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Fixation Condition Effects on Stop Signal Reaction Times: An Eye-Hand Co-ordinated Human Countermanding Task

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Fixation Condition Effects on Stop Signal Reaction Times: An Eye-Hand Co-ordinated Human Countermanding Task

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Abstract

The countermanding task requires subjects to cancel an impending movement in the presence of an imperative stop signal. The outcome of a given countermanding trial has been modeled as a race between stochastically independent GO and STOP processes and is largely dependent on the amount of time between target and stop signal presentation (the stop signal delay - SSD). Here, we investigated the effect of fixation condition on the GO and STOP processes using human subjects in eye-only, hand-only and eye-hand co-ordinated countermanding tasks. In Experiment 1, we found that duration of the STOP process, estimated through the derivation of the stop signal reaction time (SSRT), was ~20 ms shorter on trials with a 200 ms gap between fixation point removal and target presentation compared to when the fixation point remained illuminated (an "overlap" condition). Similarly, we found SSRTs were ~10 ms shorter on trials with simultaneous fixation point removal and target presentation compared to the overlap condition. However, in Experiment 2, this priming of movement inhibition due to fixation condition disappeared, when the stop signal delay for each trial was determined dynamically, based on subject performance on previous trials. Overall, we suggest the disappearance of fixation condition effects in Experiment 2 was due to smaller gap effects on reaction times and a greater variance in fixation condition effects on the STOP process in Experiment 2. We believe these differences arose due to a higher percentage of trials in Experiment 2 where the GO and STOP processes approached threshold at approximately the same time. Therefore we postulate that such trials produce a greater amount of conflict between movement generation and inhibition systems, causing both systems to rely less on fixation cues.

Keywords: Movement inhibition, countermanding, eye-hand co-ordination, motor control, saccades, oculomotor system, reaching

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I, Scott Stevenson, am submitting this research as partial fulfillment of the Master of Science Degree in the discipline of Neuroscience. As such, I have assumed a primary role in all aspects of this document including, but not limited to, design aspects, data collection and analyzing as well as producing the initial draft of the thesis. Dr. Brian D. Corneil acted as my primary supervisor for this project. He provided the framework for this project as well as providing critical advice and guidance throughout the stages of the project. He also acted as an editor to the subsequent drafts of this thesis.

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List of Abbreviations

CDF – Cumulative Distribution Function
EOG – Electro-oculography
FEF – Frontal Eye Fields
FP – Fixation Point
RT – Reaction Time
SC – Superior Colliculus
SEF – Supplementary Eye Fields
S.D. – Standard Deviation
SSD – Stop Signal Delay
SSRT – Stop Signal Reaction Time
STN – Subthalamic Nucleus
T – Target

List of Symbols

° - Degrees
deg/s – Degrees per second
Hz – Hertz
kHz – kilohertz
ms – Milliseconds
s – Seconds
± - plus or minus

Chapter 1 – General Introduction and Literature Review

1.1 – Goal Directed Action and Executive Function

In everyday life, our actions are determined by our immediate and long term goals. For example, when Tiger Woods steps to the first tee at the Masters, his immediate goal is to hit the ball in the fairway. Roger Federer's immediate goal at Wimbledon is to return his opponent's serve. Your goal is to make it to work on time even though you slept in this morning. These examples require our highly developed motor systems to execute a series of finely controlled actions to reach these desired goals. While being able to perform these complex behaviours accurately is an important part of motor control, so is inhibiting these actions when they become irrelevant or inappropriate in a continually changing behavioural context. Imagine Tiger Woods hears a camera click in his backswing; Roger Federer hears "fault" on his opponent's serve; the green light changes to yellow in front of you. All of these situations call for a change in the subject's immediate goals: Tiger Woods stops his swing to regain mental focus; Roger Federer withholds his powerful forehand down the line, and you hit the brakes as to not cause an accident.

Countless other situations can be envisioned where having excellent inhibitory control is advantageous. Think of playing baseball, where you wait until the last possible instant to decide if a pitch is going to break out of the strike-zone. While sports provide some of the most obvious examples of inhibitory control, many are encountered on a daily basis. Imagine you are about to speak, when you realize that what you are about to say may be offensive to someone in your audience. Or imagine you reach to grab a pot off the stove, but realize that the handle has been sitting above the hot element. In all of these situations, we benefit from having highly developed inhibitory control mechanisms which allow you to continue on with our daily lives.

Inhibitory control can vary from person to person and from task to task. In fact, Tiger Woods' ability to withhold his swing in mid-flight is unrivalled by almost any golfer. This inhibitory control is finely tuned from years of practice, much like Roger Federer's ability to hold off on his opponent's serve. It is unlikely that Tiger Woods or Roger Federer could rival the other's inhibitory control in each other's respective sport. Such profound differences in behaviour and cognitive control have also been observed across development (Bedard et al. 2002; Ridderinkhof et al. 1997; Williams et al. 1999) and aging (Kramer et al. 1994). In other words, these executive functions need time to develop and peak in early adulthood, before degrading slowly through the aging process. Mental illness can also affect inhibitory control and deficits have been shown to exist in Parkinson's disease (Gauggel et al. 2004), schizophrenia (Badcock et al. 2002; Carter et al. 2003) and attention deficit hyperactivity disorder (ADHD; Nigg 2001 for review; Armstrong and Munoz 2003; Oosterlaan et al. 1998; Schachar et al. 2007). In fact, some have speculated that reduced inhibitory control may be the main component contributing to the manifestation of ADHD (Barkley 1997). Therefore, it is important to emphasize that a number of factors affect our inhibitory control and that these differences play a role in our everyday lives. This ability to withhold action where appropriate is a hallmark of executive function in higher order species and is an imperative component of motor control.

1.2 - Studying Movement Inhibition

Given the number of times daily that we are required to change, or cancel our planned actions in response to a changing situational context, it is easy to see the value in studying movement inhibition. Though the six above examples require changes in the subject's immediate goals, they do not all require the same outcome. For example, when you hit the

brakes at the change of a light, you cancel your initially planned action (of pressing the gas pedal all the way through the intersection), and replace that action with another (moving your foot to the brake pedal). In the remaining five examples the subjects' changes in goals simply require them to cancel their planned action without replacement. Therefore, it is important to distinguish between two types of movement inhibition: those which require us to exchange a planned action with another competing action, and those which simply require the cancellation of a planned action.

Both types of movement inhibition have been studied under laboratory conditions. The former has been captured in the laboratory by using a double step task (Lisberger et al. 1975; Becker and Jurgens 1979; Aslin and Shea 1987), where subjects are required to make a movement to a peripheral target on the majority of the trials. However, on a subset of trials, the target jumps to an alternate location, and subjects are required to inhibit their originally planned movement to the target, and plan an alternative movement to the new target location (much like moving your foot from the gas to the brake). In studying the movement inhibition process in the double step task, it is difficult to separate the inhibition of the planned movement to the original target from the initiation process of the movement to the alternative target (Camalier et al. 2007). The second type of movement inhibition can be studied under laboratory conditions using a countermanding task (which originally evolved from the double step task; Logan and Cowan 1984; Logan 1994; Hanes and Schall 1995). In this task, subjects are also required to make a movement to a peripheral target (generally >70% of trials). However, on a small subset of trials, an imperative stop signal is presented and subjects are instructed to simply cancel their movement without replacement (much like Woods or Federer). In contrast with the double step task, the countermanding task pits movement initiation directly against movement inhibition and

thus permits the study of movement inhibition without an alternative, competing movement plan. This advantage of the countermanding task (along with others to be discussed later) has led to its rise in prominence in studies of movement inhibition.

1.3 – The Race Model

Behaviour in the countermanding task has been modelled as a race between movement initiation and inhibition. Whether a movement is generated or not has been conceptualized as a race between stochastically independent GO and STOP processes, dictating movement initiation (initiated upon target presentation), and movement inhibition (initiated upon stop signal presentation), respectively (Fig 1). Performance on a given countermanding trial depends in part on the amount of time between the onset of the peripheral target and the stop signal (deemed the stop signal delay – SSD), as this delays the initiation of the STOP process. Physiologically, however, it seems unlikely that such independent GO and STOP processes could exist, particularly in the oculomotor network, where a push-pull relationship is known to exist between fixation-holding and saccade-generating networks (e.g., Findlay and Walker 1999; Munoz and Istvan 1998; Munoz and Wurtz 1993a; Munoz and Wurtz 1993b).

Despite this, multiple countermanding studies have tested the race model and the majority have concluded that their data do not violate the race model's assumption of independence (e.g. Stevenson et al. 2009; Paré and Hanes 2003; Hanes and Carpenter 1999; Mirabella et al. 2009; Corneil and Elsley 2005; Emeric et al. 2008). The consensus has not been unanimous, as the race model's assumption of independence has been shown to fail at the shortest SSDs (Ozyurt et al. 2003). A more recent "interactive" race model suggests that the GO and STOP processes likely have an initial period of independence, but then interact for a

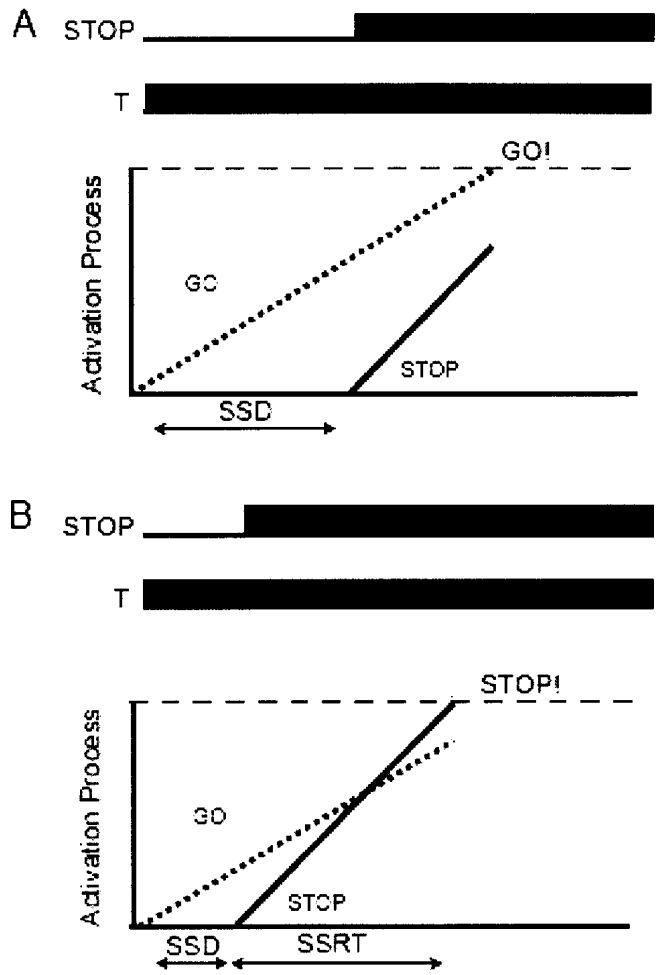

Figure 1. Schematic drawing of the race model where stochastically independent go and stop processes race toward a common threshold with the outcome of this race determining which response is generated. The go process begins with target onset, whereas the stop process begins with the onset of the stop signal. The time between target and stop signal presentation is the stop signal delay (SSD), which can vary from trial to trial. (A) the go process starts sufficiently early to beat the stop process to threshold, and hence a movement is generated. (B) the go process begins, but the stop process beats the go process to threshold, resulting in the cancellation of a movement

brief period where the GO process is potently inhibited by the STOP process (Boucher et al. 2007a). This model has the unique advantage of being able to fit not only behavioural data, but also neuronal activity associated with the countermanding task.

Regardless of whether or not the GO and STOP processes are independent for the entirety of the trial, the performance on a given countermanding trial depends upon the outcome of this race, with a movement being generated or withheld if the GO or STOP process wins the race, respectively (Fig. 1; Logan and Cowan 1984; Logan 1994). Within the countermanding task, the completion of the GO process is measured by the reaction time of the subject on the trials in which no stop signal is presented (*CONTROL* trials). On trials where a stop signal is presented (*STOP* trials) and the subject successfully inhibits their movement, a similar demarcation of the completion of the STOP process does not exist, since no overt behaviour is displayed (Fig 1B). The theory of the race model permits the mathematical estimation of the duration of the stop process (See Methods 2.5), called the stop signal reaction time (SSRT; Fig 1B). Also, by studying the GO and STOP processes, the countermanding task provides a formalized framework in which to interpret neural activity related to the immediate control of movement in both human imaging studies (Aron and Poldrack 2006; Curtis et al. 2005) and animal models (monkey: Hanes and Schall 1995; Paré and Hanes 2003; Stuphorn et al. 2000; Emeric et al. 2007; Brown et al. 2008; rat: Eagle and Robbins 2003).

1.4 – Neural Substrates of the GO and STOP processes

In the oculomotor system, the area of highest visual acuity is dedicated to a small portion of the retina ($1mm^2$), termed the fovea. In order to examine objects of interest in detail, eye movements called saccades rapidly re-align the visual axis in order to bring targets of interest

onto the fovea. The oculomotor system is the most well understood of our motor systems as it has the distinct advantage of having all of its neural circuitry above the spinal cord, accessible to modern neurophysiological techniques. Therefore, a great deal is known about the neural mechanisms underlying the GO and STOP processes of the saccadic eye movement system. The frontal eye field (FEF; e.g., Bruce and Goldberg 1985; Schall 1991), basal ganglia (e.g., Hikosaka and Wurtz 1983c; Hikosaka and Wurtz 1983b; Hikosaka and Wurtz 1983a; Hikosaka et al. 2000) and superior colliculus (SC; Schiller and Koerner 1971; Sparks 1975; Wurtz and Goldberg 1972a; Munoz et al. 2000) have all been implicated in the production of saccadic eye movements. The SC is arranged topographically such that sites moving from rostral to caudal locations code for small to large amplitude saccades, respectively (Schiller and Koerner 1971; Wurtz and Goldberg 1972b; Munoz and Wurtz 1993a; Robinson 1972). In fact, neurons in the most rostral portion of the SC have been termed "fixation neurons", while those in more caudal locations have been termed "saccade neurons" (Robinson 1972; Munoz and Wurtz 1993a). The FEF is connected to the SC (see Leichnetz and Goldberg 1988 for review), and input from the FEF is integrated in the SC before a saccade is produced. The basal ganglia are also involved in saccade production and receive input from the FEF, leading to decreased activity in the substantia nigra pars reticulata, which in turn disinhibits the SC (Hikosaka and Wurtz 1983c). The SC also receives input from the visual cortex, cerebellum and lateral intraparietal area (LIP) and this input can further affect the production of saccadic eye movements (e.g. Kase et al. 1980; Thier et al. 2002). Finally, both the SC and FEF project to the brainstem burst generator which is ultimately responsible for the production of saccadic eye movements (see Munoz et al. 2000 for review).

In order for a brain area to qualify as a neural correlate of the STOP process, the neural population being considered must show two characteristics. First, a neuron must begin both *CONTROL* and *STOP* trials in the same manner, and then have its activity diverge only after the stop signal has been presented. Secondly, this divergence must occur within the behavioural estimate of the SSRT. Thus far, neurons in the SC (Paré and Hanes 2003) and FEF (Hanes et al. 1998) have satisfied both criteria, and thus have been implicated as neural correlates of the STOP process. Human imaging studies in countermanding have also shed some light on other potential areas involved in the STOP process. For example, the ventro-lateral prefrontal cortex has been implicated in the stopping process, but whether its modulation occurs within the SSRT has yet to be determined (Leung and Cai 2007). Similarly, the subthalamic nucleus (STN) of the basal ganglia has been implicated in the limb movement STOP process (Aron and Poldrack 2006). Although its role in the immediate control of arm movement has not been determined, it has been proposed that the inferior frontal cortex excites the STN, which excites the globus pallidus, suppressing basal ganglia thalamocortical output, thus blocking the initiated GO response from being executed (Aron and Poldrack 2006). Finally, the supplementary eye fields (SEF) have been implicated in the monitoring of a subject's success on a trial by trial basis (Curtis et al. 2005). However, single unit recordings have shown that these neurons are modulated after the SSRT has elapsed (Schall et al. 2002). Therefore, while the SEF displays activity suitable for monitoring subject performance, it appears it is not involved in the immediate control of action.

