Characterizing Cortical Signatures of Inhibitory Control

by

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DISSERTATION ABSTRACT

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Title: Characterizing Cortical Signatures of Inhibitory Control

Inhibitory control - or the ability to suppress unwanted thoughts and actions - is a critical executive function that allows us to flexibly navigate dynamic environments. Previous work has established oscillatory activity in the theta and beta frequency ranges as important signatures of inhibitory processes. However, limitations inherent in the design of standard motor inhibition tasks left ambiguities surrounding the timing of this oscillatory activity with respect to the different processes involved in motor inhibition. Specifically, it is unclear how beta and theta activity relate to the cognitive (i.e. identifying task demands) and motoric (i.e. stopping a movement) components of inhibitory control. In my research, I designed a novel inhibition task - the continuous movement stop task (CMST) - which addresses the limitations of the standard paradigms by providing an unambiguous measure of motor termination on every trial. I first behaviorally validated the CMST by exploring behavioral outcome metrics. I then compared the CMST outcomes with those of an existing inhibitory control paradigm (the stop signal task or SST) then tested it in populations known to show deficits in performance on the SST. After behavioral validation, I then employed the CMST in combination with scalp electroencephalography (EEG) in Parkinson's Disease patients and intracranial EEG in epilepsy patients. This combination of scalp and intracranial EEG allowed me to explore the functional relevance of inhibition-related oscillatory dynamics in both cortical and subcortical structures,

ultimately providing a unique and essential step toward unraveling neural mechanisms of inhibitory control.

This dissertation includes previously published co-authored material.

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DEDICATION

For my brother, the reason I am a scientist.

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CHAPTER 1:

INTRODUCTION

Definition And Relevance of Inhibitory Control

Inhibitory control, or the ability to suppress inappropriate or unwanted actions, thoughts, and impulses, is a core executive function that allows us to safely and flexibly navigate dynamic environments. For example, imagine you are walking barefoot through your house when you realize you are about to step on a Lego. In this instance, the ability to terminate your next step is imperative to avoid grievous bodily harm. Similarly, we rely on inhibitory control mechanisms to refrain from responding angrily in moments of frustration or to withhold our natural tendency to check our phones when we feel it vibrate during a meeting. In fact, inhibitory control mechanisms appear to be fundamental to many cognitive and motor functions as evidenced by their involvement in a wide array of neuropsychiatric and neurological disorders ranging from reading disabilities (van der Schoot et al., 2004)to Parkinson's Disease (Jahanshahi et al., 2015). Given the far-reaching relevance of inhibitory control mechanisms, a thorough understanding of how the brain implements this critical ability holds great value for the advancement of neuroscientific research.

To date, researchers have identified at least 2 different types of inhibitory control: reactive and proactive control (Aron, 2011). Reactive control refers to a fast, stimulus-driven process that is engaged in response to an external stop signal, requiring rapid cancellation of an ongoing or imminent action (such as in the Lego example). Proactive control, on the other hand, refers to the anticipatory modulation of behavior in preparation for the possibility of needing to inhibit a response (van den Wildenberg et al., 2022). For example, if you are running toward an

intersection, you may slow down in anticipation of the possibility that there will be oncoming traffic by the time you reach it.

Methodological Approaches to Studying Inhibitory Control

Much of our current understanding of inhibitory control has been achieved via use of standard motor inhibition tasks such as the stop signal task (SST; Logan & Cowan, 1984). In this task, participants are typically instructed to make a rapid motor response to a "Go" signal (commonly a button press). On a minority of trials, a "Stop" signal is presented shortly after the Go signal, indicating that the participant should attempt to withhold their response. The key measure derived from the task is the Stop-Signal Reaction Time (SSRT)**,** which estimates the latency of the internal stopping process and serves as an index of inhibitory control efficiency. The timing between the Go and Stop signals, known as the stop-signal delay**,** is dynamically adjusted to maintain a balanced probability of successful and failed inhibition. This property allows for the modeling of stopping behavior using the independent race model (Logan & Cowan, 1984), which suggests that going and stopping are separate processes and the behavioral outcome depends on which process is completed first.

Another commonly used paradigm for investigating inhibitory control is the Go/No-Go task. This task is similar to the SST in that participants are predisposed to respond rapidly to a Go signal and are instructed to withhold this response on a minority of trials. The primary difference is that, in the Go/No-Go task, participants do not first see a Go signal followed by a Stop signal. Rather, they are presented with either a cue indicating that they should respond or a cue indicating that they should not respond. It is thought that the SST and the Go/No-Go tasks may tap different inhibitory processes, with the SST eliciting more reactive inhibitory mechanisms and the Go/No-Go eliciting proactive mechanisms (Raud et al., 2020)

Though these tasks have been enormously fruitful in uncovering mechanisms of inhibitory control, both suffer from the same limitations that must be addressed to achieve a more complete understanding of the intricacies of inhibitory mechanisms. For example, in both tasks, participants are asked to withhold a movement they are intending to make. This means that stopping is not directly observable and must rather be inferred from other task parameters. Inferring stopping time from other measures introduces ambiguity into the interpretation of task performance and limits applications of neuroscientific techniques that rely on precise time locking, such as electrophysiology. In other words, to confidently identify physiological activity associated with stopping, it is important to know when stopping actually occurred.

Another major limitation of the standard motor inhibition paradigms is that they require comparing unsuccessful-stop or go trials to trials in which participants successfully withheld movement (i.e. comparing going to stopping) when used to explore neurophysiological substrates of stopping. This comparison confounds physiological processes involved in motoric termination and the cognitive control processes preceding motoric inhibition. That is, activity underlying suppression of movement cannot be differentiated from that underlying cognitive reaction to a sudden change in environmental demands with this method. This represents a critical limitation in the field of because disruptions of the cognitive and motoric components of inhibition may be differentially affected in disorders associated with response inhibition deficits.

Additionally, these tasks are not well-suited for investigating mechanisms underlying planned termination of movement. Though proactive mechanisms can be elicited by informing participants of the probability of a stop signal appearing on a subsequent trial, a true “planned” stop in this context would be identical to planning not to move.

Finally, because both tasks require termination of a ballistic movement, they do not address mechanisms underlying termination of a continuous movement. This limits generalizability, as termination of a continuous movement might better relate to real world self-control, at least in some cases.

Neuroanatomy Of Inhibitory Control

Despite their limitations, standard motor inhibition tasks have yielded substantial insights into the neural circuitry underlying inhibitory control. Current models based on this research posit that inhibition is subserved by a cortico-basal ganglia-thalamocortical loop (CBGT). Critical cortical components of the CBGT circuit include right inferior frontal gyrus (rIFG), pre-supplementary motor area (pre-SMA), and motor cortex (M1)(Aron et al., 2007; Aron & Poldrack, 2006; Schaum et al., 2021; Sebastian et al., 2021; Swann et al., 2009, 2012). These cortical nodes of the inhibitory control system are linked with basal ganglia by anatomically and functionally distinct pathways – the hyperdirect and indirect pathways (Jahfari et al., 2011; Leunissen et al., 2016; Roseberry & Kreitzer, 2017). The hyperdirect pathway monosynaptically connects cortex with subthalamic nucleus (STN)(Aron et al., 2016; Chen et al., 2020), which is understood to play an essential role in suppressing motor output by exciting the basal ganglia output nuclei. Because these nuclei exert an inhibitory influence on thalamus, excitation via STN increases the strength of thalamic inhibition (Aron et al., 2016 for review). Thus, a monosynaptic connection with STN renders the hyperdirect pathway well-situated to carry out reactive inhibitory processes that require a rapid response to a change in environmental demands. In contrast, the indirect pathway, which multisynaptically connects cortex with STN via striatum (Alexander & Crutcher, 1990), is thought to underlie planned or proactive suppression of motor output (Adnan Majid et al., 2013; Criaud et al., 2012; Greenhouse et al., 2012; Jahfari et al.,

2012; Muralidharan et al., 2019). In other words, the indirect pathway may facilitate motor suppression that is the consequence of anticipated, internal demands while the hyperdirect pathway facilitates motor suppression in response to unanticipated changes in environmental demands.

Functional imaging studies using the SST provide additional support for the anatomical and functional distinction of the indirect and hyperdirect pathways (Behan et al., 2015; Hu et al., 2016; Li et al., 2006; Sebastian et al., 2021; Zandbelt et al., 2013; Zhang & Iwaki, 2019). For example, an fMRI study (Zhang & Iwaki, 2019) employed a modified version of the SST that elicited both reactive inhibition (theoretically facilitated by the hyperdirect pathway) and proactive inhibition (theoretically facilitated by the indirect pathway). Using functional connectivity analysis, the authors evaluated the contributions of cortical-subcortical pathways to each type of inhibition. They found a "shorter" pathway (including IFG, SMA, STN, & M1) which appeared to be more involved in reactive inhibition and a "longer" pathway (including the same regions of the shorter pathway with the addition of striatum and dorsolateral prefrontal cortex) which appeared to be more involved with proactive inhibition.

Electrophysiology Of Inhibitory Control

Inhibitory control research has largely focused on the function of neural oscillations - the rhythmic fluctuations of electrical activity generated by the brain. Theoretical models, such as that proposed by Buzsáki and Draguhn (2004), posit that oscillations serve as fundamental temporal frameworks that facilitate efficient communication and information integration across distributed neural circuits. In other words, this theory - often referred to as 'communication through coherence' (Fries, 2015) - suggests that oscillatory activity serves as a coordinator that helps organize and align the electrical activity generated by disparate neural populations.

Oscillations are separated into different frequency bands — delta (1–3 Hz), theta (4–7 Hz), alpha (8–12 Hz), beta (13–30 Hz), and gamma (>30 Hz) — each of which is associated with specific cognitive and motoric functions. Though oscillatory in most (or all) of these frequency bands may be observed during a motor inhibition task, the current preponderance of evidence supports beta and theta band activity as critically important for the implementation of motor inhibition.

Beta

Oscillatory synchrony in the beta frequency range appears to play an essential role in inhibitory control processes (Wessel & Anderson, 2024). For example, intracranial electroencephalography studies in humans using the SST have demonstrated increased beta power for successful stopping in cortical and basal ganglia regions associated with inhibitory control – including rIFG, preSMA, and STN (Fonken et al., 2016; Ray et al., 2012; Swann et al., 2009, 2012). Importantly, cortical beta observed in different nodes of the CBGT inhibitory control system may serve different functions in inhibition. For example, A transcranial alternating current stimulation study showed that beta frequency stimulation over sensorimotor cortex led to slowed movement, strongly suggesting that sensorimotor beta plays a causal role in movement suppression (Pogosyan et al., 2009). Previous work also consistently shows a decrease in beta activity prior to movement onset (Barone & Rossiter, 2021), with the extent of decreases in pre-movement beta predicting response time (Wessel, 2020). These and similar findings support the postulate that sensorimotor beta plays a causal role in termination of motor output.

Prefrontal beta, on the other hand, appears to be more involved in the cognitive aspects of inhibitory control. For example, beta in prefrontal cortex has been associated with executive

control, working memory, and preventing distractions (Schmidt et al., 2019 for review). Additionally, increases in prefrontal beta appear to be associated specifically with reactive motor termination, possibly reflecting the cognitive component of the inhibitory process (Liebrand et al., 2021). For example, in a study using an adaptation of the SST in which subjects were informed about the probability of a subsequent stop trial—ostensibly allowing them to plan to stop—elevated beta activity was only observed over sensorimotor cortex and not over prefrontal regions (Muralidharan et al., 2019). Additionally, elevated prefrontal beta was observed in an unexpected events task, providing further support for the hypothesis that beta activity in this region is associated with recognition of an unanticipated change in the environment (Wagner et al., 2018).

Though the literature consistently demonstrates the relevance of beta oscillations in inhibitory control, their precise function remains a mystery. For example, because previous work using the standard motor inhibition tasks relies on an estimate of response inhibition time, it is unclear if stopping-related increases in beta power occur early enough with respect to motor termination to be causal. Alternatively, it is possible that these beta increases are rather a reflection of sensory feedback or evaluation of motor outcomes (Schwey et al., 2023). Given the challenges with dissociating the cognitive and motoric components of inhibition described above, further research is required to determine the relevance of beta for each component.

Theta

While the importance of beta activity in motor inhibition has been more thoroughly explored, there is a considerable body of evidence suggesting that theta frequency activity (4-7Hz) may also be an important component of inhibitory control (Cavanaugh & Frank, 2014; Cavanagh et al., 2012; Eisma et al., 2021). Specifically, theta activity in midfrontal regions is

thought to reflect the cognitive control mechanisms necessary for response inhibition (Cavanaugh & Frank, 2014; Eisma et al., 2021; Singh et al., 2018; van Noordt et al., 2015). For example, Eisma et al. (2021) found elevated midfrontal theta activity during 4 different cognitive control tasks, with the highest theta power observed during a Go/No-Go task and a reactive control task. Further evidence supporting the involvement of theta band oscillations in the cognitive component of inhibition comes from a deep brain stimulation study which showed that 4Hz stimulation of STN improved cognition (Kelley et al., 2018). This study also demonstrated a short latency connection between STN and PFC, demonstrating a relationship between theta band oscillations, cognitive control, and the hyperdirect pathway.

Disorders Of Inhibitory Control

One valuable way to study mechanisms of inhibitory control is to examine contexts in which response inhibition is disrupted. Though inhibitory mechanisms appear to be disrupted in a wide variety of disorders including Schizophrenia, Attention Deficit Hyperactivity Disorder, Obsessive Compulsive disorder, and reading disabilities (Lipszyc & Schachar, 2010), here I will focus on 2 disorders: Parkinson's Disease (PD) and Nicotine Addiction.

Parkinson's Disease (PD)

Parkinson's disease (PD) is a progressive neurodegenerative disorder that results from the degeneration of dopaminergic neurons in the basal ganglia, leading to widespread dysfunction in the CBGT circuitry. PD presents a valuable opportunity to study the neural mechanisms of inhibitory control due to its profound effects on motor regulation and the suppression of unwanted actions. The dopaminergic depletion characteristic of PD disrupts the balance of excitation and inhibition within the basal ganglia, impairing both the initiation and cancellation

of motor responses. Importantly, this dysfunction presents not only with motoric deficits, but with cognitive deficits as well. In fact, cognitive disruptions are the most commonly reported non-motor symptom (Aarsland, 2021). Additionally, dopaminergic medication is thought to contribute to impulse control disorders also frequently seen in individuals with PD (Zhang et al., 2021). The common comorbidity of motoric and cognitive disruptions in PD emphasizes the imperative to dissociate neural mechanisms supporting each of these functions in the context of response inhibition.

A prominent neurophysiological feature of PD is excessive synchronization of neural activity in the beta frequency band (Hammond et al., 2007). Elevated beta oscillations have been associated with pathological maintenance of motor set, contributing to rigidity, bradykinesia, and impaired motor flexibility (Hammond et al., 2007). Moreover, abnormal beta activity is linked to deficits in reactive inhibitory control, as evidenced by impaired performance on the standard motor inhibition tasks described previously (Hammond et al., 2007; Gauggel et al., 2004; Obeso et al., 2011). Studying inhibitory control in PD, particularly in relation to beta oscillatory dynamics, offers critical insights into how rhythmic neural activity within the CBGT circuitry supports the flexible suppression of action, and how its disruption leads to characteristic motor and cognitive impairments.

Nicotine Addiction

Addiction and substance use disorders are also closely associated with inhibitory control deficits. In fact, disruptions in inhibitory control circuitry have even been proposed as an etiological factor in the development and maintenance of addiction (Feil et al., 2010; Koob & Volkow, 2016). Previous research has demonstrated both behavioral deficits on response inhibition tasks and alterations in neurophysiological substrates associated with the CBGT

circuitry. For example, a functional imaging study revealed hypoactivation of the rIFG during response inhibition as well as increased stopping latencies in a population of people living with an addiction (Luijten et al., 2011). Given the relationship between mechanisms of inhibitory control and addiction in conjunction with the prevalence of people addicted to nicotine, nicotine addicts are another beneficial population to study in the pursuit of a more comprehensive understanding of mechanisms underlying inhibitory control and their contribution to pathological behaviors.

Summary

Mechanisms of inhibitory control are relatively well-established, however, several questions remain. For instance, it is unclear to what extent previously established mechanisms underlying inhibition of an incipient, ballistic movement also apply to inhibition of an ongoing movement. Additionally, the precise role and timing of beta needs to be more concretely established. Previous work consistently demonstrates beta activity around the time of stopping, however, precisely when beta occurs with respect to actual motor termination remains to be seen. Moreover, the timing and function of beta activity specific to the cognitive components of inhibitory control also needs to be rectified.

To address these questions, I have created a novel continuous movement stop task (CMST) that addresses the previously illustrated limitations of the standard motor inhibition tasks (SST and Go/No-Go). This task (1) allows for the comparison of the same behavior (stopping) in conditions that elicit either planned or unplanned stops—balancing motor elements of the task so that cognitive aspects can be more precisely examined; (2) provides a direct measure of stopping on every trial, allowing for greater temporal precision of inhibition-related

spectral activity; and (3) requires termination of a continuous movement, promoting generalizability.

In Chapters 2 and 3, I examine the efficacy of the CMST for dissociating prepared and reactive inhibitory strategies by evaluating behavioral outcomes of the CMST in healthy subjects and patient populations. In Chapters 4 and 5, I then explore electrophysiological signals associated with different components of the task using scalp EEG and the more spatially precise stereo-EEG. With these methodologies, I leverage the novel opportunity to time-lock electrophysiological signals to the moment of movement termination to critically evaluate the timing of oscillatory dynamics with respect to the different components of the inhibitory process. This thesis therefore represents the unique opportunity to examine cortical signatures associated specifically with the cognitive (stop signal presentation) and motoric (motor termination) elements of inhibitory control.

Chapter 2 was previously published in the Journal of Cognitive Neuroscience with Dominique Denning, Venessa Hufnagel, and Nicole Swann. Chapter 3 was also previously published in the journal Brain and Behavioural Research with Bryan Mantell, Elliot Berkman, and Nicole Swann.

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CHAPTER 2:

STOPPING A CONTINUOUS MOVEMENT: A NOVEL APPROACH TO INVESTIGATING INHIBITORY CONTROL

Schultz, K. E., Denning, D., Hufnagel, V., & Swann, N. (2023). Stopping a Continuous Movement: A Novel Approach to Investigating Inhibitory Control. *Journal of Cognitive Neuroscience*, *35*(7), 1108–1132. https://doi.org/10.1162/jocn_a_01998

Introduction

Our ability to behave in a flexible, adaptive manner is critically dependent on inhibitory control. For example, imagine walking barefoot to your refrigerator when you suddenly spot a scorpion on the floor in front of you. As the goal changes from getting food to not getting stung, the ability to halt your ongoing movement is vital. Evidence suggests that the inhibitory processes underlying motor termination are also important for other forms of cognitive and behavioral control such as emotion regulation (Lewis et al., 2006), attentional control (Zavala et al., 2017), and impulse control (Schachar & Logan, 1990). Disruption of the inhibitory control system may contribute to myriad neurological and psychiatric disorders such as Parkinson's disease, obsessive-compulsive disorder, schizophrenia, attention-deficit hyperactivity disorder, and substance use disorder (Lipszyc & Schachar, 2010). Given the broad relevance of inhibitory control in degenerative and psychiatric disorders, a comprehensive understanding of this system is essential for development of treatments, interventions, and diagnostic tools.

