variability was larger in the 1 Hz condition and increased for both movement frequencies in the continuation timing condition. In all plots, error bars stand for one SD.

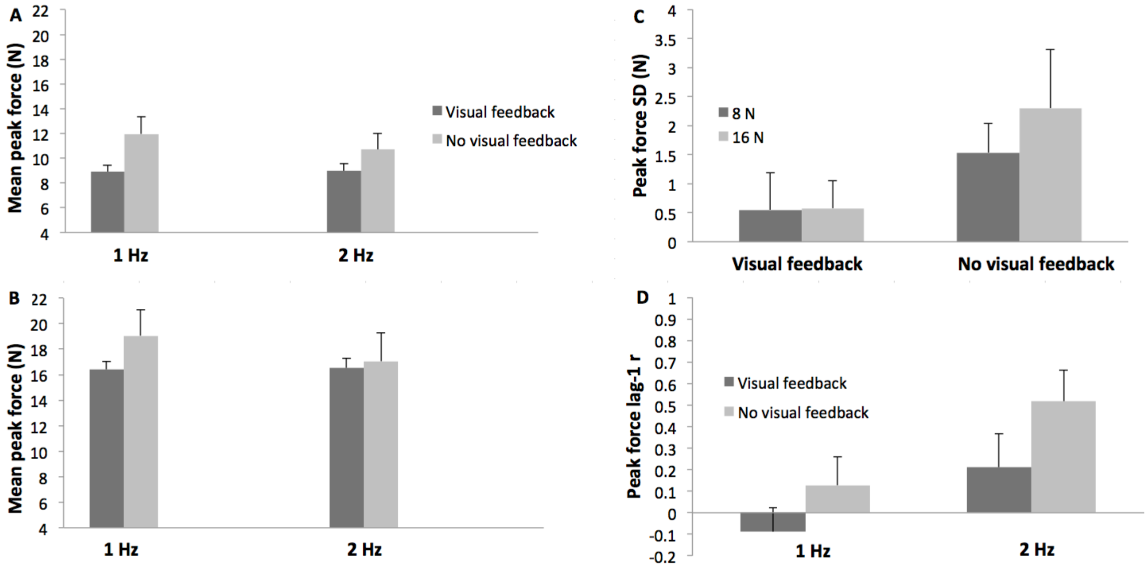

Figure 2.2. (**A-B**) Mean force output for the 8 N (**A**) and 16 N (**B**) target forces in the 1 and 2 Hz movement frequencies are plotted for both visual feedback conditions. For both force targets and movement frequencies, mean PF increased in the absence of visual feedback of force output. In the absence of visual feedback however, mean PF decreased with the higher 2 Hz movement frequency. (**C**) PF SDs for both visual feedback conditions for the 8 N and 16 N target forces. Irrespective of target force magnitude, PF variability increased in the absence of visual feedback. Without visual feedback, however, PF variability increased with target force magnitude. (**D**) Peak force lag-1 r values for both the 1 and 2 Hz movement frequencies are plotted for the two visual feedback conditions. For both movement frequencies, PF lag-1 r becomes more positive in the absence of visual feedback. For both visual feedback conditions, mean PF lag-1 r also becomes more positive for the faster movement frequency. In all plots, error bars stand for one SD.

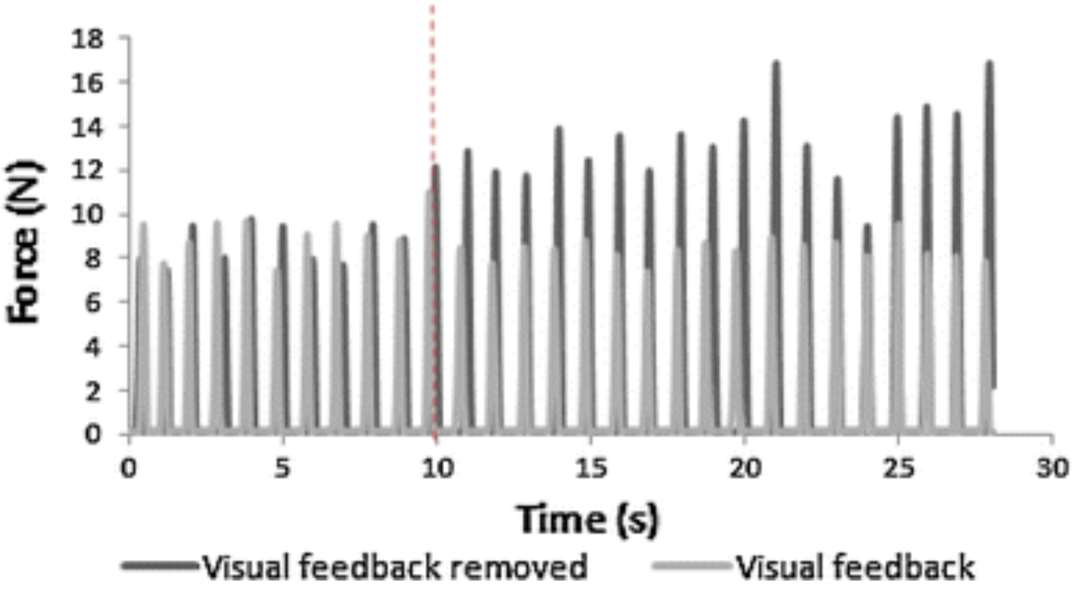

Figure 2.3. Visualizing the data: Sample force time series from one participant in the 1 Hz, continuation condition with a target force of 8 N. The vertical dotted line indicates the time at which visual feedback of force output and the pacing metronome were removed. Note the systematic increase in the peak force levels after the removal of visual feedback.

CHAPTER 3: CONTINUOUS THETA-BURST STIMULATION REDUCES THE OVERPRODUCTION OF FORCES FOLLOWING REMOVAL OF VISUAL FEEDBACK

3.1 – ABSTRACT

Forward models, generated from the efference copies of motor commands, are thought to monitor the accuracy of ongoing movement. By comparing predicted with actual afferent information, forward models also aid in the differentiation of self-produced movements from externally generated ones. Many have proposed that a consequence of this comparison is attenuation of the predicted component of incoming sensory signals. Previous work from our laboratory has shown that following the removal of an external visual reference, discrete sequential forces exceed target values. Forces produced at the fingertip were perceived as weaker, which lead to a systematic, compensatory over-production of the magnitudes required. The relatively new repetitive TMS protocol of continuous theta-burst stimulation (cTBS) has been shown to reliably depress cortical excitability for a period following stimulation. If sensory attenuation mechanisms were responsible for the overproduction of forces found in our previous results, we hypothesized that reducing cortical excitability of M1 through application of cTBS would induce discrepancy between the efference copy generated and motor output produced. As a result, we expected the overproduction of forces following visual feedback removal would be reduced after receiving cTBS. Participants produced series of pinch grip forces in time to a metronome and to visually specified force magnitudes. Visual feedback of force output was extinguished 10 s into experimental trials and participants performed continued responses for the remaining 10 s. Results confirmed our hypothesis. Mean peak force and constant error were greater and more positive in the absence of visual feedback regardless of stimulation condition; however, the magnitude

of increase was significantly reduced following cTBS compared with baseline and sham conditions. Variability was not differentially affected by stimulation condition, increasing only with removal of visual feedback contingent upon the larger forces produced in these trials. Our findings provide further evidence to support the idea that TBS may differentially affect motor output and efference copy generation.

3.2 – INTRODUCTION

It has been proposed that a function of corollary discharge from primary motor cortex (M1) is to aid in the generation of forward models of the sensory outcomes of that action (Bays et al. 2006; Bays et al. 2005; Blakemore et al. 1998a,b; Blakemore et al. 2000; Shergill et al. 2003; Shergill et al. 2005; Voss et al. 2007, Wolpert 2007, Wolpert and Ghahramani 2000). These predicted sensory outcomes are compared with incoming afferent information as a means to evaluate the success of movement execution and also to differentiate self-produced from externally sourced feedback (Bays et al. 2006; Bays et al. 2005; Blakemore et al. 1998a,b; Blakemore et al. 2000; Shergill et al. 2003; Shergill et al. 2005; Voss et al. 2007, Wolpert 2007, Wolpert and Ghahramani 2000). It is argued that this comparison process results in an attenuation of the predicted component of incoming sensory information (Bays et al. 2006; Bays et al. 2005; Blakemore et al. 1998a,b; Blakemore et al. 2000; Shergill et al. 2003; Shergill et al. 2005; Voss et al. 2007). Furthermore, this attenuation has been deemed responsible for the reduced perception of self-generated feedback compared with that from an external source (Bays et al. 2006; Bays et al. 2005; Blakemore et al. 1998a,b; Blakemore et al. 2000; Shergill et al. 2003; Shergill et al. 2005; Voss et al. 2007).

Previous work from our laboratory has found evidence for the abovementioned mechanism in the production of repetitive, discrete force pulses (Therrien and Balasubramaniam 2010; Therrien et al. 2010). Following removal of visual feedback of force output, force levels produced with each pulse were greater than target magnitudes produced when visual feedback was provided. Along with force magnitude, variability of the forces produced was also greater in these conditions. In the absence of an external reference, the forces produced were perceived as weaker leading to a systematic, compensatory over-production of the force magnitudes relative to the intended target. The results suggested that proprioceptive feedback alone was insufficient to guide the accurate production of target force magnitudes. In our task, visual feedback served to parameterize the proprioceptive system to ensure the appropriate production and scaling of force output.

Our experimental paradigm differs from those employed in previous studies of sensory attenuation mechanisms in that we do not make use of a purely externally generated stimulus. Previous literature discussing attenuated perception of self-produced feedback used forces or tactile stimuli that were applied either by the experimenters or with a robot arm (Bays et al. 2006; Bays et al. 2005; Blakemore et al. 1998a,b; Blakemore et al. 2000; Shergill et al. 2003; Shergill et al. 2005; Voss et al. 2007) The notion of visual feedback serving as an external reference in the calibration of proprioceptive feedback, however, has been noted in previous work (Withagen and Michaels 2004, 2005; Streit et al. 2007a,b). Studies of the size-weight illusion are perhaps the most common example, where the visually larger of two equally weighted objects is perceived as being lighter. Furthermore, studies of rod wielding paradigms have noted that manipulation of visual feedback can calibrate judgments of length using dynamic touch and also induce errors in perceptions of heaviness (Withagen and Michaels 2004, 2005; Streit et al. 2007a,b).

Transcranial magnetic stimulation (TMS) is an experimental technique that has grown in popularity over the last decade. While single pulses of TMS are useful in measuring corticospinal excitability, repetitive stimulation paradigms are used as a means to influence cortical excitability for periods of time following stimulation. The relatively new repetitive TMS protocol of continuous theta-burst stimulation (cTBS) has been shown to reliably depress cortical excitability for 20-60 minutes following stimulation (Huang et al. 2005; Huang and Rothwell 2004). A recent study by Voss et al. (2007) used cTBS to temporarily reduce excitability of the left M1in a force matching task. Using a force transducer and torque motor, forces of known magnitude were generated on participants' right or left index fingers. Subjects were then asked to reproduce the force level they just experienced using the opposite index finger. Results showed that in pre-TBS sessions, participants consistently over-estimated the force levels experienced. Following cTBS, however, forces produced by the right index finger were much closer to the actual target values. The authors attributed these results to cTBS inducing a mismatch between the efference copy generated and the motor commands sent to the finger, causing less attenuation of self-produced feedback.

If sensory attenuation mechanisms were responsible for the overproduction of forces noted in our own previous work (Therrien and Balasubramaniam 2010; Therrien et al. 2010), it is possible that a reduction in cortical excitability of contralateral M1 could induce a similar reduction in positive force errors following removal of visual feedback. The objective of the present study was to investigate the effect of a 40 s train of cTBS (cTBS600) to M1 on the performance of our repetitive, discrete force production task. Application of cTBS600, was compared with baseline performance (no TMS) and a sham stimulation condition. We hypothesized that application of cTBS600 to the left hemisphere of M1, would induce discrepancy between the efference copy generated and motor output. As a result, we expected that the overproduction of force magnitudes following visual feedback removal would be reduced following cTBS600 stimulation, but persist in baseline and sham conditions.

3.3 – METHOD

3.3.1 Participants

Twelve participants volunteered for this study (6 male, mean age: 22.4 yrs). All participants were students at McMaster University and were right handed according to both self report as well as the Edinburgh Handedness Inventory (mean laterality index: 88.3 ; Oldfield 1971). Participants reported no known neurological impairments or musculoskeletal impairments to the upper extremities. All had normal or corrected to normal vision at time of experimentation. All participants were screened by means of a standardized questionnaire to ensure compliance with safety standards regarding receipt of TMS (Wasserman 1998). The study was conducted in accordance with the Declaration of Helsinki and the protocol was approved by Hamilton Health Sciences/McMaster University Faculty of Health Sciences Research Ethics Board.

3.3.2 Apparatus

We used the same apparatus from Therrien and Balasubramaniam (2010). A 6 degree of freedom load cell (ATI Nano 17) mounted on a vertical stainless steel t-stand was used to collect the force data. Forces were applied on the axis perpendicular to the gripping surface (z axis). The stand was fixed to the table surface in front of a 19in, Viewsonic LCD flat panel computer monitor (refresh rate of 60 Hz), which provided participants' force contingent visual feedback. Force data were sampled at 1000 Hz with custom written Labview software (Labview 8.2, National Instruments). Load cells were calibrated with a factory generated 6x6 matrix describing the signal gain between voltage and resolved forces. This also allowed for correction of crosstalk between each measured force and moment arm. An AMTI amplifier was used to bolster voltage signals, which were then digitized with the National Instruments PCI-6220 DAQ. The ultimate resolution was 1/320 N in the z-axis. There was no hysteresis in the zero level of the resolved forces, which indicated no significant drift or offset in the force data associated with continued use of the device.

3.3.3 Experimental Protocol

We used a modified version of the repetitive force production task developed for Therrien and Balasubramaniam (2010). Participants sat in a chair with their right forearm resting on adjustable armrests on a table. They were positioned so they could comfortably reach the load cell and perform the pinch grip motion with the wrist in neutral position and no discomfort to the upper extremity. During the experiment, participants were presented with a visually specified target force of 16 N and were asked to match it by pinching the force transducer between the right thumb and index finger. The force target was presented as a column in a bar plot on the computer monitor, which was placed at a comfortable distance in front of the participant. Vertical axis labels gave participants additional information about the absolute magnitude of force. A second adjacent column represented participants' force output. Its height was contingent upon the force produced with each pinch on the load cell. The system gain was set so that a 1 N force caused a 1 cm increase in the height of the second column.

Participants were instructed to match the target force magnitude by modulating the force level produced with each pinch on the load cell. The movement rate was specified with an auditory metronome set at 2 Hz (500 ms intervals between sounds). Participants were to time each pinch with the sound of the metronome. All trials lasted 20 s. In experimental conditions (NVF), visual feedback of the target as well as the participants' current force output were removed after 10 s. Participants were asked to continue pinching the load cell, in time with the metronome, at the same force level for the remainder of the trial. In control conditions (VF), visual force feedback remained present throughout the trial. Participants were given up to 5 practice trials with each condition prior to data collection in order to familiarize themselves with the task and experimental apparatus. During data collection all conditions were presented in a pseudo-randomized order with each condition being performed twice before beginning the sequence over. The protocol was split into three sessions each performed on different days. One session tested baseline performance of the task without TMS (BL). The second session had participants undergo 40 s of cTBS prior to completing the force production task (TBS). The third session involved a sham stimulation, where the active coil was placed away from the skull and a second, inactive coil was held over participants' heads (Sham). The order of these sessions was randomized and counterbalanced across participants. Ten repetitions of each condition were performed yielding a total of 60 trials per participant after the three stimulation conditions.

3.3.4 TMS procedure

Single pulses of focal TMS were delivered with a figure of eight coil (Magstim Comp., Oakville, ON; external diameter of each coil: 9 cm) and used to elicit motor evoked potentials (MEPs) in the first dorsal interosseous muscle (FDI) of the resting right hand. The coil was oriented tangential to the head, at an angle of approximately 45 degrees from the anterior-posterior axis with the handle pointing to the posterior. MEPs were recorded using Ag/AgCl sintered electrodes placed over the FDI muscle belly and tendon, with the ground electrode placed on the Olecranon process of the elbow. The optimal stimulation site of the skull was determined as the cortical location were MEPs of 50 μV in peak-peak amplitude could be evoked in 5/10 trials, with the lowest possible stimulator output. The position was marked using Brainsight software (Brainsight 2.1.4, Rogue Research, Montreal, Canada) to allow for accurate repositioning throughout the experimental sessions.

Once the optimal stimulation site was determined, participants were asked to perform three maximum voluntary contractions (MVC) of the FDI muscle, by pinching a handheld force gauge (Baseline Evaluation Instruments 12-0235, White Plains, NY) between the right thumb and index finger. Experimental MVC was taken as the average of the three trials. Single pulses of TMS were then delivered while participants held isometric contractions at 20% of their MVC (visual feedback was provided to ensure accurate force output). Active motor threshold (AMT) was determined as the lowest stimulator intensity sufficient to produce MEPs greater than 200 μV above background EMG in at least 5/10 trials.

Continuous theta-burst stimulation (cTBS) was used for the repetitive stimulation phase of the experiment. cTBS involves continuous trains of pulses delivered in bursts of three at 50 Hz (20 ms between pulses) with a burst frequency of 5 Hz (200ms between bursts; Huang et al. 2005; Huang and Rothwell 2004). cTBS was delivered at 80% of AMT for a duration 40 s (a total of 600 pulses). This protocol is known as cTBS600 and depresses M1 cortical excitability in the stimulated area for up to 60 min following stimulation (Huang et al. 2005). Determination of the optimal cortical stimulation site and AMT remained the same in sham stimulation sessions. Repetitive stimulation, however, was performed with a second inactive coil placed over the participants' skull while the active coil was placed behind and oriented away from the head. This served to minimize perceived changes in location of the stimulator sounds between TBS and Sham conditions. Both TBS and Sham sessions were separated by at least 24 hours to ensure that participants received no more than 800 TMS pulses per day, conforming to previously determined safety guidelines (Wasserman 1998).

3.3.5 Data Analysis

Force data were stored separately for offline analysis. A custom script in MATLAB^{TM} extracted the peak force magnitude produced with each pinch on the load cell as well as the sample iteration and time at which they occurred. From these data, trial means were computed. The mean force produced was determined as the mean peak force produced in each trial. Variability was quantified using measures of coefficient of variation (CV). Errors in force output were analyzed using measurements of constant error. Lastly, the force series produced in NVF trials was broken down into mean peak force values for two trials phases: before feedback removal (t = 0-10 s) and after feedback removal (t = 11-20 s). As participants were not informed of condition prior to each trial, only data from the continuation phase was used for analysis (i.e. t = 10-20 s). Means were calculated across 10 repetitions per condition as well as across the 12 participants.

3.3.6 Statistical Analysis

SPSS software (SPSS 16.0, Chicago, IL) was used to conduct separate analysis of variance (ANOVA) with repeated measures for each dependent variable. Forces produced as well as their variability were assessed using factors of stimulation condition (BL, Sham, TBS) and visual feedback condition (VF, NVF). ANOVA with repeated measures was also used to compare mean peak forces in the two phases of the NVF trials with factors trial phase (t=0-10 s, t=11-20 s) and stimulation condition (BL, Sham, TBS). Post-hoc means comparisons were performed using Tukey's HSD.

3.4 – RESULTS

The average force-time series obtained from our data can be seen in Figure 3.1. Force-time series from VF trials are plotted in Figure 3.1A and series from NVF trials are plotted in Figure 3.1B. Analysis of mean peak force yielded a significant interaction among factors stimulation condition and visual feedback condition ($F(2,22) = 3.573$, $p < .05$, Figure 3.2A). Tukey's HSD tests showed that mean peak force was greater in NVF trials regardless of stimulation condition (p's <.01). Post-hoc means comparisons further revealed the interaction to be driven by the mean peak force in the NVF trials of the TBS condition, which was significantly lower than that produced in the BL and Sham conditions (p's < .01).

The ANOVA for peak force coefficient of variation yielded a significant main effect for visual feedback condition (*F*(1,11) = 65.571, *p* <.001, Figure 3.2B). Variability of the forces produced was greater in the absence of visual feedback.

Analysis of constant error produced a significant interaction among factors stimulation condition and visual feedback condition (*F*(2,22) = 3.575, *p* <.05, Figure 3.2C). Tukey's HSD tests revealed a general effect where errors were greater and more positive in the absence of visual feedback (*p*'s <.01). Post-hoc means comparisons also revealed the interaction to be driven by a significantly lower constant error in the NV trials of the TBS condition, compared to errors produced in the BL and Sham conditions (*p*'s <.01).