1.5 – Affecting Movement Initiation – The GO Process

A common method of manipulating the rate of completion of the GO process for eye or hand movements (reaction times - RTs) has been to alter the subject's state of fixation in a

simple RT task. In such a task, the subject foveates a central fixation point (FP) and performs a speeded movement (eye or hand) to a presented peripheral target. Altering a subject's state of fixation generally involves manipulation of the central FP prior to, or simultaneous with, target presentation. In particular, a generalized reduction in RTs is known to occur when comparing trials where the FP is removed prior to the presentation of a target (a "gap condition"), to trials where the FP remains on throughout the trial (an "overlap condition"; Saslow 1967; Dorris and Munoz 1995; Munoz et al. 2000). This generalized reduction has been referred to as the "gap effect." Multiple components contribute to the gap effect, including the benefit afforded by warning of impending target presentation (a "warning" component), and by disengaging fixation via removal of a foveal stimulus (a "foveal" component; Ross and Ross 1980; Ross and Ross 1981; Reuter-Lorenz et al. 1995; Kingstone and Klein 1993a; Juttner and Wolf 1992; Paré and Munoz 1996; Fendrich et al. 1999; Forbes and Klein 1996; Taylor et al. 1998; Pratt et al. 2000). Others have referred to the "gap effect" as the comparison in RTs between the "gap condition" and trials where the fixation point is removed simultaneously with target presentation (i.e. a gap of 0 ms; referred to as "step", or "no gap" condition; eye: Kingstone et al. 1995; hand: Mirabella et al. 2009). In order to be consistent with previous studies from our lab, we will refer to the comparison between "overlap" and "gap" conditions as the "gap effect", and refer to the difference between "step" and "gap" conditions as a "step effect." A maximal reduction in RTs occurs with a gap of ~200 ms in the gap condition (Saslow 1967; Fischer 1987; Munoz et al. 2000; Dorris and Munoz 1995) and neural correlates have been observed in both the SC and FEF (Dorris and Munoz 1995; Opris et al. 2001; Everling and Munoz 2000).

There is a rich literature in psychophysics regarding the gap effect on simple reaction time tasks. The effect was first reported by Saslow (1967), and subsequent experiments over the

past 40 years have confirmed the consistency of this effect, and its presence in both human and animal studies (see Munoz et al. 2000 for review), as well as on both eye and hand movement systems (Stevenson et al. 2009; Pratt et al. 2000; Gribble et al. 2002). The overall magnitude of this gap effect can range in magnitude from ~30-75 ms (Pratt et al. 2000; Reuter-Lorenz et al. 1995; Munoz and Corneil 1995; Stevenson et al. 2009) while the step effect is generally smaller (~20-40 ms; Kingstone et al. 1995; Reuter-Lorenz et al. 1995). Reuter-Lorenz and colleagues (1995) found a gap effect of ~45 ms on RTs, while only finding a ~20 ms step effect. A third fixation condition effect, termed the "fixation offset" effect, refers to the reduction in reaction times in the step, compared to overlap fixation condition and this effect generally ranges from 15-30 ms (Ross and Ross 1980; Ross and Ross 1981; Kingstone and Klein 1993b; Kingstone et al. 1995; Morein-Zamir and Kingstone 2006). Overall, manipulating fixation condition can produce measurable differences in subject behaviour. The neurophsyiological basis of these differences can then be investigated to gain further insight into the neural substrates underlying the immediate control of action.

1.6 – Affecting the STOP Process – Human Countermanding Studies

Similar to movement initiation, the study of behavioural estimates of the STOP process permit the study of underlying neurophysiological correlates. Whereas fixation condition effects have been well characterized in reaction time tasks (and hence their effects on the GO process are well known), the effects of these different fixation conditions on the behavioural STOP process have only recently been examined. Theoretically, three different effects on the STOP process could be predicted. First, because of the assumed independence of the GO and STOP processes, one could predict that SSRTs would be unaffected by a 200 ms gap. In support of this, a fixation

offset effect has been shown to expedite the duration of the GO process without influencing the duration of the STOP process (Morein-Zamir and Kingstone 2006; Table 1). The second potential outcome, also consistent with the independence assumption of the race model, predicts that any effect that shortens the GO process may also shorten the duration of the STOP process. Three previous reports have provided evidence for this prediction. For example, previous results from our lab (Stevenson et al. 2009) show evidence for a similar gap effect on SSRTs as seen on RTs (ie that the SSRT is shorter in the gap condition than the overlap condition; Table 1). These results are also consistent with a recent report using a double-step task, which demonstrated that both inhibitory and saccade preparatory processes could be primed in delayed- or memory-guided fixation conditions (Kapoor and Murthy 2008). Further, both the GO and STOP processes have been shown to be expedited to ispilateral versus contralateral targets in a hand countermanding task (Mirabella et al. 2006; Mirabella et al. 2009). The third and final potential effect on the STOP process predicts that any effect that shortens the GO process could potentially lengthen the duration of the STOP process. Despite the fact that this prediction would violate the race model's assumption of independence, the outcome seems realistic, especially due to the presence of the push-pull relationship known to exist between fixation-holding and saccade-generating networks in the oculomotor network (e.g., Findlay and Walker 1999; Munoz and Istvan 1998; Munoz and Wurtz 1993a; Munoz and Wurtz 1993b). Even beyond saccades, evidence for this outcome has been shown for hand movements, where SSRTs for a gap condition have been shown to be longer for arm movements than SSRTs in a "step" condition (Mirabella et al. 2009).

Table 1. Summaries of main results and methodological differences in three studies of the human countermanding task. A general comparison of the effect studied (gap, step or fixation offset), effector used (eye or hand), type of SSD calculation (fixed or staircasing) and type of stop signal used (visual or auditory). A negative step effect represents a stop signal reaction time (SSRT) that is longer in the gap fixation condition than the step fixation condition. Significant differences reported by the authors are represented by (*).

	Stevenson *et al* (2009)	**Mirabella *et al* (2009)**	**Morein-Zamir *et al* (2006)**
Gap Effect RTs	**56 ms***		
Step Effect RTs		**21 ms ***	
Fixation Offset Effect RTs			**18 ms ***
Gap Effect SSRTs	**41 ms***		
Step Effect SSRTs		**-12 ms***	
Fixation Offset Effect SSRTs			**5 ms**
Eye-only Task	✓		✓
Hand-only Task		✓	
Fixed SSDs	✓		
Staircasing SSDs		✓	✓
Visual Stop	✓	✓	✓
Auditory Stop	✓		✓

Considerable differences in results exist in regards to the effect of the STOP process on movement inhibition (Stevenson et al. 2009; Mirabella et al. 2009; Morein-Zamir and Kingstone 2006; Table 1). Methodological differences however hinder direct comparison between these studies (see Table 1 for summary). Stevenson and colleagues (2009) examined the gap effect, Mirabella and colleagues (2009) examined the step effect and Morein-Zamir and Kingstone (2006) examined the fixation offset effect. Further, Stevenson and colleagues and Morein-Zamir and Kingstone studied eye movements while Mirabella and colleagues studied hand movements. Finally, both Mirabella and colleagues and Morein-Zamir and Kingstone used a staircasing algorithm to dynamically determine the SSD for each individual trial based on performance on preceding trials. For example, if a subject were unable to cancel a planned movement, the SSD for the next trial would be shortened (to make it easier on the subject). If then the subject successfully cancels their movement on the next trial, the SSD would be increased (to make it more difficult on the subject). By dynamically "staircasing" the SSDs, the subject's behaviour converges on a movement probability of approximately 0.5 (50%). This differs from the method used by Stevenson et al (2009), where the authors used six preset SSDs for each subject that were determined based on their mean reaction time. These six SSDs were used with equal frequency and were randomly interleaved throughout blocks of trials. Finally, Stevenson and colleagues as well as Morein-Zamir and Kingstone used both auditory and visual stop signals (in different versions of their tasks), while Mirabella and colleagues used exclusively visual stop signals. Therefore, these three reports of fixation condition dependent effects on the STOP process cannot be directly compared given differences in fixation conditions (overlap, step and gap), effectors (eye or hand), modality of stop signal (central or peripheral visual, or auditory)

and method of determining the stop signal delay (fixed delays or a staircasing algorithm based on subject performance).

1.7 – Rationale and Hypotheses:

In light of these contrasting results, we sought to examine the comparative influences of fixation condition on the inhibition of eye and hand movements generated independently or in a co-ordinated manner. This study is of importance as it provides a comprehensive set of countermanding experiments in humans, examining eye and/or hand inhibition across three fixation conditions (overlap, step and gap), three effector combinations (eye-only, hand-only and eye-hand co-ordinated) and two methods of SSD determination (fixed and staircasing). The outcome provides a complete and comparable report of fixation condition dependent effects on the GO and STOP processes in a human countermanding task, while also providing the opportunity to reconcile differences in the literature. Finally, the outcome also provides a basis for examination and better understanding of task dependent differences in movement generation and inhibition mechanisms accessible by common neurophysiological techniques. Therefore, it is hypothesized that movement initiation and inhibition are affected by a subject's state of fixation and choice of effector used for a specific action.

Chapter 2 – Methods

2.1 - Human Participants

Seven right-handed human subjects (ages 22-37; three female) participated in Experiment 1 and six human subjects (ages 22-37; two female; all of whom also participated in Experiment 1), participated in Experiment 2 after providing their informed written consent. The experiments were counterbalanced and all subjects reported no history of neurological or musculoskeletal disorders, and all had normal or corrected-to-normal vision. Experimental procedures were approved by the University Research Ethics Board for Health Science Research at the University of Western Ontario in accordance with the ethical standards established in the 1964 Declaration of Helsinki (Appendix 1). Two subjects (*s1 and s2*) were the authors and hence were knowledgeable about the specific goals of the experiment. The other subjects were familiar with the countermanding task, but not with the specific goals of the experiment. Subjects were familiarized with the specifics of the countermanding paradigm used, but were not given feedback during the experiment.

2.2 – Countermanding Paradigms – Experiments 1 & 2

Subjects were seated in a straight-back chair in a dark compartmentalized room segregated by a double layer of thick black curtains to attenuate residual illumination from the experimental equipment. The experimental chair was situated 40 cm from a central fixation point (FP) and subjects had their head restrained by a chinrest positioned so that the FP was on their horizontal meridian. The bar attaching the chinrest to the subject's chair also served as an arm rest during the hand-only and eye-hand co-ordinated tasks.

In Experiments 1 & 2 our subjects performed three variants of the countermanding paradigm: an eye-only task, a hand only task and an eye-hand co-ordinated task. Each task, in both experiments, was studied on a separate day and these tasks were also counterbalanced across subjects. In Experiment 1, all seven subjects performed 1260 eye-only countermanding trials (30% stop trials – to replicate Stevenson et al 2009), 1260 hand-only countermanding trials (30% stop trials – to replicate Mirabella et al 2009), and 1260 eye-hand co-ordinated trials (30% stop trials). All tasks were performed over two days consisting of three blocks of 210 trials daily. Therefore a total of six one hour sessions per subject were collected. In Experiment 2 our six subjects performed 594 eye-only, 594 hand-only, and 1188 eye-hand co-ordinated trials (all containing 30% stop trials). Eye-only and hand-only tasks were performed on a single day consisting of three blocks of 198 trials, while the eye-hand co-ordinated task was performed over two days, with three blocks of 198 trials per day. Therefore a total of four one hour sessions per subject were collected.

Both experiments used the same three fixation conditions: overlap, step and gap. All fixation conditions began with the illumination of the central FP for an interval of 1,000, 1,166, 1,333, or 1,500 ms and this interval was selected randomly. The FP and targets consisted of single red LEDs, with the targets being placed 10 degrees to the left and right of the central FP and in the horizontal plane. In the overlap condition (Fig 2A), the FP remained illuminated for the duration of the trial, with the target being presented to the left or right of the subject. In the step condition (Fig 2B), the offset of the FP and the onset of the target were simultaneous, while in the gap condition the FP was extinguished 200 ms prior to target onset (Fig 2C). On *CONTROL* trials, the target remained illuminated for the duration of the trial for all fixation conditions. On *STOP* trials, the stop signal was presented, which consisted of the onset of six

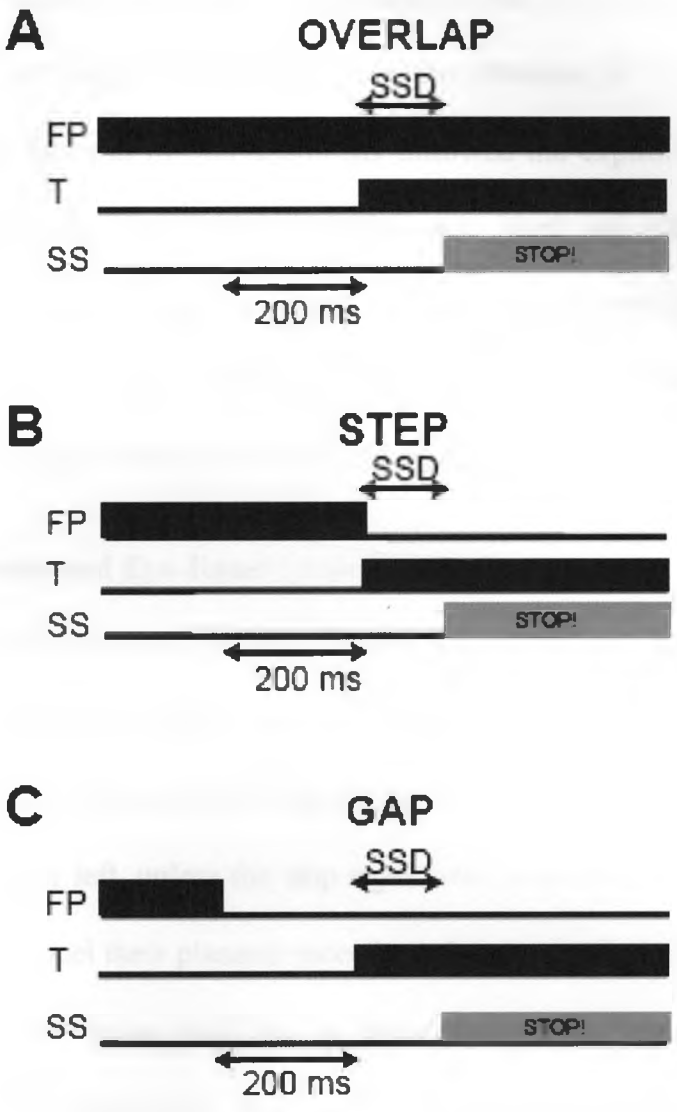

Figure 2. Schematic drawing of stop trials used in the two experiments, which comprised 30% of all trials. Both Experiments used 3 fixation conditions: overlap, step and gap. (A) The central fixation point (FP) remains illuminated for the duration of the trial, with the target being presented to the left or right of the subject. (B) The step condition involved a simultaneous offset of the FP and onset of the target. (C) The gap condition involved the disappearance of the FP 200 ms prior to target onset. In all fixation conditions, after the given stop signal delay (SSD), the stop signal (a parafoveal cluster of six red LEDs) was presented. Both experiments were identical in appearance but differed in the nature of the calculation of the SSD for a given trial.

parafoveal red LEDs located 1.5 cm above the central FP for all fixation conditions. On such trials, the stop signal and target remained on for the duration of the trial for all fixation conditions. An intertrial interval of 500–1,000 ms followed the expiration of both *CONTROL* and *STOP* trials. For both experiments, within each block of ~200 trials, all possible permutations of fixation condition (gap vs. step vs. overlap), trial type (*CONTROL* vs. *STOP*), and target direction (left vs. right) were randomly interleaved. Therefore, all aspects of experimental presentation were identical for Experiments 1 & 2.