Much of what we understand about inhibitory processes has been established using standard motor inhibition tasks, such as the stop signal task (SST; Logan & Cowan, 1984). The SST is designed to measure efficiency of response inhibition by estimating the amount of time required to inhibit an initiated response. Participants are asked to respond as quickly as possible to a 'go' signal (typically with a button press) and to inhibit their response when the 'go' signal is

followed by a 'stop' signal. The metric of interest, known as the stop signal reaction time (SSRT), is then derived from go-signal reaction time (RT), stop signal delay, and probability of correct responding (i.e. successfully stopping when prompted). SSRT can be quantified in this way using simple mathematical models, such as the independent race model, which assumes that going and stopping are two independent processes and behavioral output (or lack thereof) is determined by which process is completed first (Logan & Cowan, 1984).

Reliance on the SST and similar task designs has produced a rich understanding of reactive inhibitory control processes, specifically as they relate to stopping a movement that is not yet (or not fully) initiated. However, current designs fail to address stopping a continuous (or ongoing) movement. Although executing a continuous movement recruits different regions than a discrete movement does (Habas & Cabanis, 2008), it is often assumed that both movements recruit the same inhibitory network to implement stopping. This is based on previous work which shows that stopping a variety of movements including button presses, foot movements, speech, and eye movements all seem to engage the same brain networks (Cai et al., 2012; Coe & Munoz, 2017; Greenhouse et al., 2012). However, these approaches are all built on a framework of discrete movements and generalizability to continuous movements has not yet been established empirically. Some previous research supports the possibility of a relation between processes underlying termination of discrete and continuous movements. For example, previous work using a continuous tracking paradigm in which subjects track a target by maintaining pressure on a force sensor have shown that average time to stop a continuous response were comparable to (Morein-Zamir et al., 2006) and highly correlated with (Morein-Zamir et al., 2004, 2008) those derived from the SST. Additionally, Scheres et al. (2003) found that methylphenidate, a common pharmaceutical treatment for Attention Deficit Hyperactivity

Disorder, reduced stopping latency for both the continuous tracking paradigm and the SST, suggesting overlapping inhibitory substrates for stopping in both tasks. However, other recent work comparing behavior on the SST and a rhythmic movement task failed demonstrate a relation between stop times for each task (M. Hervault et al., 2019, 2022). Importantly, these studies focused on reactive inhibition and did not investigate the possible relation between prepared inhibition of a discrete and continuous movement. A note, that while some aspects are similar, there are also key differences between these tasks and the CMST which are delineated in the Discussion section.

Related to the previous point, the SST is not well-suited to interrogate processes underlying prepared movement termination. This is an important line of inquiry, as it has been suggested that prepared inhibitory processes and reactive inhibitory processes (i.e. stopping in reaction to an unexpected stimulus) may recruit different neural mechanisms. That is, reactive inhibition may recruit the monosynaptic 'hyperdirect' cortico-basal ganglia pathway, while prepared inhibition is thought to recruit the multisynaptic 'indirect' pathway (Aron et al., 2016; Jahfari et al., 2012; Lofredi et al., 2020). The SST can be modified to better suit this line of inquiry by giving participants a cue about the probability that they will be given a stop signal on the next trial (Greenhouse et al., 2012; Muralidharan et al., 2019; Swann et al., 2013). The foreknowledge that a stop signal may occur allows subjects to proactively engage inhibitory mechanisms that will be employed to countermand triggering of the response tendency. Studies employing this technique have found that prepared inhibition is associated with both shorter SSRT (faster stop) and longer RT (slower response), suggesting involvement of a preparatory step prior to the response onset (Aron et al, 2011). However, the utility of this approach is limited

in that one cannot fully disentangle planning to stop an initiated movement and not planning to initiate a movement at all.

To address these gaps in the literature, we developed a novel continuous movement stop task (CMST) that involves termination of a continuous movement (a circular rotation with a computer mouse) in response to a stop signal under conditions that require either prepared or reactive inhibition. Because participants are stopping an ongoing action on every trial, the CMST provides a direct measure of the time it takes to stop (henceforth referred to as stop completion time; SCT) on individual trials, rather than an estimate over many trials. Additionally, in contrast to methods that require electromyography to identify the time of motor inhibition on individual trials (Jana et al., 2020; Raud & Huster, 2017), SCT can be measured from behavior alone. The precision offered by this novel design provides a straightforward interpretation of behavioral performance as well as the ability to directly compare prepared to reactive motor termination and investigate stopping processes underlying termination of a continuous movement – a behavior which is not usually assessed with conventional tasks. Furthermore, it provides an additional opportunity to better elucidate the relation, if any, between prepared and reactive inhibition of discrete and continuous movements.

Here we present two experiments in which we (1) test and describe the performance characteristics of our novel continuous movement stop task (CMST) and (2) compare behavioral metrics between the CMST and SST.

EXPERIMENT 1

We designed and evaluated a CMST which includes two trial types: unplanned stop trials that probe predominantly reactive stopping processes and planned stop trials that probe predominantly prepared stopping processes. Four versions of this task were performed for this

experiment. We first sought to explore the influence that percentage of unplanned stop trials might have on stopping behavior. Thus, the first three versions of the task varied only in the percentage of unplanned stop trials relative to planned stop trials. We conducted a fourth version to address limitations identified in the first three versions, namely that movement data were captured unreliably in versions 1-3. The fourth version included a guide (paper circle attached to the desk) that encouraged limited movement magnitude, which allowed us to capture mouse coordinates more reliably and calculate movement speed. We also adjusted the feedback following each block to more effectively promote behavioral consistency across subjects.

Method

Participants

We analyzed data from 44 right-handed university students (27 females, 17 males) between the ages of 18 and 32 (M_{age} = 20.98, SD = .95). Each participant completed one of four task versions (**table 1**). Participants were recruited through the university's online human subjects pool using SONA-systems and through flyers posted throughout campus. All participants signed a consent form approved by the university ethics board.

Version	Unplanned Stop Trials	Movement	N	Mean Age	Sex (assigned at birth)
1	10% (24 total)	No Guide	11	19.9	5 females, 6 males
2	30% (72 total)	No Guide	13	21.3	10 females, 3 males
3	50% (120 total)	No Guide	12	20.6	6 females, 6 males
4	30% (72 total)	Includes Guide	8	20.75	6 females, 2 males

Table 1. Specific information for each task version. Each version was performed by a different group of participants (total N = 44).

Task

The CMST (**fig. 1**) required participants to move a computer mouse in a continuous circular motion while monitoring a countdown that appeared on the screen in front of them. Movement data were collected using Psychophysics Toolbox as the position of the mouse in XY coordinate space defined by the display parameters (1600x800 pixels) at a sampling rate of 500 Hz (**fig 2a**). The cursor was not visible during the countdown.

Each trial began with 3 sequential screens displaying the text "Ready", "Set", and "Go" (**fig. 1**). Each word was displayed for exactly one second, making "go" signal arrival perfectly predictable on every trial. Participants were instructed to begin moving as soon as they saw the word "Go." The countdown began after the offset of "Go" signal. The countdown started at any value from 6-3 (with equal probability across trial types) and counted down to 1 at a regular rate of one number per second. The text "Stop" was displayed one second after the countdown reached "1" (i.e., at time 0 of the

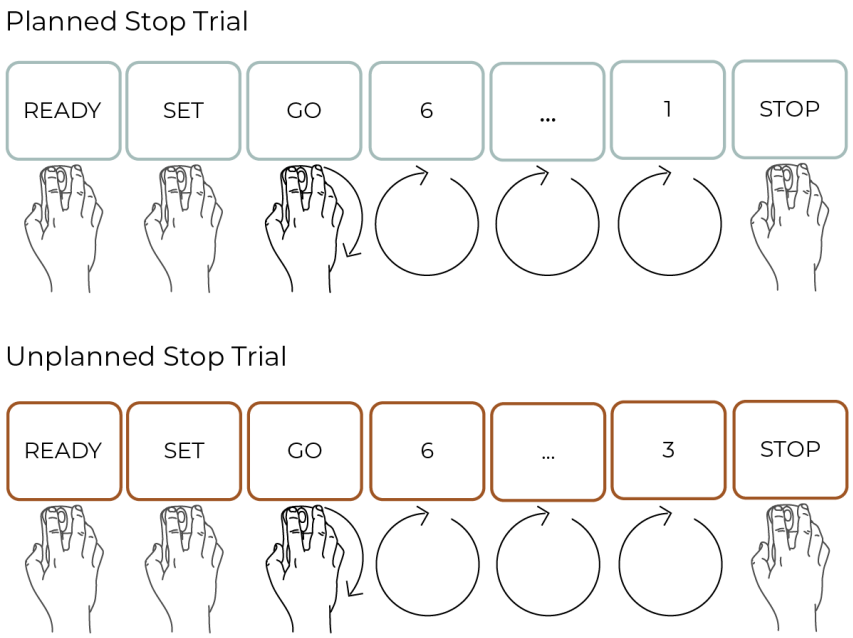

Figure 1. Depiction of task design. The start of each trial was indicated with display of the words "Ready" and "Set". Each display lasted exactly 1 second. Trials began with a go signal ("Go") which occurred immediately after the offset of the "Set" cue and was displayed for 1000ms. The countdown began at either 6, 5, 4, or 3 with equal probability for every trial. Each number of the countdown was displayed for exactly 1 second. On planned stop trials, the stop signal occurred exactly 1 second after the countdown reached one (i.e. the stop signal arrived at Time 0 of the countdown). On unplanned stop trials, the stop signal was displayed at a pseudorandom time point.

countdown) on planned stop trials and was displayed at a pseudorandom time point on unplanned stop trials. Participants were instructed to stop as soon as they saw the word “Stop”.

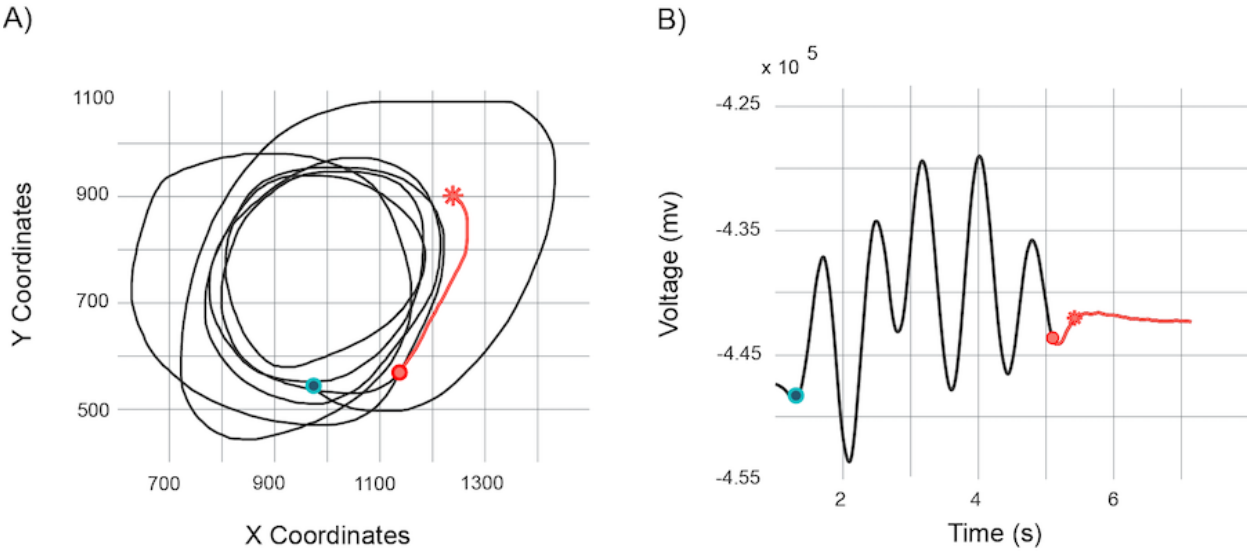

Figure 2. Example Matlab and Accelerometer data from a single trial. Red line indicates time from stop signal presentation (red circle) to movement termination (i.e. SCT; marked by a red starburst). A) Changes in computer mouse position recorded with Matlab. Mouse position is continuously recorded throughout a trial as its location in an XY coordinate system defined by monitor size and resolution. Shown here are the changes in XY position between time of go signal presentation (blue dot) and SCT. B) Accelerometer trace for the same trial. Data are shown from go signal presentation (time = 0) to 1.5 seconds after stop signal presentation.

Approximate trial length (from go-signal onset to stop signal onset) varied between 7 and ~2.5 seconds and was defined for all trials at the beginning of the task such that both conditions had an equal number of trials of comparable lengths. Stop signal presentation times for unplanned stop trials were generated using Matlab’s random number generator (*rand(N)*) plus approximate intended trial length. For example, on an unplanned stop trial intended to be approximately 4 seconds long, the stop signal presentation time would be 4 plus a random number between 0 and 1 (i.e., If the random number was 0.25 the stop signal presentation would occur at 4.25 seconds with respect to the start of the countdown.). Arrival of the stop signal during these trials was therefore not predictable. The task was programmed using the Matlab Psychophysics toolbox (Brainard, 1997).

Task training

Participants were required to correctly complete at least 5 practice trials before moving on to the rest of the experiment. If participants had not met a set of criteria after completing 20 trials, they did not move on to the rest of the experiment. During the practice stage, a circle and a cursor were visible on the screen. Participants were instructed to move the cursor around the circle at approximately one complete loop per second. The approximate speed of "one complete circle per second" was determined by pilot testing wherein movement was timed and verified to be one cycle per second and speed was derived. A range was then established around this value such that behavior could vary by +/- 4 pixels/ms. At the end of each practice trial, participants were given feedback regarding their behavioral performance. There were 6 possible error types: early start (RT< 0ms), late start (RT>1000ms), early stop (SCT<0ms), late stop (SCT>1000ms), too slow (speed of movement<10 pixels/ms) and too fast (speed of movement>60 pixels/ms). However, note that some error types were mutually exclusive (i.e., you could not start too early and too late on the same trial) so total possible errors per trial was 3. If behavior across all metrics fell within the window of acceptable behavior, participants were told their performance was "perfect". If behavioral measures fell outside this window, they were prompted to correct it. For example, if a participant waited too long to respond to the go signal (RT>1000ms), they were reminded to respond as quickly as possible when presented with the go-signal. Following successful completion of the practice trials, participants were permitted to begin the rest of the experiment. Only one participant was unable to successfully complete 5 of the 20 practice trials and therefore did not advance to the rest of the experiment and was not included in the analysis or the subject count. Overall, participants were compliant with task instructions and there were

no instances in which participants completely failed to stop on any trial. We did not include any constraints on shape or smoothness of the movement being made.

Feedback

The task included 12 blocks consisting of 20 trials (240 total trials). To promote consistent performance throughout the task and across participants, feedback similar to that given during the practice round was given at the end of each block. Participants were informed of the number of times they made each of the 6 error types. For versions 1-3, participants made at least one of the 6 possible errors on 32%, 26%, and 35% of trials respectively.

For version 4, block-wise feedback was associated with a score and a color based on performance across that block along with the number of times each error type was made. For every block, there was a total of 120 possible errors (6 error types across 20 trials). However, because some of these errors are mutually exclusive (i.e., RT can either be too long or too early) participants could realistically only make 60 of the 120 possible errors. Scores reflected percentage of errors made out of total possible errors. For example, if a participant started early, stopped late, and moved too fast on every trial, their score would be 50% (60/120 x 100). Any score above 75% was reported in green and a score of 75 or below was reported in red. As assigning a score to performance has been shown to improve behavior (Greenhouse & Wessel, 2013), we implemented these changes to encourage participants to improve performance in accordance with the feedback provided. To confirm that changes to the feedback did not differentially influence stop completion times for planned and unplanned stop trials we calculated percent change in stop completion times between blocks for planned and unplanned stop trials and compared them using a paired t-test. This analysis was performed for each subject.

We did not find any difference in percent change in stop completion times between blocks for planned compared to unplanned stop trials for any of the 8 subjects. On average, participants committed one of the 6 possible error types on 5.8% of trials (**fig. 3**). The lower error rate is possibly a product of the changes made to the feedback on this version.

Task Variants

To explore how behavior varied with percentage of unplanned stop trials, we ran 3 separate versions of the task (in 3 separate groups of participants; see **table 1**). Task versions 1-3 contained 10%, 30%, or 50% unplanned stop trials (**table 1**), respectively. In each version, the remaining trials were planned stop trials. After analysis of the first three versions of the task, we observed that the recorded magnitude of participants' circular motions frequently exceeded the limits of the

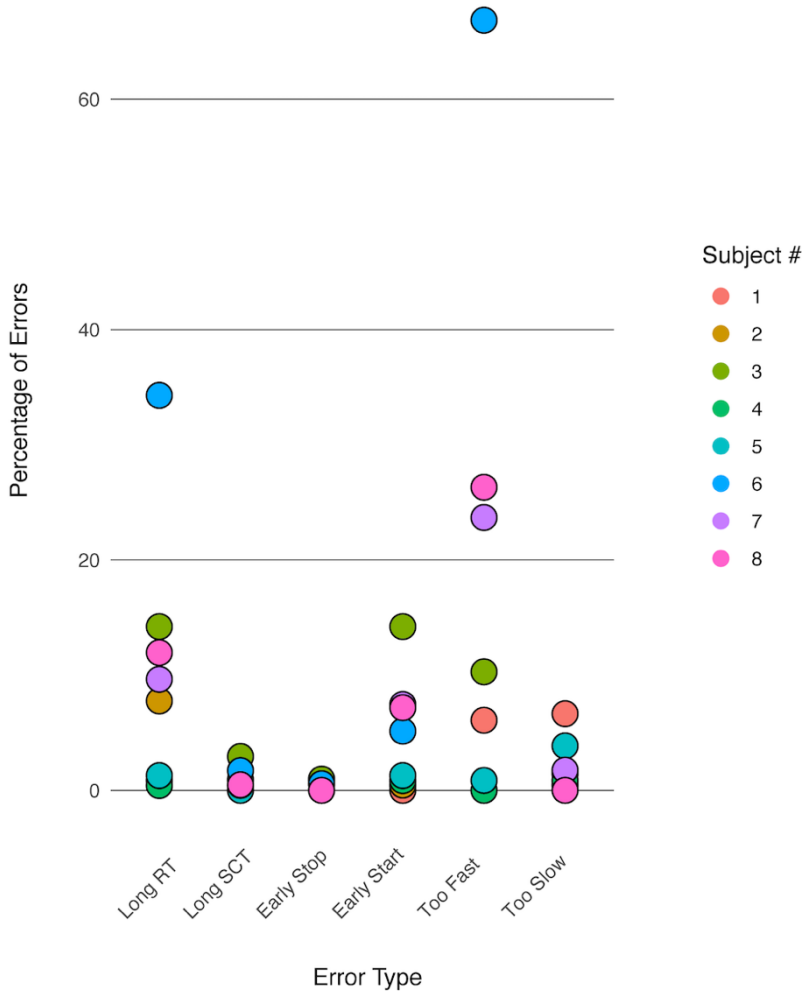

Figure 3. Percentage of errors by error type. Total errors made across the entire task were calculated for each subject and separated by error type. Here we show the total number of each error type out of the total number of trials analyzed for each subject who performed task Version 4.

coordinate plane used to identify mouse location, resulting in saturation of recorded mouse coordinate data in one dimension (X or Y) for these trials. That is, when movement of the mouse was outside the boundaries defined by the display (1600x900 pixels), it would be recorded as a change in one dimension only (i.e. change in X or Y) rather than a change in both dimensions (i.e. change in X and Y; **fig. 4a**). On average, the majority (93%) of the trials for versions 1-3 were missing more than 30% of location data and thus were deemed unsuitable for speed calculations. While a limitation, this loss of location data did not preclude our ability to calculate RT and SCT since location data was still available for one dimension. Accuracy of RT and SCT for these versions was also confirmed using accelerometry. We also used the accelerometry data to assess potential qualitative differences in movement when subjects kept their movements within the recording limits compared to when they more consistently exceeded recording limits.