Analysis of the mean peak forces produced in the two phases of NVF trials (before and after visual feedback removal) produced an interaction among factors trial phase and stimulation condition that neared significance (*F*(2,22) = 3.222, *p* = .059, Figure 3.3A). Mean force did not appear to differ across stimulation condition in the period prior to visual feedback removal. Following feedback removal, however, a trend was present where mean peak force was lower only in the TBS condition. The mean difference in force produced over these two phases also yielded a main effect for stimulation condition that neared significance (*F*(2,22) = 3.222, *p* = .059, Figure 3.3B). Once again a trend is present where the difference in mean peak force produced over the two trial phases was lower for the TBS condition, relative to BL and Sham.

3.5 – DISCUSSION

The objective of the present study was to determine whether application of a 40 s train of cTBS (cTBS600) to the FDI area of left M1 would influence the production of repetitive discrete pinch grip forces by the right hand. Based on our previous work, participants produce force magnitudes that exceed target values in the absence of visual feedback of force output. These results have been interpreted in the context of sensory attenuation mechanisms whereby self-produced forces are perceived as weaker, leading to a systematic overproduction of force magnitudes. Sensory attenuation mechanisms make use of forward models generated from efference copies of motor commands sent from M1. Voss et al. (2007) found that reducing excitability of M1, using cTBS, improved participants' force matching ability. The results were attributed to cTBS reducing the degree of sensory attenuation by inducing discrepancy between the efference copy and motor output. If attenuation of self-produced feedback was responsible for our previous results, we expected to see a reduction in the force overproduction effect in cTBS600 trials relative to baseline and sham conditions.

In accordance with our previous work, mean peak force produced, variability and constant error were all greater and more positive in the absence of visual feedback regardless of stimulation condition. Variability was not differentially affected by stimulation session. The overall increase in measures of CV associated with NVF trials, likely reflected signal-dependent noise contingent upon the larger forces produced (Wolpert and Ghahramani 2000). Interestingly the degree of increase in mean peak force was reduced following receipt of cTBS600. Analysis of constant error reflected these results showing a reduction in positive error in NVF trials of the TBS condition.

Furthermore, examination of the two phases of NVF trials revealed a trend where prior to visual feedback removal, mean peak force did not differ between stimulation conditions. While all conditions showed an increase in force output after visual feedback was removed, this increase was proportionately lower after application of cTBS600.

Overall, the present results support our hypothesis that cTBS600 to M1 would differentially affect force production relative to Sham and BL conditions. The findings also add strength to the notion that the force overproduction effect noted in our previous work may, at least in part, be the result of sensory attenuation mechanisms (Therrien and Balasubramaniam 2010; Therrien et al. 2010). As was suggested by Voss et al. (2007), it is possible that reducing excitability in the FDI area of left M1caused divergence between the efference copy generated and the motor output produced. As a result, following removal of visual feedback of force output, there was less overlap between predicted and actual feedback leading to a lesser degree of attenuation. Following the mechanism proposed in our previous work, less attenuation lead to a decrease in the degree of overproduction of forces.

We controlled for non-specific effects of receiving TMS by including a sham stimulation condition. In these sessions, participants underwent the same procedures to locate optimal stimulation sites and determine active motor threshold. The repetitive stimulation was delivered by orienting the active coil away from the participant’s head and placing a second inactive coil over the determined stimulation site. Participants did not report any perceived differences between the Sham and TBS conditions; however, it was only in the TBS condition that M1 excitability was altered. That mean peak force and constant error results were not significantly different between Sham and BL, but were significantly different in the TBS condition confirmed that the effects observed were the result of cTBS600 influence on motor cortical excitability.

One question that remains unclear from our data concerns the precise mechanism that gave rise to the incongruity between efference copy and motor output. As was suggested by Voss et al. (2007), cTBS must differentially influence the populations of neurons that generate these two products of neuronal processing. Di Lazzaro et al. (2005) found that unlike other transcranial magnetic stimulation protocols, cTBS did not change the overall excitability of corticospinal neurons. Instead it influenced cortical circuitry by altering the excitability of intracortical interneurons in M1 (Huang et al. 2005; Di Lazzaro et al. 2005). A possible explanation for our results then, is that motor cortical depression through cTBS may have stimulated changes in the processing of efference copy signals.

It has also been shown that repetitive TMS can influence a wider cortical area than just the stimulation site. Previous neuroimaging work has found that repetitive TMS to left M1 activated a network of areas outside the stimulation location, including dorsal and ventral premotor corticies (dPMC, vPMC), supplementary motor area (SMA) and contralateral (right) cerebellum (Bestmann et al. 2004; Okabi et al. 2003; Siebner et al. 2000). The cerebellum has been proposed as a likely site for the comparison between predicted sensory feedback from the forward model and actual incoming afferent information arising from movement execution (Blakemore et al. 1998b). Alternatively, Chronicle and Glover (2003) proposed that efference copies may be generated in areas upstream of M1, like premotor cortex. It is, therefore, also possible that sensory attenuation mechanisms could have been manipulated by spreading activation to cerebellar and premotor areas.

Interesting to note, however, was the slight reduction in force output following receipt of TBS even when visual feedback was presented. Although this difference was not statistically significant, it may provide some support for the role of M1 in the encoding of force as was originally proposed by Evarts (1968). It remains a possibility then, that M1 stimulation in our experiment could have induced discrepancy between efference copy and motor command by influencing force output directly.

The present study only tested performance of the limb contralateral to the stimulation site. Many studies have shown that repetitive TMS protocols also induce activity in the contralateral hemisphere of M1 and can modulate excitability of ipsilateral fibres in the corticospinal tract (Chen et al. 2003; Cincotta et al. 2006; Siebner et al. 2000; Trompetto et al. 2004). It would be interesting to expand upon the findings of the present study by including analysis of the performance of the hand ipsilateral to the stimulated hemisphere of M1.

In summary the primary finding of this study was that reducing excitability of M1 neurons, through application of cTBS600, produced a reduction in the overproduction of forces following removal of visual feedback. Force output in NVF trials was not significantly different in BL and Sham conditions; with both showing a greater magnitude of positive errors in force compared to TBS trials. These results add strength to our conclusion that the overproduction of forces seen in our previous work is the result of sensory attenuation mechanisms affecting perceptions of self-produced feedback.

cTBS600 stimulation served to disrupt sensory attenuation processes by creating incongruity between predicted and actual afferent information. While the exact mechanism of this influence remains uncertain, our results add to those of Voss et al. (2007) showing that cTBS differentially affects the populations of neurons that produce the efference copy and those that generate motor output. Furthermore, we also provide yet another example of the utility of repetitive TMS protocols in studying the effects of virtual lesions to M1 on the performance of behavioral tasks.

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3.7 – FIGURE APPENDIX

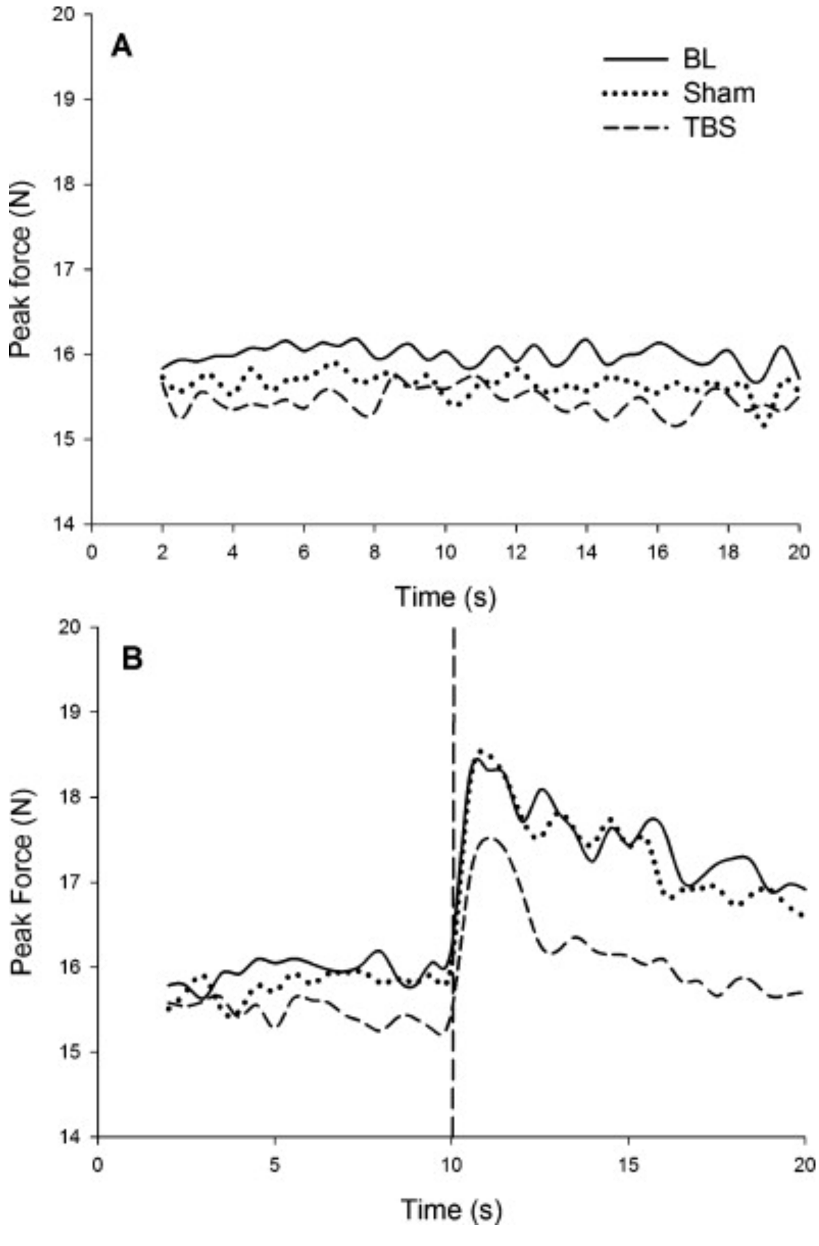

Figure 3.1. The force time series produced in VF (**A**) and NVF (**B**) trials of the three stimulation conditions, grand averaged across participants. The vertical dashed line denoted the time at which visual feedback was removed in NVF trials.

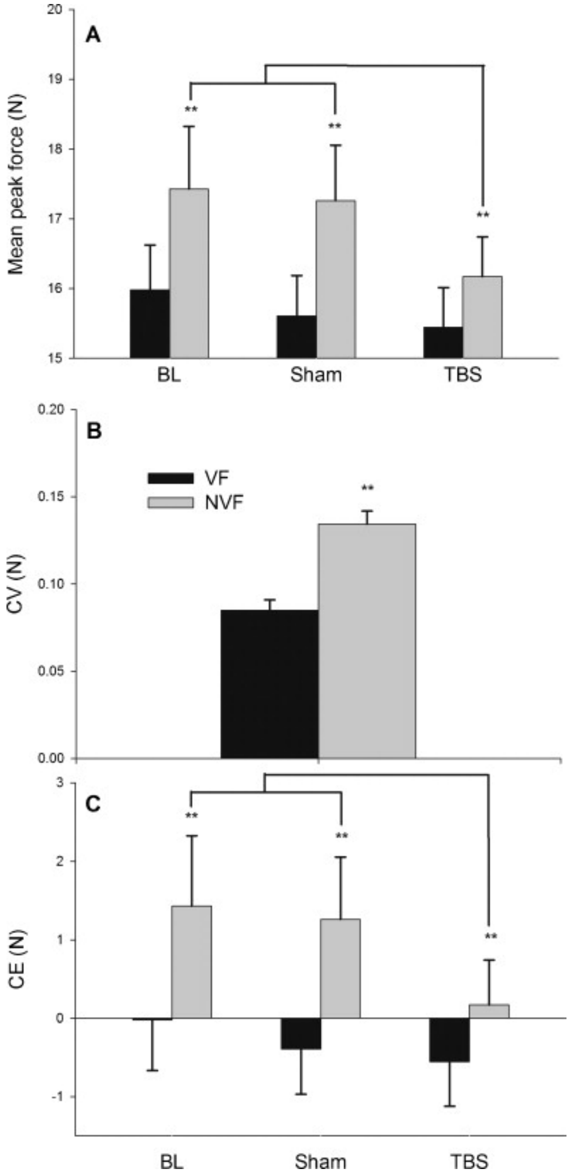

Figure 3.2. (**A**) Interaction among factors of visual feedback and stimulation condition for mean peak force. (**B**) Main effect of visual feedback for measures of coefficient of variation. (**C**) Interaction among factors visual feedback and stimulation condition for measures of constant error. In all cases, asterisks and connecting lines denote reliable pairwise comparisons, significant at $p < .01$.

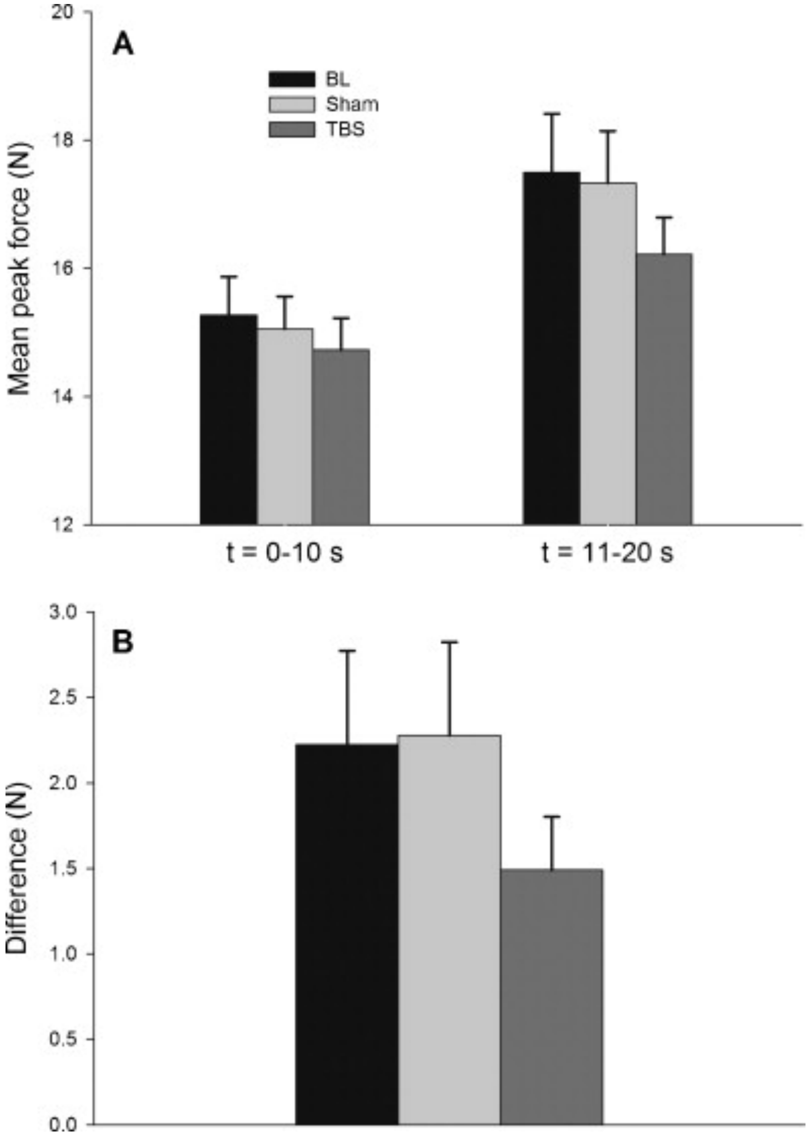

Figure 3.3. NVF trials were divided into two phases corresponding to the period of time prior to visual feedback removal (t = 0-10 s) and the period of time from feedback removal to the end of the trial (t = 11-20 s). (**A**) Non-significant interaction among factors trial phase and stimulation condition for mean peak force (*p* = .059). (**B**) Non-significant main effect for stimulation condition on the difference between mean peak forces produced in the two phases of NVF trials (*p* = .059).

CHAPTER 4: REPETITIVE FINGER FORCE PRODUCTION IN PREDICTABLE ENVIRONMENTS

4.1 – ABSTRACT

Previous research suggests that removal of visual feedback of force output in a sequential force production task, results in a continuous escalation of the force magnitudes produced. Central predictive mechanisms involving reafference result in self-generated forces being perceived as weaker, thus leading to a systematic over production of force. While this effect has been widely examined with respect to sensation of self-produced stimuli, its role in the sequential production of discrete forces has not been extensively studied. The objective of the present experiment was to further investigate the force escalation effect by examining the sequential force production task in two predictable environments where force targets progressively changed between 8 and 16 N. In one environment target force magnitudes continually increased at a predictable rate, while in the second target force magnitudes decreased at the same rate. Eight healthy participants produced a series of repetitive pinch grip forces in time to a metronome at a frequency of 2 Hz. Visual feedback of force output was removed 10 s in to the trial, with participants performing continued responses for the remaining 20 s. Following removal of visual feedback participants rapidly accrued errors in force magnitude, but slopes of the peak force series did not differ from those of the target series. Errors in magnitude were bi-directional, showing dependence on the increasing or decreasing environment in which the task was performed. The escalation and de-escalation effect observed can both be attributed to central predictive mechanisms and the force salience effect in reafference.

4.2 – INTRODUCTION

All interactions between an organism and its environment are dependent on the ability to distinguish self-generated sensory information from that which has an external source. It has been reliably shown that self-generated tactile stimuli are perceived as weaker than external stimuli of the same magnitude (Bays et al. 2006; Blakemore et al. 1998; Blakemore et al. 2000; Shergill et al. 2003; Voss et al. 2007). Many researchers have proposed that information from the motor command is used to distinguish the consequences of self-produced actions from externally sourced stimuli (Shergill et al. 2003; Voss et al. 2007). Specifically, a predictive mechanism has been proposed where a forward model (constructed from the efference copy of a motor command) anticipates the sensory consequences of an action (Bays et al. 2006). The predicted component is thought to be subtracted from the incoming sensory information, effectively attenuating the self-generated feedback (Bays et al. 2006; Blakemore et al. 1998; Blakemore et al. 2000; Shergill et al. 2003; Voss et al. 2007).

Sensory attenuation with self-produced stimuli has been documented in discrete and isometric force production tasks (Bays et al. 2006; Shergill et al. 2003; Voss et al. 2007), but this effect has not been extensively studied in sequential force production. Previous work by Therrien and Balasubramaniam (2010) suggested that when visual feedback of force output was removed in a sequential force production task, the magnitude of the produced forces increased with time. This effect was interpreted in the context of predictive mechanisms involving reafference. Self-generated forces were perceived as weaker leading to a systematic, compensatory over-production of the force magnitudes required (Shergill et al. 2003; Therrien and Balasubramaniam 2010; Voss et al. 2007). In the previously noted experiment, target force magnitudes remained constant throughout the trial. However, in most natural force production settings, such as when hammering a nail or playing the piano, we often have to scale the produced forces to target requirements. Said differently, one has to adjust the relationship between successive forces in order to produce forces of equal, less or greater magnitude. The slope of any given force time series (the rate of change) is a good indicator of how two adjacent forces are scaled within a time series.

The objective of the present experiment was to further investigate the force escalation effect by examining the sequential force production task in two predictable environments where force targets progressively changed between 8 and 16 N. To set up the experimental conditions, we modified the repetitive force production task used by Therrien and Balasubramaniam (2010). In the present experiment, pinch grip forces were rhythmically produced in two target force ramp conditions. In two conditions the target force levels increased or decreased at a constant rate throughout the trial. Consistent with the mechanism proposed in earlier results (Shergill et al. 2003; Voss et al. 2007) we predicted that regardless of the target force ramp condition, following removal of visual feedback of force output, the magnitude of the forces produced would change. If the force output to perceived to be lower than the target (due to reafference) and the target force required on the next iteration is higher, the participant would produce an even larger force that leads to escalation. In the downward ramp, the expectation of the task dictates that the force produced in a subsequent iteration is less than the previous iteration. If the force produced in the previous iteration is perceived to be less than it actually is, the level produced in the subsequent iteration will be even less thus leading to a reduction in force magnitudes (de-escalation).

In experimental terms, we made the following predictions. In the condition where the target force level was increasing throughout the target, we predicted that the removal of visual feedback would result in a further increase in the force production levels from the target (escalation effect). Conversely, in the decreasing ramp condition, we predicted that the magnitude of forces produced will be lower than those required by the target (de-escalation effect). As we did not expect visual feedback to play a role in the relative scaling between forces, we did not expect to see any changes in the slope of the force series produced by the participants and the target force series.