2.3 – Eye-only, Hand-only and Eye-Hand Co-ordinated Tasks

In the eye-only task, each trial began with the subject fixating the central FP. Since no hand movements were required, subjects rested their arms comfortably in their lap (below the arm rest). Regardless of fixation condition, the subject made a saccade to the target presented 10 degrees to either the right or left, unless the stop signal was presented. On *STOP* trials, subjects were instructed to try to cancel their planned saccade and maintain fixation on the central FP. In the hand-only task, subjects began each trial by pressing a central push button (centred 1 cm below the central FP) with their index finger. Subjects maintained fixation on the central FP while making a speeded arm movement to the target push button (left or right) centred 1 cm directly below the target LEDs. On *STOP* trials, subjects were instructed to cancel their planned arm movement. In the eye-hand co-ordinated task, subjects began by pressing in the central push button and fixating the central FP. Subjects made speeded eye and hand movements to the target LED and push button, respectively and on *STOP* trials, subjects were instructed to cancel both their planned eye and hand movements.

2.4 - Stop Signal Delay Determination:

On *STOP* trials, the stop signal was always presented with, or after target presentation and this timing was manipulated throughout both Experiments 1 & 2. The amount of elapsed time between target and stop signal presentation is termed the stop signal delay (SSD). Subjects typically exhibit an increased propensity to make a movement at longer and longer SSDs. Therefore, choosing the appropriate range of SSDs for a particular subject is imperative for creating an acceptable inhibition function. Briefly, an inhibition function is a plot of the probability of making a movement at a given SSD. Individual inhibition functions are generated for each fixation condition (see Fig 3A for an example) and these inhibition functions are required for the calculation of the stop signal reaction time (SSRT; see Methods Section 2.5 below). Historically, two methods of determining an appropriate SSD range have been used. The first generally uses a set of three to six pre-established SSDs that are separated by intervals of ~50-ms (Paré and Hanes 2003; Boucher et al. 2007b; Stevenson et al. 2009; Emeric et al. 2008; Cabel et al. 2000; Hanes and Schall 1995). For example, an individual subject may have an SSD range of 0-250 ms with individual SSDs of 0, 50, 100, 150, 200 and 250 ms. This creates a wide range, which spans the inhibition function from low to high probabilities of movement [i.e. p(movement)<0.1 @ 0ms SSD, and p(movement)>0.9 @ 250ms SSD in Fig 3A] and any of these SSDs is equally likely to be used on an upcoming trial. Further, this "fixed" SSD range is used for all fixation conditions, and an SSD from the set is pseudorandomly picked for each upcoming *STOP* trial. This set of SSDs would be determined by the subject's distribution of reaction times and propensity for movement in a practice block of trials to ensure that the entire inhibition function is spanned.

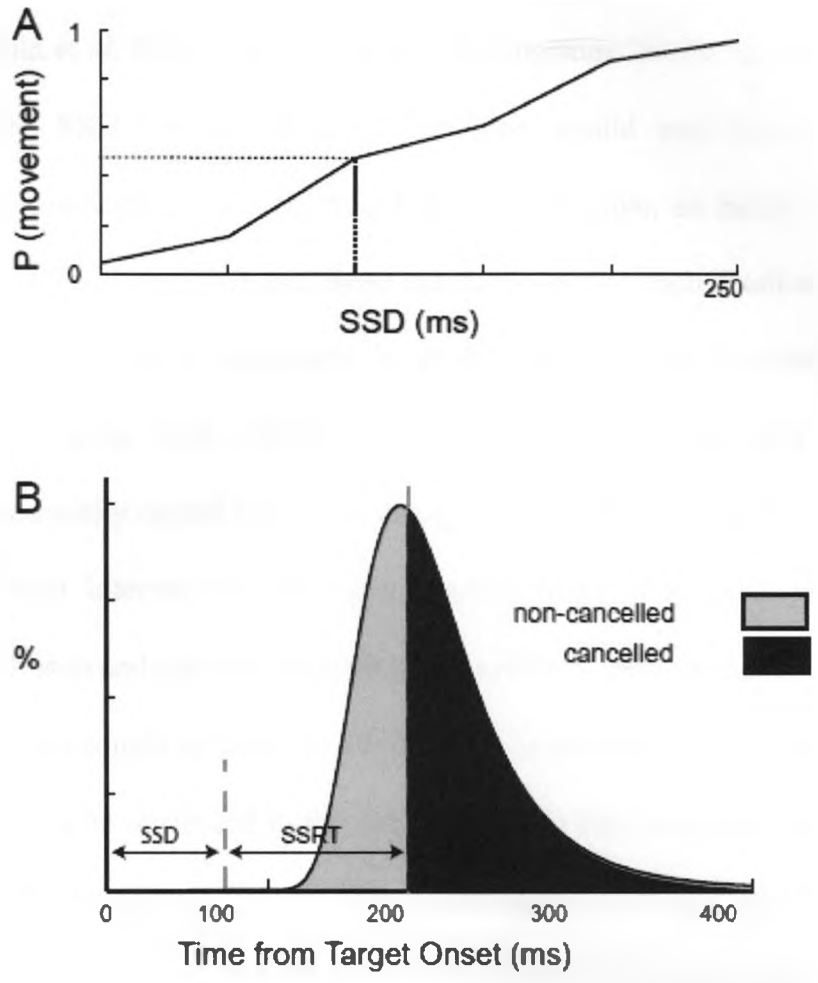

Figure 3 – A. Example inhibition function, indicating the probability of making a movement (P(movement)) at a given SSD. P(movement) increases with increasing SSD. B. A reaction time cumulative distribution function (CDF) from *CONTROL* trials. In order to calculate SSRTs via the integration method, the p(movement) is determined at each given SSD. For example, take an SSD of 100 ms in (A), which has a p(movement) of ~0.45. An integral is then run from zero to that of p(movement) in the CDF (grey section of (B)). The SSRT is then the difference between this RT and the SSD.

The second method determines the SSD dynamically for each upcoming trial (Mirabella et al. 2009; Mirabella et al. 2006; Morein-Zamir and Kingstone 2006). Instead of having a fixed range of SSDs, the SSD for each fixation condition would vary based on the subject's performance on the previous countermanding trial. For example, an initial SSD (e.g. 150 ms) and SSD interval (~50 ms) are used and these are the same for each fixation condition. If the subject were to fail to cancel a movement in an overlap trial, the "overlap SSD" would be shortened to 100 ms (initial SSD – SSD interval) for the next overlap trial. Similarly, if the subject were to successfully cancel the next overlap trial, the SSD would be increased to 150 ms (100 ms SSD + SSD interval) for the next overlap trial. The same would also happen individually for both step and gap conditions making a total of three separate "staircasing" SSDs.

In this study, we sought to determine if differences in fixation condition effects on SSRTs in previous reports may be attributed to the method of SSD determination used. Thus, the only difference between Experiments 1 & 2 existed in the method of determination of the SSD for a particular trial. It is important to note that this difference was not overtly noticeable to the subject performing the task. Experiment 1 used the first method of SSD determination mentioned above, where six fixed SSDs, in 50-ms steps, were used for each fixation condition. In the eye-only task, SSDs ranged from 0-250 ms for four subjects, 50-300 ms for one subject and 100-350 ms for two subjects. In the hand-only task, SSDs ranged from 0-250 ms for three subjects, 50-300 ms for one subject and 100-350 ms for two subjects. In the eye-hand co-ordinated task, SSDs ranged from 0-250 ms for four subjects and 100-350 ms for three subjects.

Experiment 2 used the second SSD determination method mentioned above, where SSDs were determined dynamically based on subject performance. Further, Experiment 2 was designed to replicate the findings of Mirabella et al (2009), where they used an SSD interval of

40 ms. Therefore, in all fixation conditions, SSDs began at 120 ms and staircased independently with an SSD interval of 40 ms. As above, if a subject successfully cancelled a movement on an overlap *STOP* trial, the "overlap" SSD would be increased by 40 ms to 160 ms (the "overlap" SSD would be decreased by 40 ms if the subject made a movement). The same occurred to "step" and "gap" SSDs on trials of the step and gap fixation conditions, respectively. Further, a minimum SSD was imposed of 0 ms, even if a subject failed to cancel a previous trial with an SSD of 0 ms.

In the eye-hand co-ordinated task, "eye" SSDs tracked independently of "hand" SSDs. Since only one SSD can be used on a given trial, each trial was randomly selected to be an "eye" or "hand" trial. If deemed an "eye" trial, an online saccade detector was used to determine whether or not the trial was successfully cancelled, and the "eye" SSD for that fixation condition was adjusted accordingly. Note that the SSD was adjusted based only on the eye movement, regardless of the behaviour of the hand on this particular trial. On the remaining trials, which were deemed to be "hand" trials, a hand movement occurred if the central push button was released. An online hand movement detector determined whether or not the trial was cancelled and the "hand" SSD for that fixation condition was adjusted appropriately. In total, each fixation condition had two staircasing algorithms (one for "eye" trials and one for "hand" trials). Therefore, in the eye-hand co-ordinated task in Experiment 2, there existed six simultaneous staircasing algorithms, based on fixation condition and effector. This complexity is noteworthy as we believe this made it nearly impossible for the subject to predict the SSD for an upcoming trial.

2.5 - Calculation of Stop Signal Reaction Times:

The main goal of this study is to compare estimates of the duration of the STOP process (i.e. the SSRT) across fixation conditions, effectors and SSD determination methods. Briefly, the SSRT is a derived parameter that estimates the amount of time required to cancel a planned movement. Here we used two measures of calculating the SSRT: the integration method and the mean method (Logan 1994; Hanes and Schall 1995). Calculating the SSRT via either method requires both an inhibition function from *STOP* trials and the cumulative reaction time distribution functions (CDF) from *CONTROL* trials (See Fig 3B for an example CDF). For the integration method, the SSRT is estimated at each SSD by first finding the probability of making a movement [p(movement)] from the inhibition function (see Methods Section 2.4; Fig 3A) for that SSD, then running the integral from zero to that probability in the *CONTROL* trial CDF. The SSRT is then estimated by subtracting the SSD from this value (Logan 1994; Fig 3B). The SSRT was calculated only at SSDs which were used more than 5 times for that fixation condition and had a probability of a movement between 0.1 and 0.9. This helped to ensure the capture of the linear portion of the inhibition function and cumulative RT distributions.

The mean method for estimating SSRTs assumes that the SSRT for a given subject will be the same regardless of the SSD. While this assumption seems unlikely to be true, violations of this assumption do not significantly affect the validity of the race model (Logan 1994). The mean method for calculating SSRTs simply takes the difference between the mean reaction time and the mean of the inhibition function (Hanes and Schall 1995), using a rescaling factor as suggested by Logan (1994) since the probability of making a movement does not always range from 0 and 1. The mean of the inhibition function is calculated by taking the probability of making a movement at the nth SSD (P_n), and subtracting the probability of making a movement

at the (n-1)th SSD, then multiplied by the numerical value of the nth SSD. This is done for all SSDs ($n > 1$) and the values are summed. The rescaling factor simply involves dividing this expression by the difference between the maximum (P_{max}) and minimum (P_{min}) values of the inhibition function. Therefore, the overall expression is as follows:

$$\text{Mean of the Inhibition Function} = \frac{\Sigma[(P_n - P_{n-1}) \cdot \text{SSD}_n]}{(P_{max} - P_{min})}$$

Since the mean and integration methods have been shown to produce equally valid estimates of the SSRT and both methods produced the same overall pattern of results, all reported SSRT values are an average of the mean and integration methods.

2.6 - Data Collection and Analysis:

Eye movements were recorded using bi-temporal electro-oculography (EOG) and online saccade onset was detected as an eye movement with a speed exceeding 125° per second. A hand movement was detected online as the release of the central push button which resulted in a drop in potential of 5V. Signals were filtered and amplified with a P122 AC/DC preamplifier (Grass Instruments). Horizontal eye movements were filtered (100 Hz, low pass), amplified, and digitized at a rate of 1 kHz onto a PXI controller (National Instruments). Digitized data were then transferred to a PC computer and subsequent off-line analyses were performed using customized Matlab (the Mathworks) programs. Offline, movement onsets and offsets were identified by an automarking program, which detected crossings of velocity thresholds (50°/s for eye; and 5V drop in potential from central push button for hand; velocities were filtered with a low-pass Butterworth filter with fs/fc < 17). Eye and hand movements were also analyzed via a customized Matlab Graphical User Interface permitting the data analyst to check for errors and

ensure consistency. Eye and hand reaction times, inhibition functions and SSRTs were calculated offline and saved for further analyses.

Reaction time and SSRT comparisons across fixation conditions, for Experiments 1 & 2, utilized one-way repeated measures ANOVAs followed by Bonferroni post-hoc correction tests for multiple comparisons. We also fit each inhibition function with a cumulative Weibull function of the form $W(t) = \gamma - (\gamma - \delta) \cdot \exp[-(t/\alpha)^{\beta}]$, where γ and δ are the maximum and minimum of the inhibition function, respectively, α is the time at which the inhibition function reaches 64% of its maximal growth and β is the slope (Paré and Hanes 2003). Differences in RTs, inhibition function means and SSRTs between staircasing and fixed SSD tasks for individual subjects utilized two way t-tests. Linear regression analyses were used for correlations between RTs, SSDs and SSRTs when comparing staircasing and fixed SSD tasks. Paired t-tests were used to compare the above differences (fixed versus staircasing tasks) across the entire sample. Two sample F-tests for equal variances were used in two situations. First, they were used to determine changes in the variance in the magnitudes of RTs, inhibition function means, and SSRTs between Experiments 1 & 2 across the sample. Second, they were used to determine changes in the variance of the gap, step and fixation offset effects on RTs, inhibition function means, and SSRTs between Experiments 1 & 2.

Chapter 3 - Results

3.1 – Experiment 1 – Fixation Condition Effects on the GO and STOP processes

The main goal of Experiment 1 was to determine the effect of fixation condition on the STOP process. In different sessions, subjects performed three different variants of the countermanding task (e.g. eye-only, hand-only and eye-hand co-ordinated) that utilized a fixed set of SSDs, in order to replicate and expand on the findings of Stevenson et al (2009). Briefly, RTs from each of the fixation conditions (i.e., the GO process) in each of the tasks (eye-only, hand-only and eye-hand co-ordinated) will be presented first, followed by the SSRTs (i.e., the STOP process) in each task (See Fig 4 and Table 2).