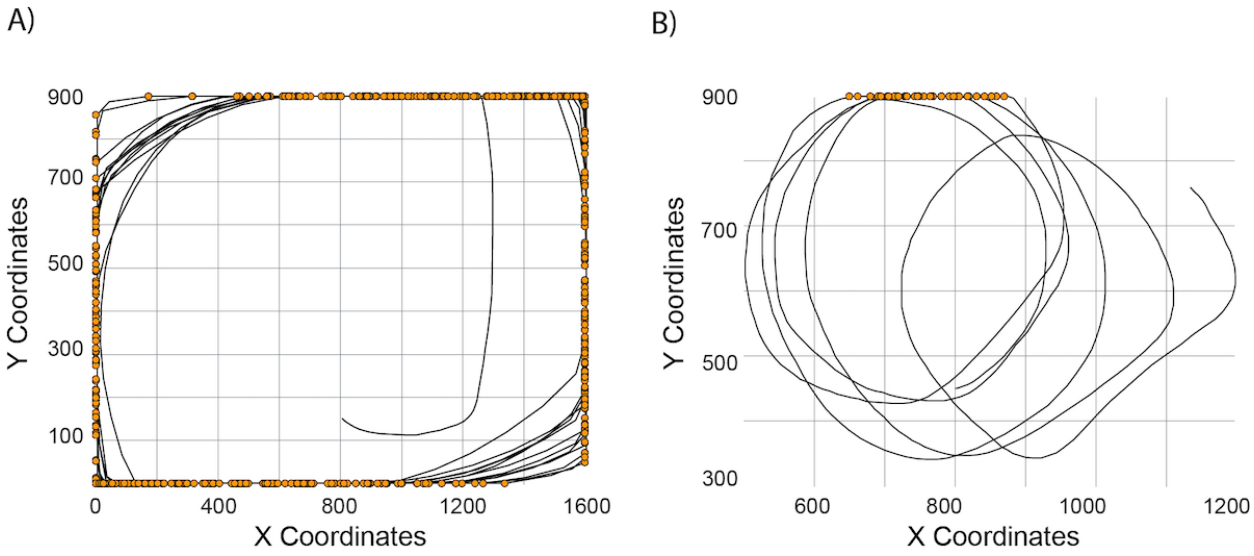

Figure 4. Examples of missing location data. A) Example trial from version 1 in which mouse movement exceeded display boundaries. Yellow dots indicate points at which mouse movement exceeded the lower limits of the Y-axis. Example is representative of trials from versions 1-3. B) Example trial from version 4 in which mouse movement exceeded display boundaries.

We did not find any discernable differences.

A fourth version of the task containing 30% unplanned stop trials was administered to a separate group of participants. In addition to the different feedback provided at the end of the block, this version also incorporated a circular paper guide with a diameter of 10 cm secured to the desk participants used. This gave participants a guide for how large their movements should be and helped constrain movement magnitude. For version 4, participants spent an average of 280ms outside display boundaries in the last 1000ms before arrival of the stop signal and participants were outside of the boundary at the time of stopping (stop completion) on 20% of trials on average. For these out of bound trials mouse coordinate position was recorded in one dimension (either x or y dimension depending on which dimension was out of bounds for each subject) and SCT was derived from changes in mouse coordinate position in this one dimension. In principle this could result in imprecision in the calculation in the case where participants were moving only in one direction with no movement at all in the other coordinate space (i.e. moving perfectly horizontal with no vertical deflection or vice versa). How often this occurred in practice was evaluated by averaging SCTs identified within boundaries and those identified in one dimension for each participant and comparing them. A paired samples t-test showed no significant difference between the two ($t(7) = 1.972$, $p=0.089$). A Bayesian t-test confirmed that these two distributions are not meaningfully different ($BF_{10}=1.242$). This finding was recapitulated for each of the 8 participants individually. Because the cursor was out of bounds more frequently for versions 1-3, a reliable comparison between SCTs identified within boundaries and those exceeding boundaries could not be made.

Data Collection

Participants were seated comfortably in a chair approximately 61cm from a computer screen. A tri-axial accelerometer (Adafruit ADXL335 - 5V ready triple-axis accelerometer)

was attached to their right wrist. To verify accuracy of behavioral measures for versions 1-3 (where mouse coordinates were often out of bounds) accelerometry data, SCT, and RT were plotted for each trial from the first 3 versions and visually inspected to confirm that onset and offset of movement as determined in Matlab corresponded to onset and offset of movement as seen in the accelerometry data (**fig. 2b**). Note that here we used accelerometry to verify behavior recorded by mouse coordinates but recording accelerometry is not necessary for the task. All participants used their right hand to control a computer mouse located to the right of the computer screen. Verbal and written instructions were given prior to the start of the task.

Data Analysis

Assumptions of normality were assessed using the Shapiro-Wilk Test for all variables used in analysis. Parametric tests, such as the Student's t-test and Pearson's correlation, were used when assumptions of normality were met and non-parametric tests, such as a Wilcoxon signed-rank test and Spearman's correlation, were used when assumptions of normality were violated.

Versions 1-3

Reaction Times

Reaction times following the go signal (RT) and stop signal (SCT) were calculated for each participant using mouse location data (**fig. 2a**). RT was defined as the first time point at which the mouse moved at least 1 pixel from its starting location. SCT was defined as the time immediately prior to the point at which change in mouse location did not exceed 1 pixel for at least 200ms. In other words, SCT is the timepoint of full motor arrest (with respect to the stop signal) that is sustained for at least 200ms. We selected a 200 ms threshold to avoid inadvertently considering very brief pauses of movement as the time of full motor arrest

Excluded Data

Behavioral and accelerometry data were collected from a total of 50 participants. Trials in which RT or SCT exceeded 1000ms were excluded from analysis. If more than 30% of trials were lost, participants were excluded from analysis altogether. Two participants from version 1, One participant from version 2, two participants from version 3, and one participant from version 4 were excluded for this reason. Of the 44 participants included in the final analyses, an average 16 trials per subject were excluded across all three versions. For a detailed report of the number of trials per condition per subject see **Table 2.**

V1			**V2**			**V3**			**V4**		
sbj	*P*	*U*	*sbj*	*P*	*U*	*sbj*	*P*	*U*	*sbj*	*P*	*U*
1	205	19	1	168	72	1	115	110	1	161	69
2	201	23	2	124	56	2	114	116	2	154	65
3	205	21	3	160	67	3	118	115	3	142	62
4	211	24	4	163	69	4	108	112	4	167	71
5	213	24	5	159	69	5	118	116	5	160	73
6	212	23	6	164	71	6	116	115	6	128	47
7	190	21	7	149	55	7	102	108	7	158	70
8	215	24	8	163	26	8	115	118	8	145	64
9	215	23	9	162	66	9	110	97			
10	203	18	10	139	61	10	105	111			
11	203	21	11	166	72	11	100	100			
			12	158	59	12	116	116			
			13	161	71						
	206.6	**21.9**		**156.6**	**62.6**		**111.4**	**111.2**		**151.9**	**65.1**

Table 2. Number of trials included in analysis per subject for all 44 subjects. *Sbj* = subject number, *P* = planned stop trials, *U* = unplanned stop trials. Bold numbers indicate the mean number of trials included for each version.

Version 4

Reaction Times

RT and SCT were defined and calculated in the same way as versions 1-3. We also explored the time at which participants began stopping (with respect to stop signal arrival). This measure, henceforth referred to as Stop Initiation Time (SIT) was defined as the last time point that preceded a consistent deceleration culminating in a stop (i.e. the time in which slowing prior to SCT first began; **fig. 5**). We also took the difference between SIT and SCT to derive a measure of how long it took the participant to fully stop (henceforth referred to as Stopping Duration). In other words, this was the time between when participants first started slowing down and when they fully stopped. We then compared this measure between planned and unplanned stop trials. We also derived coefficients of variation (CV; indicated as a subscript; i.e., SCT_{CV}) for these measures.

Speed

Speed measures for version 4 were obtained by tracking the change in mouse position in pixel space and were calculated as the rate of change in pixels per millisecond (px/ms). The paper guide was not 100% effective in constraining movement, so participants still exceeded the limits of the coordinate plane on occasion, but much less often than in the previous three versions (**fig. 4b**). A Bayesian test of equivalence, for task version 4, comparing speed for trials which included out of bounds portions compared to trials which remained entirely in bounds revealed that speed calculations performed on trials with out of bounds data (i.e. missing location data) were not significantly different than speed calculations performed excluding these data

points (BF_{10} = .56) informing our decision to include all trials from version 4 in our speed analyses.

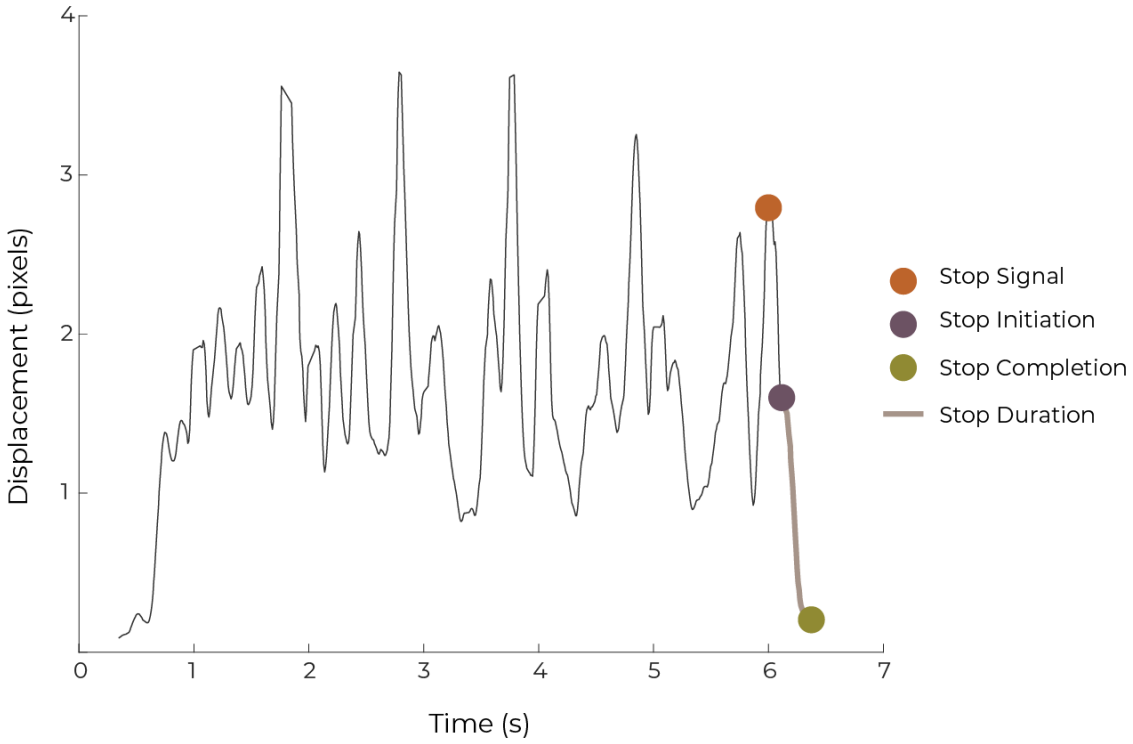

Figure 5. Example of CMST task outcome measures. Go Signal RT is defined as the time between the go signal and movement onset as identified as a change in movement over time >1. Midtrial speed is defined as the average speed in a 500ms time window that ended 1500ms before stop signal presentation. End-of-trial speed was defined as the average speed in the last 500ms before stop signal presentation. Stop initiation time (SIT) was defined as the last time point that preceded a consistent deceleration culminating in a stop. Stop completion time (SCT) was defined as the time of full motor arrest. Stop duration was defined as the difference between SCT and SIT.

Because arrival of the stop signal is predictable on planned stop trials, we expected that participants would slow their movement in anticipation of stop signal arrival, but prior to stop signal presentation. In contrast, for unplanned stopping we predicted stopping would be preceded by a slowing period only after stop signal presentation. To identify if participants moved slower in the time immediately before stop signal presentation compared to earlier in the trial, we first

calculated two speed measures: end-of-trial speed and mid-trial speed. End-of-trial speed was defined as the average speed in the last 500ms before stop signal presentation. Mid-trial speed was defined as the average speed in a 500ms time window that ended 1500ms before stop signal presentation (**fig. 6**). We then took the difference between the means of these two measures (mean mid-trial – mean end-of-trial) and compared this slowing measure between trial types. To explore the possibility that slowing influenced stopping behavior, we correlated our slowing measure (mid-trial – end-of-trial) with both SIT and SCT. We also compared average mid-trial speed and average end-of-trial speed individually between trial types. Lastly, we compared average speed across the entire trial (from RT to stop signal onset) for each trial type and evaluated the relationship between average trial speed and SCT.

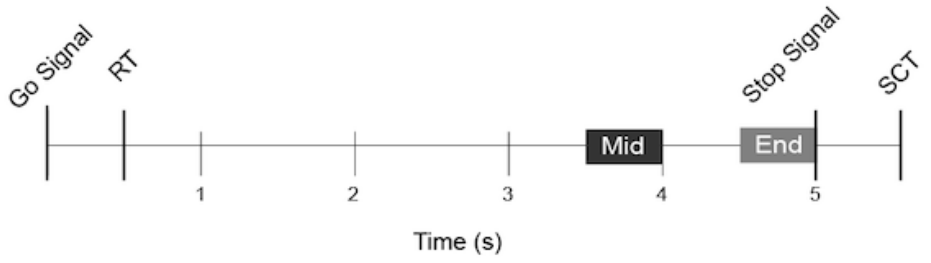

Figure 6. Example definitions of mid-trial and end of trial speed. Dark gray bar indicates mid-trial time window (1500ms-1000ms before stop signal onset), light gray bar indicates end-of-trial window (500ms before stop signal onset).

To explore the potential that subjects were moving slower at the time of stop initiation on planned compared to unplanned stop trials we identified instantaneous speed at SIT (speed at SIT) and compared this value between trial types. Finally, to examine the possibility that participants were able to stop faster when moving slower we correlated speed at SIT with SCT.

Excluded Data

Trials in which RT or SCT exceeded 1000ms or in which we were unable to confidently identify SIT (for example when participants move shortly after stopping) were excluded from analysis. If more than 30% of trials were lost, participants were excluded from analysis altogether. 1 participant was removed from analysis for this reason. Of the remaining 8 participants, an average of 23 trials per subject were excluded from analysis. For a detailed report of the number of trials per condition per subject see **Table 2.** Any variable which exceeded 10 times the standard deviation was removed from analysis. The only instance of an outlier of this magnitude was the SIT_{CV} on planned stop trials for one subject.

Statistics

Versions 1-3

Reaction Times and Stopping Times

For each task version, average RTs and SCTs for planned and unplanned stop trials were compared to one another using a student's paired t-test for significance.

Version 4

Reaction Times and Stopping Times

Means and CVs of RTs, SITs, SCTs, and Stopping Durations for planned and unplanned stop trials were all compared using a student's paired t-test for significance. We also evaluated the relations between the means and CVs of RTs, SITs, SCTs and Stopping Durations separately for each trial type. Because we did not have specific hypotheses regarding individual variable pairs in the correlation analysis (for example RT and Stopping duration), we used a Bonferroni corrected alpha of .0063 to control for multiple comparisons (8 total comparisons made).

Additionally, mean SCTs and RTs for participants from all four versions ($N = 44$) were combined and differences in these measures between trial types were evaluated using the same statistical tests. To identify any potential effect of task version on stopping behavior, a Bayesian ANOVA was performed. These tests were repeated to examine effects of condition and task version on RT.

Speed

We used a student's paired samples t-test was to evaluate differences in SIT speed, mid-trial speed, end-of-trial speed, slowing, and average total trial speed between trial types. We used a Pearson correlation to assess the relation between SCT and (1) speed at SIT and (2) slowing. A Spearman correlation was used to investigate the relation between SCT and average trial speed. We also evaluated the possible relation between slowing and SIT using a Pearson correlation.

Individual Subjects Analyses

Stopping times were also analyzed individually for each of the 8 participants who completed version 4. We used an independent samples Mann Whitney t-test to compare SIT, SCT and stopping duration between trial types.

Results

Reaction Times

SCTs were evaluated collectively (**fig. 7**), combining all four versions of the task, and individually for each of the four different versions of the CMST (**fig. 8**). Results are summarized in **table 3.** Outcomes were similar across all versions. Considered collectively, SCTs were significantly shorter for planned stop trials ($M = 338$ms, $SD = 83$) compared to unplanned stop trials ($M = 476$ms, $SD = 56$), $W = 0$, $p < .001$. RTs between conditions did not differ significantly

($M_{planned}$ = 253ms, SD = 119; $M_{unplanned}$ = 249, SD = 125), $t(44) = 1.25$, $p = .22$. The difference in SCTs for planned compared to unplanned stop trials was also consistent for all task versions when considered individually (as was the lack of a difference for the RT effects, **Table 3, fig. 8**). Additionally, a Bayesian ANOVA revealed that there was no interaction effect between task version and trial type on SCT or RT, $BF_{10\ SCT} = .031$, $BF_{10\ RT} = .004$.