4.3 – METHOD

Eight healthy participants (six male, two female) volunteered for this experiment. All were students from McMaster University and were right handed according to both self-report as well as the Edinburgh Handedness Inventory (Oldfield 1971). Participants were free of any known neurological impairment or musculoskeletal impairments to the upper extremities and had normal or corrected normal vision. In keeping with the Declaration of Helsinki, prior to participation, volunteers gave their informed consent in accordance with McMaster Research Ethics Board regulations.

Similar to the apparatus used in Therrien and Balasubramaniam (2010), force data were collected using a 6-DOF load cell (ATI Nano 17) mounted on a stainless steel stand so that forces were applied on the horizontal (z axis). The apparatus was fixed to a table with a computer monitor placed behind for subject's feedback. Force data were sampled at 1,000 Hz with data acquisition hardware (National Instruments DAQ- card-6024E) using custom software written with Labview (Labview 8.2, National Instruments). This software was customized to provide visual feedback to the subjects on a Viewsonic 19 in. flat panel display with a refresh rate of 60 Hz. The force transducers were calibrated with a 6 x 6 matrix that describes the relation of voltage gain to resolved force. The factory-generated calibration matrix allowed for correction of crosstalk between each measured force and moment axis. Furthermore, signals were amplified with the packaged AMTI amplifier, and signals digitized with the National Instruments PCI-6220 DAQ. This combination of voltage amplification and 16-bit resolution of a DAQ lead to an ultimate resolution of 1/320 N in the z axis. There was no hysteresis in the zero level of the resolved forces, which indicates no significant drift or offset in the force data due to ongoing use of the apparatus. The gain was set so that a change in force output of 1 N corresponded to a 1 cm change in amplitude.

Participants were seated in a comfortable, non-rotating chair with their right forearm resting on a table. They were positioned so that they could comfortably reach the force transducer and successfully perform the pinch grip (between the thumb and index finger) motion on it. During each testing session, participants were given a visually specified target force and were asked to match the target force magnitude by pinching the force transducer between the right thumb and index finger. The magnitude of the target force was presented as a column in a bar graph on the flat panel display placed at a comfortable distance in front of the participant. A second column adjacent to the target bar represented the current force output produced by the participant. Force levels produced were indicated by changing amplitudes with each press on the load cell. To produce the ascending and descending target force ramps, the amplitude of the target column changed 100ms before each subsequent pinch. Participants were instructed to continually match their force output with the magnitude specified by the target column by modulating their grip force with each press.

All test participants were given five practice trials with both ramp directions (ramp up and ramp down) and full visual feedback of their force output. Following this, experimental conditions were presented in a blocked manner. For a given ramp direction, participants were tested with full visual feedback prior to being tested with trials where it was removed. Participants were also counterbalanced for exposure to target ramp direction. A metronome specified movement rate with a frequency of 2 Hz, corresponding to time intervals of 500 ms between peak forces. Each trial lasted 30 s. In certain experimental conditions, visual feedback of both the current force output and target force amplitude was removed 10 s in to the trial. Participants were instructed to make continued responses for the remaining 20 s and increase or decrease their force output on each press attempting to match the rate of change of the target force ramp presented in visual feedback trials as well as the first 10 s of the trials where visual feedback was removed. Thus there were two visual feedback conditions (visual feedback and no visual feedback). Five repetitions of each condition were performed to yield a total of 40 trials per participant.

Force data were stored for offline analysis using a customized PC workstation. A custom written program in MATLAB^{TM} extracted the peak force (PF) magnitude from each pinch on the force transducer, as well as the iteration and time at which is occurred. PFs were extracted to quantify the magnitude of force produced to be compared against the target force level. Mean PF time series were then computed for each participant and group means were compiled for each ramp condition. Variability in performance was quantified through calculation of constant and variable error. Only the continuation phase (t = 10-30 s) from each trial was used for analysis. Means were calculated across 5 repetitions per condition as well as across participants. SPSS^{TM} software was used to conduct separate analysis of variance (ANOVA) with repeated measures for constant and variable error values in the two target force ramp conditions as well as independent samples t-tests comparing slope and intercept values between PF series produced by participants to those of the target PF series.

4.4 – RESULTS

The PF time series produced in the increasing and decreasing ramp conditions can be seen in Figure 4.1. Bi-directional errors in force magnitude were observed for the two ramp directions once visual feedback of force output was removed. In the ramp up direction, this resulted in the development of positive errors in force magnitude. In the ramp down direction, however, the opposite trend was noted. Once visual feedback was removed, participants' force output was continually lower than target magnitudes. Except for one subject who constantly overproduced the force levels, there were very few inter-individual differences in performance. We recognized the presence of this outlier in our subject data (see Figure 4.1B and D). However, analysis of the data after removing data from this subject revealed no major differences in the results obtained. Considering this, we included all the data from all eight subjects in our analyses.

This effect is further illustrated in Figure 4.2. A set of 2 (ramp conditions: ramp up and ramp down) x 2 (visual feedback conditions: full and no) ANOVAs with repeated measures revealed an interaction between ramp direction and visual feedback condition for mean constant error in the continuous ramp condition (Figure 4.2A; $F(1,7) = 42.55$, $p < .001$, $\eta^2 = 0.86$) . Constant error values were low and did not differ between ramp directions when visual feedback of force output was present throughout the trial. In trials where visual feedback was removed, however, the direction of errors was dependent on the ramp direction. In ramp up trials, mean constant error was positive, demonstrating that participants consistently over produced force in these trials. In ramp down trials, mean constant error was negative, indicating a continual undershooting of target force magnitudes. Despite this trend, it should be noted that the difference in constant error values between the full and no visual feedback conditions in the ramp down condition was not statistically significant. 2 x 2 ANOVAs with repeated measures were also performed for both target force ramp conditions on mean variable error. Figure 4.2B illustrates the interactions obtained for both conditions ($F(1,7) = 28.00$, $p < .01$, $\eta^2 = 0.80$). In both cases, regardless of ramp direction, mean variable error remained low and constant in the presence of visual feedback of force output. When visual feedback was removed however, an overall increase in variable error was observed, but was smaller in the ramp down direction.

To further assess these dependencies on ramp direction, independent samples t-tests were performed comparing participants' mean slope and intercept values with those of the target peak force series. Analysis of mean slope revealed a significant difference between participant and target series only in the ramp down direction, when visual feedback was removed ($t(14) = 2.41, p < .05$), Mean slope values were less steep than the target peak force series, suggesting that the result was likely due to floor effects in participants' ability to decrease their force output further.

Analysis of the mean intercept did not reveal any differences between participant data and the target force, suggesting that at the time that the visual feedback was extinguished, participants produced target forces in the range of the required force level. We chose to do the simpler analyses of slope rather than use time-series methods such as ARMA/ARIMA to look for trends for two reasons. First, our analysis adequately served to demonstrate that the (de)escalation effect resulted in increase or decrease in error accrual. Secondly, with only forty peak force observations after the visual feedback is removed, complex time series analyses (such as rescaled range analyses) are likely to be less reliable and informative (Delingieres et al. 2006).

To test the time dependency in error development following removal of visual feedback of force output, we did the following analyses. Constant error values were calculated for three time points: 10 s, 20 s and 30s. A repeated measures ANOVA was performed with the factors 3 (time points: 10, 20 and 30s) x 2 (ramp conditions: ramp up and ramp down) x 2 (visual feedback conditions: full and no). The interaction obtained is shown in Figure 4.3. A significant interaction was obtained between ramp direction, visual feedback condition and time point ($F(2,14) = 41.74, p < .01, \eta^2 = 0.53$) The bi-directional errors in force magnitude were again observed for the two ramp conditions in the absence of visual feedback of force output. While error values for the three time points did not differ when visual feedback was present, error values were dependent on the time at which they were measured after visual feedback was removed. For both ramp conditions a large increase in force magnitude error is noted between the 10 and 20 s time points. After the 20 s point however, the error stabilized confirming what was seen in the slope analyses.

4.5 – DISCUSSION

We predicted that reafference mechanisms reducing the salience of self-generated forces would result in errors in force magnitude in a sequential force production task. We expected to see evidence of this in consistently increasing positive errors in force magnitude following removal of visual feedback of force output in the ramp up condition. Almost immediately following removal of visual feedback, positive errors in force magnitude were made (see Figure 4.1B). This supported the notion of a predictive mechanism causing self-generated forces to be perceived as weaker. Participants produced more force than was required in order to compensate for the forces perceived to be weaker. In the ramp down direction the predicted trend was observed, but in the opposite direction. When target forces decreased in a predictable manner the trend was to under produce force following removal of visual feedback. In the context of the decreasing ramp, when subjects perceive that the force output in an earlier iteration was lower than it actually was, they compensated by producing even less on the subsequent iteration. Despite consistent errors in magnitude, that mean slope in both target force ramp direction conditions did not differ significantly from the slope of the target force series indicated that participants were able to accurately scale the relation between sequential forces. These results suggest that the escalation effect noted in the sequential force production tasks is not the result of accumulation of errors in the force production mechanisms themselves.

Similar preservation of accurate scaling relations but inaccurate force magnitude production in healthy individuals has been found in previous rhythmic force production tasks (c.f. Pope et al. 2006; Pope et al. 2005). This finding falls in line with evidence from functional imaging studies that the brain areas involved with controlling the magnitude of force output and scaling the relative magnitudes in a series of forces may be different. Control of force magnitude is associated with activation of primary motor and sensory areas, supplementary motor area, premotor and prefrontal areas, parietal and cingulate cortices and cerebellum (Cramer et al. 2002; Dai et al. 2001). However circuits involving the basal ganglia, specifically the subthalamic nucleus and internal segment of the globus pallidus, are activated when the accurate scaling of forces relative to one another is required (Pope et al. 2006; Pope et al. 2005).

Blakemore et al. (1998) have found neural correlates for the mechanism of reafference in self-produced stimuli using functional imaging. Stimuli from self-produced movements are associated with reduced activity in both the somatosensory cortex (S1) and cerebellum when compared with externally generated stimuli. The decrease in S1 activation correlates with neurophysiological data showing reductions in neuron activity following voluntary touch, compared to external touch of the same area (Cullen et al. 2004). The changes in S1 activity may have been mediated by the cerebellum, whose activity decreased when self-produced movements resulted in a tactile stimulus (Blakemore et al. 1998). Interestingly, cerebellar activation was not mediated by movement alone and showed increased activation when externally produced tactile stimuli were applied. Blakemore et al. (1998) took these results to suggest that the cerebellum distinguishes movements based on their specific sensory consequences. Voss et al. (2007) have shown that theta burst stimulation of the primary motor cortex during a force matching task results in decreases in the sensory attenuation known to occur with self-generated movements. Taken together, these findings further support the proposed distinction between the perception of force magnitudes and relative scaling between them in the brain.

Our results showing bi-directional changes in force magnitudes can also be explained in the context of central predictive mechanisms. It is well known that sensory input is highly variable due to noise present in the motor system and the differential manner in which self-produced and externally sourced stimuli are processed (Bays et al, 2006; Blakemore et al. 1998; Blakemore et al. 2000; Shergill et al. 2003; Voss et al. 2007; Wolpert 2007; Wolpert and Ghahramani 2000). It has been proposed that in addition to incoming sensory information, the CNS also makes use of knowledge from prior experience (Körding et al. 2004; Wolper 2007; Wolpert and Ghahramani 2000). A possible mechanism for this has been proposed using Bayesian integration, where it is hypothesized that the CNS optimally combines this prior knowledge with sensory inputs to generate a state estimate (Körding et al. 2004; Wolper 2007; Wolpert and Ghahramani 2000). Due to central modulation of incoming proprioceptive information, the self-generated feedback from each press on the load cell gave an unreliable estimate of the force produced when visual feedback of force output was absent (Pope et al. 2005). This sensory input was then combined with the prior knowledge that the target force series was increasing or decreasing in a predictable manner. Combination of the present state estimate of the motor output with prior knowledge of the target force series could also create an over-production effect in the ramp up condition and a de-escalation in the ramp down condition. Thus our results provide an interesting problem to model using Bayesian methods. Körding et al. (2004) have found evidence for Bayesian integration in force estimation in a task that required the production of an experienced force. The possibility of a similar mechanism working in a sequential task warrants further study. In all of these studies, an issue that remains unclear is whether the escalation of forces has an upper bound. This issue has not been looked at in the seminal paper of Shergill et al. (2003) or the present study.

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4.7 – FIGURE APPENDIX

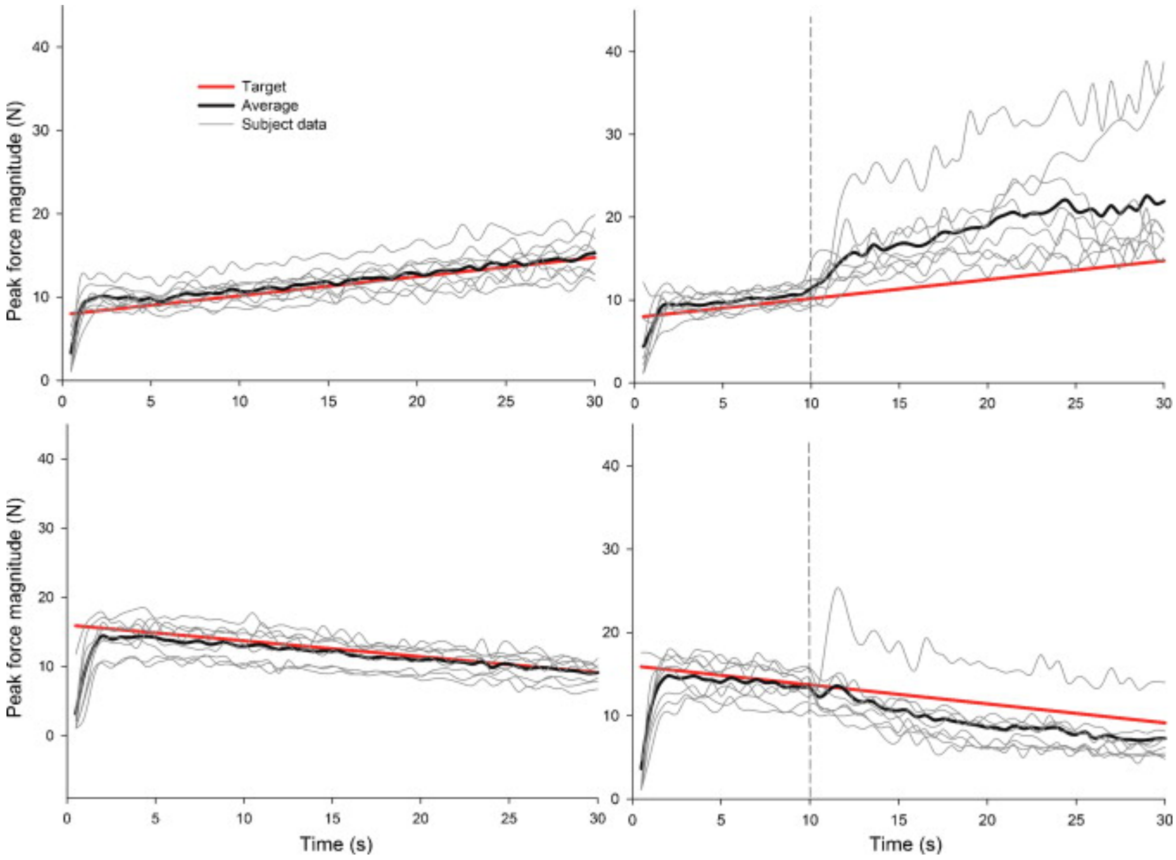

Figure 4.1. The peak force series are plotted for both ramp directions and visual feedback conditions. Top panel: Peak force series produced in the ramp up direction. Bottom panel: Peak force series produces in the ramp down direction. (**A**) and (**C**) Visual feedback remained present throughout the trial. (**B**) and (**D**) Visual feedback of force output was removed after 10 s. Vertical dotted lines indicate the time at which visual feedback was removed.

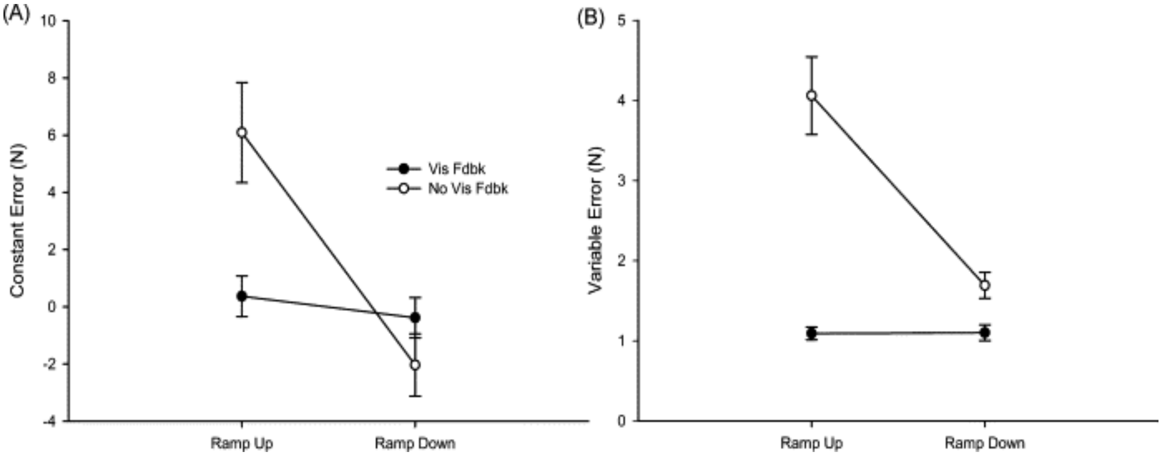

Figure 4.2. (**A**) Constant error values are plotted for both ramp directions as well as both visual feedback conditions. Removal of visual feedback resulted in a positive mean error in the ramp up direction, whereas it resulted in a negative mean error in the ramp down direction. (**B**) Variable error values are plotted for both ramp directions as well as both visual feedback conditions. In the absence of visual feedback, mean variable error decreased in the ramp down direction. Error bars indicate standard error of the mean.

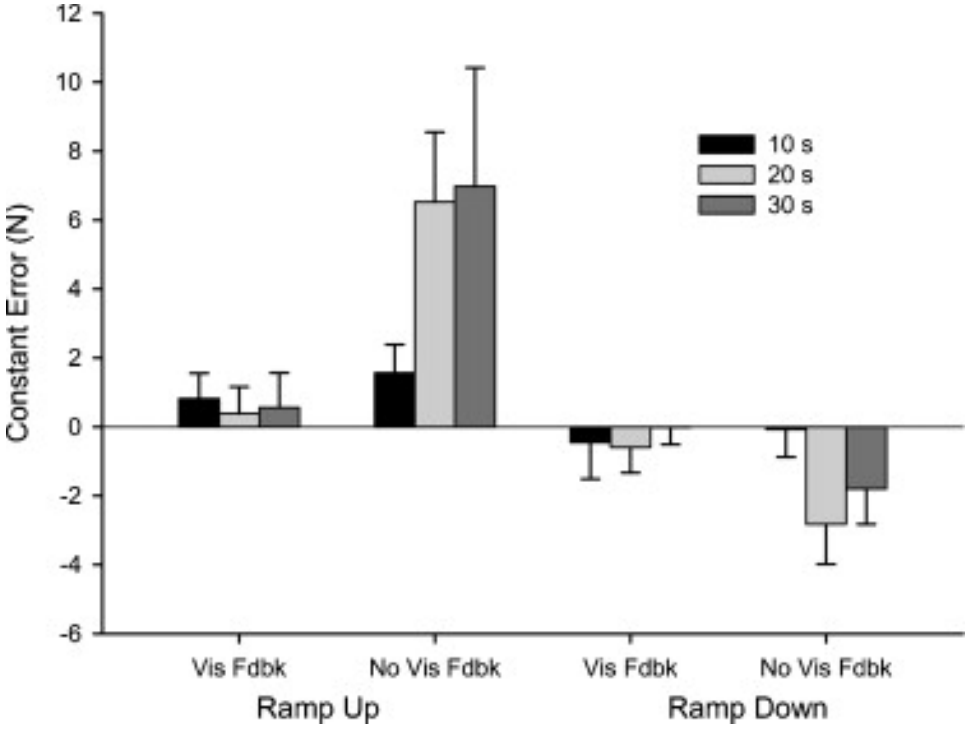

Figure 4.3. Constant error values at three time points (t = 10 s, 20 s and 30 s) are plotted for both ramp directions as well as both visual feedback conditions. Bi-directional errors in force magnitude are visible for the two ramp directions in the absence of visual feedback. Error values were also dependent on the time at which they were measured. There is an initial increase in errors between 10 and 20 s followed by stabilization of errors, although the force magnitudes keep increasing and decreasing.