The results from Experiment 1 further confirm that the GO process can be affected by fixation condition (Fig 4; Left Panel). Regardless of the type of movement produced, we observed a significant effect of fixation condition on RTs ($P<0.001$ for all tasks; One-way repeated measures ANOVA followed by Bonferroni post-hoc test for multiple comparisons). Overall, we observed a significant reduction in RTs from overlap to gap fixation conditions in all tasks (i.e. eye-only, hand-only, eye-hand co-ordinated). The magnitude of this reduction (gap effect) varied across the tasks with the smallest gap effects occurring in the eye-only (66 ± 29 ms; mean ± S.D.) and eye portion of the eye-hand co-ordinated tasks (66 ± 29 ms) and the largest occurring in the hand-only (77 ± 22 ms) and hand portion of the eye-hand co-ordinated task (77 ± 19 ms). Further, we observed a consistent reduction in RTs from step to gap for all tasks. Similar to the gap effect, the magnitude of the step effect varied with the smallest step effects occurring in the eye-only (33 ± 23 ms) and eye portion of the eye-hand co-ordinated task (36 ± 25 ms) and the largest occurring in the hand-only (54 ± 14 ms) and hand portion of the eye-hand

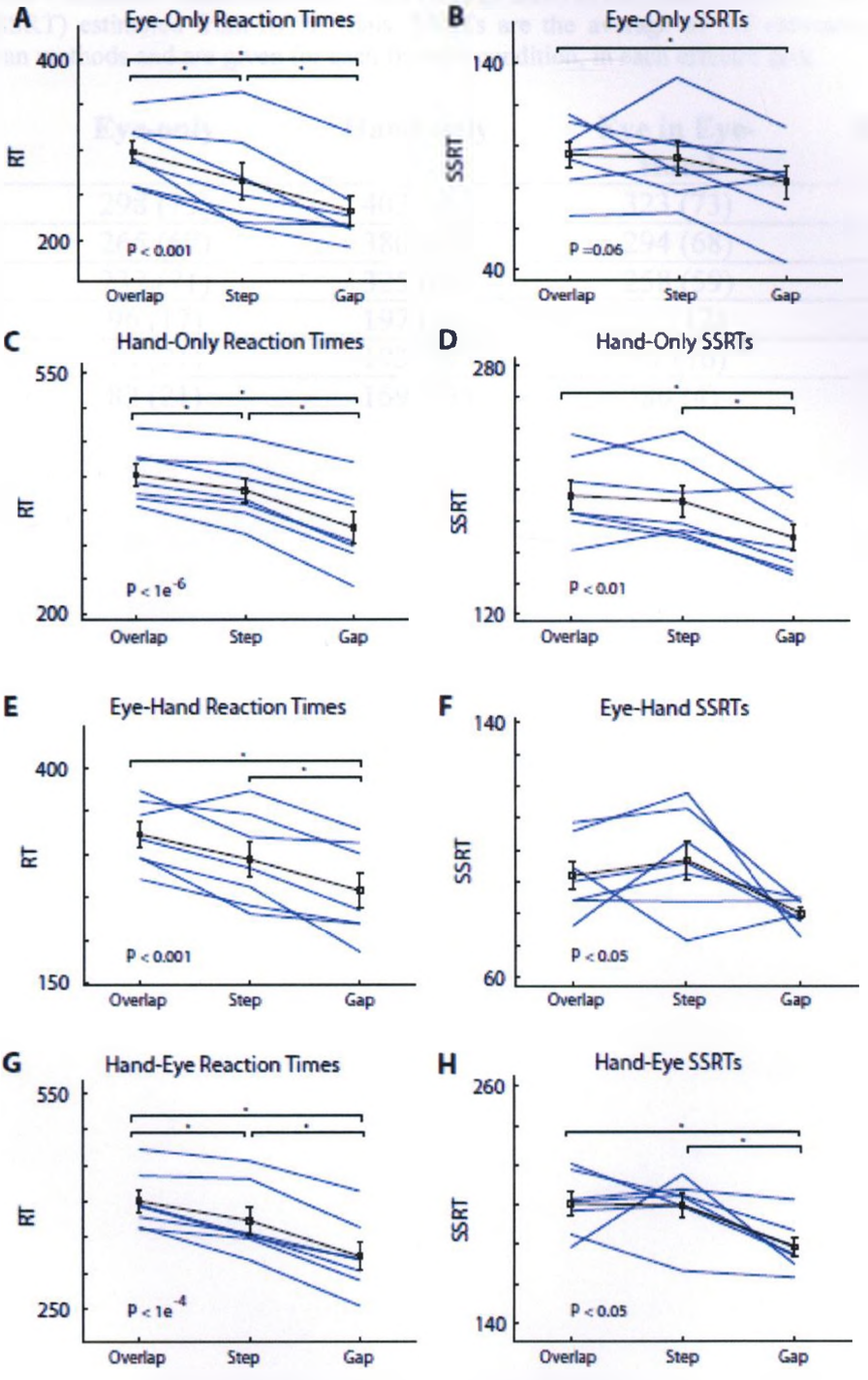

Figure 4 –Fixation condition effects on both the GO and STOP processes using fixed SSDs. Experiment 1's results confirm that a gap effect does exist on SSRTs when using fixed SSDs. Significant gap, step and fixation offset effects are seen on reaction times for eye, hand and hand in eye-hand tasks (A,C,G). Gap and step effects are observed on reaction times for eye movements in the eye hand task, but no significant fixation offset effect is observed (E). A gap effect is seen on SSRTs in the eye-only, hand only, and hand portion of the eye-hand co-ordinated task (B, D, H). There is no fixation offset effect in any task (B, D, F, H) but a "step" effect on SSRTs existed in both the hand-only and eye-hand co-ordinated tasks (D, H).

Table 2 – Experiment 1 Results – mean Reaction Times (RT) (± S.D.) in ms from *CONTROL* trials and Stop Signal Reaction Times (SSRT) estimated from *STOP* trials. SSRTs are the average of the estimates derived from the Integration and Mean methods and are given for each fixation condition, in each effector task.

	Eye-only	**Hand-only**	**Eye in Eye-Hand**	**Hand in Eye-Hand**
Overlap RT	298 (75)	402 (41)	323 (73)	401 (63)
Step RT	265 (67)	380 (47)	294 (68)	374 (60)
Gap RT	232 (71)	325 (60)	258 (59)	323 (69)
Overlap SSRT	96 (17)	197 (26)	92 (12)	201 (16)
Step SSRT	94 (21)	193 (27)	97 (16)	200 (16)
Gap SSRT	82 (21)	169 (23)	80 (4)	178 (13)

co-ordinated task (50 ± 14 ms). Finally, we observed a significant decrease in RTs from the overlap to step fixation conditions (33 ± 28 ms) in the eye-only task. Similarly, we observed significant fixation offset effects in the hand-only (22 ± 11 ms) and hand portion of the eye-hand co-ordinated task (27 ± 17 ms), while in the eye portion of the eye-hand co-ordinated task, this fixation offset effect (29 ± 30 ms) did not reach significance.

Similar to the GO process, we also observed an effect of fixation condition on the STOP process (Fig 4; Right Panel). In all tasks (eye-only, hand-only and eye-hand co-ordinated), the effect of fixation condition on the STOP process reached, or approached significance ($p < 0.05$ except for eye-only ($p = 0.06$); One way repeated measures ANOVA with Bonferroni's post hoc test for multiple comparisons). Similar to Stevenson et al (2009), we observed an overall reduction in SSRTs from overlap to gap fixation conditions in all tasks and this gap effect reached significance in the eye-only, hand-only and hand portion of the eye-hand co-ordinated tasks. The magnitude of the gap effect varied across the tasks with the smallest gap effects occurring in the eye-only (14 ± 11 ms) and eye portion of the eye-hand co-ordinated tasks (12 ± 14 ms; $p = 0.08$) and the largest occurring in the hand-only (27 ± 20 ms) and hand portion of the eye-hand co-ordinated task (22 ± 17 ms). Further, we observed a consistent, significant reduction in SSRTs from step to gap for the hand tasks (Fig 4D, H), but not for the eye tasks (Fig 4B, F). The magnitude of the step effect varied and only reached significance in the hand-only (23 ± 16 ms) and hand portion of the eye-hand co-ordinated task (21 ± 15 ms). Finally, we observed no significant change in SSRTs from the overlap to step fixation conditions for any task.

These results from Experiment 1 further confirm the existence of a gap effect on the STOP process as seen in Stevenson et al (2009), and that this effect is also seen on hand

movements (Fig 4D,H). Further, we show that, at least with fixed SSDs, a step effect also exists on the hand STOP process that is in the opposite direction to that seen by Mirabella et al. (2009). Finally, consistent with Morein-Zamir and Kingstone, we see a fixation offset effect on the GO process, but not on the STOP process. Overall, Experiment 1 shows that both the GO and STOP processes can be affected by fixation condition and that these effects are consistently observed whether the subject is performing eye, hand or eye-hand co-ordinated movements.

3.2 - Experiment 2 - Fixation Condition Effects on the GO and STOP processes

The results from Experiment 1 are generally in agreement with previous reports (Stevenson et al. 2009; Morein-Zamir and Kingstone 2006). However, in marked contrast to Mirabella and colleagues (2009), we observed an expedited STOP process (i.e. lower SSRTs) in the gap versus step condition. One difference between their setup and ours in Experiment 1 is their use of a dynamic, staircasing algorithm to determine SSDs on each countermanding trial. Therefore, Experiment 2 was set up as closely as possible to replicate the findings of Mirabella and colleagues (2009).

The main goal of Experiment 2 is to determine if the fixation condition effects on the STOP process also existed using staircasing SSDs. It is once again important to note that Experiments 1 & 2 were counterbalanced (i.e. half of our subjects performed Experiment 2 first) and that Experiment 2 differed from Experiment 1 only in the method of determining SSDs for a particular trial. All other aspects of presentation were identical and we do not believe the different methods of determining SSDs were overtly obvious to the subject performing the experiment.

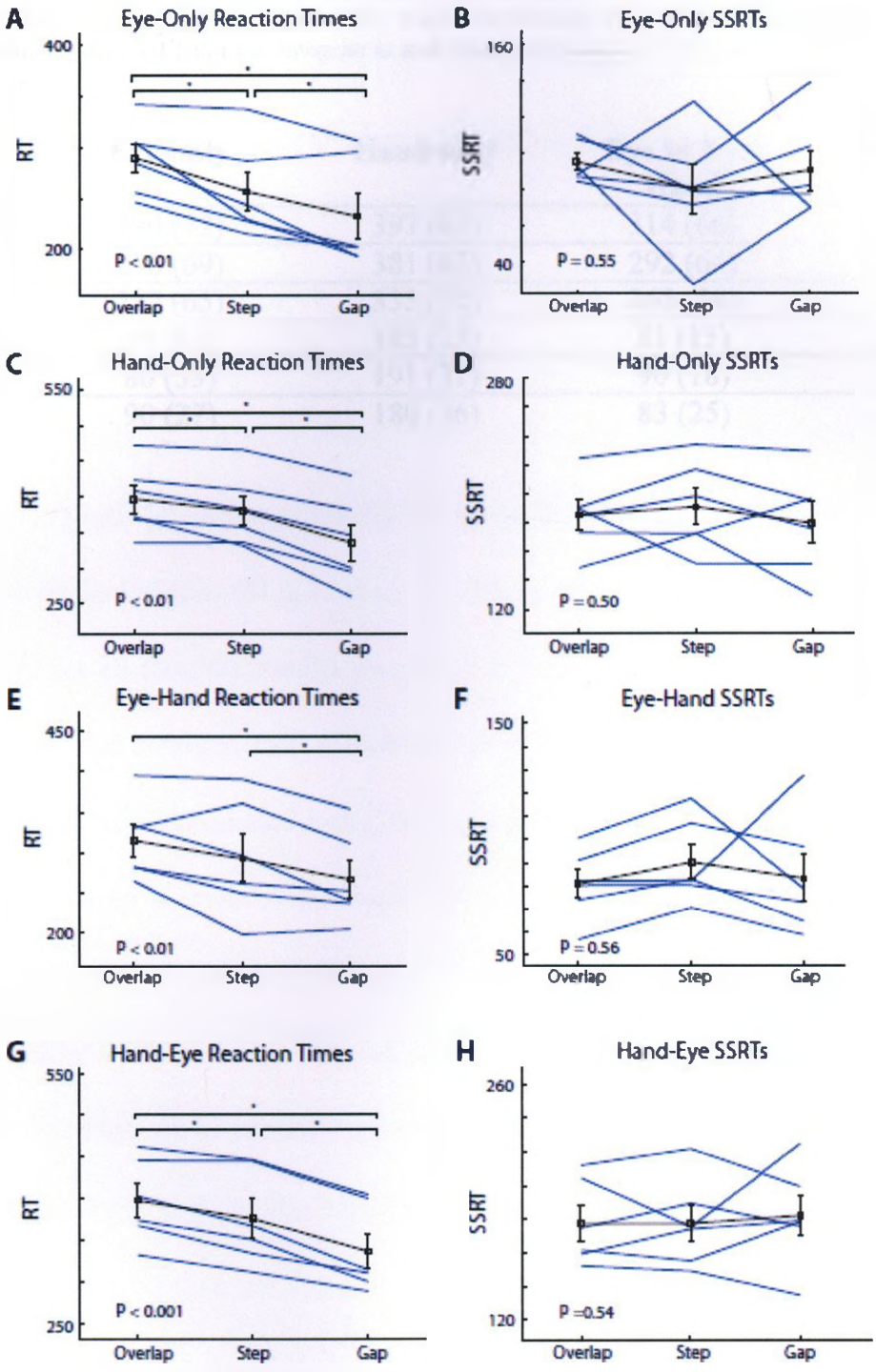

Figure 5 – Fixation condition effects on the GO but not the STOP process using staircasing SSDs. Significant gap, step and fixation offset effects are seen on reaction times for eye, hand and hand in eye-hand tasks (A,C,G). As in Experiment 1, gap and step effects were observed on reaction times for eye movements in the eye hand task, but no significant fixation offset effect was observed (E). No effect of fixation condition is seen on SSRTs in any of the eye-only, hand only, or eye-hand co-ordinated tasks (B, D, F, H).

Table 3 – Experiment 2 Results – mean Reaction Times (RT) (± S.D.) in ms from *CONTROL* trials and Stop Signal Reaction Times (SSRT) estimated from *STOP* trials. Values in brackets denote standard deviations. SSRTs are the average of the estimates derived from the Integration and Mean methods and are given for each fixation condition, in each effector task.

	Eye-only	**Hand-only**	**Eye in Eye-Hand**	**Hand in Eye-Hand**
Overlap RT	290 (72)	397 (65)	314 (66)	398 (59)
Step RT	256 (69)	381 (63)	292 (64)	376 (58)
Gap RT	232 (65)	335 (70)	265 (58)	337 (65)
Overlap SSRT	95 (11)	185 (25)	81 (15)	178 (25)
Step SSRT	80 (33)	191 (31)	90 (18)	178 (26)
Gap SSRT	90 (27)	180 (36)	83 (25)	182 (30)

The results from Experiment 2 further confirm that the GO process can be affected by fixation condition (Fig 5; Left Panel; Table 3). Regardless of the type of movement produced, we observed a significant effect of fixation condition on RTs ($P<0.01$ for all tasks; One-way repeated measures ANOVA with Bonferroni's post hoc test for multiple comparisons). Similar to Experiment 1, we observed a significant reduction in RTs from overlap to gap fixation conditions in all tasks. The magnitude of the gap effect varied across the tasks with the smallest gap effects occurring in the eye-only (57 ± 38 ms) and eye portion of the eye-hand co-ordinated tasks (49 ± 27 ms) and the largest occurring in the hand-only (62 ± 28 ms) and hand portion of the eye-hand co-ordinated task (61 ± 17 ms). Further, we observed a consistent reduction in RTs from step to gap for all fixation conditions. Similar to the gap effect, the magnitude of the step effect varied with the smallest step effects occurring in the eye-only (25 ± 20 ms) and eye portion of the eye-hand co-ordinated task (26 ± 25 ms) and the largest occurring in the hand-only (46 ± 16 ms) and hand portion of the eye-hand co-ordinated task (39 ± 13 ms). Finally, we observed a significant decrease in RTs from the overlap to step fixation conditions, and this fixation offset effect (33 ± 24 ms) reached significance in the eye-only condition. In the eye portion of the eye-hand co-ordinated task, this fixation offset effect (22 ± 33 ms; $p = 0.07$) approached significance while in the hand-only (16 ± 15 ms) and hand portion of the eye-hand co-ordinated task (21 ± 23 ms), we observed significant fixation offset effects.