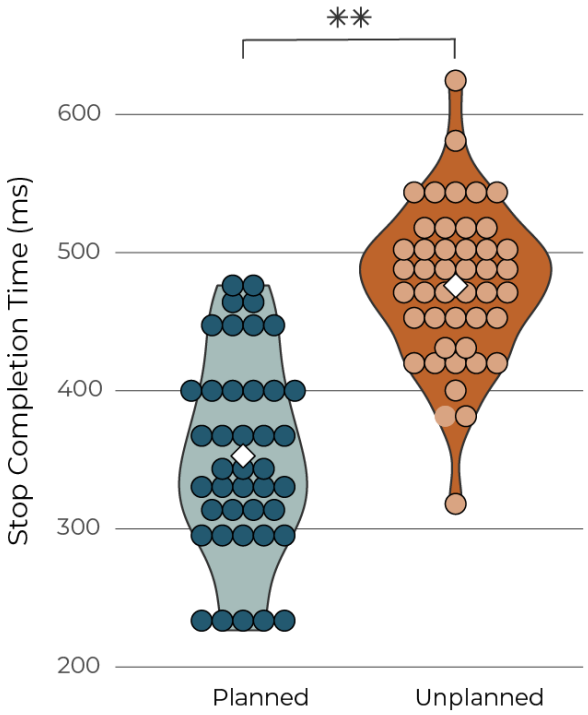

Figure 7. Combined SCTs from all 4 task versions (N=44). Dots represent individual subjects. White diamond indicates group mean. ** indicates p<.001. SCTs for planned stop trials (M = 338ms, SD = 83) were significantly shorter than unplanned stop trials (M = 476ms, SD = 56), W = 0, p < .001

For version 4 (where additional measures could be evaluated), we found that SIT occurred significantly earlier on planned (M = 157ms after stop signal, SD = 65) compared to unplanned stop trials (M = 306ms after stop signal, SD = 38), $t(7) = -7.283$, $p < .001$, $d = -2.575$, CI = [-4.05, -1.07] (**fig. 9**). Average Stopping Duration was not significantly different for planned (M = 174ms, SD = 42) compared to unplanned stop trials (M = 173ms, SD = 23), $t(7) = .056$, $p = .957$. The Stopping Duration$_{CV}$ was also not significantly different between planned (M = .449, SD = .078) and unplanned stop trials (M = .397, SD = .063); $t(7) = 1.837$, $p = .109$. We did however

find a significant difference in the SIT_{CV} ($M_{planned}$ = 1.455, SD = 2.038; $M_{unplanned}$ = .305, SD = .055; W = 36, p = .008, d = 1, CI = [1, 1]) and SCT_{CV} ($M_{planned}$ = .342, SD = .227; $M_{unplanned}$ = .171, SD = .072; $t(7)$ = 2.406, p = .041, d = .885, CI = [.035, 1.693]; **fig. 10**) with planned stopping being more variable in both cases. Additionally, we found that the SIT_{CV} was significantly greater than the SCT_{CV} for both planned (M_{SIT} = .743, SD = .317; M_{SCT} = .384, SD = .201; $t(6)$ = -5.235, p = .002, d = -1.979, CI = [-3.28, -.64]) and unplanned

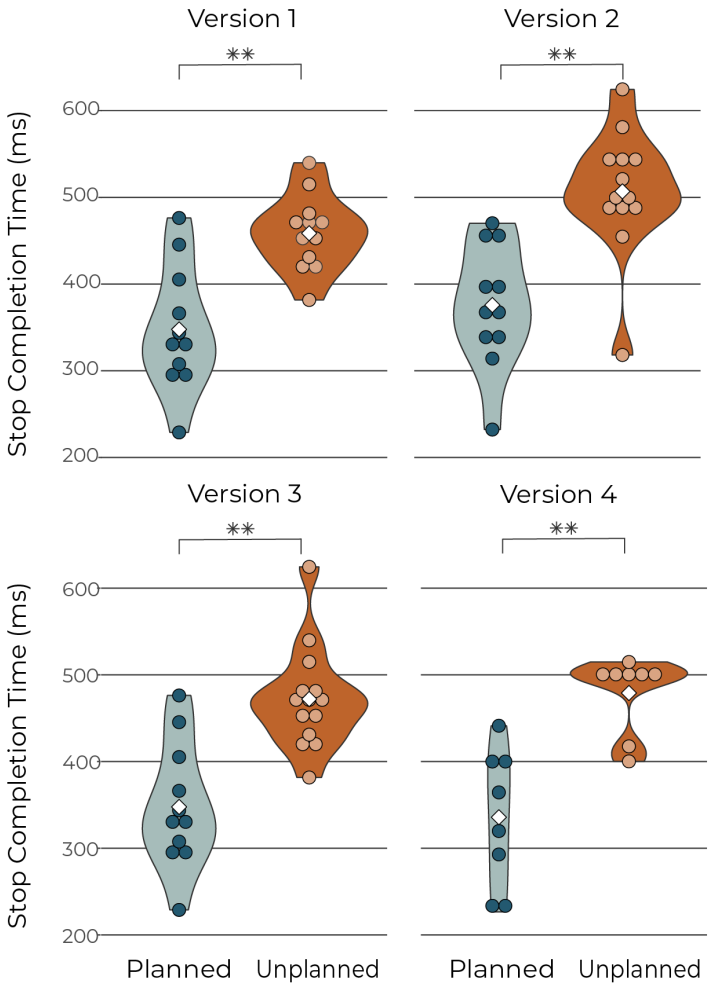

Figure 8. SCTs for each task version. Dots represent individual subjects. White diamond indicates group mean. ** indicates p<.001. **A)** Version 1: 10% unplanned stop (N=11). SCTs were significantly shorter for planned (M = 336ms, SD = 88) than unplanned stop trials (M = 536ms, SD = 9), t(10) = -6.33, p < .001. **B)** Version 2: 30% unplanned stop (N=12). SCTs were significantly shorter for planned (M = 346ms, SD = 97) than for unplanned stop trials (M = 507ms, SD = 73), t(12) = -5.81, p < .001. **C)** Version 3: 50% unplanned stop (N = 12). SCTs for planned stop trials (M = 335ms, SD = 82) were significantly shorter than those for unplanned stop trials (M = 459ms, SD = 43), t(11) = -8.84, p < .001. **D)** Version 4: 30% unplanned with movement constraint (N = 8). SCTs were significantly shorter for planned (M = 336ms, SD = 79) compared to unplanned stop trials (M = 479ms, SD = 44), t(7) = -5.94, p < .001.

stop trials (M_{SIT} = .305, *SD* = .055; M_{SCT} = .193, *SD* = .034; $t(7) = -7.66$, $p < .001$, $d = -2.708$, CI = [-4.24, -1.14]; fig 10).

SCT			
VERSION	**PLANNED STOP**	**UNPLANNED STOP**	**PLANNED V. UNPLANNED**
1 (10% unplanned)	*M* = 336ms, *SD* = 88	*M* = 536ms, *SD* = 93	$t(10) = -6.33$, $p < .001$, $d = -1.91$, CI = [-2.91, -0.88]
2 (30% unplanned)	*M* = 346ms, *SD* = 97	*M* = 507ms, *SD* = 73	$t(12) = -5.81$, $p < .001$, $d = -1.61$ CI = [-2.43, -.76]
3 (50% unplanned)	*M* = 335ms, *SD* = 82	*M* = 459ms, *SD* = 43	$t(11) = -8.84$, $p < .001$, $d = -2.55$, CI = [-3.73, -1.35]
4 (30% unplanned)	*M* = 331ms, *SD* = 80	*M* = 480, *SD* = 46	$t(7) = -5.94$, $p < .001$, $d = -2.1$, CI = [-3.4, -.8]
All versions	*M* = 337ms, *SD* = 84	*M* = 476, *SD* = 56	$W = 0$, $p < .001$, $d = -1$, CI = [-1, -1]
RT			
VERSION	**PLANNED STOP**	**UNPLANNED STOP**	**PLANNED V. UNPLANNED**
1 (10% unplanned)	*M* = 204ms, *SD* = 96	*M* = 197ms, *SD* = 103	$t(10) = .56$, p = .59
2 (30% unplanned)	*M* = 267ms, *SD* = 155	*M* = 266ms, *SD* = 160	$t(12) = .19$, $p = .85$
3 (50% unplanned)	*M* = 235ms, *SD* = 90	*M* = 230ms, *SD* = 97	$t(11) = .84$, $p = .418$
4 (30% unplanned)	*M* = 284ms, *SD* = 140	*M* = 279ms, *SD* = 146	$t(7) = .58$, $p = .58$
All versions	*M* = 253ms, *SD* = 119	*M* = 249ms, *SD* = 125	$t(44) = 1.25$, $p = .22$

Table 3. Behavioral results for task versions 1-4 and for all four versions combined. *M* = mean, *SD* = standard deviation. Effect size and 95% confidence intervals reported for all significant results.

After correcting for multiple comparisons for correlations between measures (Bonferroni corrected $\alpha = .0063$), we found correlations between the following variable pairs for planned stop trials: mean SCT and mean SIT ($r = .91$, $p = .005$), mean SCT and SCT_{CV} ($r = -.93$, $p < .001$), SCT_{CV} and mean SIT ($r = -.93$, $p = .002$), mean SIT and SIT_{CV} ($r = -.95$, $p = .001$), and Stopping $Duration_{CV}$ and mean SIT ($r = -.94$, $p < .001$). For unplanned stop trials we found correlations between the following variable pairs: mean and SCT_{CV} ($r = .86$, $p = .006$) and mean SIT and RT_{CV} ($r = .905$, $p = .005$).

Speed

We found that participants slowed significantly more between the end-of-trial window and the mid-trial window on planned (*M* = .166, *SD* = .106) compared to unplanned stop trials

(M = -.096, SD = .252), $t(7)$ = 2.483, p = .043, d = .878, CI = [.03, 1.68] (**fig. 11a**). Slowing, however, was not correlated with SCT, r = .188, p = .655 or with SIT, r = .1, p = .814. Average end-of-trial speed was significantly slower on planned (M = 3.236, SD = .87) compared to unplanned stop trials (M = 3.5, SD = 1.01), $t(7)$ = -3.065, p = .018, d = -1.08, CI = [-1.95, -.173]. Average mid-trial speed did not differ between planned (M = 3.4, SD = .9) and unplanned trials (M = 3.41, SD = .89), $t(7)$ = -.076, p = .941. Mean speed across the entire trial was also not significantly different between planned (M = 3.5px/ms, SD = .86) and unplanned stop conditions (M = 3.4 px/ms, SD = .91), $t(7)$ = .52, p = .619. We did not find a correlation between trial average speed and SCT, r = .071, p = .882. Additionally, speed at SIT was not significantly different between trial types ($M_{planned}$ = 3.47px/ms, SD = .89; $M_{unplanned}$ = 3.7px/ms, SD = 1), $t(7)$ = -1.46, p = .187, but was correlated with SCT, r = .832, p = .01 wherein faster speed at the time of SIT was associated with slower SCT.

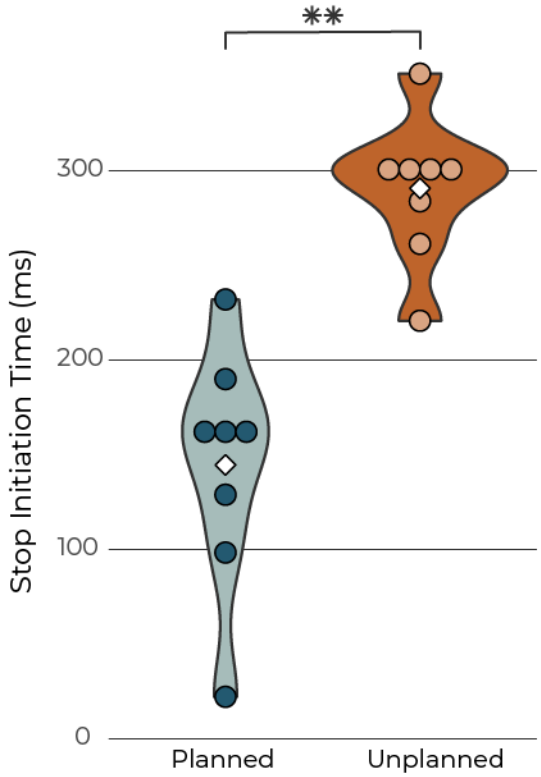

Figure 9. Stop initiation. SIT occurred significantly earlier on planned (M = 195ms, SD = 63) compared to unplanned stop trials (M = 346ms, SD = 33), t(7) = -8.175, p < .001.

Individual Subjects

Individual subject analyses revealed 43 out of 44 subjects showed a significant difference in SCT between planned and unplanned stop trials ($p < .05$).

Analyses of the 8 subjects who completed version 4 revealed that stop completion and stop initiation times differed significantly between planned and unplanned stop trials for all

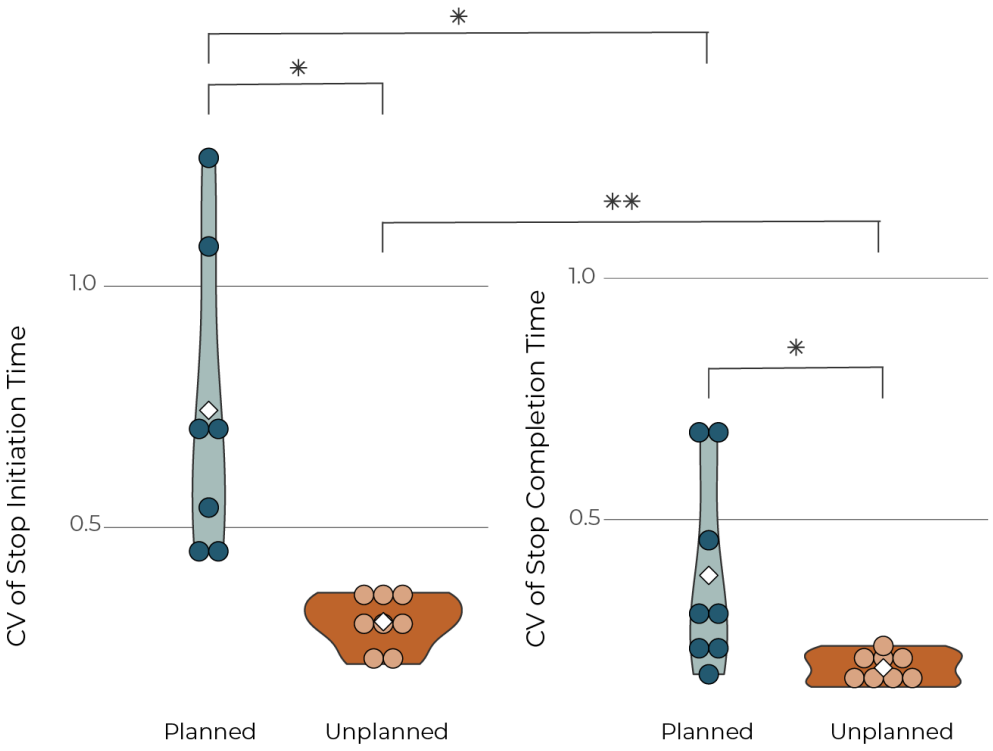

Figure 10. Stopping variability. Dots represent individual subjects. White diamond indicates group mean. * indicates p<.05. ** indicates p<.001. SIT_{CV} was significantly different between planned (M = 1.455, SD = 2.038) and unplanned (M = .305, SD = .055) stop trials, W = 36, p = .008. SCT_{CV} was significantly different between planned (M = .342, SD = .227) and unplanned (M = .171, SD = .072) stop trials, t(7) = 2.406, p = .041. The variability of SIT was significantly greater than the variability of SCT for planned stop trials (M_{SIT} = .743, SD = .317; M_{SCT} = .384, SD = .201; t(6) = -5.235, p = .002) and unplanned stop trials (M_{SIT} = .305, SD = .055; M_{SCT} = .193, SD = .034; t(7) = -7.66, p < .001).

subjects (**fig. 12**). Stopping duration differed significantly for 1 of 8 subjects. Outcomes are summarized in **Table 4**.

EXPERIMENT 2

To better understand the relationship between stopping continuous and discrete movements that are not yet fully initiated, we performed an experiment in which participants completed both the CMST and the SST. We additionally sought to explore the potential behavioral relevance of stop signal expectation by modifying both tasks to include blocks in which the subject knew their movement would never be interrupted by a stop signal (never-interrupt blocks) in addition to those in which subjects were unsure if their movement would be interrupted by a stop signal on each trial (maybe-interrupt blocks) – similar to trials in Experiment 1. We hypothesized that stopping behaviors in each task (SIT and SCT for the CMST and SSRT for the SST) would correlate with one another. Additionally, we expected never-interrupt blocks to influence movement speed during the CMST and never-stop blocks to decrease goRT during the SST. We compared outcome measures between tasks and evaluated behaviors for each task individually.

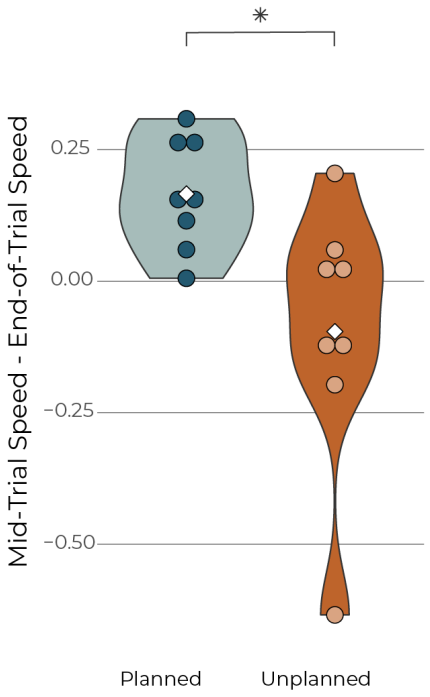

Figure 11. Slowing. Dots represent individual subjects. White diamond indicates group mean. * indicates p<.05. **A)** Participants slowed significantly more in the last 500ms before stop signal onset on planned (M = -2.61, SD = 6.65) than on unplanned stop trials (M = 16.05, SD = 14.85), t(7) = -3.6, p = .009.