CHAPTER 5: CONTINUOUS THETA-BURST STIMULATION TO PRIMARY MOTOR CORTEX REVEALS ASYMMETRIC COMPENSATION FOR SENSORY ATTENUATION IN BIMANUAL REPETITIVE FORCE PRODUCTION

5.1 – ABSTRACT

Studies of fingertip force production have shown that self-produced forces are perceived as weaker than externally generated ones. This is due to mechanisms of sensory reafference where the comparison between predicted and actual sensory feedback results in attenuated perceptions of self-generated forces. Without an external reference to calibrate attenuated performance judgments, a compensatory overproduction of force is exhibited. It remains unclear whether the force overproduction seen in the absence of visual reference stimuli differs when forces are produced bimanually. We studied performance of two versions of a bimanual sequential force production task compared to each hand performing the task unimanually. When the task goal was shared, force series produced by each hand in bimanual conditions were found to be uncorrelated. When the bimanual task required each hand to reach a target force level, we found asymmetries in the degree of force overproduction between the hands following visual feedback removal. Unilateral continuous theta-burst stimulation to the left primary motor cortex yielded a selective reduction of force overproduction in the hand contralateral to stimulation by disrupting sensory reafference processes. While variability was lower in bimanual trials when the task goal was shared, this influence of hand condition disappeared when the target force level was to be reached by each hand simultaneously. Our findings strengthen the notion that force control in bimanual action is less tightly coupled than other mechanisms of bimanual motor control and show this effector specificity may be extended to the processing and compensation for mechanisms of sensory reafference.

5.2 – INTRODUCTION

Previous work from our laboratory has shown that in the absence of a visual reference, self-generated, discrete, repetitive force pulses tend to exceed target magnitudes (Therrien and Balasubramaniam 2010, Therrien et al. 2011). This phenomenon of force overproduction has been attributed to mechanisms of sensory reafference affecting perceptions of self-produced, somatosensory feedback (Therrien et al. 2011). Specifically, it has been proposed that corollary discharge from the primary motor cortex (M1) is used in the generation of forward models of the sensory outcomes of a given motor act (Bays et al. 2006; Bays et al. 2005; Blakemore et al. 1998; Blakemore et al. 1998; Shergill et al. 2003; Voss et al. 2007; Wolpert and Ghahramani 2000). These sensory predictions are compared with incoming afferent information as a means of evaluating the accuracy of motor execution as well as to establish agency over self-generated movements. (Bays et al. 2006; Bays, et al. 2005; Blakemore et al. 1998; Blakemore et al. 1998; Shergill et al. 2003; Voss et al. 2007; Wolpert and Ghahramani, 2000). This comparison process is thought to result in attenuation of the predicted component of incoming afferent information, reducing the salience of self-generated sensory feedback (Bays et al. 2006; Bays et al. 2005; Blakemore et al. 1998; Blakemore et al. 1998; Shergill et al. 2003; Voss et al. 2007). In the case of fingertip force production, self-produced forces are perceived as being weaker. Without visual reference stimuli, to calibrate somatosensory performance judgments, participants exhibit a systematic overproduction of force to compensate.

Our previous work has examined only unimanual sequential fingertip forces. It remains unclear whether the systematic force overproduction seen in the absence of visual reference stimuli differs when forces are produced in a bimanual context. While strong coupling has been found between the limbs in studies of bimanual motor timing, the control of force in bimanual tasks seems to be less tightly coupled. Studies of both continuous isometric and repetitive force production have reported similar force output errors between unimanual and bimanual conditions (Davis 2007; Inui and Hatta 2002). In addition, Inui and Hatta (2002) provided unilateral visual feedback of either the dominant or non-dominant hands in a bimanual repetitive force production task and found that removal of this reference stimuli induced asymmetric effects on the force output of the two hands. Specifically, feedback of the dominant hand resulted in similar force output for the two limbs, but non-dominant limb feedback resulted in asymmetrical performance variability. Together, these results suggest that mechanisms compensating for visual feedback manipulations may operate independently for each limb in cases of bimanual force production.

In our task, comparison of the force overproduction effect between unimanual and bimanual contexts could provide insight into the nature of sensory reafference processing. If sensory reafference mechanisms function in an effector specific manner, each limb in a bimanual force production task should exhibit the force overproduction phenomenon, perhaps to differing extents, and show little correlation, or coupling, between the hands. Conversely, if these mechanisms encode context-specific information about the limbs in a bimanual task, some degree of coupling, or synergistic correlation, between them might be expected, similar to what has been found in previous studies of oscillatory multi-finger force production (Latash et al. 2001; Scholz et al. 2002). In our task, this coupling could differentially influence the force overproduction exhibited following removal of visual feedback. Here we focus on a bimanual extension of the sequential force production task employed by Therrien and Balasubramaniam (2010). Our objective was to test the hypothesis that, if the forces produced by the two limbs in a bimanual context are controlled asymmetrically, as previous literature suggests, then sensory reafference signals may also be processed asymmetrically for each limb in a bimanual force production task.

5.3 – METHOD

5.3.1 - Ethics Statement

The McMaster University Research Ethics Board and the Hamilton Health Sciences/McMaster University Faculty of Health Sciences Research Ethics Board approved the experimental protocols presented here. All participants provided informed consent prior to participation.

5.3.2 - Experimental Apparatus

Force data were collected using two 6 degrees of freedom load cells (ATI Nano 17) mounted on vertical stainless steel t-stands. Forces were applied on the axes perpendicular to the gripping surface (z axes) of each transducer. The stands were placed in parallel, approximately 22 cm apart, and fixed to the table surface in front of a 19 in., Viewsonic LCD flat panel computer monitor (refresh rate of 60 Hz) that provided participants' force contingent visual feedback. Force data were sampled at 1000 Hz with custom written Labview software (Labview 8.2, National Instruments). A factory generated 6 x 6 matrix, describing the signal gain between voltage and resolved forces, was used to calibrate each load cell. This calibration matrix also allowed for correction of crosstalk between measured forces and moment arms. An AMTI amplifier was used to bolster voltage signals, which were then digitized with the National Instruments PCI-6220 DAQ. The ultimate resolution of each transducer was 1/320 N in the z-axis. There was no hysteresis in the zero level of the resolved forces, which indicated no significant drift or offset in the force data associated with continued use of the device.

5.3.3 - Bimanual Sequential Force Production Task

Participants sat in a chair with both forearms resting on adjustable armrests, located in front of each force transducer, on a table surface. They were positioned so they could comfortably reach each load cell with the appropriate arm and perform the pinch grip motion with the wrists in neutral position. During each experiment, participants were presented with a visually specified target force level, of either 8 N or 16 N, in the form of a column in a bar plot. They were asked to match this force level by repetitively pinching either one or both of the load cells between the thumb and index finger of the right hand only (UR), left hand only (UL) or both hands simultaneously (Bi). Participants were to synchronize their pinch rate with an auditory metronome set to 2 Hz (corresponding to 500 ms between sounds), which remained present throughout each trial. Each pinch of the load cell modulated the height of a second column, adjacent to the target column, on the bar plot in manner contingent upon the force level produced. The goal of the task was to match the height of the target column, with the second column, by modulating the force level produced with each pinch of the load cell. The system gain was set so that a 1 N increase in force, produced a 1 cm increase in the height of the second column.

All trials lasted 20 s. In experimental conditions (NV), visual feedback of the target as well as participants' current force output were removed after 10 s. In these conditions, participants were asked to continue repetitively pinching the load cell in time with the metronome and at the same force level for the remainder of the trial. In control conditions (V), visual force feedback remained present throughout the trial. In all experiments, participants were given up to 5 practice trials with each condition prior to data collection in order to familiarize themselves with the task and experimental apparatus. Participants were instructed as to which hand(s) (UR, UL, Bi) to use prior to the start of each trials, but were not informed of experimental condition (8N or 16 N, V or NV).

Experiment 1: Bimanual shared goal task. Right-handed volunteers, (n = 10, 5 male, 5 female, mean age: 24.6 years old, mean Edinburgh Handedness Inventory laterality index: 73.3; Oldfield 1971) performed the bimanual sequential force production task. The UL and UR hand conditions involved performing the pinch grip motion only on the left or right load cell with the corresponding hand. In these trials, the total force visible on the screen corresponded to the force output of the active hand. In the Bi condition, participants produced pinch grip forces on both the right and left force transducers with the corresponding hands. The visual display of the total force produced in Bi trials corresponded to the summed output forces of the two hands. Trial conditions were presented in a randomized order with 5 repetitions of each trial type. For 3 hand conditions (UL, UR, Bi), 2 force target force levels (8 N, 16 N) and 2 visual feedback conditions (V, NV), this yielded a total of 60 trials per participant.

Experiment 2: Bimanual independent goal task. Without specific force targets for each hand in the Bi condition of Experiment 1, analysis of any force overproduction by each hand in NV trials was limited. To better analyze the force overproduction effect in each hand in the bimanual sequential force production task, a second group of right-handed volunteers (n=12, 6 male, 6 female, 22.1 ± 3.7 years, mean Edinburgh Handedness Inventory Laterality Index: 82.5; Oldfield, 1971) was recruited to perform a variant of the protocol employed in Experiment 1. In this task the UR and UL hand conditions involved producing pinch grip forces with the right or left hand only. In the Bi trials however, the target force level was to be reached with each hand simultaneously, rather than be shared across the two effectors. In this version of the bimanual sequential force production task the visual feedback was structured such that a single force target of 16 N was presented as the center column of a 3-column bar plot on the computer monitor. The two remaining columns represented participants' force output. These were located on either side of the center target column and directly in front of the corresponding load cell. The height of these columns was contingent upon the force produced with each pinch of the corresponding load cell. This meant that the leftmost column of the visual display corresponded to the left transducer and represented the force output of the left hand. The rightmost column of the visual display corresponded to the right transducer and represented the force output of the right hand. The height of the center target column remained fixed at 16 N throughout the experiment. Forces were analyzed for four hand conditions (UR, UL, BiR, BiL) and two visual feedback conditions (V, NV). Six repetitions were performed for each condition yielding 36 trials per participant.

Experiment 3: Unilateral TMS in the bimanual independent goal task. In Therrien et al. (2011) we used continuous theta-burst stimulation (cTBS) to reduce the excitability of left M1 and found that this resulted in a systematic reduction in the force overproduction exhibited by the contralateral hand in NV trials by inducing discrepancy between efference copy and motor output signals. The idea behind the present experiment was to test whether perturbing one hemisphere of M1, would induce an effector-specific modulation of the force overproduction effect in the bimanual repetitive force production task. The same group of volunteers from Experiment 2 participated in two additional testing sessions where they performed the same bimanual force production task as Experiment 2 after receiving either real or sham cTBS.

TMS procedures. A figure of eight coil (Magstim Comp., Oakville, ON; external diameter of each coil: 9cm) was placed tangential to the head, at an angle of approximately 45° from the anterior-posterior midline, with the handle pointing to the posterior. The coil was used to deliver single pulses of focal TMS over left motor cortex and elicit motor evoked potentials (MEPs) in the first dorsal interosseous muscle (FDI) of the resting right hand. MEPs were recorded using electromyography (EMG). Ag/AgCl sintered electrodes were placed over the FDI muscle, in belly-tendon configuration, with a ground electrode placed on the Olecranon process of the elbow. The site for repetitive stimulation was determined as the cortical location where MEPs of 50 μV in peak-peak amplitude could be evoked in at least 50% of trials, with the lowest stimulator output.

This optimal stimulation site was recorded with Brainsight software (Brainsight 2.1.4, Rogue Research. Montréal, PQ) to allow for precise repositioning of the coil throughout both TBS and Sham stimulation sessions.

After determining the optimal stimulation site, participants performed 2-3 maximum voluntary contractions (MVCs) of the FDI muscle by pinching a handheld force gauge (Baseline Evaluation Instruments 12-0235, White Plains, NY) between the right thumb and index finger. Final MVC was taken as the average of these trials. To determine active motor threshold (AMT), single pulses of TMS were delivered while participants held isometric contractions at 20% of their MVC. A dial on the force gauge provided visual feedback to ensure an accurate force level was attained. AMT was determined to be the lowest stimulator intensity sufficient to produce MEPs greater than 200 μV above background EMG in at least 50% of trials.

As in Therrien et al. (2011), cTBS was used for the repetitive stimulation phase of the experiment. In cTBS, continuous trains of TMS are delivered in bursts of three at 50 Hz (20 ms between pulses) with a burst frequency of 5 Hz (200 ms between bursts; Huang et al. 2005; Huang and Rothwell 2004). cTBS was delivered at an intensity of 80% AMT for a duration of 40 s (to yield a total of 600 pulses). This protocol, termed cTBS600, is known to depress cortical excitability in the stimulated region for up to 60 minutes post-stimulation (Huang et al. 2005). For the sham stimulation sessions, the same procedures outlined above were used to determine the optimal stimulation site and AMT. Unbeknownst to participants however, repetitive stimulation was performed with a second inactive coil placed over the participant's skull while the active coil was moved behind and oriented away from the head. Both TBS and Sham stimulation sessions were separated by a minimum 24 hours to ensure compliance with previously determined safety guidelines (Wasserman 1998).

5.3.4 - Data analysis

Force data were stored separately for offline analysis. A custom-written script in MATLAB^{TM} was used to extract the peak force magnitude produced with each pinch of the load cell as well as the corresponding sample iteration and the trial time at which the peak occurred. Trial means were calculated from these data. To prevent contamination from transient behavior as participants adjusted to each new trial, the first 2 s of data (corresponding to the first 4 peak forces) were discarded from each trial. Mean force was defined as the mean peak force produced in each trial. Variability of each trial was quantified using coefficients of variation (CV). Only continuation phase data (t = 11-20s) was used for these analyses, i.e. after the feedback was removed in NV trials. Pearson product-moment correlations were performed for the detrended force series produced by each hand in the bimanual conditions of all three experiments. In *Experiments 2 and 3*, the force errors produced by each hand when visual feedback was removed were quantified relative to the mean force level produced by participants prior to feedback removal. Trials were separated into mean peak force values for two trial phases: before feedback removal (t = 2 -10 s) and after feedback removal (t = 11-20 s). The difference between the mean force levels produced in these two trial phases was taken as a measurement of the average change in force level over the course of the two trial phases. This method of quantifying force errors was chosen over measures relative to the target force magnitude only (i.e. constant error) to account for differing baseline levels of force output that were exhibited by participants even when visual force feedback was provided. All means were calculated across condition repetitions as well as across the study participants.

5.3.5 - Statistical analysis

Separate analyses of variance (ANOVAs) with repeated measures were calculated for each dependent variable using SPSS software (SPSS 16.0, Chicago, IL). In *Experiment 1* the forces produced and the associated variability were assessed using factors of hand condition (UR, UL, Bi), target force level (8 N, 16 N) and visual feedback condition (V, NV). In *Experiment 2*, the forces produced, the associated variability and the change in force level over the two trial halves were assessed using factors of hand condition (UR, UL, BiR, BiL) and visual feedback condition (V, NV). The same analysis was performed for *Experiment 3*, but with an additional factor of stimulation condition (Sham, TBS). Post-hoc means comparisons were performed using Tukey's HSD.

5.4 – RESULTS

The goal of *Experiment 1* was to assess the differences between sequential force pulses produced either unimanually by the right or left hand or bimanually through shared effort by the two hands together. Force-time series for the 16 N target force magnitude can be seen in Figure 5.1. Grand mean data from the two unimanual and the overall bimanual (combined output of the two hands) conditions are plotted in Figures 5.1A and B. Force series produced by each hand of a representative subject in the bimanual condition of Experiment 1 are shown in Figures 5.1C and D. Representative subject data was chosen over grand mean data due to high variability from shifts in how forces were distributed over the two hands in this condition. Analysis of mean peak force produced a main effect of target force magnitude, which indicated that participants successfully produced two significantly different force levels corresponding to the 8 and 16 N force target conditions ($F(1,9) = 674.045$, $p <.001$). Mean peak forces were slightly above the target magnitudes, but were comparable across participants (9.0N and 16.7N for the 8 and 16 N force target conditions, respectively). An interaction among the factors hand condition, force target magnitude and visual feedback condition was significant ($F(2,18) = 3.624$, $p <.05$, Figure 5.2A) with post-hoc means comparisons revealing it to be driven by significantly greater forces produced in the absence of visual feedback in all conditions, except when the target force magnitude was 16N and forces were produced unimanually by the left hand. Post-hoc analysis also revealed an interesting effect where the mean peak force produced in NV trials of the bimanual hand condition, exceeded the mean peak force produced in the NV trials of the unimanual conditions. This difference between the bimanual and both unimanual hand conditions was significant for the 16 N target force magnitude, but only reached significance between the bimanual and unimanual left hand conditions for the 8 N target force magnitude.

Analysis of peak force coefficient of variation also yielded a significant interaction between the factors hand condition, force target magnitude and visual feedback condition ($F(2,18) = 7.645$, $p <.01$, Figure 5.2B). Post-hoc means comparisons revealed peak force variability to be larger in the absence of visual feedback regardless of target force or hand condition. Post-hoc analysis also revealed an interesting pattern where force variability in the bimanual hand condition was lower compared with forces produced unimanually, despite the tendency for greater mean peak force in this hand condition. Force variability in the bimanual hand condition for the 8 N target force magnitude was significantly reduced compared to both unimanual right and unimanual left hand conditions. This reduction only reached significance between the bimanual and unimanual left conditions for the 16 N target force magnitude.

The bimanual task in this experiment involved the target force magnitude being reached through the summed output of the two hands. As participants were not instructed as to a specific strategy to use when dividing the target force magnitude between the two hands, analysis of any force overproduction by each hand in NV trials of this hand condition was limited. Pearson product-moment correlations were performed comparing the detrended force series produced by each hand in the bimanual hand condition; the results of this analysis can be seen in Table 5.1. When visual feedback was present the forces produced by each hand showed weak negative correlations that failed to reach significance When visual feedback was removed the forces series show smaller correlations that were weakly positive for the 8 N target force magnitude and approached zero for the 16 N target force magnitude. Thus, it seemed the force output of the two hands showed no significant synergistic correlation when producing a shared force bimanually; however, whether this was due to each hand expressing the force overproduction phenomenon independently remained unclear.

In *Experiment 2* the force task in the bimanual hand condition was modified to better analyze the force output behavior of each hand when visual feedback was removed.

Instead of reaching the force target through the combined effort of the two hands, the goal of bimanual task in this experiment was to attain the target force level simultaneously with both hands. Grand mean force-time series obtained from our data can be seen in Figure 5.3. The force-time series from the unimanual hand conditions are plotted in Figure 5.3A, while the force-time series from the bimanual hand conditions are shown in Figure 5.3B. Clear differences were present in the performance of the two hands for both the unimanual and bimanual hand conditions. The left hand consistently produced larger forces than the right, even when visual feedback was present. Upon removal of visual feedback, both hands produced positive force errors. While the magnitude of these errors was similar when both hands acted unimanually, the errors were greater and more positive for the right hand in the bimanual hand condition. A significant interaction among factors of hand and visual feedback condition for mean peak force mirrored these results ($F(3, 33) = 6.315$, $p < .01$, Figure 5.4A). Post-hoc means comparisons revealed mean peak forces produced in the absence of visual feedback to be greater in all conditions except when the left hand was acting in the bimanual task. The right hand produced lower mean peak forces than the left hand when visual feedback was present and this difference was significant for the bimanual hand condition. Pairwise means comparisons also revealed that mean peak forces produced by each hand in the absence of visual feedback were greater in unimanual hand conditions than when the hands produced forces bimanually.

Analysis of the mean change in force level over the course of a trial revealed a similar pattern of results. A significant interaction between factors of hand and visual feedback condition showed that positive force errors were displayed for all conditions except when the left hand acted in the bimanual task ($F(3, 33) = 6.753$, $p < .01$, Figure 5.4B). Independent samples t-tests were used to compare means obtained for conditions where visual feedback was present against zero. No significant differences were obtained (p's $< .05$) demonstrating that the biases in force output seen in these conditions in Figure 5.4A, were consistent throughout the trial. While the degree of force overproduction exhibited by the two hands in NV trials was similar in unimanual conditions, post-hoc means comparisons revealed significant differences between them in the bimanual hand condition. Pairwise means comparisons also showed within hand differences between the unimanual and bimanual contexts of the task. The mean change in force output seen when visual feedback was removed did not change for the right hand across unimanual and bimanual contexts; however, the degree of force overproduction exhibited by the left hand following visual feedback removal was significantly reduced when the limb acted in a bimanual task.