Unlike Experiment 1, the STOP process was not affected by fixation condition for eye or hand movements in Experiment 2 (Fig 5; Right Panel). In all tasks, the effect of fixation condition on the STOP process did not reach, or even approach significance ($P > 0.50$ in all tasks; One way repeated measures ANOVA). We observed no gap effect on SSRTs in the eye-only (5 ± 25 ms), hand-only (6 ± 22 ms) or eye or hand portions of the eye-hand co-ordinated

task (both -2 ± 23 ms). Also unlike Experiment 1, we observed no step effect on SSRTs in the eye-only (-10 ± 38 ms), hand-only (11 ± 23 ms) or eye (-6 ± 24 ms) or hand (-9 ± 7 ms) portions of the eye-hand co-ordinated task. Finally, we observed no significant change in SSRTs from the overlap to step fixation conditions, for the eye-only (15 ± 35 ms), hand-only (-6 ± 24 ms) or eye (-9 ± 7 ms) or hand (7 ± 28 ms) portions of the eye-hand co-ordinated task.

In summary, the GO process is affected by fixation condition regardless of which method of SSD determination is used. However, the fixation condition only influences the duration of the STOP process when a fixed range of SSDs is used. Considering that the same subjects were used for both experiments and the experiments were counterbalanced, it seems there is a fundamental difference between Experiments 1 & 2, particularly that dynamically determining the SSD negates the effect of fixation condition on movement inhibition.

3.3 – Comparative Analysis between Experiments 1 & 2

The absence of fixation condition effects on SSRTs in Experiment 2 was very surprising, especially when compared to the results from Experiment 1. Here, we examine a number of possible potential mechanisms for this result. Recall that the estimation of the SSRT (see Methods Section 2.5) requires both the cumulative distribution function of reaction times, as well as the inhibition function. Therefore, we first sought to determine if a systematic difference in the magnitude of reaction times between Experiments 1 & 2 existed. Thus we compared mean reaction times for each subject in the eye-only, hand-only and eye-hand co-ordinated tasks across Experiments 1 & 2.

In doing so, we found no significant systematic differences in reaction times between the two experiments for any task. Therefore, we grouped the mean RTs all tasks (eye-only, hand-

only and eye-hand co-ordinated) together to increase the statistical power (Fig 6, Left Panel; 6 subjects x 4 tasks). We found that individual significant differences in reaction times between Experiments 1 & 2 did exist, but these differences did not occur consistently in the same direction. Despite the individual reaction time differences which reached significance between Experiments 1 & 2, overall, RTs showed strong correlations ($r > 0.90$; $p < 1e^{-8}$ for all fixation conditions). Given these strong correlations, it was not surprising that we still found no significant, systematic differences in RTs between Experiments 1 & 2 for any fixation condition ($p > 0.11$ for all fixation conditions) when all tasks were pooled. Finally, we observed no significant differences between RT variances between Experiments 1 & 2 ($p > 0.73$ in all fixation conditions; two sample F test). Therefore, we observed no differences in reaction time magnitude between the two experiments and thus, magnitudinal changes in RTs cannot explain the differences seen in SSRTs between Experiment 1 & 2.

Since the inhibition function is also required to estimate the SSRT, we sought to determine if a systematic difference in the mean of the inhibition functions existed between Experiments 1 & 2. For each subject, the 50% point of the Weibull fit (See Methods Section 2.6) was extracted as the mean of the inhibition function for each fixation condition in each task. As with RTs, we grouped all tasks together to increase the statistical power (Fig 6, Middle Panel) since no systematic differences in inhibition function means were found for any task. Still, after doing so, we found no significant, systematic differences overall in inhibition function means between Experiments 1 & 2 for any fixation condition ($p > 0.40$ for all; Fig 6B,E,H). Further, inhibition function means showed strong correlations ($r > 0.56$ for all) and these correlations were highly significant ($p < 0.005$ for all). Finally, no significant differences existed between the variances of inhibition function means between Experiments 1 & 2 ($p > 0.20$ in all fixation

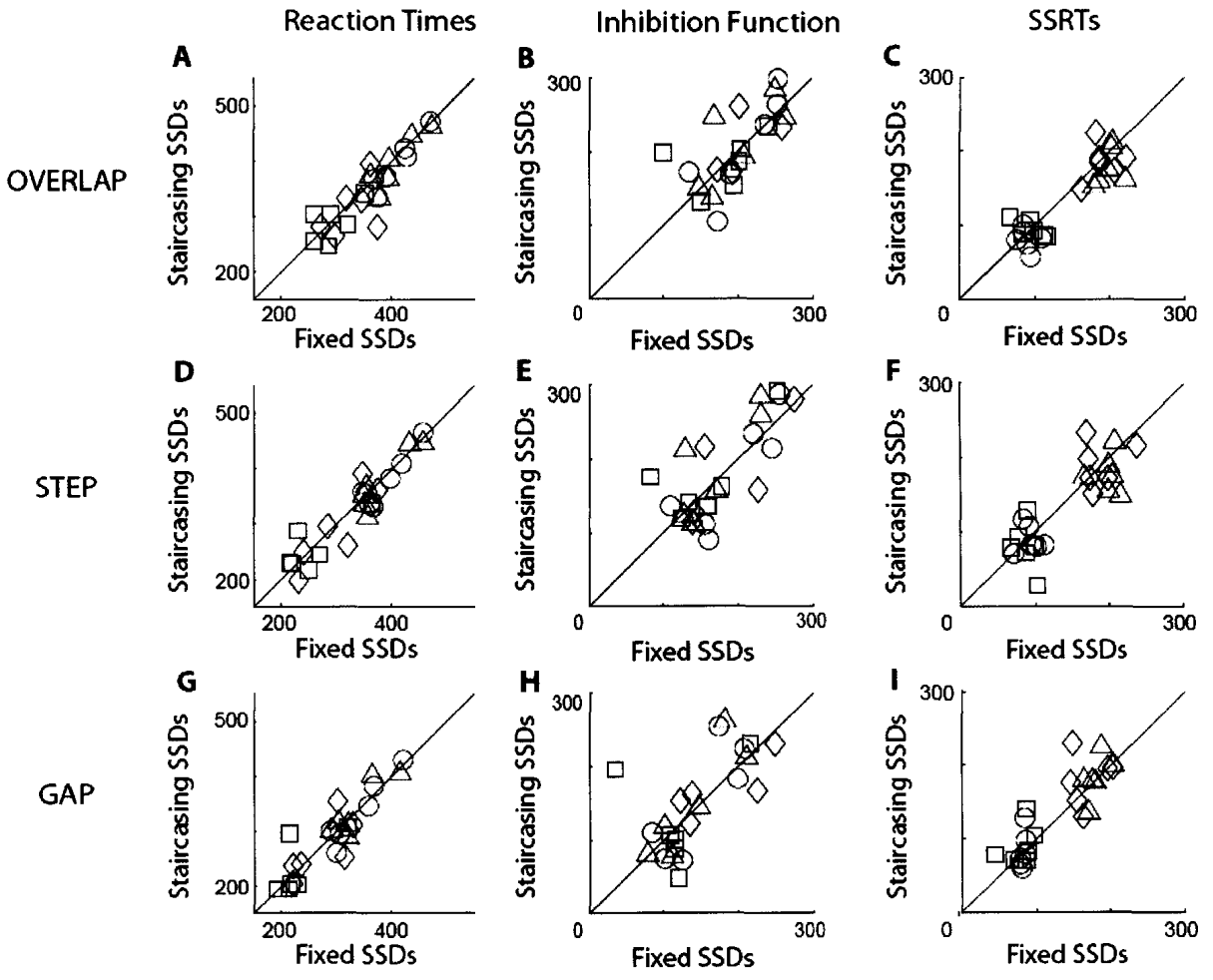

Figure 6 – Comparative analysis of Experiments 1 & 2 to determine if magnitudinal changes in RTs (Left Panel), Inhibition Function Means (Middle Panel) or SSRTs (Right Panel) in any fixation condition may have led to the disappearance of gap and step effects on SSRTs in Experiment 2. In all subplots (□) represents data from the Eye-only task, (◊) from Hand-only, (○) from Eye portion and (Δ) from Hand portion of eye-hand co-ordinated task. No significant differences existed between RTs in Experiment 1 (Fixed SSDs) and Experiment 2 (Staircasing SSDs) for overlap (A), step (D) or gap (G) fixation conditions. Significant correlations existed between RTs in the two experiments. Similarly, no significant differences existed between inhibition function means in Experiment 1 & 2 for overlap (B), step (E) or gap (H) fixation conditions. Significant correlations existed between inhibition function means in the two experiments. Finally, no significant differences existed in the magnitude of SSRTs in Experiment 1 & 2 for overlap (C), step (F) or gap (I) fixation conditions. Further, significant correlations existed between SSRTs in the two experiments.

conditions; F test). Therefore, like reaction times, we can conclude that no systematic change in the mean of the inhibition functions occurred between experiments, and that both were equally variable whether fixed or staircasing SSDs were used. Thus, magnitudinal changes in RTs and inhibition function means cannot explain the differences in SSRTs between Experiments 1 & 2.

Although no systematic differences have been seen in RTs or inhibition function means across fixation conditions between Experiments 1 & 2, we still sought to determine if SSRTs change systematically in magnitude from Experiment 1 to Experiment 2. Since both the RT cumulative distribution function and inhibition function were used to calculate the SSRT, it was not surprising that we found no significant, systematic differences in SSRTs between Experiments 1 & 2 for any fixation condition ($p > 0.12$ for all; Fig 6C,F,I) when we grouped all tasks together to increase the statistical power. Further, SSRTs showed strong correlations ($r > 0.84$ for all) and these correlations were highly significant ($p < 1e^{-6}$ for all). Furthermore, we observed no significant differences between SSRTs variances between Experiments 1 & 2 ($p > 0.67$ in all fixation conditions; F test).

In sum, we can conclude that no systematic change in the magnitude of RTs, inhibition function means or SSRTs occurred between experiments, and that all were equally variable whether fixed or staircasing SSDs were used. Therefore, changes in the absolute magnitude of the GO or STOP processes cannot account for the absence of any influence of fixation condition on the duration of the STOP process seen in Experiment 2.

3.4 - Range and Number of SSDs used in Experiments 1 & 2

The above results show that no significant, systematic differences in RTs, inhibition function means or SSRTs existed between Experiments 1 & 2. However, the possibility exists that differences in the sampling of SSDs between experiments may have led to the absence of fixation condition effects in Experiment 2. Since the staircasing algorithm is known to converge on the mean of the inhibition function, the number and range of SSDs used in Experiment 2 may not have been the same as Experiment 1. Here, we sought to determine if the number of valid SSDs (see Methods Section 2.5) used by each subject differed between Experiments 1 & 2, could have led to the disappearance of fixation condition effects on the STOP process in Experiment 2. In doing so, in the eye-only task of Experiment 1, subjects used a mean of 4.2 SSDs which met the criteria for a valid SSD (means combined across fixation conditions: 3.9 SSDs for overlap, 4.3 SSDs for step and 4.4 SSDs for gap). In the hand-only task, and eye and hand portions of the eye-hand co-ordinated task, subjects used 3.6, 3.5 and 3.2 SSDs which met the SSD criteria, respectively (Table 4). In Experiment 2, in the four tasks, subjects used an average of 3.7, 4.1, 4.11 and 4.5 SSDs, respectively (Table 4). Paired t-tests revealed significant differences for all tasks between experiments and surprisingly, three tasks (hand-only, eye in eye-hand and hand in eye-hand) used a greater number of valid SSDs when a staircasing algorithm was used.

However, Experiment 2 used smaller SSDs steps, so while the number of SSDs used in Experiment 2 was, on average, higher the range may not have been. Therefore, we calculated the mean range of SSDs for both experiments by multiplying the number of valid SSDs used by the SSD step (50 ms in Experiment 1, and 40 ms in Experiment 2) and these data are also shown in Table 4. Despite the smaller number of SSDs used, Experiment 1 had a significantly larger

Table 4 – Mean number of valid SSDs and range of valid SSDs used by each subject for each task. Left three columns: mean number of valid SSDs used by subjects in each task. On average, Experiment 2 used a larger number of valid SSDs. Right three columns: Range of valid SSDs used by subjects in each task (# of valid SSDs x the SSD step). SSD step was 50 ms in Experiment 1, 40 ms in Experiment 2. Overall, Experiment 1 had a larger range of valid SSDs used. P values, as determined by paired t-tests, with significant differences being determined by values less than 0.05.

Task	# of SSDs Expt 1	# of SSDs Expt 2	P (paired t-test)	SSD range Expt 1 (ms)	SSD range Expt 2 (ms)	p (paired t-test)
Eye-only	4.22	3.66	<0.05	211	146	<0.001
Hand-only	3.56	4.06	<0.05	178	162	<0.01
Eye in Eye-Hand	3.50	4.11	<0.05	175	164	<0.05
Hand in Eye-Hand	3.22	4.50	<0.001	161	180	0.85
OVERALL	**3.6**	**4.1**	**<0.01**	**181**	**162**	**<0.01**

overall range of valid SSDs due to the larger SSD step ($p < 0.01$; paired t-test). This difference reached significance for three of the four tasks (eye-only, hand-only and eye in eye-hand). In sum Experiment 1, on average, used a smaller number of valid SSDs per subject, but had a larger range due to the larger SSD step. Therefore, it is possible that the smaller range of valid SSDs sampled could have led to the disappearance of fixation condition effects in Experiment 2.

3.5 – SSD sampling differences contribute to the disappearance of gap and step effects

Knowing that subjects used a smaller range of valid SSDs in Experiment 2, we sought to determine whether the same results would have been borne out in Experiment 1, had subjects only been exposed to the SSDs used in Experiment 2. To this end, we used the Weibull functions that were fit to the inhibition functions in Experiment 1 and calculated the probability of making a movement at each valid SSD (See Methods Section 2.5) from Experiment 2. More specifically, if a subject's SSDs in the overlap condition were 40, 80, 120 and 160 ms in Experiment 2, we would then use the Weibull fit to calculate the p(movement) for those SSDs using the overlap data from Experiment 1. Therefore, using the same inhibition function fit and RT distributions from Experiment 1, we could determine whether sampling a smaller range of SSDs in Experiment 2 could have contributed to the disappearance of the gap and step effects. Thus, we re-calculated each subject's SSRTs in each task via both the mean and integration methods, and plotted the means in Figure 7.