Method

Participants

We analyzed data from 15 right-handed university students (10 females, 5 males) between the ages of 18 and 37 (M_{age} = 20.9 SD = 4.74). Participants were recruited through the university's online human subjects pool using SONA-systems and through flyers posted

throughout campus. All participants signed a consent form approved by the university ethics

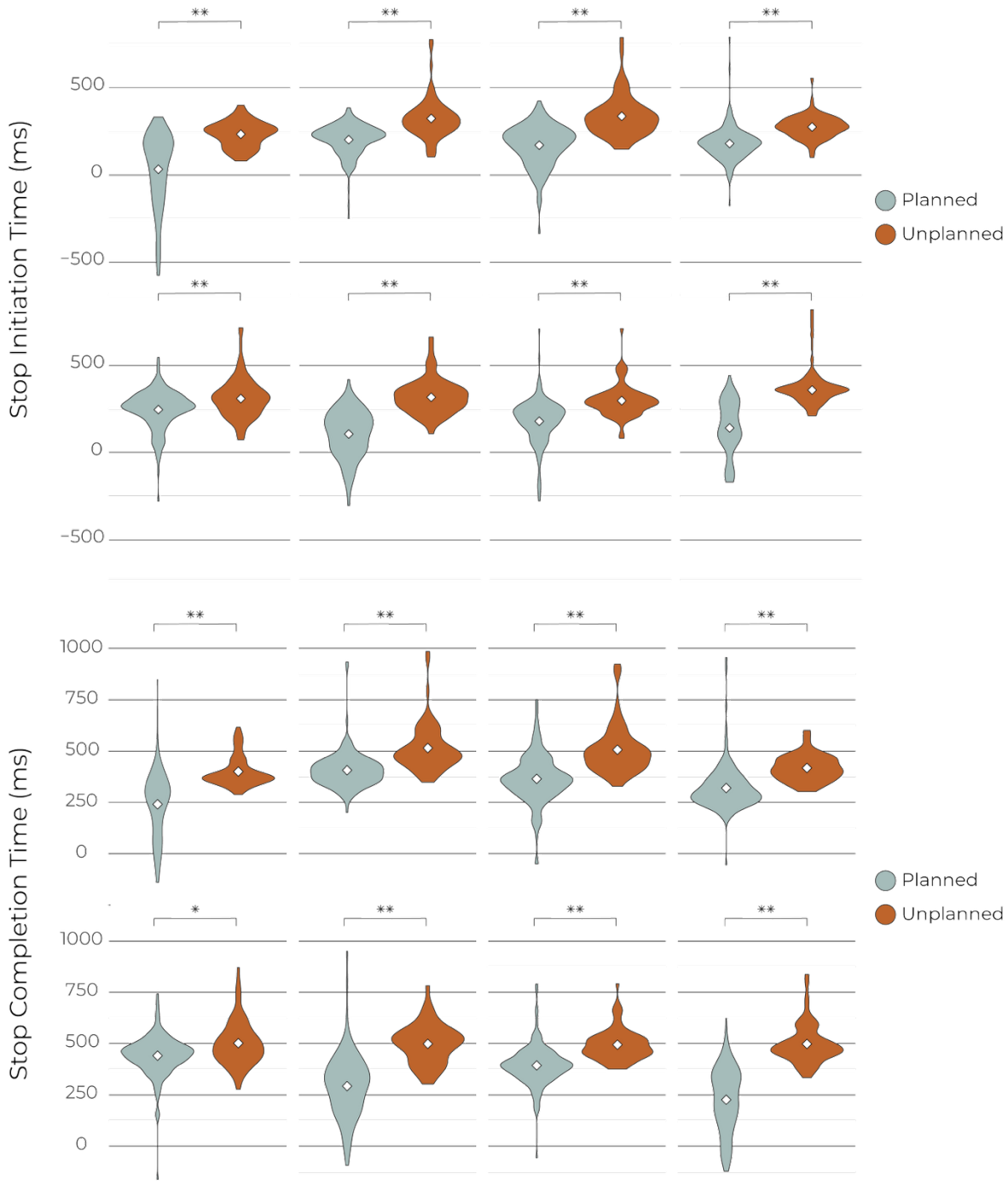

Figure 12. Individual Subjects. * indicates p<.05. ** indicates p<.001. Stop completion and stop initiation times differed significantly between planned and unplanned stop trials at p = .003 for one subject and p<.001 for the others

board.

STOP INITIATION								
	Planned		**Unplanned**		**Independent Samples t-test**			
Sbj #	*Mean*	*SD*	*Mean*	*SD*	*Stat*	*p-value*	*d*	*C.I.*
1	33	211	234	72	2241	<.001	-0.66	-0.74, -0.56
2	202	90	323	118	1879	<.001	-0.66	-0.74, -0.56
3	170	118	336	120	1224	<.001	-0.72	-0.8, -0.63
4	180	97	275	66	1871	<.001	-0.69	-0.77, -0.6
5	146	112	309	110	4322	<.001	-0.29	-0.43, -0.14
6	106	134	317	93	601	<.001	-0.84	-0.88, -0.77
7	179	128	297	90	2113	<.001	-0.63	-0.71, -0.52
8	141	152	357	78	766	<.001	-0.84	-0.88, -0.78
STOP COMPLETION								
	Planned		**Unplanned**		**Independent Samples t-test**			
Sbj #	*Mean*	*SD*	*Mean*	*SD*	*Stat*	*p-value*	*d*	*C.I.*
1	227	156	393	61	1605	<.001	-0.73	-0.8, -0.64
2	398	71	514	117	1828	<.001	-0.67	-0.75, -0.57
3	362	111	509	121	1305	<.001	-0.7	-0.78, -0.57
4	320	110	417	64	1784	<.001	-0.70	-0.77, -0.6
5	443	101	492	109	4634	.003	-0.24	-0.38, -0.14
6	287	131	499	99	649	<.001	-0.82	-0.87, -0.75
7	391	93	508	81	1591	<.001	-0.72	-0.79, -0.63
8	229	155	500	95	422	<.001	-0.91	-0.94, -0.88
STOPPING DURATION								
	Planned		**Unplanned**		**Independent Samples t-test**			
Sbj #	*Mean*	*SD*	*Mean*	*SD*	*Stat*	*p-value*	*d*	*C.I.*
1	194	118	160	65	6605	.121		
2	195	73	190	54	5539	.996		
3	191	86	172	70	4938	.167		
4	132	56	145	69	5345	.154		
5	197	68	183	66	6645	.249		
6	181	82	183	77	3458	.583		
7	212	96	211	75	5455	.701		
8	88	42	143	67	2300	<.001	-0.512	-0.63, -0.38

Table 4. Summary of statistics performed on 8 subjects who completed version 4 of the task.

Tasks

Each participant completed both the CMST and the SST in a 1-hour session. Task order was counterbalanced across participants. Both tasks were programmed using the Matlab Psychophysics toolbox (Brainard, 1997).

CMST

The CMST used for Experiment 2 contained 30% unplanned stop trials and was identical to those used in Experiment 1, version 4 with three exceptions: (1) the CMST for Experiment 2 included 10 blocks of 15 trials rather than 12 blocks of 20 trials, (2) on 2 of the 10 blocks, subjects were informed that they would never see the stop signal before the countdown ended (i.e., no unplanned stop trials), and (3) the longest possible trial duration was reduced from 7 seconds to 6 seconds to reduce time needed to complete the task and enable us to do the SST as well in the same experimental session. We also instructed subjects to make circular motions with the mouse using only their wrist and emphasized the importance of remaining still until the start of the next trial after stopping. Emphasis on moving only with the wrist resulted in participants exceeding the boundaries of the display much less often, 2.48% of the time on average.

SST

The SST was designed in accordance with best practices as identified by Verbruggen et al. (2019). The primary task was a 2-choice reaction time task. Subjects were instructed to respond as quickly as possible to the presentation of an arrow pointing to the left or the right (go signal) by pressing the corresponding arrow key on a keyboard. All trials began with presentation of a white fixation cross in the center of their screen that was displayed for 300, 400, 500, or

600ms. The fixation cross was replaced by an arrow which was displayed until a response was detected, the stop signal was presented, or for a maximum of 500ms. This task included 5 blocks of 50 trials. On 33% of trials (stop trials), presentation of an arrow was followed by presentation of a red X. Order of stop and go trials was randomized using the *randperm* function in Matlab. The interval between presentation of the arrow and the stop signal, the stop signal delay (SSD), was determined using a tracking procedure in which 1 of 3 different staircases starting at 150, 200, and 250ms were increased by 50ms following successful stop trials and decreased by 50ms following failed stop trials. On 1 of the 5 blocks subjects were informed that they would not see a stop signal during that block. The position of this 'never-stop' block was randomly assigned using the Matlab *randperm* function. After each block subjects were shown a graph of their average reaction time from the current block and all preceding blocks. Participants were offered the opportunity to take a break for as long as they wanted following feedback.

Data Analysis

Assumptions of normality were assessed using the Shapiro-Wilk Test for all variables used in analysis. Parametric tests, such as the Student's t-test and Pearson's correlation, were used when assumptions of normality were met and non-parametric tests, such as a Wilcoxon signed-rank test and Spearman's correlation, were used when assumptions of normality were violated.

Excluded Data

We collected data from 24 total subjects. Of these, 4 were excluded due to technical issues that arose during task performance (i.e., computer malfunction and a bug in the task code), 2 were excluded due to violating assumptions of the independent race model for the SST (i.e., probability of responding on a stop trial < 25% and failed stop RT > go trial RT), and 3 were

excluded due to poor performance on the CMST (determined using the same criteria as in Experiment 1). Thus, a total of 15 participants were included in our analyses.

CMST and SST

To thoroughly explore all possible relations between measures of reactive stopping and stopping variability observed in the two tasks, we evaluated the relationship between mean SSRT and (1) mean SCT, (2) mean SIT, and (3) mean stopping duration as well as the relation between $SSRT_{CV}$ and (1) SCT_{CV}, (2) SIT_{CV}, and (3) $Stopping\ Duration_{CV}$. These correlations were performed separately for planned and unplanned stop trials. A Bonferroni corrected alpha of .0083 was used to control for multiple comparisons (6 total comparisons).

We also performed a correlation analysis to evaluate the relationship between measures of preparatory inhibition from the CMST and from the SST. We used slowing as a measure of preparatory inhibition in the CMST. We took the difference between average go signal RT within never-interrupt blocks and average go signal RT within maybe-interrupt blocks as an index of preparatory inhibition in the SST.

Finally, to see if there was a relationship between movement onset on the two tasks, we examined the correlation between mean goRT and mean RT for planned and unplanned stop trials.

CMST only

We performed the same analyses as in Experiment 1. In addition to these analyses, we compared reaction time and speed measures between block types (i.e., never-interrupt blocks and maybe-interrupt blocks).

SST only

SSRT was calculated using the integration method (Verbruggen et al., 2019). We also compared goRT means between maybe-interrupt and never-interrupt blocks.

Statistics

CMST and SST

Pearson's correlations were used to assess the relation between variables that met the assumptions of normality as determined using the Shapiro-Wilk test for Bivariate Normality. These correlations are reported using the following notation: r^{p}. Variables that did not meet this assumption were analyzed using Spearman's correlations. These correlations are reported using the following notation: r^{S}.

CMST only

We used a student's t-test to compare all variables that met the assumptions of normality as determined by the Shapiro-Wilk Test of Normality. A Wilcoxon signed-rank test was used to compare all variables that did not meet the assumptions of normality. Pearson's (r^{p}) or Spearman's (r^{S}) correlations were used for all comparisons depending on whether or not the variable pair met the assumptions of normality as described above.

SST only

We used a student's paired samples t-test to compare goRT means between maybe-stop and never-stop blocks.

Results

CMST And SST

There were no significant correlations found between means or CVs of stopping measures or go signal RT measures for the two tasks (**Table 5).** We did, however, find a (modestly) significant correlation between our measures of proactive slowing on the SST (M = -.014, SD = .014) and planned stop trials (M = .204, SD = .18; r^S = .529, p = .045) but not unplanned stop trials (M = .085, SD = .095; r^P = .242, p = 384).

	CMST (means)	**SST (means)**	**R**	**P**	**CMST (CV)**	**SST (CV)**	**R**	**P**
Planned Stop Trials	SCT	SSRT	r^p = .210	0.452	SCT	SSRT	r^S = -.025	0.934
	SIT	SSRT	r^p = .219	0.433	SIT	SSRT	r^S = -0.150	0.593
	Duration	SSRT	r^p = .061	0.830	Duration	SSRT	r^S = .071	0.802
	RT	goRT	r^S = .179	0.524	RT	goRT	r^p = .209	0.455
Unplanned Stop Trials	SCT	SSRT	r^p = .405	0.135	SCT	SSRT	r^S = -.093	0.743
	SIT	SSRT	r^p = .420	0.119	SIT	SSRT	r^S = -.257	0.354
	Duration	SSRT	r^S = .207	0.460	Duration	SSRT	r^S = -.364	0.182
	RT	goRT	r^p = .112	0.692	RT	goRT	r^p = .298	0.281

Table 5. Correlations between CMST and SST

CMST Only

Reaction Times

Observations from Experiment 1 were recapitulated here. Mean SIT and SCT both differed significantly between planned stop trials (SIT: M = 217ms, SD = 86; SCT: M = 347ms, SD = 97) and unplanned stop trials (SIT: M = 295ms, SD = 47; SCT: M = 435ms, SD = 64), $t_{SIT}(14)$ = -4.92, p < .001, d = -1.27, CI = [-1.95, -.57]; $t_{SCT}(14)$ = -5.87, p < .001, d = -1.52, CI = [-2.26, -.75] (**fig. 13 a & b**). SIT_{CV} and SCT_{CV} were significantly greater for planned (SIT: M =

.78, *SD* = .647; SCT: *M* = .418, *SD* = .205) compared to unplanned stop trials (SIT: *M* = .303, *SD* = .152; SCT: *M* = .195, *SD* = .064), *W* = 117, *p* < .001, *d* = 0.95, CI = [.85, .98]; $t_{SCT}(14) = 4.46$, *p* < .001, *d* = 1.15 CI = [.48, 1.8]; **fig. 13 c & d**). SIT_{CV} was also significantly greater than the SCT_{CV} for both trial types (planned: M_{SIT} = .78, *SD* = .647; M_{SCT} = .418, *SD* = .205; *W* = 0, *p* < .001, *d* = -1, CI = [-1, -1]; unplanned: M_{SIT} = .303, *SD* = .152; M_{SCT} = .195, *SD* = .064; *W* = 0, *p* < .001, *d* = -1, CI = [-1, -

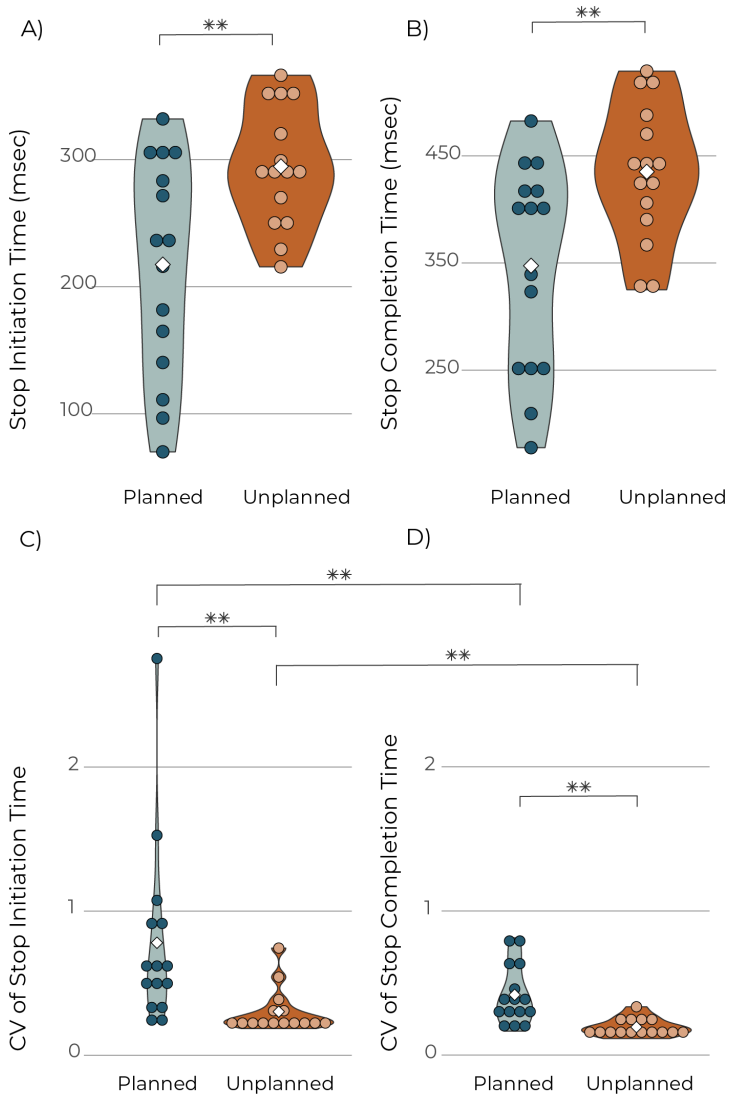

Figure 13. Stop initiation and stop completion times. ** indicates p<.001. **A)** Mean SIT was significantly earlier for planned (M = 217ms, SD = 86) than unplanned stop trials (M = 295ms, SD = 47), t(14) = -4.92, p < .001. **B)** Mean SCT occurred significantly earlier on planned (M = 347ms, SD = 97) compared to unplanned stop trials (M = 435ms, SD = 64), t(14) = -5.87, p < .001. **C)** The SIT_{CV} were significantly greater for planned (M = .78, SD = .647) compared to unplanned stop trials (M = .303, SD = .152), W = 117, p < .001. **D)** SCT_{CV} were significantly greater for planned (M = .418, SD = .205) compared to unplanned stop trials (M = .195, SD = .064), $t_{SCT}(14)$ = 4.46, p < .001. Additionally, the SIT_{CV} was significantly greater than the SCT_{CV} for both trial types (planned: W = 0, p < .001; unplanned: W = 0, p < .001).

1]; **fig. 13 c & d**). Stopping $Duration_{CV}$ was not significantly different between planned (M = .504, SD = .091) and unplanned trials (M = .465, SD = .099), $t(14) = 1.588$, $p = .135$. Mean RT was also not significantly different between trial types ($M_{planned}$ = 307ms, SD =140; $M_{unplanned}$ = 306ms, SD = 115), $W = 54$, $p = .762$.

Unlike the previous experiment, we found that average Stopping Duration did differ significantly between planned (M = 130ms, SD = 26) and unplanned stop trials (M = 141, SD = 30), $t(14) = -3.598$, $p = 0.003$, $d = -.929$, CI = [-1.53, -.31].

Correlations that were significant after correcting for multiple comparisons (Bonferroni corrected $\alpha = .0063$, 8 total comparisons) for planned and unplanned stop trials are reported in **table 6a** and **table 6b** respectively.

(a) Significant Correlations for Planned Stop Trials				**(b) Significant Correlations for Unplanned Stop Trials**			
Variable pairs				*Variable Pairs*			
SCT_M	SCT_{CV}	$r^p = -.776$	$p < .001$	SCT_M	SI_M	$r^p = .898$	$p < .001$
	SI_M	$r^p = .966$	$p < .001$		$Duration_M$	$r^s = .693$	$p = .005$
	SI_{CV}	$r^s = -.800$	$p < .001$	SI_{CV}	SCT_{CV}	$r^s = .900$	$p < .001$
SCT_{CV}	SI_M	$r^p = -.733$	$p = .002$		$Duration_{CV}$	$r^s = .704$	$p = .005$
	SI_{CV}	$r^s = .971$	$p < .001$				
SI_M	SI_{CV}	$r^s = -843$	$p < .001$				

Table 6. Significant correlations for planned and unplanned stop trials. Subscript M indicated mean. Subscript CV indicates coefficient of variation.

Speed

Again results from Experiment 1 were replicated: participants slowed significantly more on planned (M = .204, SD = .18) compared to unplanned stop trials (M = .085, SD = .095), W = 110, $p = .003$, $d = .833$, CI = [.55, .94] (**fig. 14**). Participants also moved significantly slower in the 500ms end-of-trial window on planned (M = 2.64, SD = .92) than on unplanned stop trials (M

= 2.93, *SD* = 1.06), *t*(14) = -2.599, *p* = .021, *d* = -.671, CI = [-1.22, -.099]. We did not find a significant difference in average mid-trial speed between planned (*M* = 2.841, *SD* = .994) and unplanned stop trials (*M* = 3.02, *SD* = 1.12), *t*(14) = -1.498, *p* = .156, *d* = -.387, CI = [-.91, -.15] or average speed across the entire trial ($M_{planned}$ = 2.66px/ms, $SD_{planned}$ = .84; $M_{unplanned}$ = 2.69px/ms, $SD_{unplanned}$ = .94, *t*(14) = -.294, *p* = .773). Average speed was not correlated with SCT (r^P = -.402, *p* = .137) or SIT (r^P = -.28, *p* = .312). SIT speed was also not significantly different between trial types ($M_{planned}$ = 2.75px/ms, *SD* = .869; $M_{unplanned}$ = 2.97px/ms, *SD* = 1.394), *t*(14) = -.83, *p* = .421, and was not correlated with SCT (r^P = .121, *p* = .666) or SIT (r^P = -.002, *p* = .994).