Analysis of peak force coefficient of variation yielded only one significant main effect of visual feedback condition ($F(1,11) = 34.792$, $p < .001$, Figure 5.4C) in which variability was greater in absence of visual feedback. As in *Experiment 1*, correlational analysis was performed on the detrended force series produced by each hand in the bimanual condition to assess coupling between the limbs in these trial. The results of this analysis can be seen in Table 5.2. Correlation coefficients were again weakly negative when visual feedback was present, but became smaller when it was removed; although, values failed to reach significance in either condition.

Taken together the results of this experiment suggest that, while the variability of the forces produced did not differ as a function of hand condition, expression of the force overproduction effect noted in our previous work did differ between unimanual and bimanual contexts as well as between hands within the bimanual task. Non-significant correlations again suggested independent action by each hand in the bimanual task; however, it still remained unclear whether the difference in overproduction errors exhibited by each hand in NV trials of this condition were rooted in asymmetric processing of reafferent feedback from the self-generated force pulses. We sought to investigate this question in Experiment 3.

In *Experiment 3* we used a 40 s train of cTBS to the FDI area of left M1 to induce a period of unilateral cortical depression. In Therrien et al. (2011) we used this TMS protocol on a unimanual sequential force production task and found it to result in significant reductions in the degree of force overproduction seen following removal of visual feedback. This result was attributed to a TMS-induced discrepancy between sensory predictions and actual afferent feedback resulting in reduced attenuation of self-generated somatosensory feedback. The goal of the present experiment was to investigate whether a unilateral perturbation to this mechanism would result in differential effects for the unimanual and bimanual force production tasks used in Experiment 2. The mean force-time series obtained from our data in Experiment 3 is plotted in Figure 5.5. Data from the UR and UL hand conditions can be seen in Figures 5.5A and B, respectively. Data from the BiR and BiL hand conditions can be seen in Figures 5.5C and D, respectively. Clear differences can again be seen in the performance of the two hands.

Like in Experiment 2, the left hand was biased to produce greater forces than the right hand, even when visual feedback was present. Upon removal of visual feedback, both hands produced positive force errors in unimanual conditions (although, this effect is more pronounced in the right hand), but only the right hand shows the force overproduction phenomenon in the bimanual condition. Interestingly, following receipt of cTBS, the magnitude of these force errors by the right hand (contralateral to the stimulation site) is selectively reduced.

Repeated measures ANOVA for mean peak force yielded a significant interaction among factors of stimulation session, hand condition and visual feedback condition that showed a similar pattern of results ($F(3, 33) = 3.258$, $p < .05$, Figure 5.6A). Post-hoc means comparisons revealed that mean peak forces produced in the absence of visual feedback were consistently greater than those produced when it was present in all conditions except when the left hand acted in the bimanual task. There was also a non-significant trend for the left hand to produce greater forces than the right when visual feedback was present. Furthermore, an additional effect was present where the degree of force overproduction in NV trials was selectively reduced for the right hand in both the unimanual and bimanual hand conditions following receipt of cTBS.

Analysis of the mean change in force level produced over the course of a trial also yielded a significant interaction among factors stimulation session, hand condition and visual feedback condition ($F(3, 33) = 3.422$, $p < .05$, Figure 5.6B). Significant positive force errors were seen in the absence of visual feedback for all conditions except when the left hand acted in the bimanual hand condition. T-Tests comparing the change in force level in conditions where visual feedback was present to zero again revealed no significant differences (*p*'s < .05). While there was a trend for the left hand to show reduced force overproduction errors when acting in the bimanual compared to the unimanual condition, this failed to reach significance. Similar to the mean peak force results, positive force errors produced in the absence of visual feedback were reduced for the right hand in both the unimanual and bimanual hand conditions following receipt of cTBS. Together these results suggest that unilateral cTBS influenced the processing of reafferent feedback selectively for the hand contralateral to stimulation. Analysis of peak force coefficient of variation yielded only a single main effect of visual feedback condition ($F(1,11) = 95.367$, $p < .001$, Figure 5.6C), suggesting that force variability was not differentially affected by either hand condition or the stimulation sessions of our task. This is in line with previous results (Therrien et al., 2011).

Pearson product-moment correlations performed on the detrended force series produced by each hand in the bimanual task can be seen in Table 5.2. As in the previous experiments, correlation coefficients did not reach significance for either visual feedback condition or stimulation session, suggesting a lack of coupling between the hands overall. Interestingly, while correlations were weakly negative in the Sham stimulation session, becoming less correlated in NV trials, correlation coefficients were weakly positive following receipt of cTBS and became slightly stronger after visual feedback withdrawal. Together, the results of Experiment 3 suggest that unilateral cTBS influenced the processing of reafferent feedback from self-produced forces in our task, and this influence was selective for the limb contralateral to stimulation.

5.5 – DISCUSSION

Our goal was to investigate the processing of reafferent feedback in a bimanual sequential force production task. Two groups of volunteers participated in either a task where the bimanual hand condition required a target force magnitude to be achieved through the shared output of both hands, or a task where each hand was to produce the same target force magnitude simultaneously. In both, the bimanual production of force was compared with conditions in which each hand performed the sequential force production task unimanually. In *Experiment 1* we found that forces tended to exceed target magnitudes in the absence of visual feedback; however, this was less reliable for the left hand. In addition, the forces produced bimanually in this condition did not simply show a pattern of results consistent with the combination of the behavior exhibited in the unimanual hand conditions. With the larger target force magnitude, forces produced in the bimanual hand condition without visual feedback tended to exceed the forces produced by either hand unimanually without visual feedback. With the smaller target force magnitude, this was not the case. Following visual feedback removal, forces produced bimanually were similar to those produced by the dominant, right, hand acting in a unimanual task. Without specific force targets for each hand in the bimanual task, any investigation into the force overproduction phenomenon in this condition was limited. Correlational analyses performed for the force series produced by the two hands in bimanual trials yielded no significant results indicating a lack of significant coupling between the limbs in this condition overall. Interestingly though, correlation coefficients were weakly negative when visual feedback was present, but became smaller and more positive when it was removed. These results suggested the presence of some synergistic coviariation (Latash et al. 2001; Scholz et al. 2002) that was reduced upon removal of visual feedback. Despite this reduced coupling, variability of the force series was lower in bimanual trials following removal of visual feedback.

In *Experiment 2* we showed that when the target force magnitude was specified for each hand in a bimanual task, the force overproduction phenomenon did not occur equally for both. When acting in a unimanual task, forces produced by both the right and left hands exceeded target magnitudes following removal of visual feedback. When acting bimanually though, force overproduction was only seen reliably in the dominant hand. Unlike in Experiment 1, variability was not differentially affected by hand condition suggesting that when the two hands act bimanually to produce independent force targets, variability of the forces produced is comparable to unimanual tasks. *Experiment 3* replicated the differences in expression of the force overproduction phenomenon between the right and left hands in bimanual, compared to unimanual, trials. Interestingly, a period of unilateral motor cortical depression, induced by application cTBS600, resulted in a reduction of positive errors in force output following visual feedback removal that was selective for the hand contralateral to stimulation. Variability of the forces produced was significantly influenced neither by hand condition, nor stimulation session – a result that was in line with Experiment 2 as well as our previous work (Therrien et al., 2011).

Overall, the results of this study support our hypothesis that sensory reafference signals may be processed asymmetrically (and possibly separately) for each limb in a bimanual force production task. A lack of significant correlation between the hands in bimanual trials of *Experiment 1* suggested independent control, rather than synergistic covariation, of the hands following removal of visual feedback of force output. *Experiments 2 and 3* further investigated this hypothesized asymmetric control and found that while force overproduction was consistently exhibited by the right hand following feedback removal, the effect was less reliable for the left hand in bimanual conditions. Our study participant pools were strongly right handed (values greater than +40 on the Edinburgh Handedness Inventory indicate right hand dominance; Oldfield 1971). It is possible that the observed asymmetry in force overproduction was due to strength differences between the dominant and non-dominant limbs; however, in that case, one would have expected reduced force overproduction by the left hand when it acted unimanually as well. Both neurophysiological and neuroimaging studies have routinely shown that strongly right handed individuals have more well developed efferent and afferent connections with their dominant side (Bernard et al. 2011; Dassonville et al. 1997; Siebner et al. 2002). An alternative possibility is that forward model predictions may be more precise for the dominant limb in this population. Following the mechanism proposed in our earlier work (Therrien et al. 2011), in the absence of visual feedback, more precise sensory predictions would result in increased overlap with actual somatosensory feedback stemming from motor execution. This would lead to an augmented degree of sensory attenuation, which would in turn amplify the degree of compensatory overproduction of force by the right hand in bimanual tasks.

The notion of asymmetric processing of reafferent feedback is further supported by the observation that the effect of unilateral cTBS was selective to the hand contralateral to stimulation for both unimanual and bimanual hand conditions. The unimanual results are in line with our previous experiment (Therrien et al. 2011) and strengthen the notion that reducing excitability in the FDI area of M1, through application of cTBS, may have induced discrepancy between predicted and actual sensory feedback. Following removal of visual reference stimuli, there was reduced overlap between these two signals, which lead to reduced sensory attenuation and, in turn, to a decrease in the degree of force overproduction following stimulation. Additionally, the bimanual results suggest possible effector-specificity in sensory prediction signals. One would expect context-specific forward models to contain sensory predictions averaged over the two limbs in a bimanual task. Unilaterally perturbing one hemisphere would induce a global mismatch with incoming afferent feedback and such error signals would likely result in global updates to subsequent motor commands that would have affected the behavior of both limbs following stimulation.

It is important to note that, as in our previous study, our data do not provide any information regarding the mechanism that gave rise to a discrepancy between the sensory predictions generated and motor output produced. It is possible that application of cTBS induced changes in the processing of efference copy signals by altering the excitability of intracortical interneurons (DiLazzaro et al. 2008). The cerebellum has been suggested as the neural locus for a forward model comparator (Blakemore et al. 1998) and there exists evidence that efference copies may be generated upstream of M1 (Chronicle and Glover 2003). Spreading activation to any of these areas could have also disrupted sensory attenuation mechanisms in our task (Bestmann et al. 2004; Okabe et al. 2003; Siebner et al. 2000).

In addition to comparisons between the behavior of each hand in a bimanual sequential force production task, our study involved investigation of two kinds of bimanual tasks: one where the goal force was to be achieved through the shared output of the two hands and one where the two hands were to each produce the target force concurrently. Analysis of any differences between the magnitudes of forces produced by the two hands when the task goal was shared, versus not, was limited due to a lack of prescribed force sharing strategy in *Experiment 1*. Measures of force variability however, revealed differences between the two bimanual tasks. In the shared-goal task, a trend was present for variability to be reduced in the bimanual compared to unimanual hand conditions. This was interesting, as similar reductions in variability in the absence of feedback have been noted in studies of motor timing (Drewing and Aschersleben 2003; Helmuth and Ivry 1996; Kelso et al. 1979). Yet, when the bimanual task was altered so that the goal was no longer shared, this effect of hand condition on force variability disappeared. Both bimanual tasks employed here involved a shared temporal goal between the hands. Our finding of changes in force variability between the two tasks suggests that something unique occurs when this shared temporal goal was paired with a shared force level goal that served to stabilize the forces produced, despite the positive errors and overall lack of coupling they exhibited. While negative covariation between the hands has been seen consistently in studies of motor timing and temporal coordination, one might wonder why the control of force level would reveal such capacity for independence. There are hemispheric asymmetries in the processing of somatosensory feedback (Goble and Brown 2007; Goble et al. 2006; Goble et al. 2005). Furthermore, it has been proposed that this asymmetry in somatosensory processing has lead to distinct specializations in motor performance between the limbs (Sainburg 2002). That negative covariation has been found in previous studies of bimanual motor timing, does not run counter to this hypothesis as bimanual tasks often involve a shared goal; therefore, temporal coordination between independent actions of the two hands is necessary for accurate task execution. Rather, findings of asymmetry between the hands during control of bimanual forces and similarity between the two hands during the control of bimanual movement timing suggest that these two aspects of motor control may be specified at different levels of motor program generation (Ivry 1986).

The present study is the first, to our knowledge, to examine compensation for attenuated reafferent feedback form self-produced forces in a bimanual task. While our results are preliminary, the effects of sensory reafference on bimanual motor output warrant further study. First, examination of the data in all three of the present experiments reveals a trend for a gradual decrease in force output as trials progressed following visual feedback withdrawal that was present in all hand conditions; although, this was least marked when the right hand acted unimanually. Decays in force output following visual feedback removal have been noted in studies of unimanual and bimanual production of isometric forces and have been attributed to the decay of visuomotor memory of the target force level (Davis 2007; Vaillancourt and Russell 2002). It is possible that a similar process may be at work in our task. Future study of this slow decay, perhaps in longer trials, and potential differences between the right and left hands in its expression may provide further insight into the nature of asymmetric processing of reafferent feedback between dominant and non-dominant hemispheres. Secondly, with respect to the TMS manipulation of *Experiment 3*, the present study involved only unilateral stimulation of left M1. Given the anatomical and physiological asymmetries between dominant and non-dominant hemispheres of right-handed individuals (Bernard,et al.,2011; Dassonville,et al.,1997; Siebner et al. 2002), it would be interesting to expand upon the current findings to investigate the effects of stimulation to the contralateral hemisphere of M1.

In summary, previous studies of unimanual sequential forces has shown that the magnitudes produced tend to exceed target values in the absence of visual feedback of force output. This has been attributed to compensation for the sensory attenuation that results from the reafferent processing of self-generated somatosensory feedback. In the present study we examined this effect in two bimanual extensions of the sequential force production task. Differences in expression of the force overproduction phenomenon between unimanual and bimanual tasks could provide insight into the effector-specificity or context-specificity of sensory prediction signals. Results showed that unimanual sequential forces produced following visual feedback removal exceeded target values for both limbs. Forces are produced bimanually however, did not show the same symmetrical overproduction. Indeed, unilaterally depressing excitability in one hemisphere of M1 to disrupt sensory prediction processes induced behavioral alterations selectively for the hand contralateral to stimulation. Overall our findings fall in line with previous literature suggesting that the control of force by the two hands in a bimanual task may be less tightly coupled than other mechanisms of motor control. The present results also add to this literature by showing that the asymmetrical control of bimanual force may also extend to the processing of reafferent somatosensory feedback and compensation for the resulting attenuation of its salience.

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5.7 – FIGURE APPENDIX

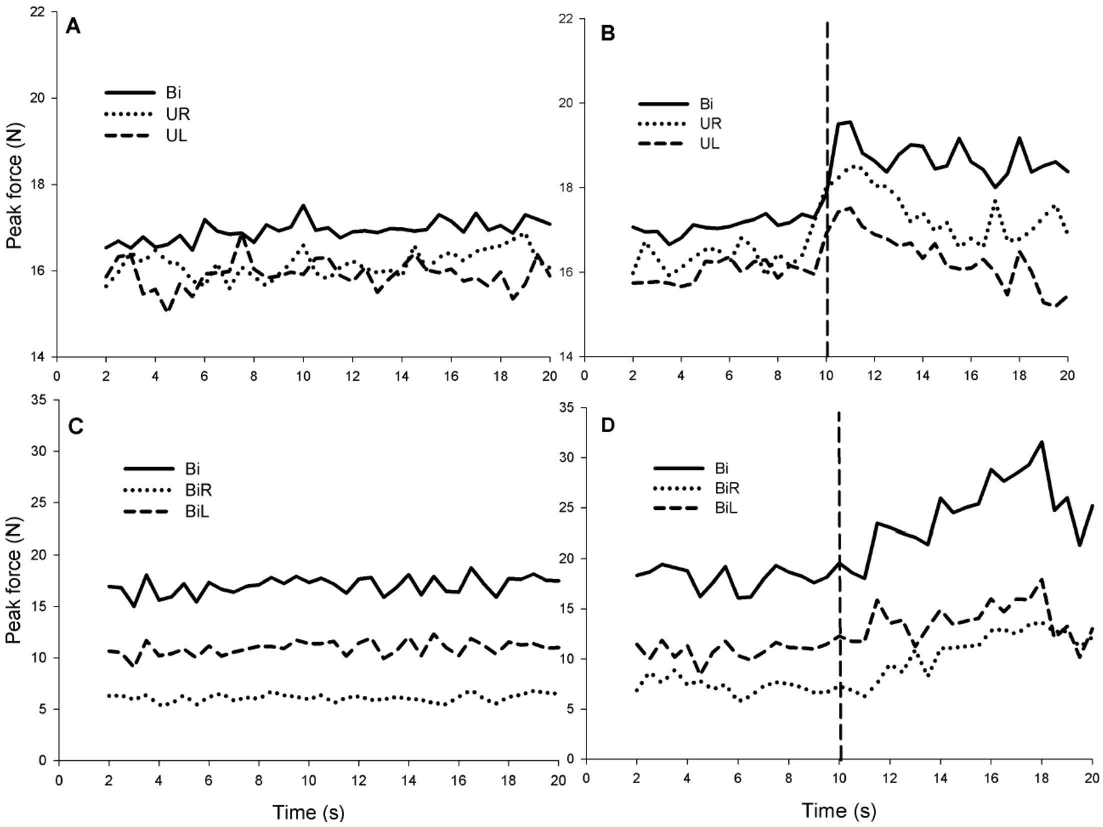

Figure 5.1. Force time series produced for the 16N target force magnitude in the two unimanual and the shared-goal bimanual hand conditions of *Experiment 1*. Mean force time series are plotted for (**A**) conditions where visual feedback of force output remained present throughout as well as (**B**) where where feedback was removed. Due to high variability from shifts in force distribution by the two hands in the shared-goal bimanual task, rather than mean data, force output data from each hand in these conditions is plotted from a representative subject in panels **C** (conditions where visual feedback remained present throughout the trial) and **D** (conditions where visual feedback was removed). Vertical dashed lines represent the time at which visual feedback was removed.

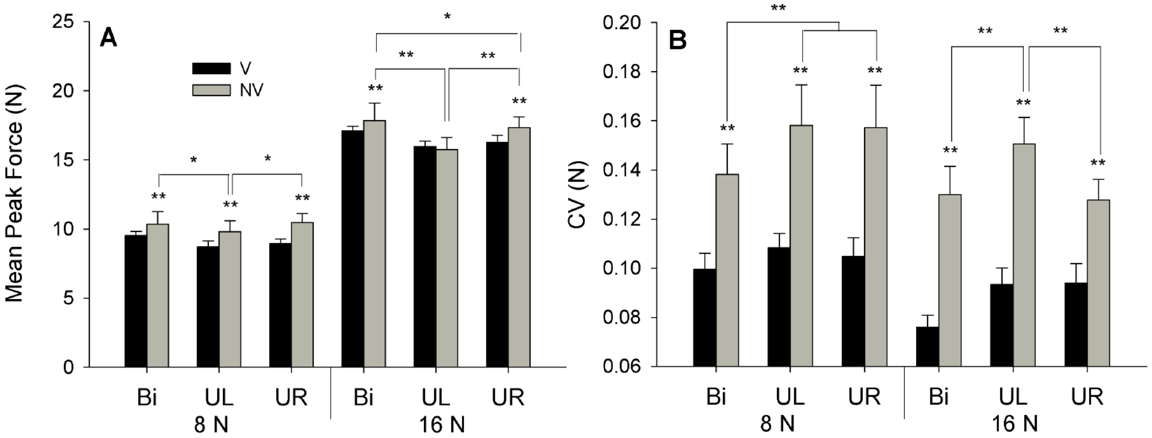

Figure 5.2. Significant interactions among factors target force magnitude, hand condition and visual feedback condition for (**A**) mean peak force and (**B**) peak force coefficient of variation in *Experiment 1*. Asterisks and connecting lines denote reliable pairwise means comparisons, * = $p< .05$, ** = $p< .01$.