In the eye- and hand-only tasks, the effect of fixation condition on the STOP process approached, but did not reach significance ($P < 0.11$ for both; Fig 7A & B). However, in both the eye-movement and hand movement portions of the eye-hand co-ordinated task, we observed a significant effect of fixation condition on SSRTs. In the eye movement portion (Fig 7C), we

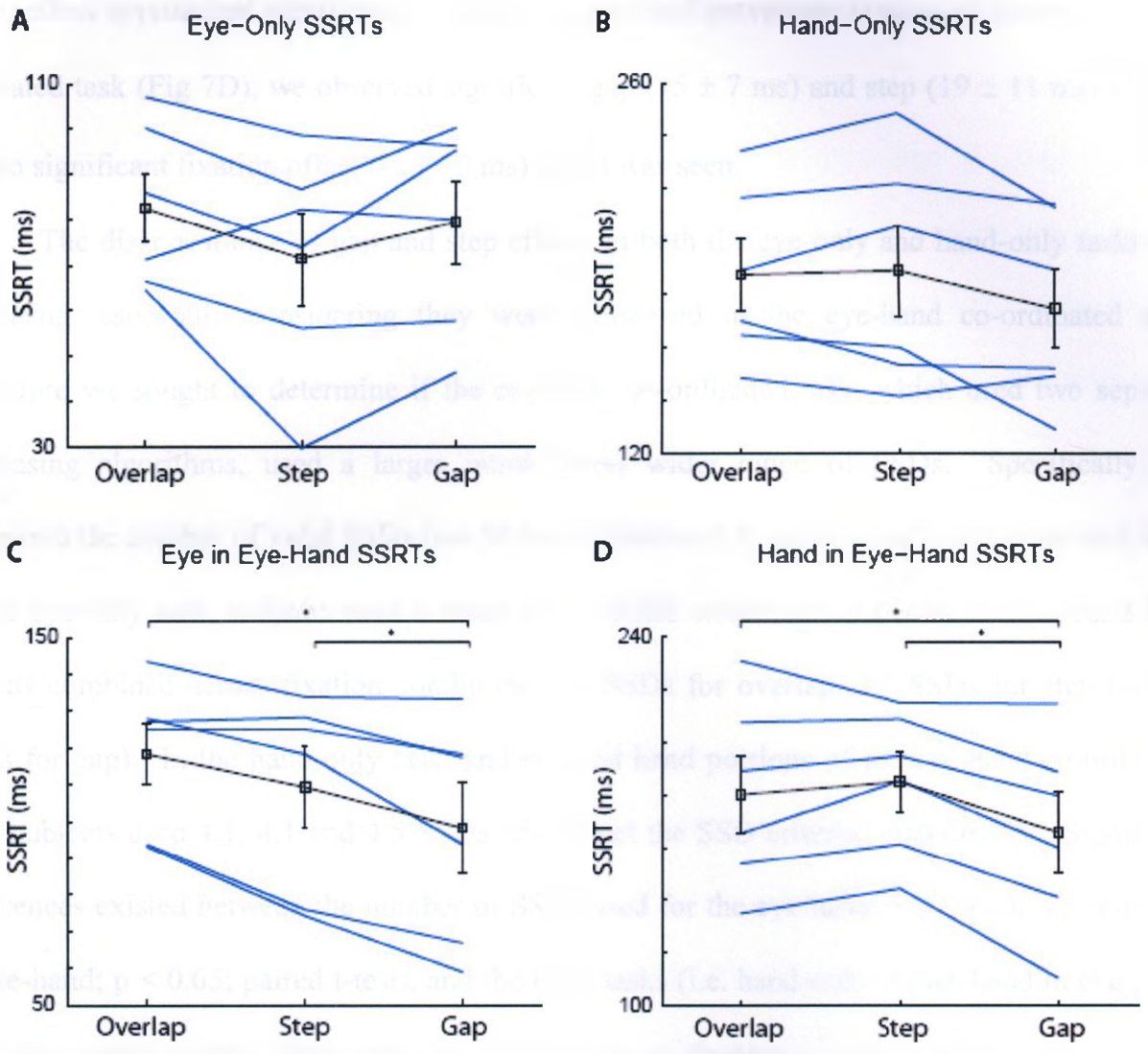

Figure 7 – Recalculation of SSRTs using both the Weibull fit and reaction time cumulative distribution function from Experiment 1, but the SSDs from Experiment 2. A. The gap effect on SSRTs seen in Experiment 1 disappeared when the SSDs from Experiment 2 were used. B. Similarly, both gap and step effects on SSRTs seen in Experiment 1 disappeared when the SSDs from Experiment 2 were used. C. Although gap and step effects on SSRTs approached significance in Experiment 1 for the eye portion of the eye-hand task, we observed significant gap and step effects on SSRTs when using the SSDs from Experiment 2. D. Similar to Experiment 1, gap and step effects were conserved in the hand portion of the eye-hand co-ordinated task when the SSDs from Experiment 2 were used to recalculate the SSRTs.

observed significant gap (20 ± 13 ms) and step (11 ± 8 ms) effects, while the fixation offset (9 ± 9 ms) effect approached significance. Finally, in the hand movement portion of the eye-hand co-ordinated task (Fig 7D), we observed significant gap (15 ± 7 ms) and step (19 ± 11 ms) effects, but no significant fixation offset (-5 ± 12 ms) effect was seen.

The disappearance of gap and step effects in both the eye-only and hand-only tasks was surprising, especially considering they were conserved in the eye-hand co-ordinated task. Therefore we sought to determine if the eye-hand co-ordinated task, which used two separate staircasing algorithms, used a larger number and wider range of SSDs. Specifically, we compared the number of valid SSDs (see Methods Section 2.5) used by each subject in each task. In the eye-only task, subjects used a mean of 3.7 SSDs which met the criteria for a valid SSD (means combined across fixation conditions: 3.5 SSDs for overlap, 3.7 SSDs for step and 3.7 SSDs for gap). In the hand-only task, and eye and hand portions of the eye-hand co-ordinated task, subjects used 4.1, 4.1 and 4.5 SSDs which met the SSD criteria, respectively. Significant differences existed between the number of SSDs used for the eye tasks (i.e. eye-only versus eye in eye-hand; $p < 0.05$; paired t-test), and the hand tasks (i.e. hand-only versus hand in eye-hand; $p < 0.05$; paired t-test). Therefore, the conservation of fixation condition effects on the STOP process in Experiment 2 can be attributed, at least in part, to the smaller range and number of SSDs used in the eye-only and hand-only task, versus the eye-hand co-ordinated task. Thus we can conclude that SSD sampling does have an effect on fixation condition effects on the STOP process.

3.6 – Fixation Condition Effect Differences between Experiments 1 & 2

If SSD sampling were the only explanation for the absence of fixation condition effects on the STOP process, we should have seen fixation condition effects on SSRTs in the eye-hand co-ordinated task in Experiment 2. Therefore we sought to determine if smaller average differences *between* fixation conditions on RTs in Experiment 2 (ie a smaller gap effect), or greater variances in these differences on a subject by subject basis could explain Experiment 2's absence of fixation condition effects. Therefore, we compared the magnitudes and variances of gap, step and fixation offset effects between Experiments 1 & 2. As above, we have combined the effects across effector tasks to increase statistical power for RTs, inhibition function means, and SSRTs.

When contrasting the gap effect on reaction times in Experiment 1 versus Experiment 2, we found a significantly smaller gap effect, on average, in Experiment 2 ($p < 0.01$; Fig 8A; paired t-tests). However, we also observed strongly correlated gap effects ($r = 0.83$; $p < 1e^{-5}$), indicating that the smaller gap effect on RTs in Experiment 2 was consistent across the sample and across effectors. Further confirming this consistency, we observed no significant difference in the variances in the magnitudes of the gap effect between Experiments 1 & 2 ($p = 0.26$; F test). Similar to the gap effect, we observed a significantly smaller step effect, on average, in Experiment 2 compared to Experiment 1 ($p < 0.05$; Fig 8D; paired t-test). Also similar to the gap effect, we observed strongly correlated step effects ($r = 0.82$; $p < 1e^{-6}$) and the variances in the magnitudes in Experiments 1 & 2 did not differ significantly ($p = 0.73$; F test). The fixation offset effect showed a trend towards being smaller in Experiment 2, though this difference did not reach significance ($p = 0.09$; Fig 8G; paired t-test). Similar to both the gap and step effects, we observed strongly correlated fixation offset effects ($r = 0.89$; $p < 1e^{-8}$) and the variances in the

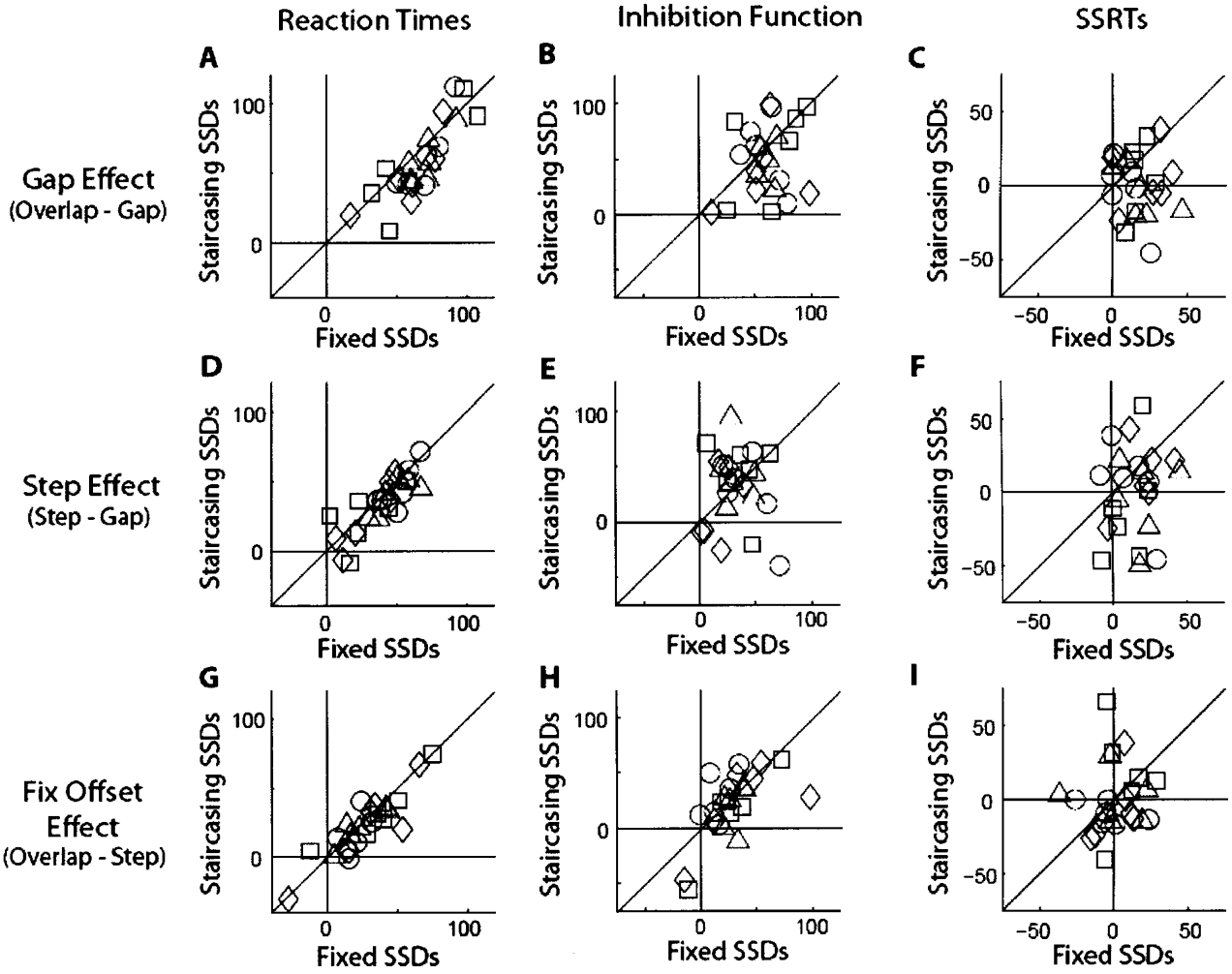

Figure 8 – Comparative analysis of fixation condition effects on RTs, (Left Panel), Inhibition Function Means (Middle Panel) and SSRTs (Right Panel) in Experiments 1 & 2 to determine the cause of the disappearance of gap and step effects on SSRTs in Experiment 2. In all subplots (□) represents data from the Eye-only task, (◊) from Hand-only, (○) from the Eye portion and (Δ) from the Hand portion of eye-hand co-ordinated task. Smaller gap (A) and step (D) effects existed in Experiment 2 (Staircasing SSDs) compared to Experiment 1 (Fixed SSDs) while no fixation offset effect existed (G). Further, significant correlations existed between RTs in the two experiments. However, no significant differences existed between inhibition function means in Experiment 1 & 2 for gap (B), step (E) or fixation offset (H) effects. Further, no significant correlations existed between fixation conditions effects on inhibition function means and the variance of these effects was significantly larger in Experiment 2. Finally, no significant differences existed in the magnitude of gap (C), step (F) or fixation offset (I) effects on SSRTs between Experiments 1 & 2. However, significant differences existed in the variances of gap (C) and step effects (F) on SSRTs. This variance was greater in Experiment 2 (Staircasing SSDs) where gap and step effects are equally likely to be positive or negative while in Experiment 1, both gap and step effects are almost exclusively positive. Finally, no significant difference in variance existed for the fixation offset effect (I).

magnitudes of the step effect in Experiments 1 & 2 did not differ significantly ($p = 0.83$; F test). Therefore, we saw smaller fixation condition effects on the GO process when staircasing SSDs were used and since the estimation of SSRT requires the reaction time CDF, these differences likely contribute to the absence of fixation condition effects on the STOP process in Experiment 2.

Since the inhibition function is also used to estimate the SSRT, we sought to determine if fixation condition effects on the mean of the inhibition function were smaller in Experiment 2 as well. Although the term "gap effect" has generally been reserved for RTs and SSRTs, we believe that any difference in inhibition function means between overlap and gap fixation conditions also fit the criteria as a "gap effect." Similarly, step and fixation offset effects could also be used when describing fixation condition differences between means of the inhibition functions. Thus, we extracted the "mean SSD" for each fixation condition; that is the SSD at which p(movement) = 0.5 from the Weibull fit as above (Section 3.4). Therefore, subtracting the mean SSD from the gap condition, from the mean SSD in the overlap condition produced the "gap effect" on the mean of the inhibition function. Similarly, we also calculated both the step and fixation offset effects on inhibition function means. Overall, unlike reaction times, we saw no systematic difference in the magnitude of the gap (Fig 8B), step (Fig 8E) and fixation offset (Fig 8H) effects on the mean of the inhibition functions in Experiment 1 versus Experiment 2 ($p > 0.20$ for all; paired t-tests). Further and importantly, we observed poorly correlated gap and step effects on the inhibition function means ($r < 0.26$ for both; $p > 0.32$ for both) and the variances in the magnitudes of the gap and step effects in Experiment 2 were both significantly larger than Experiment 1 ($p < 0.05$ for both; F test). Recall that we observed no significant fixation offset effect on SSRTs in either experiment, thus it is not surprising that we observed

significantly correlated fixation offset effects ($r = 0.62$; $p < 0.001$), and these effects showed no significant difference in variance ($p = 0.36$; F test). Therefore, the larger variance in fixation condition effects on inhibition function means in Experiment 2 likely also contributed to the absence of gap and step effects on SSRTs.

Similar to reaction times, when contrasting the gap effect on SSRTs in Experiment 1 versus Experiment 2, we found significantly smaller gap effects, on average, in Experiment 2 ($p < 0.01$; Fig 8C). Similar to inhibition function means, we found these gap effects on SSRTs to be poorly correlated ($r = -0.11$; $p = 0.61$). Further, the variances in the magnitudes of the gap effects in Experiments 1 & 2 were significantly different ($p < 0.05$; F test). This difference in variance is noticeable in Fig 8C, where the gap effect has a small range and is consistently positive (range: -1 to 46 ms; 21/24 positive) when using fixed SSDs. On the contrary, when using staircasing SSDs, the gap effect has a wider range and is equally likely to be positive or negative (range: -45 to 38 ms; 12/24 positive). Similar to the gap effect, we found significantly smaller step effects on SSRTs, on average, in Experiment 2 compared to Experiment 1 ($p < 0.05$; Fig 8F). Similar to inhibition function means, step effects were poorly correlated ($r = 0.15$; $p = 0.49$) and the variances in the magnitudes of the step effect in Experiments 1 & 2 were significantly different ($p < 0.001$.; F test). As with the gap effect, this difference in variance is noticeable in Fig 8F, where the step effect has a smaller range and is more consistently positive (range: -8 to 46 ms; 21/24 positive) when using fixed SSDs. When using staircasing SSDs, the step effect has a wider range and is less likely to be positive (range: -45 to 38 ms; 15/24 positive). Unlike reaction times, the fixation offset effect on SSRTs did not show any trend towards being smaller in Experiment 2 ($p = 0.86$; Fig 8I). Similar to both gap and step effects, we found fixation offset effects to be poorly correlated ($r = 0.10$; $p = 0.63$) and the difference in

their variances between Experiments 1 & 2 approached significance ($p = 0.054$). Once again, Experiment 2 showed a wider range of fixation offset effects (Experiment 1 range: -37 to 28 ms; Experiment 2 range: -41 to 66 ms), however, both experiments showed equal likelihood of producing a positive fixation offset effect on SSRTs (Experiment 1: 13/24 positive; Experiment 2: 14/24 positive).