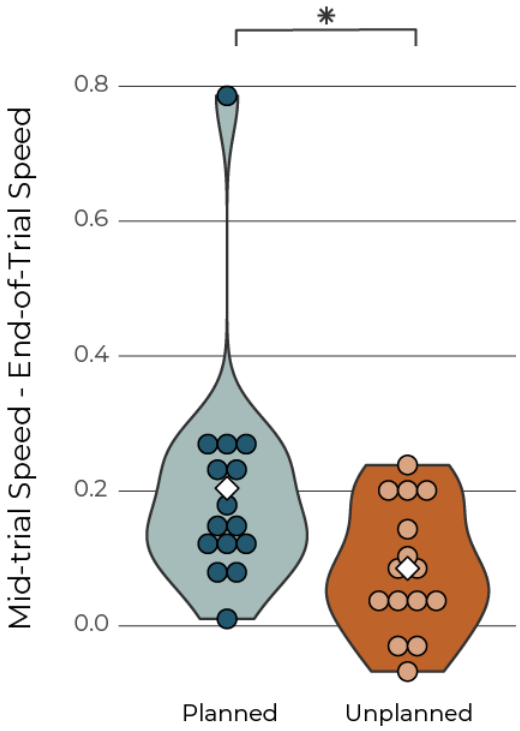

Figure 14. Slowing. * indicates p<.05. Participants slowed significantly more on planned (M = .204, SD = .18) compared to unplanned stop trials (M = .085, SD = .095), W = 110, p = .003.

Maybe vs. Never Blocks

There were no differences in the means of any behavioral measures from planned stop trials between maybe-interrupt and never-interrupt blocks. Outcomes are summarized in **Table 7**.

SST Only

We found that average failed stop RT was shorter than goRT and that participants failed to stop on approximately 50% of stop trials, which confirms that assumptions of the independent race model were upheld. SST performance characteristics are summarized in **Table 8**. GoRT means were significantly different between maybe-interrupt (M = 447ms, SD = 99) and never-interrupt blocks (M = 394, SD = 73), $t(14) = 3.891$, $p = .002$, $d = 1.01$, CI = [.367, 1.619].

Variable	Statistic	Maybe-Interrupt	Never-Interrupt
SCT	$t(14) = .196$, $p = .847$	$M = 348$, $SD = 100$	$M = 345$, $SD = 102$
SIT	$t(14) = .082$, $p = .936$	$M = 218$, $SD = 88$	$M = 217$, $SD = 89$
Stopping Duration	$W = 71$, $p = .561$	$M = 131$, $SD = 25$	$M = 129$, $SD = 33$
Trial average speed	$t(14) = .664$, $p = .518$	$M = 2.69$, $SD = .84$	$M = 2.58$, $SD = 1$
End speed	$t(14) = .463$, $p = .65$	$M = 2.66$, $SD = .92$	$M = 2.58$, $SD = 1.1$
Slowing	$t(14) = 1.071$, $p = .302$	$M = .212$, $SD = .18$	$M = .185$, $SD = .2$
SIT speed	$t(14) = .619$, $p = .546$	$M = 2.79$, $SD = .82$	$M = 2.65$, $SD = 1.3$

Table 7. Summary of t-test outcomes for comparison of Maybe and Never blocks

Variable	Mean & Standard Deviation
SSRT (ms)	$M = 216.98$, $SD = 66$
SSD (ms)	$M = 241.9$, $SD = 92$
Failed stop (%)	$M = 49.39$, $SD = 7.08$
Go RT (ms)	$M = 432$, $SD = 90$
Unsuccessful stop RT (ms)	$M = 384$, $SD = 68$
Failed go (%)	$M = 0.8$, $SD = 1.62$

Table 8. SST behavioral summary

Discussion

In the present study, we tested and evaluated a novel stop signal task that requires termination of an ongoing, continuous, movement under conditions which elicit prepared

(planned) or reactive (unplanned) stopping processes and compared behavioral metrics between the CMST and SST. Our aims were to describe the performance characteristics of the CMST, independently explore prepared and reactive stopping processes, and evaluate how stopping a continuous movement relates to stopping behavior in the SST, where a discrete button press is stopped just before or during initiation. Previous experiments have sought to explore similar questions. For example, Hervault et al. (2019, 2021, 2022) also investigated the relation between stopping a continuous, rhythmic movement and a discrete movement (i.e., SST). Similarly, Morein-Zamir et al. (2003) employed a continuous movement stopping paradigm in which subjects used a computer mouse to track a moving target and aborted their action when presented with a stop signal. Finally, Hannah et al. (2022) designed a comparable stop signal task in which the primary response is the movement of a computer mouse toward a target. However, none of these experimental designs differentiated between instances where the movement termination was planned compared to unplanned. Additionally, stopping tasks designed by Hervault et al. and Hannah et al. included a stop signal delay (i.e., the time between the 'go' and 'stop' signals) of ~100-600 ms, which is more comparable to the SST than the delay between the 'go' and 'stop' signals used in the present design (3000-7000 ms), which ensured that the terminated movement was truly ongoing. Other work from Morein-Zamir and colleagues (2004, 2006, 2008) employed a continuous response paradigm in which subjects performed a tracking task by pressing on a force sensor and releasing pressure when presented with a stop signal. This task design is somewhat similar to the lifting task described by Byblow and colleagues where a button is depressed and then released in response to stimuli (Coxon et al., 2007). In both cases, the action being performed is a static hold which is then released, as opposed to on ongoing,

dynamic movement that is terminated – two behaviors which may be associated with different neurophysiological processes.

Here we presented two experiments. In Experiment 1, we tested and evaluated a novel stop signal task that requires termination of a continuous movement under conditions which elicit prepared (planned) or reactive (unplanned) stopping processes. We found a consistent difference in mean SCT between planned and unplanned stop trials across all versions of the task (**fig. 7**), suggesting that the effect was robust, and that proportion of unplanned stop trials does not have a significant effect on the behavior. This is a beneficial feature of this task in that it allows for flexibility in total task length without compromising integrity or interpretability of the data. For example, a 50% unplanned stop version could be used in a shortened version of the task, reducing the temporal demand on the participants without compromising the ability to behaviorally differentiate planned and unplanned stopping. It is possible that our small sample size obscured subtle differences between the tasks. However, we believe this interpretation is less likely given our Bayes factor of .031, which strongly suggests that all versions of the task are equivalent.

Our finding that participants stopped earlier on planned compared to unplanned stop trials is consistent with existing literature concerning proactive inhibitory control and may be at least partially explained by proactive engagement of inhibitory mechanisms (Aron, 2011 for review). In previous research employing the SST, the degree of proactive inhibition (indexed by an increase in RT) was negatively correlated with SSRT, meaning that the more participants slowed their responses the faster they stopped (Aron et al., 2007; Jahfari et al., 2009). Although proactive inhibitory mechanisms are largely studied in the context of inhibiting a prepared discrete movement, it is possible similar mechanisms are involved in terminating an ongoing

movement. We also observed that participants slowed prior to stop signal arrival significantly more on planned than unplanned stop trials, again supporting the suggestion that participants were preparing for stopping when it arrived at a predicable time.

In addition to SCT (defined by full motor arrest), we were able to capture behavioral changes reflecting initiation of the stop process. 'Stop initiation time' (SIT) was defined as the time point that immediately preceded a consistent deceleration eventuating in full motor arrest (**fig. 5**). SITs observed on unplanned stop trials in the present study were comparable to those observed in other studies that involved similar ongoing movements (Hervault et al., 2019, 2021; Morein-Zamir & Meiran, 2003). We found that participants initiated stopping significantly earlier on planned than unplanned stop trials (**fig. 9**). We suspect that SIT partially reflects attentional aspects of the inhibitory process (signal detection). Our finding that SIT occurs earlier on planned stops may be understood in the context of the temporal orienting hypothesis which suggests that expectation of stimulus occurrence at a particular time facilitates perception of the stimulus and motoric preparation of a response to that stimulus (Miniussi & Nobre, 2001). It also could be a reflection of participants initiating motoric stopping (as opposed to preparing to initiate) in anticipation of the stop signal.

Our data also revealed that the variability of stop initiation and stop completion was greater for planned than unplanned stop trials (**fig. 10**). We take the differences in SCT variability between trial type to suggest that inhibitory processes underlying unplanned motor termination are more stereotyped than those underlying planned motor termination. Our finding that SIT was more variable for planned than unplanned stop trials could possibly reflect aspects of motor planning similar to those observed in previous work showing that reaction time variability during a go/no-go task was greater when go-signal onset was predictable than when it was not

predictable (Wodka et al., 2009). Previous research in non-human primates performing a highly practiced reach task showed that about half of the observed variability in movement could be explained by variability in neural activity immediately preceding a reach (Churchland et al., 2006). In other words, variability observed during movement is largely produced in motor preparation. It is possible that the planning phase on planned stop trials contributed to the increase in variability seen on planned stop trials compared to unplanned stop trials. Additionally SIT was more variable than SCT for both trial types (**fig. 10**), which could suggest that SIT captures processes related to anticipatory preparation, attention, and signal detection in addition to response selection/suppression and that these processes are more variable than the inhibitory processes captured by SCT.

Finally, we recapitulated our primary findings for each of our 8 subjects who completed version 4 of the task. The ability to conduct individual subject statistics demonstrates an advantage of the CMST over typical inhibitory control tasks in that it allows for fine-grained examination of behavior on every trial. The consistency of findings across subjects also highlights the robustness of the observed differences in stopping behavior between trial types.

In Experiment 2 we assessed the relation between reactive inhibition of a discrete movement, which is inhibited before or during initiation, and the prepared and reactive inhibition of a continuous movement by comparing stopping behavior measured by the SST and the CMST. We also explored the potential influence of stop signal expectation on behavior by modifying both tasks such that each contained blocks in which participants knew their movement would never be interrupted. We examined the relationships between prepared inhibition in both tasks by correlating slowing prior to stop signal arrival (a measure of preparatory inhibition on the CMST) and the difference between goRT in never-interrupt blocks and maybe-interrupt blocks (a

measure of preparatory inhibition on the SST). We found a modest, significant correlation between our measure of prepared inhibition from the SST and prepared inhibition from the CMST (observed as slowing prior to stop signal arrival) for planned but not unplanned stop trials. This suggests that mechanisms underlying preparatory inhibition elicited prior to terminating a continuous movement may overlap with those elicited on the SST. This is an area that should be further investigated in future studies.

Contrary to our expectations, we did not find any significant correlations between our measures of reactive inhibition on the SST and the CMST, suggesting that reactive inhibition of discrete movements (at least those recruited in the SST) and inhibition of continuous movements (recruited in the CMST) elicit different inhibitory processes. This finding contradicts previous research by Morein-Zamir et al (2004, 2008) that demonstrated a relationship between stopping times measured with a continuous tracking task and stopping times measured with the SST. The continuous tracking paradigm employed by Morein-Zamir et al. (2004, 2006, 2008) required subjects to track a moving target by maintaining pressure on a force sensor with their finger until the target stopped moving, at which point they were to release the pressure. Despite similar stop initiation and stop completion times between the CMST and the tracking task (Morein-Zamir et al., 2004), there are several differences between the two tasks that may explain the lack of relation between these two stopping measures and SSRT. Most notably, the movement being terminated in the continuous tracking task (continuous press of a button) may bear substantially more similarity to the movement being inhibited in the SST (discrete press of a button) than does the CMST (where an ongoing movement is terminated). Thus, it is possible that the go process terminated in the tracking task was sufficiently different from the go process terminated in the CMST such that it tapped into different inhibitory mechanisms.

This potential is supported by previous work by Hervault et al (2019), which also demonstrated a lack of relation between stop times measured using a similar continuous movement stop task and those measured with the SST. More recent work from Hervault et al. (2022) employed discrete and continuous stop tasks in which the behavior being terminated in both tasks was more similar to the behavior terminated in the CMST. Specifically, subjects either moved a stylus from the center of the screen to either the left or right side of the screen (discrete movement) or they oscillated rhythmically between the two sides of the screen (continuous movement). In both conditions, there was the possibility that an unanticipated stop signal might appear, indicating they should terminate their response. They found evidence supporting the putative discrepancy in substrates contributing to inhibition of discrete and continuous movements using electroencephalography. They also replicated their previous findings (Hervault et al., 2019) of a null relationship between stop times observed in the discrete and continuous task. This raises the possibility that inhibiting an ongoing static movement, such as that used in the continuous tracking task (Morein-Zamir et al., 2004), may be critically different than inhibiting an ongoing, continuous movement, such as that employed in the present study and by Hervault et al (2019, 2022). The lack of a correlation between reactive stopping behavior in the CMST and the SST highlights the importance of future research on unplanned termination of ongoing movements.

Surprisingly, we observed a near absence of slowing (i.e., mid-trial speed – end-of-trial speed) in anticipation of the stop signal on unplanned stop trials as well as no significant slowing on planned stop trials for the blocks where unplanned stopping might occur (“maybe-interrupt" blocks) compared to blocks where participants knew no unplanned stop trials would occur (“never-interrupt” blocks) in Experiment 2. This conflicts with what might be expected based on

typical behavior observed in the SST where participants slow their response time when a stop signal is anticipated. It is possible this is because in the SST, people tend to slow their behavior in response to an error that is typically apparent as soon as it is made. In other words, people are aware of a failure to stop and are thus motivated to alter their strategy. Performance errors on the SST are also binary (i.e., you successfully stopped or you didn't). In contrast, there is a range of acceptable stop completion times on the CMST. Stop completion errors on the CMST are also not obvious as they are being made (i.e., participants don't necessarily know if it took them 900ms, which is an acceptable albeit long stop time, or 1010ms to stop, which exceeds the limit we defined as acceptable. Participants are also only given information regarding their performance at the end of each block. Thus, it is possible that because there was no immediate, apparent feedback about stop completion time there was not the same motivation to adopt a strategy of slowing. It is possible that this is also because, in our data, slowing did not seem to be associated with a shorter SCT at least at the trial-by-trial level. So, perhaps this was not an adaptive strategy here. Overall, we did not find a correlation between slowing and SCT, which suggests that, in this context, anticipatory adjustment of motor programs did not necessarily facilitate faster stopping.

Finally, contrary to our expectations, we found that behavior on the CMST did not differ significantly between maybe-interrupt and never-interrupt blocks, suggesting that the likelihood of a stop signal did not influence task performance. However, for the SST we found that average goRT on never-interrupt blocks was significantly faster than on maybe-interrupt blocks, suggesting that stop signal expectation did have an appreciable influence on behavior in the SST.

Limitations

Although the present study represents an exciting next step in inhibitory control research, there are limitations that should be addressed in future research. One limitation of Experiment 1 is the small sample of participants who completed version 4, the only version in Experiment 1 for which we could confidently evaluate speed of movement. Although data collection was stopped prior to our target sample size of 12 (due to the COVID-19 pandemic), a post-hoc power analysis performed on all significant findings using G*power (Faul et al., 2007, 2009) revealed that our sample of $N = 8$ provided sufficient power, at the recommended power level of 0.8 and $\alpha = .05$, to detect the observed effect sizes for all significant results with two exceptions: (1) our comparison of the SCT_{CV} between planned and unplanned stop trials, which only achieved a power of .728 and (2) our comparison of slowing between trial types, for which we only achieved a power of .722. Furthermore, our sample size did not provide sufficient power to detect an effect size smaller than $d = 0.95$ or a correlation weaker than $r = 0.75$, thus it is possible that potentially informative differences in behavior associated with this portion of the experiment were obscured by our small sample size.

Additionally, because larger movements could not be reliably captured with our set-up, we were unable to evaluate the possibility that magnitude of movement impacts stopping behavior. It is possible that the loss of location data (particularly in experiment 1) affected other calculations such as SCT. These limitations may be effectively addressed with behavioral constraints that are more compelling than a circular paper guide. One method we have found success with is asking participants to use only their wrist when making the circular motions. The impact that recruiting different effectors to carry out the continuous movement (i.e., using the wrist, elbow, or elbow and shoulder) may have on stopping behavior is unclear. However, given

the similarity between stop times observed for all task versions used in the present study and the stop times observed in the continuous tracking paradigm in which only a single digit was recruited (Morein-Zamir et al., 2004; 2006; 2008), we believe this impact is minimal at most. Nevertheless, we cannot rule out the possibility that results may have differed if a different effecter were used.

Furthermore, we cannot determine if the greater variability we observed in stop initiation and stop completion times on planned stop trials was driven by the degree to which stopping was prepared or reflected lapses in attention on some trials. That is, because planned stop trials can include instances in which participants successfully plan to stop and instances in which they do not successfully plan to stop (i.e., stopping that is reactive rather than prepared), greater variability in stopping on planned stop trials may reflect an attentional component or the use of different stopping strategies.

Finally, our design is unable to disentangle the impact of temporal acuity on SCT for planned stop trials. That is, variability in planned stop SCT may be caused by an over- or under-estimation of the 1-second interval duration before the stop signal is presented rather than variability within the inhibitory control system itself.

Interpretations of results from the Experiment 2 are also constrained by some limitations. First, reduction in trial number and addition of never-interrupt and maybe-interrupt block types resulted in relatively few unplanned stop trials (mean number per subject = 32). It is possible that relations between stopping behavior on unplanned stop trials and stopping behavior on the SST were obscured by the limited trial number. Our sample size of 15 provided sufficient power at the recommended power level of 0.8 and $\alpha = .05$, to detect the observed effect sizes for all significant results. However, it did not achieve sufficient power to detect small or moderate

correlations and effect sizes. Additionally, though our results support the hypothesis that reactive inhibition of discrete and continuous movements recruits dissimilar inhibitory control processes, it is possible that other differences between the tasks were driving this outcome. Future research should investigate potential relations between termination of continuous movements with other tasks that elicit inhibition of discrete movements such as the go/no-go task, which has recently been shown to probe stopping behavior that is distinct from that probed by the SST (Raud et al., 2020).