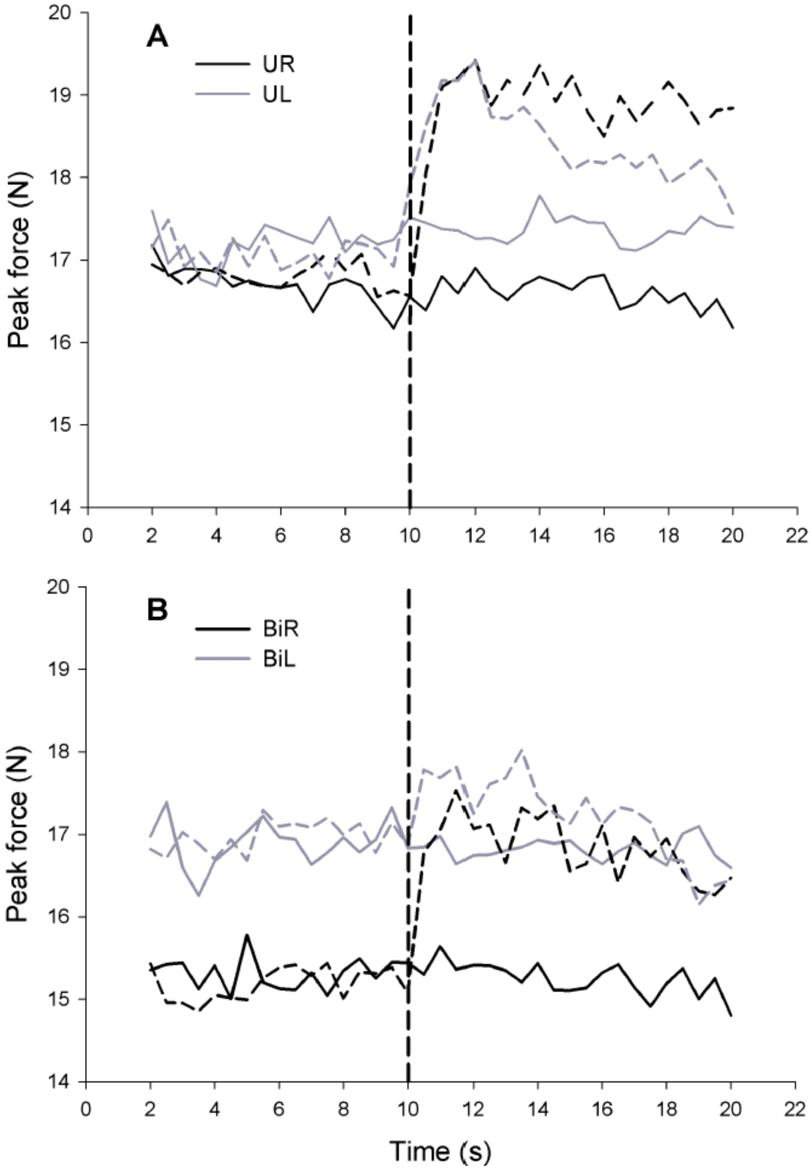

Figure 5.3. Mean force time series produced in (**A**) the two unimanual and (**B**) the two bimanual hand conditions of *Experiment 2*. Solid lines represent conditions where visual feedback of force output remained present throughout the trial. Dashed lines represent conditions where visual feedback was removed. Vertical dashed lines denote the time at which visual feedback was removed.

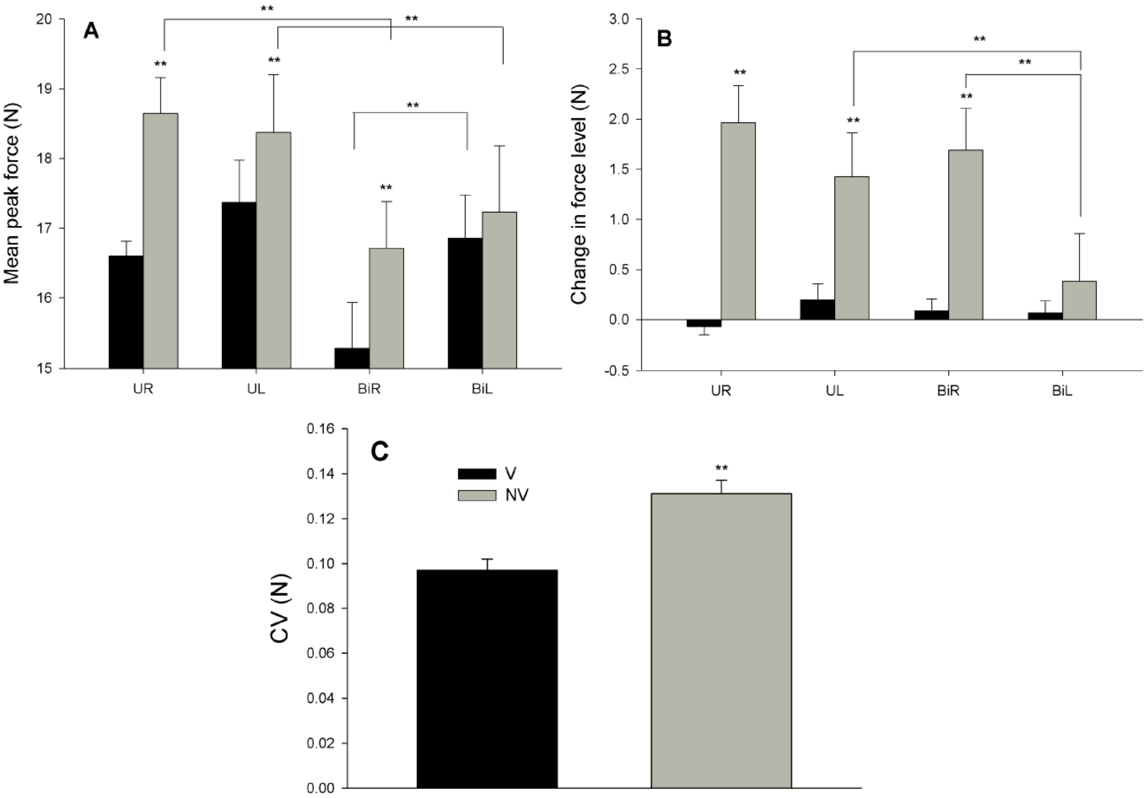

Figure 5.4. Significant interactions among factors hand condition and visual feedback condition for (**A**) mean peak force and (**B**) the mean change in force level over the course of a trial for *Experiment 2*. (**C**) Significant main effect of visual feedback condition for peak force coefficient of variation in *Experiment 2*. Asterisks and connecting lines denote reliable pairwise means comparisons, ** = $p < .01$.

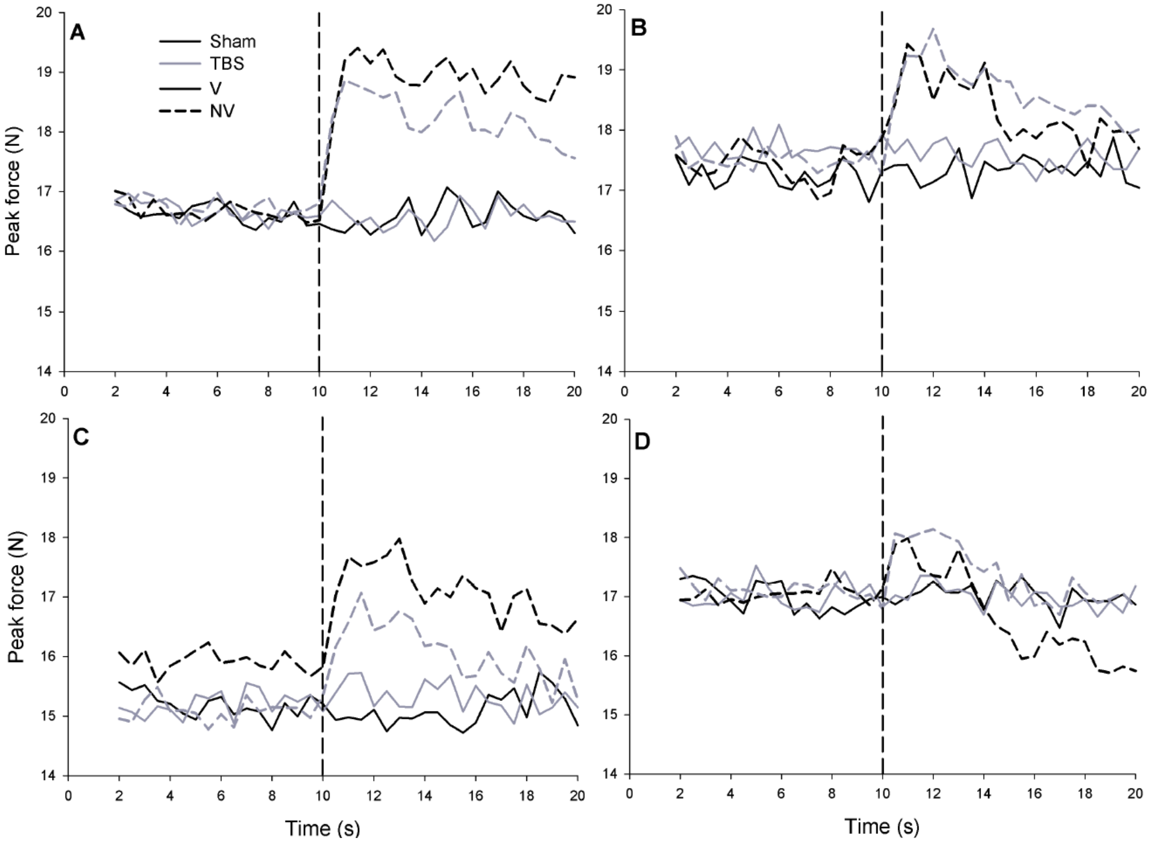

Figure 5.5. Mean force time series produced in the (**A**) unimanual right, (**B**) unimanual left, (**C**) bimanual right and (**D**) bimanual left hand conditions of *Experiment 3*. Solid lines represent conditions where visual feedback remained present throughout the trial. Dashed lines represent conditions where visual feedback was removed. Vertical dashed lines denote the time at which visual feedback was removed.

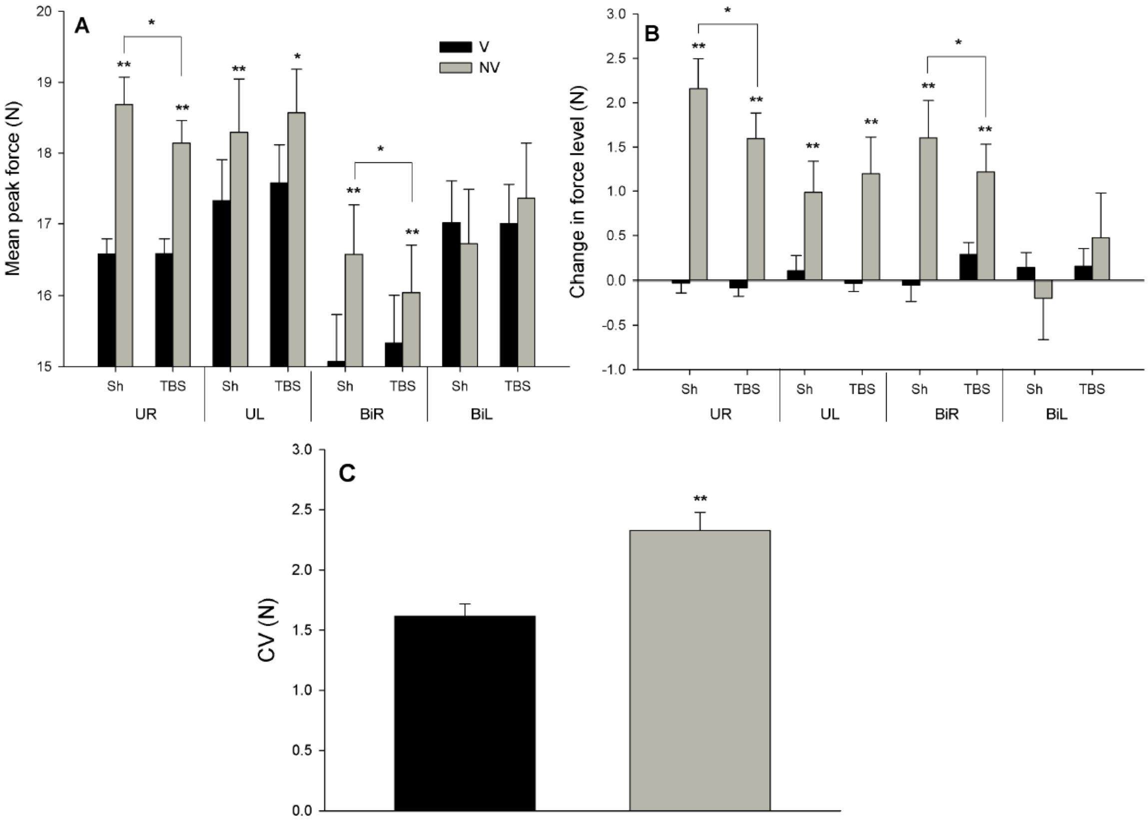

Figure 5.6. Significant interactions among factors stimulation session, hand condition and visual feedback condition for (**A**) mean peak force and (**B**) mean change in force level over the course of a trial in *Experiment 3*. (**C**) Significant main effect of visual feedback condition on peak force coefficient of variation in *Experiment 3*. Asterisks denote reliable pairwise means comparisons. * = $p < .05$, ** = $p < .01$.

Table 5.1
Pearson product moment correlation coefficients for the force series produced by the right and left hands in the bimanual hand condition of Experiment 1.

	Target Force Magnitude	
	8 N	16 N
Visual Feedback		
V	-.353	-.123
NV	.405	-.061

Note. N = 10 for all analyses.

Table 5.2
Pearson product moment correlation coefficients for the force series produced by the right and left hands in the bimanual hand conditions of Experiments 2 and 3.

	Experiment 2	*Experiment 3*	
		Stimulation Condition	
		Sham	TBS
Visual Feedback			
V	-.505	-.323	.212
NV	-.122	-.171	.491

Note. N = 12 for all analyses.

CHAPTER 6: SENSORY ATTENUATION OF SELF-PRODUCED FEEDBACK: THE LOMBARD EFFECT REVISITED

6.1 – ABSTRACT

The Lombard effect describes the automatic and involuntary increase in vocal intensity that speakers exhibit in a noisy environment. Previous studies of the Lombard effect have typically focused on the relationship between speaking and hearing. Automatic and involuntary increases in motor output have also been noted in studies of finger force production, an effect attributed to mechanisms of sensory attenuation. The present study tested the hypothesis that sensory attenuation mechanisms also underlie expression of the Lombard effect. Participants vocalized phonemes in time with a metronome, while auditory and visual feedback of their performance were manipulated or removed during the course of the trial. We demonstrate that providing a visual reference to calibrate somatosensory-based judgments of current vocal intensity resulted in reduced expression of the Lombard effect. Our results suggest that sensory attenuation effects typically seen in fingertip force production play an important role in the control of speech volume.

6.2 – INTRODUCTION

It is commonly observed that when trying to speak with someone who is listening to music over headphones, they will respond loudly and sometimes even shout. This automatic and involuntary increase in vocal intensity that speakers exhibit in a noisy environment is known as the Lombard effect, named after French otolaryngologist, Étienne Lombard (Garnier et al. 2010; Lane and Tranel 1971; Letowski et al. 1993; Lombard 1911; Patel and Schell 2008; Pick et al. 1989; Smotherman 2007; Tonkinson 1994; Zollinger and Brumm 2011). Despite the large body of literature that has been published since its initial discovery in 1911, the precise mechanism behind the Lombard effect remains unclear.

Lombard (1911) initially attributed his observations to an automatic self-monitoring process involving auditory feedback. As a result, studies of the Lombard effect have typically focused on the relationship between vocal output and auditory input. Important to remember, however, is that somatosensory feedback from the articulators is equally important for accurate vocal control. Indeed, this has been corroborated by findings in the speech motor learning literature. Alterations of auditory feedback have been shown to induce compensatory changes to pronunciation, demonstrating that the central nervous system actively monitors somatosensory errors signals (10). In addition, both normally hearing and post-lingually deaf adults have shown adaptation to perturbing loads applied to the jaw during speech, despite those loads producing no measurable acoustical change (Nasir and Ostry 2006, 2008; Tremblay et al. 2003).

With respect to the Lombard effect, there exists evidence showing that individuals can be trained to use non-auditory sources of sensory feedback in the regulation of vocal intensity. Tonkinson (1994) found that experienced singers were able to learn to use instructions to consciously resist the Lombard effect when performing in chorus. Pick et al. (1989) also examined the effect of instructions on individuals' ability to inhibit the Lombard effect in an unconstrained, free speech task. When simply instructed to resist any changes in vocal intensity, participants were unsuccessful; however, when visual feedback of their vocal intensity was provided, participants could be trained to inhibit the Lombard effect in conditions where masking noise prevented any auditory feedback of their vocal output. The authors suggested that visual feedback of vocal intensity might serve to calibrate somatosensory information from the speech effectors, which allowed participants to use this feedback to maintain a steady voice level. Inherent in this interpretation is the assertion that somatosensory feedback, on it own, is unreliable in generating perceptions of motor output.

Changes in vocal intensity are mediated through changes in subglottic pressure, which are achieved through adjustments of expiratory force (Smotherman 2007). Previous work from our laboratory studying self-produced, discrete, repetitive finger forces has noted automatic and involuntary increases in output when visual feedback of force level is removed. (Therrien and Balasubramaniam 2010; Therrien et al. 2010' Therrien et al. 2011). These increases in force output were attributed to sensory attenuation mechanisms affecting perceptions of self-produced somatosensory feedback. Specifically, it has been proposed that corollary discharge from primary motor cortex is used to generate predictions of the sensory outcomes of an action (Bays et al. 2006; Bays et al. 2005; Blakemore et al. 1998; Shergill et al. 2003; Voss et al. 2007; Wolpert and Ghahramani 2000). When that action is executed, the predicted outcomes are compared with incoming afferent information in order to evaluate the success of motor execution as well as to discern self-produced from externally generated feedback (Bays et al. 2006; Bays et al. 2005; Blakemore et al. 1998; Shergill et al. 2003; Voss et al. 2007; Wolpert and Ghahramani 2000) . The comparison process is thought to result in attenuation of the predicted component of incoming sensory information and this attenuation may be responsible for a reduced percept of self-generated sensory feedback compared with that from external sources (Bays et al. 2006; Bays et al. 2005; Blakemore et al. 1998; Shergill et al. 2003; Voss et al. 2007). In the case of force production, self-produced forces are perceived as being weaker; therefore, in the absence of more reliable reference stimuli, participants exhibit a compensatory over-production of the force magnitudes required.

It is important to underscore that re-afference mechanisms do not operate exclusively in situations of tactile perception and force production. Indeed, the attenuation of self-generated changes in visual feedback is thought to aid in maintaining stability of the visual scene during eye movements (Paus et al. 1995). These attenuation processes, however, render sensory signals from self-movement less reliable. When other feedback modalities are present, they are used to calibrate attenuated somatosensory-based judgments of performance and modulate motor output in subsequent actions. Situations similar to the Lombard phenomenon involve auditory information being rendered unreliable due to increases in levels of ambient noise. As a result, to estimate vocal intensity, the Central Nervous System (CNS) must shift its reliance to favor somatosensory feedback from the speech effectors. Due to the abovementioned sensory re-afference mechanisms, perceptions of self-generated somatosensory feedback are attenuated. In vocal control, reduced salience of somatosensory information could lead to a compensatory increase in vocal intensity following removal of auditory reference stimuli.

If sensory attenuation of somatosensory feedback also underlies the increases in vocal intensity associated with the Lombard effect, then provision of another form of sensory reference, such as visual feedback of vocal output, should calibrate attenuated somatosensory signals and result in reduced positive errors in vocal intensity level following removal of auditory feedback. The objective of the present study was to examine the interplay between auditory and somatosensory feedback modalities in the control of vocal intensity by having participants perform a repetitive vocalization task while auditory and visual feedback stimuli were independently manipulated. We hypothesized that providing a visual reference of participants' voice level would serve to calibrate somatosensory-based judgments of current vocal intensity. We contend that this would result in reduced expression of the Lombard effect when auditory feedback was masked, compared with conditions where no reference stimuli were provided.

6.3 – METHOD

6.3.1 Ethics Statement

The study was conducted in accordance with the Declaration of Helsinki and the protocol was approved by the McMaster University Research Ethics Board. Written informed consent was obtained from all participants prior to their participation in the study.

6.3.2 Participants

Eight participants volunteered for this experiment (6 male and 2 female, mean age: 22.0 years). All participants were students at McMaster University, free of any known speech or hearing impairments and had normal or corrected-to-normal vision at time of data collection.

6.3.3 Apparatus

Participants spoke in to a small, collar-mounted microphone (Nexxtech omni-directional PC microphone) that was placed out of the breath stream and at a fixed distance of approximately 8 cm from the lips. The microphone output was fed directly to the microphone input of a PC workstation (Dell Precision T7500) where it was recorded by the on-board sound chip set (Intel SoundMAX), then sampled at a rate of 44 100 Hz and processed using custom-written LabView software (LabView 8.5, National Instruments). This software fed the speech signal to a visual feedback display on a 24-inch LCD computer monitor as well as to the computer headphone output. Participants received all auditory feedback through a pair of noise-attenuating headphones (Sennheiser HD280 Pro) connected directly to the headphone output of the PC workstation. In experimental conditions, LabView software delivered a 90 dB pink noise signal to both earphones in place of the microphone output.