Overall, fixation condition effects on the STOP process seem to be absent from Experiment 2 for two reasons. First, the smaller fixation condition effects on the GO process can explain the smaller fixation condition effects on the STOP process. Secondly, the greater variability in fixation condition effects on the inhibition function means can explain the larger variance in fixation condition effects on the STOP process. Importantly, both of these differences are relative, not absolute (i.e. *between* fixation conditions, rather than systematic changes in the overall length of the GO and STOP processes). Together, these relative changes led to smaller, more variable and ultimately insignificant fixation condition effects on movement inhibition in Experiment 2.

3.7 – GO and STOP process differences in Eye-Hand Co-ordination

On a different note, upon analyzing the GO process between tasks, we noticed that eye RTs in the eye-hand co-ordinated task were noticeably longer than in the eye-only task. We found this effect consistently in Experiment 1 and Experiment 2 across all fixation conditions and all tasks. Therefore, all fixation conditions, and both tasks were combined to increase statistical power. Upon doing so, we determined that subjects had significantly longer RTs (35 ± 39 ms) when saccades were accompanied by a hand movement (Fig 9A). Performing the same analysis on hand movements in the hand-only and eye-hand co-ordinated tasks, we found no

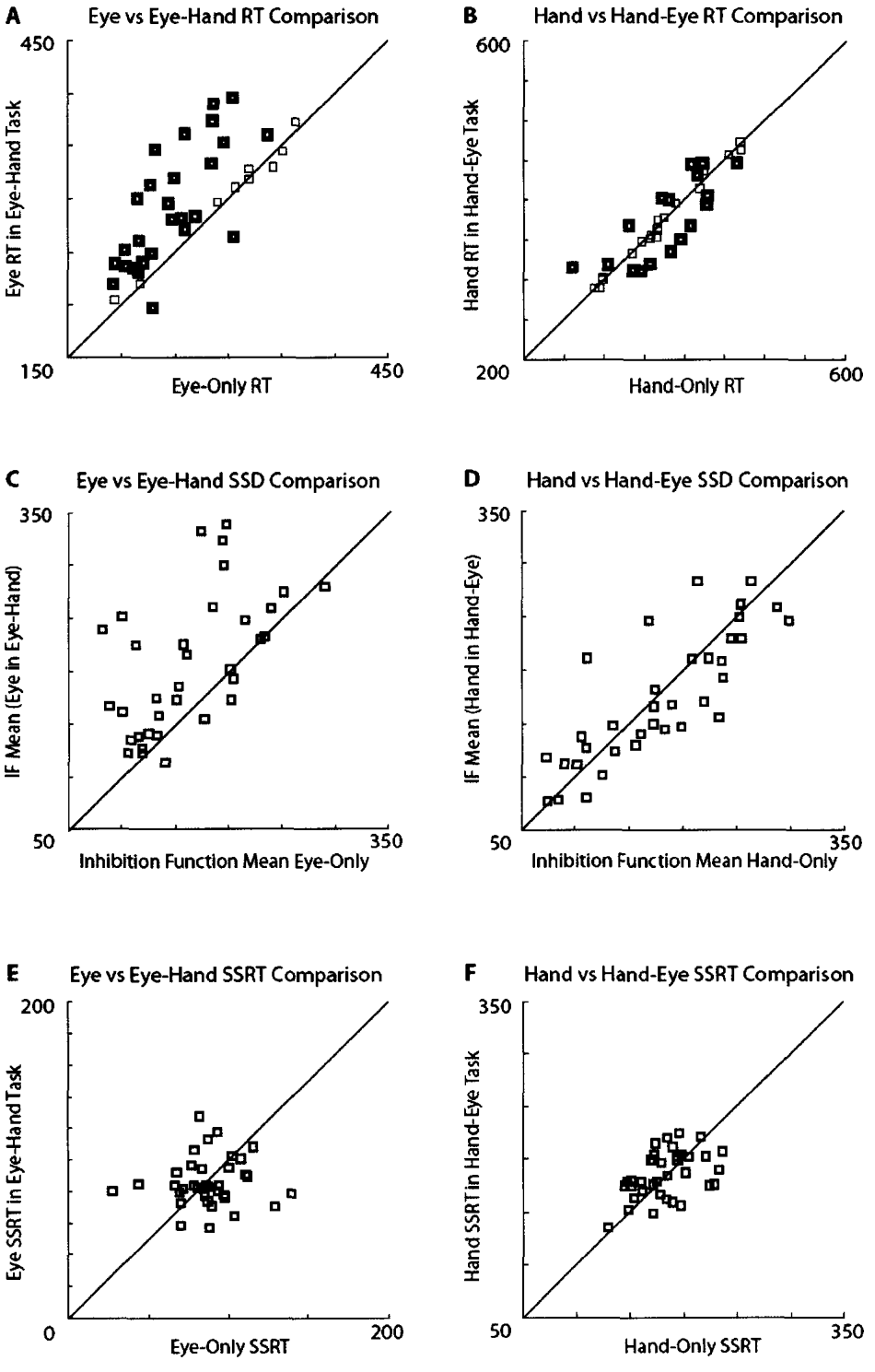

Figure 9 – Correlations of Reaction Times, SSDs and SSRTs between the eye-only and eye in eye-hand co-ordinated tasks (A,C,E) as well as the hand-only and hand in eye-hand co-ordinated tasks (B,D,F). The eye movement GO process is longer with an accompanying hand movement (A,C), while the STOP process is unaffected (E). Both the hand GO and STOP processes are unaffected by an accompanying eye movement (B,D,F). All plots are combined data from across all 3 fixation conditions and significant differences ($p<0.05$) represented by bold squares.

significant effect on reaction times when hand movements were accompanied by an eye movement (Fig 9B; 3 ± 24 ms; 8/17 RTs showing significant differences were longer). Similar to the eye GO process, the mean of the inhibition functions (as determined by the Weibull fit) shifted to the right (ie occurred at a longer SSD) in the eye-hand co-ordinated task (Fig 9C; 49 ± 58 ms) and, these inhibition function means showed strong and significant correlations ($r = 0.55$; $p < 0.0005$). Similar to the hand GO process, the mean of the inhibition functions did not differ significantly between the hand-only and eye-hand co-ordinated tasks (Fig 9D; mean difference: 4 +/- 37 ms; range: -78 to 101 ms; $p = 0.49$) and these means showed tight correlations ($r = 0.83$; $p < 1e\text{-}9$). While the eye GO process was, on average, longer in the eye-hand co-ordinated task, we found no significant effect on the eye STOP process despite an accompanying hand movement (Fig 9E; 1 ± 25 ms). Further, these values no longer showed a significant correlation ($r = 0.07$; $p = 0.69$) providing further evidence to suggest that while the eye GO process is affected by an accompanying hand movement, the eye STOP process is not. Similar to the hand GO process, the hand STOP process showed no significant effect when accompanied by an eye movement (Fig 9F; -1 +/- 26 ms). Further, these values no longer showed a significant correlation ($r = 0.07$; $p = 0.69$) providing further evidence to suggest that both the GO and STOP processes for the hand are unaffected by an accompanying eye movement.

Therefore, it appears that given the longer reaction times of arm movements, in an eye-hand co-ordinated movement, the eye GO process slows down to accommodate the slower hand movement. However, if the eye movement needs to be cancelled, this process need not be slowed by whether it is to be accompanied by a hand movement.

3.8 – Tests of the Race Model

One assumption of the Race Model is that the GO and STOP processes are stochastically independent. Therefore, the growth of the GO process should not affect the growth of the STOP process, and vice-versa. One test of such independence is to see how well reaction times of non-cancelled saccades can be predicted using control trial reaction times (Logan 1994). To do this, we compared non-cancelled *STOP* trials from a given SSD (≥ 10 non-cancelled saccades for a given subject) with their corresponding *CONTROL* trials whose reaction times were less than the sum of the subject's SSRT plus the given SSD. Over all three experiments, and all fixation conditions, we found that the representative non-cancelled portion of the *CONTROL* RT distribution predicted the actual RTs of non-cancelled saccades well (for simplicity, we present here the prediction based on the mean SSRT, averaging the integration and mean methods together). Table 5 (Test 1) summarizes the number of violations of the race model for each fixation condition in each task for both Experiments 1 & 2. In Experiment 1, for the eye-only condition, the mean observed non-cancelled RTs for the overlap, step and gap conditions exceeded the predicted RTs by 7.8, 0.3 and 6.9 ms respectively, with the differences on a per-SSD basis reaching significance in 6/21 (overlap), 4/25 (step) and 9/30 (gap) comparisons. In the eye-only task in Experiment 2, the mean observed non-cancelled RTs for the overlap, step, and gap conditions exceeded the predicted RTs by 2.3, 10.7, and 18.0 ms respectively, with the differences on a per-SSD basis reaching significance in 1/4 (overlap), 1/6 (step) and 1/5 (gap) comparisons. The remainder of the tasks produced similar findings and are summarized in Table 5. Overall, the frequency of race model violations is higher than those reported previously from our lab (Stevenson et al. 2009), occurring at nearly 30% of the SSDs. Since not all subjects used the same set of SSDs in either experiment, we rank ordered each subjects' set of SSDs from

Table 5 – Race model tests for Experiments 1 & 2. Test 1 shows the number of significant differences between non-cancelled and predicted RTs over the number of total comparisons for each fixation condition. Test 2 shows the p-value of the repeated measures ANOVA (or paired t-test) comparing non-cancelled RTs at each SSD. Overall, RTs increased (often significantly) with increasing SSDs, as predicted by the race model.

		Race Model Tests – Experiment 1		**Race Model Tests – Experiment 2**	
Task	**Fixation Condition**	**Test 1**	**Test 2**	**Test 1**	**Test 2**
Eye-only	OVL	6/21	0.06	1/4	0.54
	STP	4/25	<0.0001	1/6	0.16
	GAP	9/30	<0.0001	1/5	0.14
Hand-only	OVL	11/24	0.22	2/5	N/A
	STP	7/27	<0.05	1/3	N/A
	GAP	9/33	<0.0001	0/4	N/A
Eye in Eye-Hand	OVL	4/12	0.98	3/15	0.08
	STP	2/20	<0.05	4/15	<0.05
	GAP	5/22	<0.05	1/13	0.34
Hand in Eye-Hand	OVL	4/18	0.41	8/17	0.34
	STP	5/25	<0.005	3/18	0.77
	GAP	8/30	<0.0001	6/18	<0.005

shortest to longest. Similar to a previous report (Ozyurt et al. 2003), the greatest number of violations occurred at each subject's shortest SSDs. At the shortest SSDs, the race model's independence assumption was violated 80% and 85% of the time in Experiments 1 & 2 respectively. At the longest SSD, however, the independence assumption was violated less than 10% of the time for both experiments. Further, we observed no substantial differences between Experiments 1 & 2 for any task. Therefore, no significant differences in race model validity existed between experiments and these data are generally consistent with previous reports regarding the assumption of independence of the GO and STOP processes.

A second test of the independence assumption in the race model is that the RTs for non-cancelled saccades should increase progressively for longer SSDs, as the delayed STOP process should eliminate less of the upper tail of the control RT distribution at longer SSDs (e.g., imagine how Fig. 3B would look for longer SSDs). Our observations validated this prediction as the observed RT for non-cancelled saccades increased for longer SSDs for all fixation conditions in both experiments (Table 5, Test 2). Overall, these increases reached significance in 9/12 total fixation conditions from the four tasks (Table 5) for Experiment 1 (for inclusion, at least 3 subjects had to have at least 10 non-cancelled saccades at a given SSD). In Experiment 2, given that the staircasing algorithm created different and generally smaller overall ranges of SSDs for each subject, fewer SSDs had three subjects with 10 or more non-cancelled saccades – particularly in the eye-only and hand-only tasks. Therefore, in the eye-only condition, while none of the fixation conditions produced significantly longer RTs for longer SSDs, all displayed an increasing trend (two-way t-tests). Further, there did not exist two qualifying SSDs in the hand-only task for any fixation condition, therefore no comparison could be made. In the eye-hand co-ordinated task, with 1200 trials and two separate staircasing algorithms, sufficient

numbers of SSDs qualified and 3/6 fixation conditions from the two parts of the task reached significance. Therefore, all tasks and fixation conditions with sufficient numbers of qualifying SSDs showed a trend towards increasing RTs for longer SSDs as predicted by the race model.

Chapter 4 – Discussion

The aim of this study was to determine the influence of fixation condition on movement inhibition. To this end, we performed a comprehensive study of how humans countermand movements, examining the inhibition of eye and/or hand movements across three different fixation conditions. This study provides the opportunity to learn more about movement inhibition, particularly in light of the known influences of fixation condition on movement generation. Secondly, it provides the opportunity to reconcile discrepancies in the literature that were not directly comparable previously. Although we did observe some influences of fixation condition on movement inhibition, surprisingly, we observed that such influences depended on the method of stop signal delay determination we used. Further, the SSD determination method also influenced fixation condition effects on the GO process, which was extremely surprising, given the infrequency of STOP trials. Overall, this study provides a comprehensive report of human countermanding across multiple fixation conditions, effectors, and SSD determination methods. The establishment of these fixation condition effects and task dependent differences permits study of their neurophysiological basis in animal models.

4.1 – Comparison to previous countermanding studies

To our knowledge there are only three other reports that have examined the influence of fixation conditions in countermanding paradigms. First, Stevenson et al. (2009) analyzed the gap effect on RTs and SSRTs using fixed SSDs for eye-only movements. In regards to the GO process, our results from both Experiment 1 & 2 are in agreement with Stevenson and colleagues as we observed a significant gap effect on RTs in the eye-only task and this effect was similar in magnitude (~56 ms in Stevenson et al 2009; ~66 ms and ~58 ms in Experiments 1 & 2

respectively). Similarly, we observed a gap effect for all effector combinations in both experiments. Interestingly, the gap effect approached 80 ms three of the four effector tasks in Experiment 1 (See Table 3), which was substantially larger than most gap effects seen in simple reaction time tasks (Pratt et al. 2000; Reuter-Lorenz et al. 1995; Munoz and Corneil 1995). These differences could be subject related or perhaps related to the nature of the countermanding task (as postulated in Stevenson et al 2009). For example, it is known that RTs on *CONTROL* trials in the countermanding task are longer than in simple RT tasks (Lappin and Eriksen 1966). Therefore, if both overlap and gap RTs were lengthened by a similar percentage, due to the presence of infrequent *STOP* trials, it could lead to the larger gap effect seen in these tasks.

In regard to the STOP process, we also observed a significant gap effect on SSRTs for eye-only, hand-only and hand portion of the eye-hand co-ordinated tasks for the fixed SSD task. However, the gap effect on SSRTs (~15-25 ms depending on which effector task) in this study was somewhat smaller than that reported by Stevenson and colleagues (~40 ms). Three subjects participated in both studies and two of the three had very similar gap effects on SSRTs between the two studies. Thus it is likely that these differences were subject related.

Further, while simultaneous priming of the GO and STOP processes seems improbable, especially due to the interconnected neural networks responsible for each, these results are also consistent with reports studying movement inhibition not necessarily related to fixation condition effects. In an arm countermanding task which analyzed ipsilateral and contralateral trials separately, it has been found that both the ipsilateral GO and STOP processes are expedited (Mirabella et al. 2006). Overall, these results provide further evidence for the independence (at least in part) of the GO and STOP processes.

The second human countermanding report that is pertinent to the current study is that of Morein-Zamir and Kingstone (2006) who examined human performance in an oculomotor countermanding task. The authors reported a negligible fixation offset effect on SSRTs, despite a modest decrease in saccadic reaction times on *CONTROL* trials (which averaged ~18 ms; Table 1). Both experiments in the current study corroborated these findings, as no effector in either experiment showed a significant fixation offset effect on SSRTs. Therefore, we emphasize that when studying fixation condition effects, using a gap interval (as opposed to a step) is optimal to study the influences of fixation point manipulations on processes related to movement inhibition, as reductions in saccadic RTs are greatest for gaps ranging between 200-400 ms (Munoz et al. 2000; Dorris and Munoz 1995; Juttner and Wolf 1992).