Conclusion

We found a reliable difference in SCT for all task versions with subjects requiring less time to stop (shorter SCTs) for planned compared to unplanned stop trials. We also found that subjects initiated stopping sooner on planned than unplanned stop trials and that stop initiation and stop completion were more variable for planned than for unplanned stop trials. These data support the hypothesis that prepared and reactive motor termination recruit separable inhibitory processes. They also support the efficacy of the CMST for evaluating prepared and reactive termination of continuous ongoing movement. Additionally, we found that SIT was more variable than SCT for both trial types, supporting the hypothesis that these two measures capture different aspects of inhibition. Finally, we found an absence of correlations between CMST and SST performance with respect to reactive inhibition suggesting that each task probes a distinct form of inhibitory control. Our CMST is an important addition to the field of inhibitory control research as it provides an unambiguous behavioral measure of stopping on individual trials, allows for direct comparison of prepared and reactive inhibitory processes, yields a rich set of behavioral measures to examine, and provides an opportunity to evaluate termination of a

continuous movement- a currently understudied aspect of inhibitory control. If used in conjunction with neuroscientific techniques such as EEG or fMRI, this measure could provide a clearer picture of the timing and mechanisms underlying stopping ongoing movements than is currently available.

Bridge

Here, our results suggest that the CMST is effectively behaviorally dissociating planned and unplanned stop trials. We were surprised, however, by the lack of correlation between the CMST and the SST. To better situate the CMST in the context of existing inhibitory control paradigms, we decided to employ this task in a population previously shown to express deficits in performance on inhibitory control tasks – people with a nicotine addiction.

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CHAPTER 3:

PREPARED AND REACTIVE INHIBITION IN SMOKERS AND NON-SMOKERS

Schultz, K. E., Mantell, B., Berkman, E., & Swann, N. (2023). Prepared and Reactive Inhibition in Smokers and Non-Smokers. *Behavioural Brain Research*, *437*.

Introduction

Cigarette smoking is the leading cause of preventable death in the United States (NIDA 2021). Most cigarette smokers are addicted to nicotine and struggle to quit despite their desire to do so. Between 2000 and 2015, 68% of smokers indicated a desire to quit, but only 7.4% were able to do so successfully (Babb et al, 2017). Neurophysiological models of addiction have identified disruption in cortico-striatal circuits underlying inhibitory control, or the ability to inhibit inappropriate or unwanted behaviors, as one factor in the development and maintenance of addictive behaviors (Feil et al., 2010; Koob & Volkow, 2016). In other words, if the neural circuitry that allows for deliberate control or suppression of automatic behaviors (such as picking up a cigarette) is disrupted, the ability to resist the impulse to smoke is diminished and addictive behaviors persist. Neuroimaging and electrophysiological studies in smokers support the role of dysfunction in inhibitory control circuits in nicotine addiction (Bell & Froeliger, 2021; De Ruiter et al., 2012; Froeliger et al., 2017; Kozink et al., 2010; Luijten et al., 2011; Nestor et al., 2011; Spinella, 2002). Previous research also suggests that the relationship between inhibitory control dysfunction and nicotine consumption may be dose-dependent in the sense that individuals who consume a greater amount of nicotine also express greater deficits in measures of inhibitory control (Billieux et al., 2010; Galván et al., 2011).

Inhibitory control is commonly studied using simple motor inhibition tasks, such as the stop signal task (SST; Logan & Cowan, 1984; Verbruggen et al., 2019). In this task subjects develop a pre-potent response, typically to rapidly press a button in response to a "go" cue, but on a minority of trials must withhold the button press when presented with a stop signal ("stop" trials). Efficiency of response inhibition is measured as an estimate of the time required to successfully prevent a response, or the stop signal reaction time (SSRT). A prominent model of inhibitory control implicates right inferior frontal gyrus (rIFG), pre-supplementary motor area (pre-SMA), and motor cortex as essential cortical components of the inhibitory control system (Aron et al., 2007; Swann et al., 2009, 2012). Cortical nodes of the inhibitory control system are linked with basal ganglia by anatomically and functionally distinct pathways. Two of these pathways are the hyperdirect and indirect pathways (Jahfari et al., 2011; Leunissen et al., 2016). The hyperdirect pathway is well-situated for fast and cue-dependent inhibition, here called *reactive inhibition*, and is implicated in sudden termination of motor output that requires cognitive processes (Aron, 2011; Zhang & Iwaki, 2019). For example, if one suddenly notices one is about to step on a Lego, the ability to stop oneself depends on cognitive processes underlying identification of the threat and determination of an appropriate reaction (i.e., stopping)(Aron et al., 2007, 2016; Miocinovic et al., 2018; Nambu et al., 2002; Wagner et al., 2018). Reactive inhibition is postulated to be reflected in increased activity in pre-frontal regions such as the rIFG and pre-SMA (Liebrand et al., 2021). The specific roles rIFG and pre-SMA play in reactive inhibition are still unclear. Planned suppression of motor output without the need for cognitive control processes, such as stopping movement at the end of a dance is thought to recruit the indirect pathway and to be mediated primarily by motor cortex, without significant influence from rIFG and pre-SMA (Adnan Majid et al., 2013; Greenhouse et al., 2012; Jahfari et

al., 2012; Muralidharan et al., 2019). For example, in a study using an adaptation of the SST in which subjects were informed about the probability of a subsequent stop trial—ostensibly allowing them to plan to stop—increased activity was only observed over sensorimotor cortex and not over prefrontal regions (Muralidharan et al., 2019).

Previous research suggests that substance use disorder may be associated with specific deficits in the prefrontal-basal ganglia circuits that mediate reactive inhibition and not necessarily those that mediate planned inhibition. For example, studies using functional magnetic resonance imaging (fMRI) reveal hypoactivation of rIFG during motoric inhibition tasks in individuals with an addiction (Luijten et al., 2011). An fMRI study of nicotine-dependent individuals also demonstrated that activity in right inferior frontal cortex was modulated by nicotine withdrawal during a motor inhibition task (Kozink et al., 2010). Interestingly, this study showed that pre-SMA was unaffected by nicotine. The authors suggest that nicotine preferentially affects attentional control aspects of inhibition which may be mediated by rIFG – a key node of the reactive inhibition network. Additionally, neural stimulation of rIFG improved performance on a motoric inhibition task in nicotine-dependent individuals (Newman-Norlund et al., 2020).

Though the current literature supports disruption of the prefrontal circuits that mediate reactive inhibitory control processes in substance use disorders, the relationship between disorders of addiction, such as nicotine dependence, and planned inhibitory processes is unclear. The goal of the present study is to examine the extent to which reactive and planned inhibitory processes are differentially disrupted in nicotine-dependent individuals. To this aim, we employed a novel stop signal task that explicitly separates planned and reactive inhibitory processes and assessed (1) group differences in task performance between smokers and non-

smokers and (2) the continuous relation between task performance and smoking behaviors within the smoking group. On the basis of the prior clinical literature reviewed above, we predicted deficits in reactive inhibitory control in smokers relative to non-smokers and a dose-dependent relationship such that greater reactive inhibitory control impairment would increase with nicotine exposure among smokers. The neurophysiological literature also supports a specificity hypothesis whereby the effects observed between and within groups on reactive control would not generalize to planned stopping. We also anticipated that individuals who smoked more recently (i.e., within the last 30 mins) would stop faster than those who last smoked longer ago (i.e., 24 hours or more) given the previous literature demonstrating cognitive enhancements following acute consumption of nicotine and deficits following nicotine abstinence (Ashare & Hawk, 2012; Bell & Froeliger, 2021; Charles-Walsh et al., 2014; Dawkins et al., 2007).

Method

This study was approved by the University of Oregon ethics board and took place entirely online. All subjects completed a demographic questionnaire and the Continuous Movement Stop Task (CMST), a simple motor inhibition task in which subjects terminated an ongoing movement under conditions that elicited either planned or reactive motor termination processes (Schultz et al., 2021; **Chapter 2 Fig. 1**). In this task, participants moved a computer mouse (or used a trackpad) in a continuous circular motion while monitoring a countdown displayed on their screen. On the majority of trials (75%), the countdown proceeded to “1” before the stop signal was displayed indicating that the participant should cease their movement (planned stop). In other words, participants could predict the onset of the stop signal and prepare to terminate their movement accordingly. On the remaining trials (25%), and without warning to the participant, the stop signal was displayed before the countdown reached “1” (unplanned stop). Location data

were collected from each participant's mouse (or trackpad), allowing for identification of movement termination. The amount of time between the stop signal and full motor arrest, henceforth referred to as 'stop time', provided a measure of efficiency of the inhibitory control system. Because the arrival of the stop signal on planned stop trials was predictable, these trials assessed planned or prepared inhibitory processes whereas the unplanned stop trials elicited unplanned or reactive processes.

Subjects who identified as smokers also completed the (1) Fägerstrom Test of Nicotine Dependence (FTND) (Heatherton et al., 1991), a standard measure used to evaluate the intensity of physical addiction to nicotine through questions about smoking frequency and urge strength and (2) a brief nicotine product usage survey which identified other forms of nicotine consumption besides combustible cigarettes (e.g., e-cigarette, hookah, etc.).

Participants

Participants were recruited through Amazon's Mechanical Turk (MTurk) and were paid upon completion of the experiment. All subjects provided a digital signature indicating their informed consent. Of the 653 participants that consented 422 identified as smokers, 229 identified as non-smokers, and 2 did not answer the question. Only 281 of the 422 participants who identified as a smoker and 164 of the 229 participants who identified as a non-smoker completed the demographics questionnaire and at least 100 trials of the CMST.

Given the possibility that excessively long response times indicated a lapse in attention, trials in which subjects took more than 1 second to respond to the GO signal or the STOP signal were removed from analysis. After removal of these trials, subjects who had fewer than 30 trials of either trial type were removed from all analyses. 161 smokers and 34 non-smokers were excluded from analysis for this reason. Of the subjects included in the analyses, 11% of trials

were excluded on average in the smoker group (range = 0-44%) and 3% of trials were excluded on average in the non-smoker group (range = 0-46%). To qualify as a smoker, participants needed to identify as a smoker and consume an average of at least 2mg of nicotine (~1 cigarette) per day. 29 self-identified smokers did not meet this criterion and were excluded from analysis. Inclusion in the non-smoker group required that subjects identified as a non-smoker and, if a former smoker, had quit one year or more before completing the experiment. 25 participants who identified as a non-smoker indicated that they quit smoking within the last year and were excluded from analysis.

Participants were asked to indicate their age, the sex they were assigned at birth, their racial identity, if they had a neurological diagnosis, and if they take neurological medications (**Table 9**). We did not specify examples of neurological diagnoses or neurological medications, thus it is possible participants with psychiatric diagnoses or who are taking psychiatric medications answered in the affirmative to these questions. Participants were not excluded on the basis of neurological

Demographic Information		**Smokers**	**Non-smokers**
Age (years)	*Range*	25-65	21-66
	Mean	38.1	37.92
	SD	9.15	10.31
Sex	*Male*	56 (62%)	61 (57%)
	Female	34 (37%)	45 (42%)
	Intersex	0	0
Racial Identity	*White*	74 (81%)	82 (77%)
	Black/ African American	9 (10%)	10 (9%)
	Asian	5 (5%)	12 (11%)
	Native American/ Native Alaskan	3 (3%)	1 (1%)
Neurological	*Diagnosis*	28 (31%)	9 (8%)
	Medication	31 (34%)	10 (9%)

Table 9. Demographic information for both the smoking and non-smoking groups.

disease or medication but this information was included in the statistical models as a covariate. After exclusion, 91 smokers and 106 non-smokers remained for analysis.

Participants in the smoker group consisted of 91 individuals who identified as a smoker and reported consuming a daily average of at least 2mg of nicotine (~1 cigarette/day). 89 subjects reported smoking cigarettes, 54 of the 89 subjects reported smoking e-cigarettes in addition to combustible cigarettes, and 2 reported smoking only e-cigarettes. One of the 56 subjects who reported smoking e-cigarettes did not report level of nicotine content, so we cannot confirm the e-cigarettes this subject used contained nicotine. Information regarding nicotine consumption can be found in **Table 10**.

	Mean	**SD**	**Range**	**Number of Responses**
Cigarettes/Day	9	6.5	2-35	89
Cigarette Nicotine Consumption (Cigarettes/Day * 1.5)	13.48	9.73	3-52.5	90
E-Cig puffs/day	18.86	37.4	1-200	56
E-Cig Nicotine Consumption (Nicotine level * puffs/day)	0.48	1.25	.01-8	54
Total Nicotine Consumption	13.52	9.79	3-52.5	91
Dependence Score	4.54	2.18	0-10	91

Table 10. Nicotine consumption information

Although the chemical composition of e-cigarette liquid is different than that of combustible cigarettes and the dependence-related effects of the two products may differ somewhat (Ponzoni et al., 2015), we consider consumption of either product to merit inclusion in the smoker group because the pharmacokinetics of the two are comparable due to their identical administration route (i.e inhalation) (St. Helen et al., 2015). Additionally, total plasma nicotine

concentration produced by e-cigarettes has been shown to reach similar levels as that produced by combustible cigarettes (Fearon et al., 2018).

Participants in the non-smoker group consisted of 106 individuals who identified as a non-smoker and reported that they had not formerly been a smoker who quit within the last year.

A one-way ANOVA showed that there was not a significant difference in age between the smoking and non-smoking groups; $F(1,195)=.017$, $p=0.896$. A chi-squared test of sex indicated that there was not a significant difference between groups; $X^2(1, N=196) = 0.19$, $p=.66$

Behavioral Measures

Reaction Times

Reaction times following the stop signal (Stop Time) were calculated for each subject using location data from their mouse (or trackpad). Location data were recorded using a Java Script event listener as XY coordinates in pixel space defined by the display parameters of the computer each subject used. Reaction time to the go signal (RT) was defined as the time point at which subjects moved at least one pixel from their starting location. Stop time was defined as the time from the onset of the stop signal to the point at which change in XY coordinates was 0. We hypothesized that on planned stop trials participants will attempt to stop as close to the stop signal as possible – in line with the task instructions. This could result in participants stopping very close to the time of stop signal onset or even just before the stop signal. Thus, we included in our analysis trials where participants stopped moving anywhere from 200ms before to 1 second after the stop signal. Trials where participants stopped (no more than 200ms) prior to the stop signal were given a negative value, trials where participants stopped at the time of the stop signal were recorded as a 0ms stopping time, and trials where participants stopped (no more than

1s) after the stop signal were given a positive stopping time). Variability in response times to the stop signal and the go signal were also evaluated by calculating the coefficient of variability (CV) for each measure.

Heaviness of Smoking

Heaviness of smoking was measured as the estimated average amount of nicotine consumed daily. Participants who used tobacco were asked to report the average number of cigarettes they smoked per day, if they used e-cigarettes and, if so, the range of nicotine levels in the cartridges they use and how many puffs per day they take (**Table 10**). Nicotine levels for cartridges were divided into low (<8mg), medium (8-16mg), and high (>16mg).

According to the National Institute on Drug Abuse (NIDA, 2021), a smoker will consume between 1-2mg of nicotine per cigarette. Previous research on e-cigarettes shows that, on average, smokers will consume approximately 0.2% of the total nicotine content per puff (Goniewicz et al., 2013). To estimate daily nicotine consumption from cigarettes, we multiplied the number of cigarettes smoked per day by 1.5mg (the middle of the range reported by NIDA). Nicotine consumption from e-cigarettes was estimated by finding the median of the range of nicotine levels reported, taking 0.2% of this number and multiplying the product by the number of puffs reported. We determined the range to be 1-8mg for low levels and the range was 16-24 for high levels (Goniewicz et al., 2013). Estimated nicotine from cigarettes and e-cigarettes were then added together (when participants used both) to produce an estimate of daily average nicotine consumption.

Dependence

Nicotine dependence was derived from the FTND (Heatherton et al., 1991). This test consists of 6 questions pertaining to nicotine consumption habits and compulsion to smoke. There are 3 yes/no items scored 0 (no) and 1 (yes) and 3 multiple choice items scored 0-3. These items are then summed to produce a score of 0-10. These scores are then categorized in different classes of nicotine dependence including very low (0-2), low (3-4), moderate (5), high (6-7), and very high (8-10).

Time Since Last Cigarette

We attempted to identify nicotine state (i.e., sated or in withdrawal) by asking participants to report the approximate amount of time that had elapsed between the time they were participating in the experiment and the time the smoked a cigarette. Considering that participants may not be likely to remember the precise time at which they last smoked a cigarette, we asked them to simply report whether their last cigarette was (a) less than 30 minutes ago, (b) about an hour ago, (c) 3 or more hours ago today, or (d) more than 24 hours ago.

Data Analysis

Data were compiled using custom MATLAB (2019a) scripts and all statistical tests were performed using JASP (JASP Team, 2021). Distributions of variables were evaluated for normality using the Shapiro-Wilk test. In cases where the assumption of normality was violated, non-parametric tests were used.

Between Groups

Between-group differences in average stop times for planned and unplanned stop trials, coefficients of variation (CV) for planned and unplanned stop times, average go-signal reaction times (RT) and the CV of RTs were all evaluated using a one-way ANOVA. Neurological diagnosis and/or the use of neurological medication were examined as covariates using ANCOVA. Participants reported if they had a neurological diagnosis and/or if they take neurological medication

Within Groups

A one-way ANOVA was used to assess within-group differences in average planned and unplanned stop times and differences in stop time variability between planned and unplanned stop trials. Pearson's correlations were used to evaluate the relations between variables in all cases except for instances when the assumptions of pair-wise normality were violated as determined by the Shapiro-Wilk test for bivariate normality. Instances in which Spearman's correlations were used are noted in the results section.

Results

Between Groups

Smokers stopped significantly more slowly than non-smokers on planned stop trials ($F(1,195) = 48.17$, $p < 0.001$, $d = .997$; $M_{smokers} = 465.942$ms, $SD_{smokers} = 158$ms; $M_{non\text{-}smokers} = 329.93$ms, $SD_{non\text{-}smokers} = 116.86$ms; **fig. 15a**) and unplanned stop trials ($F(1,195) = 67.27$, $p < 0.001$, $d = 1.178$; $M_{smokers} = 610.86$ms, $SD_{smokers} = 156.24$ms; $M_{non\text{-}smokers} = 467.7$ms, $SD_{non\text{-}smokers} = 107.53$ms ;**fig. 15b**). Surprisingly, we found that the non-smoker group expressed greater variability in stop times on planned stop trials than the smoker group, $F(1,195) = 9.97$, $p = .002$,

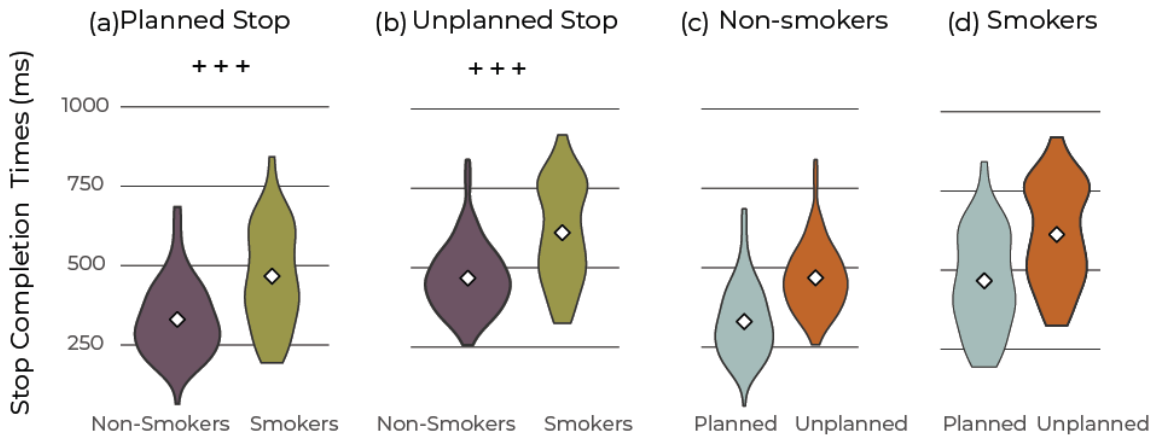

Figure 15. Stop times by trial type and group. White bar indicates group mean. +++ = p<.001 **(a)** Stop times on planned stop trials for non-smokers (M=329.9, SD=107.5) and smokers (M=466.2, SD=157.1). **(b)** Stop times on unplanned stop trials for non-smokers (M=467.7, SD=107.5) and smokers (M=612.4, SD=156). **(c)** Stop times for planned and unplanned stop trials for the non-smoker group only. **(d)** Stop times for planned and unplanned stop trials for the smoker group only.

d = .454; $M_{smokers}$ = .485, $SD_{smokers}$ = .204; $M_{non\text{-}smokers}$ = .591, $SD_{non\text{-}smokers}$ = .263 **(fig. 16a).** There was not a difference between groups in the CV of stop times for unplanned stop trials ($M_{smokers}$ = .277, $SD_{smokers}$ = .131; $M_{non\text{-}smokers}$ = .304, $SD_{non\text{-}smokers}$ = .11), $F(1,195) = 2.38$, $p = .125$ **(fig. 16b).**

We did not find a difference in average RT between smokers (M = 364.76, SD = .24) and non-smokers (M = 328.03, SD = 110.36), $F(1,195) = 3.27$, $p = .072$. We did, however, find that the smoker group expressed significantly greater variability in RT (M = .749, SD = .423) than the non-smoker group (M = .566, SD = .24), $F(1,195) = 14.384$, $p < .001$, $d = .545$.