6.3.4 Procedure

Participants sat in a non-moving chair with their arms resting comfortably in their lap. They were fitted with a pair of headphones, a small, collar-mounted microphone and were positioned so they could comfortably see the visual display while maintaining a seated upright posture. Participants were reminded to keep this posture throughout the experiment in order to maintain a constant distance between the microphone and lips. During the experiment, participants were asked to repeat the phoneme, /ba/, at an utterance rate specified by a visual metronome, in the form of a blinking light on the visual display, that was set at 1 Hz (corresponding to 1000 ms between blinks). Participants were to time each utterance with the blink of the metronome. Participants were also presented with a visually specified target volume level of 80 dB SPL and were asked to match it by modulating the intensity of their voice with each successive utterance of the phoneme, /ba/. The volume target was presented as a red line on a continuous line graph on the computer monitor. A second yellow tracing provided online feedback of participants' vocal intensity. The system gain was set so that a 1 dB SPL increase in vocal intensity caused a 1 cm increase in the amplitude of the trace. All trials lasted 20 seconds.

An illustrated depiction of our experimental conditions can be viewed in Figure 6.1. During the experiment, the visual display of vocal intensity and the auditory voice feedback were manipulated independently resulting in four experimental conditions: the visual feedback of vocal intensity being removed 10 s in to the trial (A-NV), the auditory voice feedback being replaced with masking pink noise 10 s in to the trial (NA-V) or both occurring 10 seconds in to the trial (NA-NV). Following the feedback manipulation, participants were required to continue uttering the phoneme, /ba/, in time with the visual metronome and at the same vocal intensity level for the remainder of the trial. In control conditions (A-V) both visual feedback of vocal intensity and auditory voice feedback remained present throughout the trial. Participants were not informed of the experimental condition prior to beginning each trial. They were given up to 5 practice trials with each condition prior to data collection in order to familiarize themselves with the task and experimental apparatus. During data collection all conditions were presented in a pseudo-randomized order, with each condition being repeated twice before beginning the sequence over. 10 repetitions of each condition were performed, yielding a total of 40 trials per participant.

6.3.5 Data Analysis

Pressure data (Pascals, Pa) from the microphone output were stored separately for offline analysis. To avoid contamination from transient changes in behavior as participants adjusted to each new trial, the first 2 seconds of data were discarded. To avoid contamination from synchronization errors associated with the visual metronome, the last 2 seconds of data from each trial were also discarded. A custom script in MATLAB^{TM} was used to convert pressure values from Pa in to dB SPL as well as extract the peak dB SPL produced with each utterance, the corresponding sample number and time at which they occurred in the trial. From these data, trials means were computed. Overall vocal intensity was determined as the mean peak dB level from each utterance produced in the last 8 seconds of each trial. Variability was quantified using measures of standard deviation (SD) and coefficients of variation (CV). The vocal intensity-time series produced with each trial were broken down in to mean vocal intensities for two trial phases: before feedback removal (i.e. t = 2 -10 s) and after feedback removal (i.e. t = 11-18 s). The difference between these means was then calculated to determine the change in mean vocal intensity over the two trial phases. Lastly, the mean onset time of the 10th utterance (corresponding to t = 10 above) was calculated as this utterance corresponded to the time point when feedback manipulations occurred. Any asynchrony with the metronome on this utterance would have affected the trial phase (described above) in which it occurred. Means were calculated across 15 repetitions of each condition as well as across participants.

6.3.6 Statistical Analysis

SPSS software (SPSS 16.0) was used to conduct separate analysis of variance (ANOVA) with repeated measures for each dependent variable. Overall vocal intensity, change in mean vocal intensity, vocal intensity variability as well as the iteration time for the 10th utterance were assessed using factors of auditory feedback condition (A, NA) and visual feedback condition (V, NV). Post-hoc means comparisons were performed using Tukey's HSD.

6.4 – RESULTS

The average vocal intensity time series obtained from our data can be seen in Figure 6.2. Analysis of overall vocal intensity yielded a significant interaction among factors of auditory feedback condition and visual feedback condition (F (1,7) = 13.759, $p < .01$, $\eta^2 = .663$, Figure 6.3A). Post-hoc means comparisons revealed overall vocal intensity to be significantly greater in the absence of auditory voice feedback regardless of visual feedback condition; however, overall vocal intensity was greatest when both auditory and visual feedback were absent (*p*'s < .01). The ANOVA for change in mean vocal intensity also yielded a significant interaction among factors of auditory feedback condition and visual feedback condition (F (1,7) = 10.478, $p < .01$, $\eta^2 = .599$, Fig. 6.3B). Post-hoc means comparisons revealed that, again, the mean change vocal intensity was greater and more positive in the absence of auditory feedback, regardless of visual feedback condition; however, the change was greatest and most positive in the absence of both auditory and visual feedback (*p*'s < .01). Examination of Figure 6.2 reveals a trend for vocal intensity on the 10th utterance (corresponding to the utterance at which feedback was removed) to be slightly, though not significantly, greater in the two NA conditions, compared to the same utterance in trials where auditory feedback remained present throughout the trial. Analysis of the 10th utterance in all conditions revealed mean response times of 10. 265 ± 0.055 s (A-V), 10.233 ± 0.097 s (NA-V), 10.234 ± 0.132 s (A-NV), and 10.233 ± 0.052 s (NA-NV). Together these yielded an average response lag of 0.241 ± 0.016 s for the 10th utterance. ANOVA for the 10th utterance means revealed no significant main effects or interactions (*p's* > .05), suggesting no significant differences between experimental conditions. Further inspection of Figure 6.2 revealed great variability in the vocal intensities produced across participants, a finding that is commonly noted in the auditory perturbation literature. Grand mean variability, collapsed over all four experimental conditions was 1.172 ±0.068 dB and 0.014 ±0.001 dB for SD and CV values respectively. Despite the large between-subject variability, analysis of SD and CV values did not yield any significant main effects or interactions (*p's* > .05); thus, variability of vocal output intensity was not differentially affected by the removal of auditory and/or visual feedback in our task.

6.5 – DISCUSSION

The objective of the present study was to investigate the effects of auditory and visual feedback manipulations on expression of the Lombard effect in a non-communicative, repetitive vocalization task. Previous work from our lab has found that following removal of visual feedback, self-produced, repetitive, discrete finger forces were greater than target magnitudes produced when visual feedback of force output was provided (Therrien and Balasubramaniam 2010; Therrien et al. 2010; Therrien et al. 2011). These results were interpreted in the context of sensory attenuation mechanisms, whereby self- generated forces were perceived as being weaker leading to a systematic overproduction of the force magnitudes required. Changes in vocal intensity associated with the Lombard effect show a similar pattern of automatic and involuntary increases when the, more reliable, auditory feedback of one's own voice is masked by background noise. If sensory attenuation mechanisms also underlie these increases in vocal intensity, we expected that providing a visual reference of vocal output would result in decreased expression of the Lombard effect in conditions where auditory feedback was masked.

In accordance with previous literature, vocal intensity levels in the present experiment immediately increased when auditory voice feedback was masked with noise, regardless of visual feedback condition. This overall effect of auditory feedback on expression of the Lombard effect is in line with previous research suggesting a central reliance on audition (Lane and Tranel 1971; Laugesen et al. 2009). The degree of increase in vocal intensity was reduced, however, when visual feedback of output volume was provided in combination with auditory masking noise. This result is in line with those of Pick et al. (1989) and suggests a special role for somatosensory feedback from self-produced speech in expression of the Lombard effect. Measures of variability did not reveal any significant main effects or interactions, suggesting that variability associated with vocal output was not differentially affected by the auditory or visual feedback manipulations employed in this experiment. There was a non-significant trend in both NA conditions for vocal intensity on the 10th utterance, corresponding to the utterance where feedback was removed, to be slightly greater compared with conditions where auditory voice feedback remained present throughout the trial. Statistical analysis of response times at this utterance revealed that average responses lagged slightly behind the metronome – a result that is in line with previous work studying asynchronies associated with the use of a visual metronome (Chen et al. 2002). Removal of both visual and auditory feedback stimuli was synchronized with the metronome; therefore, both were removed simultaneously with the 10th metronome blink. Considering this, the trend for a slight increase in vocal intensity is likely an artifact resulting from peak intensity levels that were obtained from responses lagging behind the metronome, when both visual and auditory voice feedback had already been removed. The notion of vocal responses to auditory feedback perturbations occurring on such time scales is in line with previous studies of vocal adaptations to pitch-shifted feedback (Burnett et al. 1998; Curio et al. 2000). Overall, these results indicate that the central nervous system is not normally prepared to use somatosensory information from the speech effectors as a primary source of sensory feedback when trying to control vocal intensity. When participants are provided with an alternate source of feedback to calibrate somatosensation, however, they are able to regulate their vocal intensity and resist the Lombard effect.

When Lombard (1911) first discovered his effect, he attributed it to processes of internal self-monitoring that required auditory feedback of the voice in order to maintain consistent vocal intensity. Subsequent attempts to elucidate the Lombard effect's underlying mechanism have shown a primary focus on the relationship between vocal output and auditory input. Given the results of the present experiment, as well as work studying repetitive production of discrete finger forces (Therrien and Balasubramaniam 2010; Therrien et al. 2010; Therrien et al. 2011), we propose an alternate mechanism that is centered on the processing of somatosensory feedback from self-produced vocalizations.

Specifically, we propose that increases in vocal intensity associated with the Lombard effect may, at least in part, be the result of compensation for the sensory attenuation of self-produced somatosensory feedback. Vocal production involves motor commands being sent from primary motor cortex to the articulators. Corollary discharge from the motor cortex is used in the generation of predictions of the sensory consequences those commands will yield (Bays et al. 2006; Bays et al. 2005; Blakemore et al. 1998; Shergill et al. 2003; Voss et al. 2007; Wolpert and Ghahramani 2000). When vocal action is executed, the predicted sensory outcomes are compared with incoming afferent signals in order to evaluate the success of motor execution and distinguish self-produced from unexpected sensory feedback (Bays et al. 2006; Bays et al. 2005;

Blakemore et al. 1998; Shergill et al. 2003; Voss et al. 2007; Wolpert and Ghahramani 2000). Many have hypothesized that this comparison process results in attenuation of the predicted component of incoming sensory signals resulting in a reduced percept of self-generated sensory feedback compared with that which was unexpected or externally-sourced (Bays et al. 2006; Bays et al. 2005; Blakemore et al. 1998; Shergill et al. 2003; Voss et al. 2007). The effects of this attenuation process have been shown previously in cases of tactile sensation and peripheral force production (Therrien and Balasubramaniam 2010; Therrien et al. 2010; Therrien et al. 2011; Bays et al. 2006; Bays et al. 2005; Blakemore et al. 1998; Shergill et al. 2003; Voss et al. 2007). In the case of vocal control and the Lombard effect, self-produced vocalizations are perceived as being of lower intensity; therefore, without more reliable sensory information to calibrate vocal output, participants automatically and unconsciously increase vocal intensity to compensate.

The notion of such a mechanism in the control of vocalization is well supported by current literature. Neurophysiological evidence of sensory attenuation during self-produced vocalizations has been found in the form of reduced auditory cortex activity in both humans (Curio et al. 2000; Crone et al. 2001; Ford et al. 2001; Houde et al. 2002) and non-human primates (Eliades and Wang 2005, 2006, 2008). Somatosensory association cortex in humans has also been found to show suppressed activation during self-produced speech relative to silent repetitive movements of the tongue and jaw (Dhanjal et al. 2008). Finally, Paus et al. (1996) showed that speech-related motor activity modulated changes in cerebral blood flow to secondary auditory cortex, demonstrating the existence of direct motor-to-sensory feedback regulation in vocal control centers of the human brain.

With respect to the Lombard effect itself, indirect evidence for the presence of internal models based on sensory predictions can be drawn from previous work showing that individuals can be trained to inhibit increases in vocal intensity over the long term (Pick et al. 1989; Tonkinson 1994). Furthermore, the Lombard effect has been shown in a wide variety of non-human animals ranging from primates to whales, which suggests a more generalized mechanism than one specific to humans (Smotherman 2007). A recent study by Love and Bee (2011) failed to show the Lombard effect in tree frogs, leading the authors to suggest that the phenomenon could not be generalized to all vertebrates. The mammals in which the Lombard effect has been demonstrated possess a higher evolved cerebellum relative to reptiles (Larsell 1923). The cerebellum has been proposed as a likely neural locus for the formation and evaluation of sensory predictions, which are processes integral to mechanisms of sensory attenuation (Blakemore et al. 1998).

Many studies investigating the control of vocal intensity have noted a reversal of the Lombard effect, known as the Sidetone effect, in situations where enhanced auditory feedback of the voice is provided in place of masking noise (Chang-Yit et al. 1975; Garnier et al. 2010; Laukkanen et al. 2004). Indeed, the results of the present study showed a non-significant trend for overall vocal intensity to decrease in trials where only auditory voice feedback was provided. Computational frameworks of motor control offer a parsimonious explanation of these results (Wolpert and Ghahramani 2000). Auditory feedback delivered at a volume levels greater than the vocal intensity of the speaker would be discrepant with central predictions of sensory feedback. To reduce this discrepancy, subsequent motor commands would then be updated to produce a lower vocal intensity on the next utterance. More direct study of the Sidetone effect is needed, however, before specific mechanisms can be implicated in its expression.

In this article we presented results examining the Lombard effect in a non-communicative, repetitive vocalization task. Our results show that both auditory voice feedback and somatosensory information from the speech effectors are important in the regulation of vocal intensity. We propose a possible for mechanism for the Lombard effect that centers on mechanisms of sensory attenuation affecting somatosensory feedback from self-produced vocalizations. While this mechanism is currently speculative, its role in the expression of the Lombard effect warrants further study. Changing the relative weighting of various sensory feedback modalities in response to auditory feedback perturbations like those seen in the Lombard effect, alters the speech effector system as a whole. Erickson (2002) found that increases in vocal intensity on emphasized syllables could be accomplished through movements of the jaw and tongue. It would be of interest, then, to study the behavior of the supraglottal articulators to determine whether similar compensatory strategies are employed in expression of the Lombard effect.

Aside from increases in vocal intensity, the Lombard effect has been associated with automatic and involuntary changes to other vocal parameters, such as pitch (Garnier et al. 2010; Lane and Tranel 1971; Letowski et al. 1993; Lombard 1911; Patel and Schell 2008; Pick et al. 1989; Smotherman 2007; Tonkinson 1994; Zollinger and Brumm 2011).

In addition, many studies have found enhanced expression of the Lombard effect in communicative situations (Garnier et al. 2010; Lane and Tranel 1971; Letowski et al. 1993, Patel and Schell 2008; Pittman and Wiley 2001). The mechanisms controlling voice pitch are complex and pitch-shifted auditory feedback has been shown to induce other automatic, involuntary changes to vocal output (Laydon et al. 2003; Smotherman 2007; Toyomura et al. 2007). Recent evidence suggests that perturbations to vocal pitch and intensity may be processed differently in the auditory cortex of non-human primates (Eliades and Wang 2008); therefore, it is possible that vocal modulations of pitch and intensity in the Lombard effect may be controlled independently. Nonetheless, more study is needed to elucidate the relationship between somatosensory and auditory feedback modalities in the regulation of vocal parameters other than output intensity, especially in situations where verbal comprehension is stressed.

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6.7 – FIGURE APPENDIX

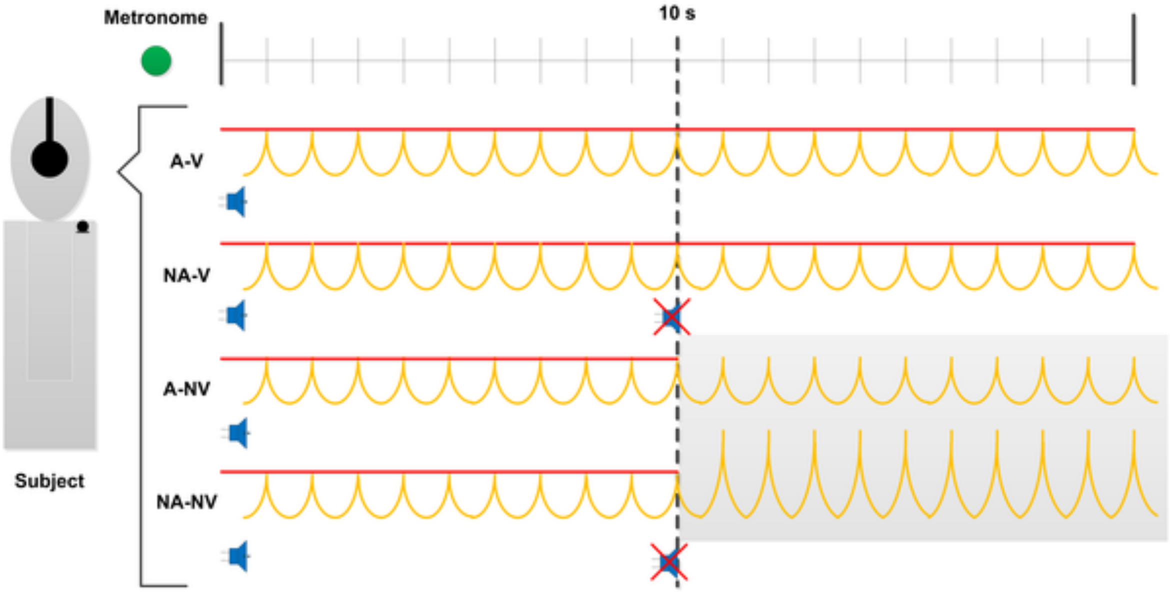

Figure. 6.1. Schematic illustrating the four experimental conditions studied in our protocol. Auditory voice feedback either remained present throughout the trial (A), or was replaced with masking noise after 10 s (NA). Similarly, visual feedback of vocal intensity relative to the 80 dB SPL target either remained present throughout the trial (V), or was removed after 10 s (NV). Following feedback manipulations, participants were instructed to make continued responses synchronized with the visual metronome and at the target vocal intensity for the remainder of the trial. We hypothesized that provision of visual reference stimuli would calibrate attenuated somatosensory signals and result in reduced expression of the Lombard effect following removal of auditory voice feedback.

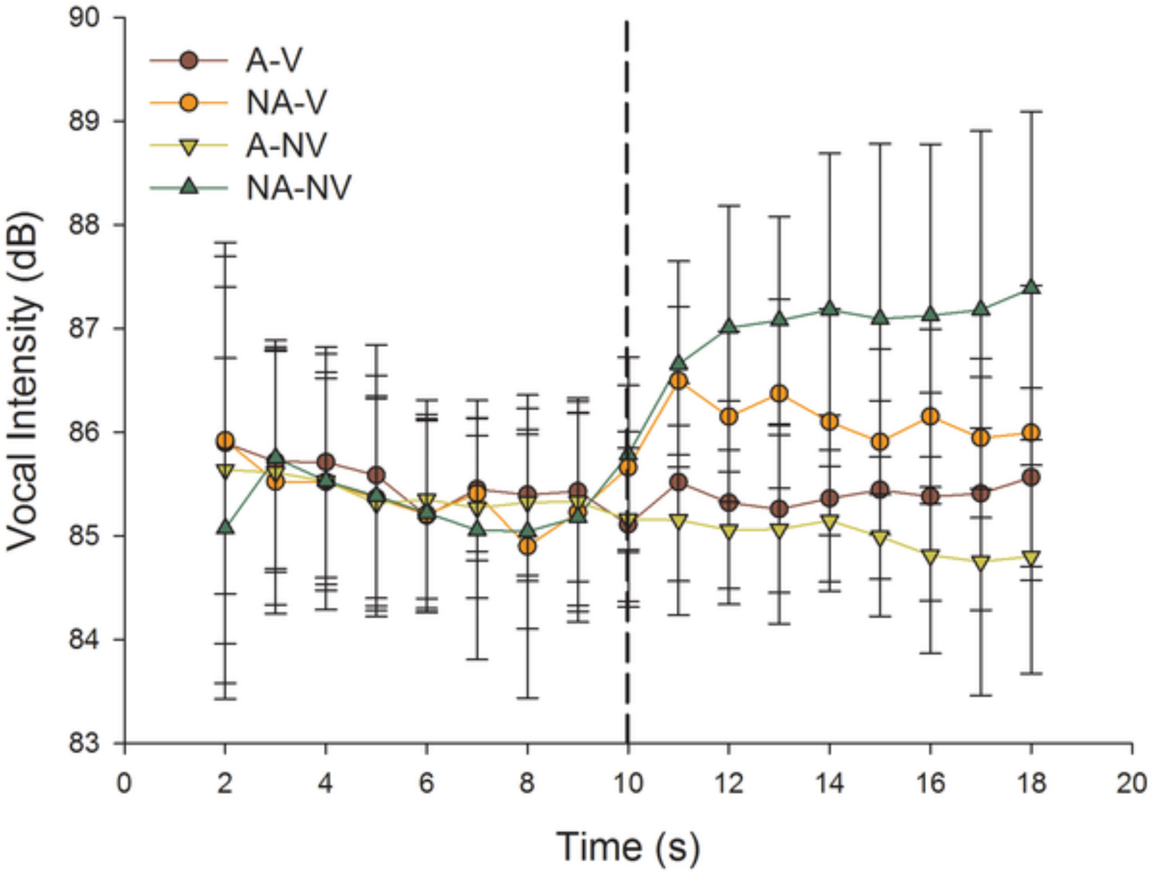

Figure. 6.2. The vocal intensity time series for all conditions, grand averaged across participants. Error bars represent SD. The vertical dashed line represents the time at which auditory voice feedback, visual feedback of vocal intensity or both were removed.