The final previous human countermanding report stands in contrast to the current findings (Mirabella et al. 2009). This study reports that SSRTs for arm movements increase when a gap interval is increased from 0 ms to 212 ms, despite decreases in the reaction times of arm movements on *CONTROL* trials (Table 1). Originally, we postulated that effector-related differences between the oculomotor and limb-movement systems could be the cause for this discrepancy (Stevenson et al. 2009). This explanation would have been consistent with previous reports which have suggested an independence between STOP processes for eye and hand movements (Logan and Irwin 2000; Boucher et al. 2007b). However, in Experiment 1, we found a step effect on SSRTs in the opposite direction to that found by Mirabella and colleagues for both eye movements and hand movements. We were even more surprised to find that this effect disappeared entirely in Experiment 2, where staircasing SSDs were used. Regardless of which experiment is considered, we never observed an increase in SSRTs from step to gap as found by Mirabella and colleagues. However, we postulate that since four of six subjects showed an

increase in SSRT in the eye-only task with staircasing SSDs, it is possible that a significant result could be obtained using a staircasing SSD algorithm. Further, we have seen a substantial change in fixation condition effects on the STOP process in this study due to what we believe to be a relatively small change in SSD determination between the two experiments. Therefore, while our setup was designed to resemble Mirabella and colleagues as closely as possible, differences did still exist which could have led to the differences seen between these two studies. For example, they had subjects perform blocks consisting of only trials of the "gap" fixation condition, then a block of the "step" fixation condition. They also used a touch screen which may have led to intensity differences in both the targets and stop signals. This could potentially explain why we observed a much larger step effect on reaction times in both experiments (~21 ms in Mirabella et al (2009); ~55 ms and ~46 ms in the hand-only task for Experiments 1 & 2, respectively). We believe that these differences, coupled with a staircasing procedure for determining SSDs, could produce the results found by Mirabella and colleagues.

4.2 – Fixation Condition Effects: Staircasing versus Fixed stop signal delays

The current results show a disappearance of fixation condition effects on movement inhibition when a dynamic method of SSD calculation is used. However, it is important to emphasize that no changes in SSRT magnitude were observed for any fixation condition between the two experiments. Therefore, we propose three potential reasons for the disappearance of relative differences *between* fixation conditions on SSRTs. First, Figure 7 illustrates that having a limited range and number of SSDs can decrease fixation condition effects on SSRTs. Despite the fact that the same data (RT CDF and Weibull fit of the inhibition function from Experiment 1) were used, both gap and step effects on SSRTs disappeared in the eye- and hand-only tasks

when the more limited range of SSDs from Experiment 2 was used for SSRT recalculation (Fig 7A & B). Further, when SSRTs were recalculated using Experiment 1's data for the eye-hand co-ordinated task, the gap and step effects on SSRTs were conserved (Fig 7C & D). Recall that the eye-hand co-ordinated task used two separate staircasing algorithms per fixation condition (one for eye and one for hand), and thus had a larger number and range of SSDs. Therefore, the first reason for the disappearance of the gap and step effects on SSRTs in Experiment 2 lies in the smaller range and number of SSDs used in the eye- and hand-only tasks in Experiment 2.

However, if this were the only reason for this disappearance, we would have expected to find gap and step effects on SSRTs for the eye-hand co-ordinated task in Experiment 2 (Fig 5F & H). Since this was not the case, other factors must have also influenced fixation condition effects on the STOP process. In particular, Figure 8 illustrates that smaller gap and step effects on RTs existed in Experiment 2. Considering the experiments were counterbalanced, this change was not due to ordering effects. This was especially surprising that the SSD determination method could influence the GO process, especially given the infrequency of the STOP signal. Further, despite the fact that the gap and step effects were smaller, they were strongly correlated (Fig 8A & D), indicating that this effect was consistent across the sample. This was especially surprising, as it would have been more plausible that a smaller gap effect would occur in Experiment 1 where the same range of SSDs was used for each fixation condition. Although subjects could not predict the exact SSD of an upcoming trial, they would know the general range of SSDs that could be chosen, and this range would be the same for any fixation condition. Therefore, it would not have been surprising if subjects behaved similarly in all fixation conditions (for movement initiation or inhibition) in Experiment 1, leading to smaller fixation condition effects on both RTs and SSRTs. Further, the staircasing algorithm would converge on the "true" mean SSD for

a subject in Experiment 2 potentially creating different inhibition function means for each fixation condition. Therefore, since the general trend followed that the mean of the inhibition function was found at the shortest SSD for gap and the longest SSD for overlap (with step in between), it would not have been surprising if these means were further spread out in Experiment 2, leading to exacerbated fixation condition effects on RTs and SSRTs. However, this was not the case. Therefore, it is likely that the both the fixed range and staircasing SSDs used captured the "true" mean of the inhibition function and this was confirmed by the lack of significant difference between inhibition function means in Figure 6 (B, E, H).

Despite the fact that no magnitudinal changes occurred in inhibition function means across the two experiments, gap and step effects on inhibition function means and SSRTs became more variable in Experiment 2. Since both the reaction time CDF and inhibition function are required for the estimation of SSRT, we believe the increase in variability in fixation condition effects on inhibition function means to be the third contributing factor to the disappearance of fixation condition effects on the STOP process. We believe that this increase in variance could have arisen for the following reason. Firstly, Boucher and colleagues' (2007) interactive race model states that the interaction of the STOP process on the GO process is virtually instantaneous. However, we believe that if the GO and STOP process both approach threshold at the same time, they may have a subtle, but important interaction before the completion of the race. Therefore, in such situations, a greater amount of conflict may exist, which may have led to the greater variance in fixation condition effects on inhibition function means and SSRTs in Experiment 2. This would seem plausible, since a higher percentage of trials in Experiment 2 would challenge the point where the stochastic GO and STOP processes reach threshold at approximately the same time. Alternatively, Experiment 1 would have a larger

percentage of trials where the race is clearly won by the GO or STOP process and if these SSDs are still produce a p(movement) between 0.1 and 0.9, then these "non-conflicting" SSDs are used in the estimation of SSRT. Therefore, the higher the percentage of SSDs used to calculate the SSRT which fall into the "conflicting" category, the greater amount of potential conflict between the GO and STOP processes and this may have caused the greater variability and ultimate disappearance of fixation condition effects on the STOP process in Experiment 2. Further, this may not only affect the STOP process, as the results also suggest that movement generation systems may rely less on visual cues in situations of greater conflict. Therefore, perhaps an interesting future experiment would be to conduct a countermanding experiment with fixed SSDs, where each fixation condition's mean SSD is centred on the mean SSD from the staircasing SSD task. Further, these SSDs could be normally distributed, such that more trials use SSDs close to the mean SSD, with fewer and fewer used at SSDs progressively further from the mean. This would mimic a situation of greater conflict, while still using a fixed set of SSDs.

4.3 – Effects of Eye-hand Co-ordination

Both Experiments show that the eye movement GO process is longer in an eye-hand co-ordinated task than an eye-only task. A dependency of eye movement reaction time has been documented previously but the effects have not necessarily been in agreement. For example, two previous studies have shown that eye movement reaction times are faster with a co-ordinated hand movement (Lunenburger et al. 2000; Snyder et al. 2002) while another has shown them to be slower (Boucher et al. 2007b; in agreement with our results). Despite the fact that eye reaction times were longer with an accompanying hand movement, the finding that the eye GO process was affected by an accompanying hand movement was not surprising. It is has long been shown that eye movements are "yoked" to hand movements (Fisk and Goodale 1985). In

this study, hand movements to ipsilateral space were faster than those to contralateral space and this lateralization effect has been reported consistently (Velay and Benoit-Dubrocard 1999; Barthelemy and Boulinguez 2001; Barthelemy and Boulinguez 2002; Cavina-Pratesi et al. 2004). However, they also found that when eye movements were co-ordinated with a hand movement, saccades were also faster to ipsilateral compared to contralateral targets. It is logical to accept that in order to make a co-ordinated eye and hand movement to a target, the amplitude and direction of *both* the eye and hand movement should be specified prior to the initiation of either movement. Further, it has been shown that due to neuromuscular delays and greater inertia of the limb, the eye movement begins prior to an arm movement. Although saccades are typically initiated 40-100 ms prior to limb movement onset, electromyographic (EMG) activity in the arm begins before, or simultaneous with, saccade onset (Gribble et al. 2002). This permits the subject to foveate the target prior to the hand reaching the target. For these two reasons it is not surprising that the initiation of eye movements is "yoked" to the initiation of hand movements.

The fact that the GO process for eye movements and hand movements are yoked would suggest a similar outcome for the STOP process. On the contrary, we found that the STOP process for eye movements was unaffected by an accompanying hand movement, which lends further support to the independence of the GO and STOP processes. Further, a previous report has suggested that independent stopping mechanisms exist for eye and hand movements (Boucher et al. 2007b; Logan and Irwin 2000), suggesting that while the eye is yoked to the hand during the initiation of an eye-hand co-ordinated movement, it need not be when the movement is inhibited. However, further research is required to determine a potential neural mechanism for this phenomenon.

Finally, while eye movements are yoked to hand movements, we found no evidence for hand movements being similarly yoked to eye movements. Neither the GO, nor the STOP process for hand movements was affected by an accompanying eye movement, suggesting that the planning of the direction and amplitude of the hand movement may be the rate limiting step of an eye-hand co-ordinated movement. That is to say that the execution of an eye movement is delayed until the hand movement is fully planned. One concern we had with Mirabella and colleagues' (2009) study was that they did not specify whether or not they excluded trails where the eye moved with the hand. These findings suggest that even if the eyes were allowed to move during this hand-only task, it would not have significantly affected their hand RT or SSRT estimates.

4.4 – Are the Eye and Hand STOP processes independent?

Both the eye and hand STOP processes are similarly affected by fixation condition as the fixation condition effects seen on the eye STOP process in Experiment 1 are also seen on the hand STOP process. Further, no fixation condition effects are seen on either STOP process in Experiment 2. Therefore, perhaps at least in early sensory processing, the eye and hand STOP processes are similarly affected by fixation condition. In finding that neither the eye nor the hand STOP processes are yoked to each other, this suggests that the eye and hand may not share common inhibitory control. A previous report (Boucher et al. 2007b) has also proposed independent stopping mechanisms for eye and hand movements, citing the observation of some eye-hand co-ordinated error trials with hand-only errors and others with eye-only errors. This study corroborates these findings as we observed trials in the eye-hand co-ordinated task where subjects made hand-only errors, as well as trials where subjects made eye-only errors.

Alternatively, a previous report from our lab has suggested a similar inhibitory mechanism for the eye and head in eye-head gaze shifts (Corneil and Elsley 2005), despite a percentage of trials with head-only errors. The authors only reported trials with head-only errors and never observed any trials where the subject made an eye-only error. Thus they suggested a dual-threshold hypothesis, where the eye and head are under a similar inhibitory control mechanism, but the threshold to evoke a head movement is lower than that of the eye. Since we observed both eye-only and hand-only errors, a dual threshold cannot explain our results. Further, since neither the eye nor hand STOP processes are yoked, our results support independent inhibitory mechanisms for the eye and hand.

4.5 – Models of Inhibition

On the surface, the results of the current study appear similar to those of Kapoor and Murthy (2008). In that study, a double step task was employed to examine the effect of covert attention on compensating for a shifting target, or goal. Using delayed visually guided, memory guided, or simple visually guided saccades, they showed that the GO process was expedited in the visually guided and memory-guided tasks on simple reaction time trials (60% of trials). On the remainder of trials, the target stepped to an alternate location. They were able to estimate the time necessary for the subject to change their planned movement (to the original target) and make a saccade to the new target using a metric called the Target Step Reaction Time (TSRT). Interestingly, TSRTs were also shorter for the delayed visually guided and memory guided saccades compared to simple visually guided saccades. Thus, similar to the current study, both movement initiation and movement inhibition can be expedited in the same fixation condition.

However, while the behavioural outcome in the two tasks appears similar, it is likely that the neural activity underlying the behaviour is quite different between the two studies. In both the delayed visually guided and memory guided saccade tasks, the target is flashed so the subject can plan the saccade, but must withhold it momentarily. Once the fixation point is extinguished the previously planned saccade can be rapidly executed (hence the expedited GO process). Similarly, if the target were to step to an alternate location, this covert inhibition would make it relatively easy for the subject to withhold the saccade (since the saccade is already being withheld) to the original target and plan a saccade to the new target. On such trials, the flash of the target would likely cause an initial decrease in fixation neuron activity, but as the saccade is required to be withheld, these neurons would increase their activity to maintain fixation. At the same time, saccade neurons likely also begin to increase as saccade is planned. Their activity would then level off, waiting for the fixation point to be extinguished. In this situation, both the movement initiation and movement inhibition systems are primed with increases in both fixation and saccade neuron activity. Since there is a known push-pull relationship between fixation and saccade neurons (mentioned above; e.g., Findlay and Walker 1999; Munoz and Istvan 1998; Munoz and Wurtz 1993a; Munoz and Wurtz 1993b), it would seem that in order to have an increase in activity in both neuronal populations, an external signal would have to be provided and this could arise from the basal ganglia.

Similarly, the model of inhibition proposed by Stevenson et al. (2009) outlines fixation neuron activity in both overlap and gap fixation conditions. In this model, the expedited GO signal is a result of decreased fixation neuron activity in the gap compared to overlap condition. It is also proposed that the expedition of the stop process may be due to an extra-collicular signal, potentially arising from the basal ganglia, markedly increasing fixation neuron activity

leading to shorter SSRTs in the gap condition. This is quite different from the above model for Kapoor and Murthy. Instead of having an extra-collicular signal causing an increase in both saccade and fixation neuron activity simultaneously, we believe that fixation neuron activity would initially decrease in the gap condition (as previously shown; Paré and Hanes 2003) and only after the stop signal is presented would an extra-collicular signal cause a *rebound* of fixation neuron activity that is stronger and earlier in the gap condition compared to the overlap condition. While we propose different models of inhibition for each of these studies, we do not believe that either model invalidates the other. Both models require an extra-collicular signal to modify the activity of both saccade and fixation related neurons in the SC. Given that neuronal activity is substantially affected by fixation condition, it is not surprising that the underlying neural mechanisms would differ substantially in two different tasks. Although we believe that both of these models are valid, they both require testing using an animal model.

4.6 – General Conclusions

Overall, the length of time necessary to generate, or inhibit a movement can be manipulated by altering the situational context. Specifically, the magnitude of the GO and STOP processes change with differing fixation conditions. However, smaller task specific differences like the method of SSD calculation used, do not affect the overall magnitude of the GO or STOP processes for a given effector. Rather, only the consistency and magnitude of the relative changes *between* fixation conditions are sensitive to such task specific differences. Those task related differences which lead to a greater amount of conflict (such as a smaller range of SSDs clustered around the mean) can lead to smaller differences and greater variability in the movement inhibition process. Specifically, the GO and STOP processes, when approaching

threshold at the same time, may interact to produce more variable outcomes. In conclusion, differences in situational context seem to matter less when closely competing movement initiation and inhibition processes exist.

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Appendix 1

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Use of Human Subjects - Ethics Approval Notice

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Sponsor:
Ethics Approval Date: May 15, 2007 — **Expiry Date:** May 31, 2008
Documents Reviewed and Approved: Revised Study End Date
Documents Received for Information:

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

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

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the HSREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of monitor, telephone number). Expedited review of minor change(s) in ongoing studies will be considered. Subjects must receive a copy of the signed information/consent documentation.

Investigators must promptly also report to the HSREB:

a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) all adverse and unexpected experiences or events that are both serious and unexpected;
c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to this office for approval.

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

Chair of HSREB: Dr. John W. McDonald
Deputy Chair: Susan Hoddinott

Ethics Officer to Contact for Further Information		
Jennifer McEwen	Denise Grafton	Ethics Officer

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

cc: ORE File