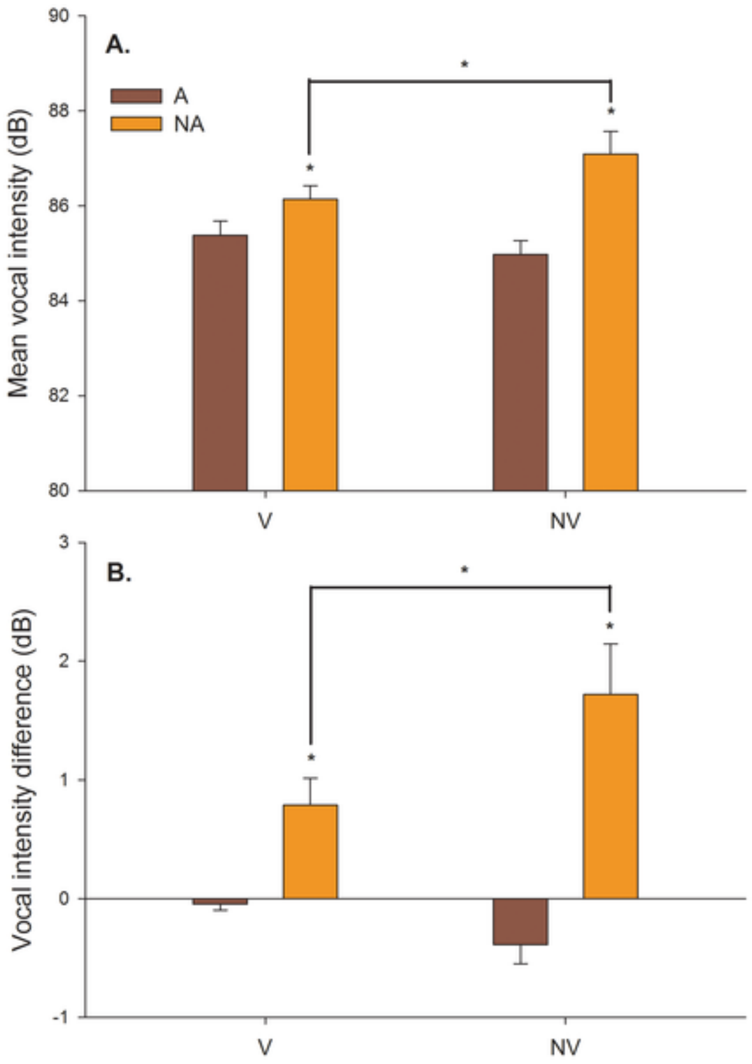

Figure. 6.3. (**A**) Interaction for overall vocal intensity among factors of auditory feedback condition and visual feedback condition. (**B**) Interaction for the difference in mean vocal intensity over the two trial phases corresponding to the period before feedback removal (t = 2-10s) and the period following it (t = 11-18s). In all cases, asterisks and connecting lines represent reliable pairwise comparisons, significant at $p < .01$. Error bars represent standard error.

CHAPTER 7: GENERAL DISCUSSION

7.1 – THESIS SUMMARY

Many daily motor actions require the concurrent regulation of muscle force and motor timing (e.g. playing the piano or hammering a nail). While an extensive literature has studied the control of these movement parameters in isolation, much of the neural mechanisms used to simultaneously manage force and time remain unclear. This thesis has examined the roles of visual and somatosensory feedback modalities in the control of sequential periodic forces. Our task involved the repetitive production of pinch-grip forces to a visually specified target magnitude and in synchrony with an external pacing stimulus, while the availability of either was manipulated. Broadly, we hypothesized that force output errors produced without vision may be related the processing of reafferent somatosensation and that the removal of visual information would affect force output ability, but would not differentially influence motor timing behavior as dictated by the Wing and Kristofferson model (1973). This conjecture was examined in Chapters 2 and 3. Following this we applied our hypothesis to extensions of the sequential force production task in order to assess the interplay between vision and somatosensation in tasks with changing target forces (Chapter 4) as well as in tasks requiring that forces be produced bimanually (Chapter 5). Lastly, we expanded our investigation to include sequential force production by the vocal effector system. Specifically, we adapted our task to assess the relationship between auditory and somatosensory feedback in the control of vocal intensity. Overall, our behavioral findings add to current knowledge of the integration of reafferent somatosensory feedback in the presence of other reference stimuli in the control of timed force output behavior. A more detailed summary of these findings, their theoretical implications and potential directions for future research is included below.

7.2 – A ROLE FOR VISION IN THE CALIBRATION OF ATTENUATED REAFFERENT SOMATOSENSORY FEEDBACK

In Chapter 2 we studied the effect of removing visual feedback on force level control in a sequential force production task, performed unimanually with the dominant right hand. Following withdrawal of visual reference stimuli, we found that force output increased, with mean values exceeding target magnitudes and autocorrelation data suggesting that this occurred consistently for the remaining length of the trial. Without vision, participants had to judge force performance relative to the remembered target using somatosensory feedback from the active hand. Previous literature showing similar positive force errors in a task where individuals were required to match experienced forces using somatosensation attributed the effect to compensation for the attenuation of reafferent somatosensory feedback (Shergill et al. 2003).

In Chapter 3 we tested the hypothesis that mechanisms of sensory reafference may have also been responsible for the force overproduction errors noted in our task. Our results showed that inducing discrepancy between predicted and actual sensory signals, through application of cTBS to M1, reduced positive errors in force output following removal of visual feedback. In line with Voss et al. (2007), this finding supported the assertion that force output errors produced in our task without visual reference stimuli were linked to the processing of reafferent somatosensory feedback. Interestingly, TMS to M1 did not influence force performance when visual feedback was present.

This latter finding of Chapter 3, combined with the finding that force overproduction errors were not exhibited when visual feedback was present in Chapter 2 and the anecdotal observation that these errors are not typically exhibited in daily life suggests that visual information might serve as an external reference in the calibration of attenuated reafferent somatosensation. Specifically, for the control of motor output in our task, we propose a mechanism where visual feedback may be integrated with reafferent somatosensory signals in the estimation of current force level. Somatosensory information from self-generated forces is unreliable due to the attenuating effects of reafference processing. Thus, when it is available, visual information is favored in the generation of force output estimates. When visual feedback is removed however, only attenuated reafferent somatosensation is available to assess force performance, which yields an errant estimation of reduced force output. If this estimate is to be compared with a remembered visual estimate, as is the case in our task, the resultant discrepancy can be fed back to the motor system to initiate a corrective increase in output on subsequent iterations. An illustration of this mechanism is included in Figure 7.1.

The notion of visual feedback tuning somatosensory perception is well supported by the sensory integration literature. Indeed, the size-weight illusion, where the visually smaller of two equally weighted objects is perceived to be heavier, is a classic example of visual dominance (Charpentier 1891 as reviewed by Murray et al. 1999). While the size-weight illusion was originally thought to be the result of discrepant sensory prediction, Flanagan and Beltzner (2000) found it to persist even after participants learned to appropriately scale grip force to the true object weight (a sign of accurate sensorimotor prediction). In line with our proposal, this finding signaled the involvement of perceptual mechanisms, which operate separately from the forward model comparator, in the final estimation of object weight. Ernst and Banks (2002) later showed that in the estimation of current state this visual perception is optimally integrated with somatosensation and visual dominance results when lower uncertainty is associated with this sensory modality. Interestingly, studies of rod-wielding paradigms have found that perception still favors visual-spatial information even when variance in this domain is experimentally manipulated (Riley and Turvey 2000). This suggests a natural tendency for visual dominance, which may be related to the unreliable nature of reafferent somatosensation.

What remains unclear from the work in Chapters 2 and 3 is the manner in which visual feedback may tune attenuated performance judgments. Previous literature examining continuous isometric force production has found that visual information stabilizes performance through mechanisms of intermittent feedback control (Slifkin et al. 2000). It is possible that vision adjusts for attenuated somatosensation through similar mechanisms; however, it is important to note that intermittent control processes are influenced a by a number of factors including the spatial (Kuznetsov and Riley 2010; Sosnoff and Newell 2006) and temporal (Slifkin et al. 2000; Sosnoff and Newell 2005a) regularity of visual feedback, the magnitude of force being produced (Sosnoff and Newell 2005a) as well as movement frequency (Sosnoff and Newell 2005b). Future research studying the effect of these factors on the interplay between vision and somatosensation in the control of sequential forces may help to elucidate the precise mechanism of visual calibration.

7.3 – COMPENSATION FOR SENSORY REAFFERENCE IN THE ABSENCE OF AN EXTERNAL REFERENCE

Chapters 4 and 5 of this thesis probed the effect of varying task parameters on sequential force production in the absence of visual reference stimuli. In Chapter 4 participants produced series of unimanual pinch-grip forces with continuously increasing or decreasing magnitudes while visual feedback of force output was periodically removed. Results of this study revealed two main findings. First, errors produced following visual feedback withdrawal were consistent with a perceived shift in magnitude, indicating that the attenuation of reafferent somatosensory feedback does not disrupt participants' ability to scale the relative difference between successive force levels. Secondly, a systematic dependence was observed between the direction of force errors following visual feedback withdrawal and the slope of the target force series. While force overproduction was associated with conditions where target forces continuously increased, an undershoot bias was found for conditions where target forces progressively decreased. These bi-directional errors suggest that in the absence of an external reference, behavior compensating for the effects of sensory reafference may be dependent on prior task constraints.

This latter result of Chapter 4 is particularly interesting given that literature studying continuous force production has found that force output typically decays without visual feedback (Davis 2007; Vaillancourt & Russell 2002). In our task rather, the general observation has been an increase in force level following removal of visual information (Chapters 2, 3, 5 and 6). It is possible that the production of continuous versus sequential forces imposes task constraints that could contribute to this discrepancy in results. Chapter 4 discussed Bayesian Decision Theory (Wolpert 2007) as a potential mechanism through which the increasing or decreasing force demands of the task could have contributed to the pattern of errors observed. Modeling this problem using Bayesian methods could help to clarify the issue of discrepant findings between continuous and sequential force production tasks in the future.

In Chapter 5 we again modified task parameters, this time to study the effects of removing visual feedback on performance of two bimanual extensions of the sequential force production task. In the first task, target force magnitudes were reached through the combined effort of the two hands; whereas, bimanual conditions of the second task required that each hand reach the target force simultaneously. Our objective was to determine whether the effector-specific control that has been associated with bimanual force production (Inui and Hatta 2002; Rinkenauer et al. 2002) might also be extended to the processing of reafferent somatosensory feedback. Results showed a lack of significant coupling between the forces produced by the two hands when the bimanual task goal was shared. Furthermore, when the bimanual task goal was to be reached simultaneously with both hands, the degree of force overproduction exhibited by each was asymmetric and unilateral cTBS applied to the left M1 selectively influenced force overproduction errors by the hand contralateral to stimulation. Thus, it seems that in the absence of an external reference to calibrate force output estimates, both the processing of and compensation for the attenuation of reafferent feedback may be programmed in an effector-specific manner.

While the control of bimanual forces has shown capacity for between-hand independence (Inui and Hatta 2002; Rinkenauer et al. 2002), previous literature has found evidence for coupled force output in bimanual tasks. Ranganathan and Newell (2008) reported switches from error-compensation behavior (negative correlation) to between-hand enslaving (positive correlation) with degradation of visual feedback quality in bimanual discrete isometric force production. Additionally, interference effects have been observed when bimanual force production tasks involve asymmetric targets for the two hands (Hu and Newell 2011), which are enhanced when little time is allotted for motor programming (Masumoto and Inui 2013; Steglich et al. 1999). Although the trend results of Chapter 5 are generally in line with the findings of Ranganathan and Newell (2008), none of our correlations reached significance suggesting a lack of true coupling in our study. Nonetheless, it would be interesting to further assess effector-specific processing of reafferent somatosensory feedback when the intermittency of visual information is manipulated as well as in bimanual tasks requiring asymmetric force production by the two hands.

7.4 – THE CALIBRATION OF REAFFERENT SOMATOSENSATION BEYOND THE MANUAL EFFECTORS

In Chapter 6 we devised a vocal analog to the basic sequential force production task used in Chapters 2-5. Here, participants made repetitive utterances at a prescribed sound intensity and in synchrony with a visual metronome. The task was motivated by the Lombard effect (Lombard 1911), a common observation in audiology literature that individuals placed in a noisy environment show immediate and involuntary increases in vocal loudness. Increases in vocal intensity following auditory feedback masking in the Lombard effect resemble the force overproduction effect found in Chapters 2-5. Since vocal intensity is mediated through force output by the respirators (Smotherman 2007), we hypothesized that in the Lombard effect, auditory feedback may serve to calibrate attenuated reafferent somatosensation from the speech effectors. Our results revealed that when auditory voice feedback was present, or was masked and replaced with a visual reference, expression of the Lombard effect was lessened. When the only source of sensory feedback available was somatosensation however, the Lombard effect was exhibited to significantly greater extent suggesting a distinct role for reafference effects in its expression. We proposed a novel mechanism for the Lombard effect that involves the same interplay between audition and somatosensation in the control of force by the vocal effectors as that posited for vision and somatosensation in the control of force by the manual effectors.

In addition to providing a novel explanation for the Lombard effect, the mechanism proposed in Chapter 6 also provides a new lens through which the control of vocal intensity can be studied more generally. Motor disorders of the basal ganglia, such as Parkinson’s disease, are associated with deficits in vocal intensity control (Walsh and Smith 2012). Inducing the Lombard effect has been shown to improve symptoms of hypophonia in this patient group (Coutinho et al 2009); however, the underlying mechanism remains unclear. Parkinson’s patients also exhibit impairments in somatosensory processing from the speech effectors (Hammer and Barlow 2010) as well as enhanced vocal responses to auditory feedback manipulations relative to healthy controls (Liu et al. 2012). It would be beneficial for future research to further examine the role of reafferent somatosensation in the Lombard effect, as it may reciprocally help to further our understanding of the mechanisms underlying the symptoms of certain motor disorders, like Parkinson's disease.

Interesting to consider as well, are findings of enhanced expression of the Lombard effect in situations where verbal communication is stressed (Garnier et al. 2010; Lane and Tranel 1971; Letowski et al. 1993; Patel and Schell 2008; Pittman and Wiley 2001). Given the finding that behavioral responses to sensory attenuation effects can be task dependent and the discussion of a Bayesian mechanism in Chapter 4, the communicative enhancement of the Lombard effect poses an interesting avenue for future research. In Lombard-type situations where the available somatosensory information is unreliable, a Bayesian integration process would yield a response that favors the more reliable prior (Wolpert 2007). In communicative tasks this prior would be to enhance the intelligibility of vocal output, which could augment the increase in vocal intensity seen in the Lombard effect.

7.5 – MOTOR TIMING IN THE CONTEXT OF SEQUENTIAL FORCE PRODUCTION

Motor timing during simultaneous control of force was examined in Chapter 2 and discussed further in Chapter 5. In Chapter 2 we used an information processing approach to assess whether removing visual feedback of force output would influence the interval timing ability in a synchronization-continuation timing task. Overall, the findings of Chapter 2 revealed that despite a change in force control mechanisms, which occurred as a result of visual feedback removal, motor timing ability remained independent of force level estimation. Such a distinction between force and time at the level of parameter specification is in broad agreement with the findings of previous literature (Ivry 1986; Keele et al. 1987); however, our results did not rule out all possible interaction between these two control processes. Force performance was influenced by both visual feedback and movement frequency (Chapter 2). Sosnoff and Newell (2005b) found that, rather than influencing the mean and variability of intervals at which forces were produced, manipulating the intermittency of visual feedback affected temporal control in terms of the quantity and rate of force output error corrections. While autocorrelations performed on the force series revealed no error correction following visual feedback removal at lag 1 (Chapter 2), future work could use our paradigm to assess longer-range correlations in the force data.

In Chapter 5 we did not assess motor timing directly; however, our results showed a strong capacity for independence between the limbs in the processing of and compensation for reafferent somatosensory feedback. When paired with previous findings of strong between-hand coupling in bimanual timing (Rinkenauer et al. 2002), these findings also supported autonomy between force estimation and temporal parameterization processes. Bimanual force coupling has been found to vary as a function of time, such that longer intervals are associated with more asymmetric control (Masumoto and Inui 2013; Steglich et al 1999). It would be interesting for future research to assess the bimanual sequential force production tasks of Chapter 5 performed over a range of movement frequencies to determine whether a similar pattern of results occurs for somatosensory processing.

7.6 – CONCLUDING STATEMENTS

This thesis has examined the sensorimotor control of sequential forces. Collectively, the research presented in Chapters 2 through 6 has provided novel insight into the roles of visual and auditory feedback in the calibration of reafferent somatosensation to control force output by the manual and vocal effectors respectively. In addition we have shown that in the absence of external reference stimuli, behavioral compensation for the effects of sensory reafference may be dependent on prior task constraints and function in an effector specific manner. Lastly, we have demonstrated that while removal of external reference stimuli significantly affects the amplitude of forces produced, temporal production remains intact suggesting independence between force and motor timing control processes at the level of parameter specification. Our findings add to current literature studying the mechanisms through which sensory feedback contributes to the timed control of force and offer many promising avenues for future research.

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7.7 – FIGURE APPENDIX

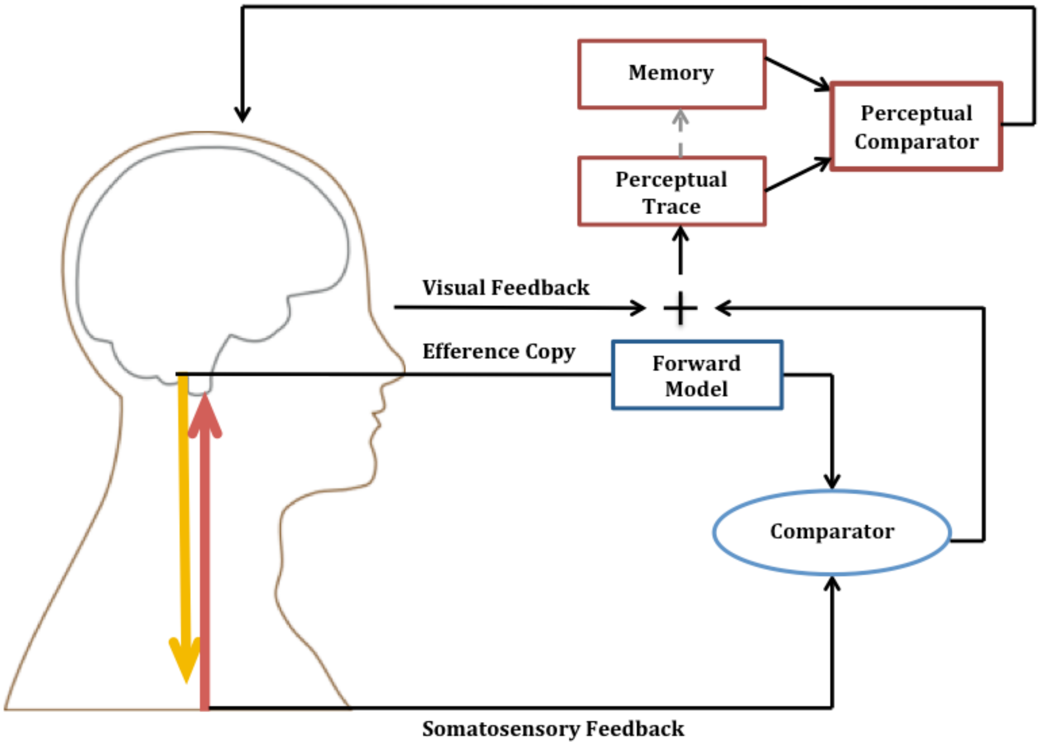

Figure 7.1. Schematic illustrating the proposed mechanism of visual calibration of reafferent somatosensory feedback in the sequential force production task.