An ANCOVA showed no interaction effect between neurological diagnosis and group ($F(1,193) = 2.07$, $p = 0.152$) or neurological medications and group ($F(1,193) = 3.842$, $p = .051$) for planned stops or for unplanned stops ($F(1,193) = 1.25$, $p = .265$ and $F(1,193) = 3.86$, $p = .051$).

Figure 16. Variability in stopping. White diamond indicates group mean. ++ = p<.05, +++ = p<.001 **(a)** The CV of stop times on planned stop trials is greater for non-smokers (*M*=.6, *SD*=.3) compared to smokers (*M*=.5, *SD*=.2), *p*=.002. **(b)** The CV of stop times on unplanned stop trials is not significantly different between smokers (*M*=.3, *SD*=.1) and non-smokers (*M*=.3, *SD*=.1) *p* = .125. **(c)** The CV of stop times on planned stop trials is greater than the CV of stop times for unplanned stop trials among non-smokers, *p<.001*. **(d)** The CV of stop times on planned stop trials is greater than the CV of stop times for unplanned stop trials among smokers, *p<.001*.

Within Groups

Non-Smokers

The non-smoker group stopped significantly more slowly on unplanned (*M* = 467.702 *SD* = 107.531) compared to planned (*M* = 329.925, *SD* = 116.862) stop trials, *F*(1,210) = 79.785, *p* < .001, *d* = 1.23 (**fig. 15c**). To control for the possibility of confounding variables such as age, neurological diagnosis, and neurological medication, we estimated a post hoc linear model with stop times as the dependent variable, trial type as a fixed factor, and the afore mentioned variables as covariates. The effect of trial type remained significant in this model (*F*(1,207) = 81.266, *p* < .001, *d* = 1.244). Additionally, we found that there was less variability in stop times

on unplanned stop trials (M = .304, SD = .11) compared to planned stop trials (M = .591, SD = .263), $F(1,210) = 107.86$, $p < .001$, d = 1.433 **(fig. 16c).**

Smokers

Like the non-smoker group, the smoker group took significantly longer to stop on unplanned (M = 610.86, SD = 156.24) compared to planned (M = 465.94, SD = 610.86) stop trials, $F(1,180) = 38.713$, $p < .001$, d = .928 (**fig. 15d**). We found that smokers also demonstrated significantly less variability in stop times for unplanned (M = .277, SD = .131) compared to planned stop trials (M = .485, SD = .131), $F(1,180) = 65.411$, $p < .001$, d = 1.206 (**fig. 16d).** To control for the possible mediating influence of variables such as age, neurological diagnosis and neurological medications, and dependence as well as nicotine use measures including cigarettes per day and estimated daily nicotine consumption, we estimated a post hoc linear model with stop time as the dependent variable, trial type as a fixed factor, and all of the above mentioned variables as covariates. The effect of trial type remained significant in this model ($F(1,170) = 47.25$, $p < .001$, d = 1.025).

Number of cigarettes smoked per day was inversely and significantly related to stop times for both planned (r = -0.219, p = .039) and unplanned (r = -.237, p = .025) stop trials. Among smokers, more cigarettes per day related to faster stopping on both trial types. To rule out the possibility of age as a confounding factor, we conducted a post-hoc analysis evaluating the relation between age and number of cigarettes smoked per day. A spearman correlation revealed that age is not significantly related to number of cigarettes smoked per day (r = .19, p = .076).

Estimated daily average nicotine consumption (in milligrams) was also inversely and significantly related to stop times for both planned (r = -.212, p = .044) and unplanned (r = -.236,

p = .024) stop trials. That is, greater daily average nicotine intake related to faster stopping on both trial types. To rule out the possibility of age as a confounding factor, we conducted a post-hoc analysis evaluating the relation between daily average nicotine consumption and age. A spearman correlation indicated that age is not related to average nicotine consumption (r = .173, p = .102).

Dependence was significantly and positively related to stop times for planned stop trials (r = .221, p = .035) but was unrelated to stop times on unplanned stop trials (r = .14, p = .187; **fig. 17**).

Recency of last cigarette was not significantly related to stop times for planned (r = -.036, p = .735) or unplanned (r = -.042, p = .692) stop trials.

Mean RT and the CV of planned stop times, unplanned stop times, and RT did not significantly relate to any measures of nicotine consumption or dependence.

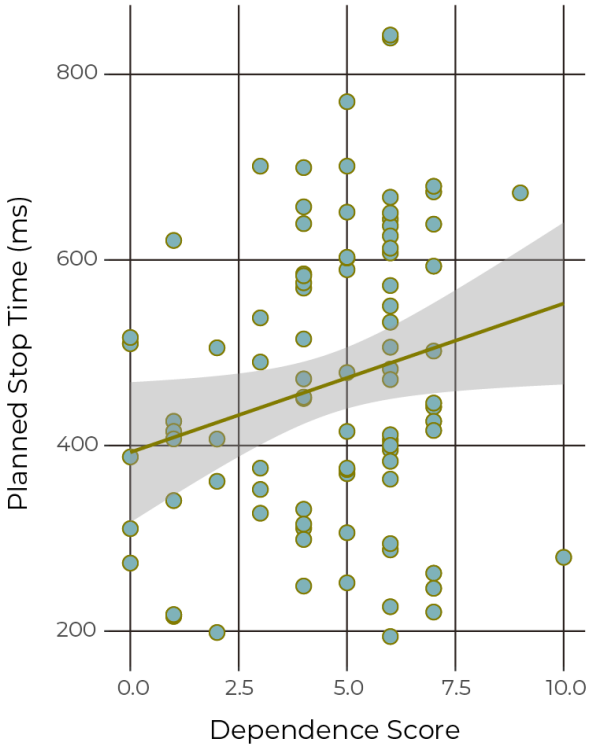

Figure 17. Correlation between nicotine dependence and SCT on planned stop trials. Dependence score was significantly and positively related to stop times for planned stop trials (r =0.217, p=0.038). Green line indicates line of best fit. Gray shadow is the 95% confidence interval.

Discussion

In this study we used the CMST to investigate group differences between smokers and

non-smokers in prepared (i.e. planned) and reactive (i.e. unplanned) movement termination. We found that smokers stopped significantly more slowly than non-smokers when movement cessation was planned and when it was unplanned (**fig. 15**). We also found that stop times were significantly more variable for planned than for unplanned stop trials for both groups and that stop times for planned stop trials were significantly more variable in the non-smoker group compared to the smoker group (**fig. 16**). There was not a difference in average RT between groups. However, variability in RT was significantly greater for smokers than for non-smokers. The measure of dependence derived from the FTND was significantly related to stop times on planned but not those on unplanned stop trials. Further investigation of the relationship between nicotine consumption and both types of inhibitory processes revealed that estimated daily nicotine consumption and average number of cigarettes smoked per day were significantly negatively related to stop times for both planned and unplanned stop trials. Recency of the last cigarette smoked was not related to either planned or unplanned stop times. We did not identify any relations between average RT or the CVs of planned stop times, unplanned stop times, and RT and any measure of nicotine consumption.

Between Group Differences

Reaction Times

Our finding that smokers stopped significantly more slowly than non-smokers supports a model of nicotine addiction characterized by inhibitory control deficits in smoking. Furthermore, it extends this model to include disruptions in both reactive and prepared inhibitory processes. Our observation of group differences is in line with findings in some previous studies (Flaudias et al., 2016; Luijten et al., 2011; Nestor et al., 2011; Spinella, 2002), but not others (Smith et al., 2014 for review). It is possible that the CMST offers a more sensitive measure of inhibitory

control processes than other inhibition tasks, such as the stop signal task, that provide only a single estimate of inhibitory efficiency for each subject. Additionally, the CMST may elicit inhibitory processes critically involved with nicotine addiction that cannot be measured with other standard tasks.

We observed a discrepancy in the exclusion rate of trials and of subjects between groups. 11% of trials in the smoker group and 3% of trials in the non-smoker group were excluded as a result of excessively long reaction times. Additionally, 57% of all respondents who identified as a smoker and 21% of non-smokers were removed from analysis due to an insufficient number of acceptable trials following removal of trials with excessively long reaction times. We suspect this is in part a reflection of the tendency for smokers to take longer to stop than non-smokers. That is, because stop times for smokers are longer overall, they are more likely to reach and exceed our stop time cutoff of 1000ms. This finding may also be a reflection of lapses in attention that are hypothesized to be more common among chronic smokers than non-smokers (Poorthuis & Mansvelder, 2013).

Variability

Stop times for planned stop trials were significantly more variable than stop times for unplanned stop trials for both smokers and non-smokers. We take this to suggest that the processes underlying reactive stopping are more stereotyped than those underlying prepared stopping. Additionally, we found that stop time variability for planned stop trials was significantly greater for non-smokers than for smokers. This may reflect attentional lapses in the smoker group that resulted in reactive stopping on some planned stop trials. If individuals in the smoker group lost focus toward the end of the countdown to the stop signal, they may react to the stop signal on planned stop trials in a similar way they would on unplanned stop trials – with

reduced variability. Though acute nicotine administration can improve attention, chronic exposure to nicotine can impair attention by disrupting cholinergic signaling in pre-frontal cortex through desensitization of nicotinic acetylcholine receptors (Poorthuis & Mansvelder, 2013 for review). Fluctuations in attention within the smoker group may also explain the observed increase in RT variability with respect to the non-smoker group.

Smokers

Dependence

The observed correlation between dependence and inhibitory control is in line with previous research showing a relationship between dependence (as measured by the FTND) and reductions in performance on various measures of inhibitory control (Billieux et al., 2010; Flaudias et al., 2016; Wilson & MacLean, 2013). Interestingly, the present study reveals this relationship is specific to prepared inhibitory control processes as opposed to reactive inhibitory processes.

It is important to note that this finding does not necessarily contradict studies such as that conducted by Billieux and colleagues (2010), which showed a correlation between dependence and performance on a Go/No Go task – a task that requires unanticipated inhibition of a prepotent response. As a result of the requirement that participants intend to move on every trial (which precludes the option to provide foreknowledge of an impending stop signal) reactive inhibition cannot be cleanly separated from prepared inhibition on that task. That is, knowing with certainty that a stop signal is about to appear on the Go/No-Go task would permit participants simply to plan to not respond, as opposed to reactively withhold a response. Previous research has shown that proactive inhibitory mechanisms, or “breaking” mechanisms that are

employed prior to movement onset, facilitate reactive mechanisms in inhibitory control tasks such as the Go/No Go or the Stop Signal Task (Chikazoe et al., 2009; Criaud et al., 2012; Zandbelt et al., 2013). Proactive inhibitory control is commonly observed as a slowing of go-signal reaction time. For example, when provided with information about the probability of a stop signal during a standard stop signal task, participants proactively engage inhibitory mechanisms to facilitate movement suppression. On trials in which participants are erroneously expecting a stop signal, preparatory engagement of inhibitory control manifests as a delayed response to the go signal. Although proactive inhibition as measured using the stop signal task may differ from preparatory mechanisms recruited in the present experiment, it is possible that the slowing in reactive inhibitory processes observed by Billieux and colleagues (2010) are influenced by deficits in preparatory response inhibition.

A key advantage of the CMST used in the present study is that the planned stop condition removes reactive processes from stopping, allowing for differentiation between the two. Because participants are aware that at some point in every trial they will be instructed to stop, we do not assert that the unplanned stop condition in the CMST recruits exclusively reactive inhibitory processes and that there is no involvement of prepared inhibitory mechanisms. In other words, preparatory inhibitory mechanisms may always be engaged to some extent in anticipation of the stop signal. However, it is unlikely that the planned stop condition elicits reactive processes to the same degree as the unplanned stop condition. Thus, the contrast between the unplanned and planned conditions allows us to quantitatively separate the processes.

It is important to note that the observed correlation was relatively weak and may not reflect a useful relation between dependence measures and inhibitory control. Additionally, it is possible that our measure of dependence was not sufficiently sensitive to provide an accurate

picture of the relation between nicotine dependence and inhibitory control. Further research into the relation between prepared inhibitory control deficits and nicotine abuse is needed.

Heaviness of Smoking

Surprisingly, we found an inverse relationship between nicotine consumption and stop times for both planned and unplanned stop trials. Despite the overall reduction in performance of smokers compared to non-smokers, smokers who consumed more nicotine daily expressed greater inhibitory capacity relative to those who consumed less. This is in contrast to work showing that diminished inhibitory capacity was associated with quantity of cigarettes consumed daily (Billieux et al., 2010). Previous work has shown a decline in inhibitory control capacity following bouts of nicotine abstinence (Charles-Walsh et al., 2014). It is possible that smokers who smoke more often are more consistently sated and less likely to express abstinence-related deficits than smokers who smoke less often. However, future inquiry into this possibility is needed. Additionally, the correlational values obtained were small and may not reflect a relation that is meaningful.

It is important to note that this finding is not necessarily inconsistent with the observed relation between dependence and inhibitory control. Though dependence and smoking frequency are often correlated, they measure different aspects of nicotine use. Dependence reflects the psychological aspects of nicotine use to a greater degree than smoking behavior per se (Bainter et al., 2020). For instance, separate genes have been identified for nicotine dependence, on the one hand, and smoking behavior, on the other (Loukola et al., 2008).

Time Since Last Cigarette

Given the previous work demonstrating the short-term cognitive enhancement following acute nicotine use and the deficits following nicotine abstinence (Ashare & Hawk, 2012; Bell & Froeliger, 2021; Charles-Walsh et al., 2014; Dawkins et al., 2007), we anticipated that individuals who smoked more recently (i.e., within the last 30 mins) and were presumably in a more sated nicotine state would stop faster than those who last smoked longer ago (i.e., 24 hours or more) and were possibly closer to a withdrawal state. Thus, our finding that recency of the last cigarette smoked was not correlated with stop times from either trial type was unexpected. Although the cognitive benefits of nicotine consumption are well-documented, inhibitory control deficits in abstinent smokers are not always observed (Bekker et al., 2005; Flaudias et al., 2016; Lesage et al., 2020; Xue et al., 2020). Additionally, it is possible that this lack of observed relation was a product of how the data were collected rather than a true representation of reality. Time since last cigarette was reported as a categorical variable (i.e. less than 30 minutes ago, about an hour ago, etc) rather than as a continuous variable. The categorical nature of this variable may have reduced sensitivity enough to obscure an existing relation.

Limitations

Though the present study represents an exciting contribution to the nicotine addiction literature, there are limitations that should be addressed in future research. First, our sample consisted predominantly of light to moderately dependent smokers with only 2 subjects falling into the very highly dependent category. As previous work has shown differences in inhibitory control capacity between moderately and heavily dependent smokers (Flaudias et al., 2016), future research including a more representative sample would provide an important addition to this line of inquiry.

Additionally, subjects were not asked to report the duration of their nicotine use (i.e., how long since they started smoking) or any previous attempts at quitting. Specifics regarding preferred cigarette brand were also not collected, which would have provided a more accurate assessment of the total quantity of nicotine consumed daily. Furthermore, nicotine content in e-cigarette cartridges is extremely variable and not always accurately identified on product labels (Goniewicz et al., 2013; Pagano et al., 2016; Taylor et al., 2021). Variability in puff topography (puff duration, velocity, inter-puff interval, number of puffs) and device features such as heating element design and voltage also affect total nicotine yield per bout of smoking (Talih et al., 2015). These variables obscure actual nicotine consumption when estimated based on number of puffs and nicotine concentration alone, thus our estimate of daily nicotine consumption is an approximation of actual consumption. Our measure of nicotine state is also imprecise. To estimate nicotine state we asked subjects to report approximately when they last consumed a cigarette. Subjects provided a ballpark estimate that was collected as a categorical variable and thus may not be sensitive enough to accurately reflect possible relationships with our behavioral measures. Additionally, subjects may smoke during the task, after they have answered the cigarette recency question, in which case their answer would be irrelevant. In future research, a precise quantification of nicotine consumption could be provided by evaluating plasma nicotine levels following a smoking session.

Lastly, we did not collect information regarding alcohol use, a potentially confounding factor known to commonly co-occur with nicotine use and to influence response inhibition. Future research should include investigation of the possibility that alcohol use mediates the relationship between nicotine use and stopping behavior.

Conclusion

The present study revealed group differences between smokers and non-smokers on a novel measure of prepared and reactive inhibitory control. Additionally, we found task performance to be weakly related to dependence and heaviness of smoking. This study provides an exciting contribution to the existing literature, but future research addressing the present limitations is needed to provide important insight into mechanisms of nicotine addiction and potential treatment options.

Bridge

The experiment presented in this chapter yielded important insight into the relation between the CMST and standard motor inhibition paradigms that was not captured in Chapter 2. That is, our observation that people with a nicotine addiction exhibited diminished performance on the CMST - as has been previously observed using other motor inhibition tasks - supports the possibility that inhibitory control mechanisms elicited by the CMST overlap with those elicited by the standard paradigms. The outcome of this experiment contributes to our understanding of the generalizability of the standard paradigms and allows us to speculate that oscillatory activity observed during performance of the CMST may overlap with that previously observed with the SST and go/no-go tasks.

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CHAPTER 4:

INVESTIGATING THE EFFECT OF L-DOPA ON THE COGNITIVE AND MOTORIC ASPECTS OF MOTOR TERMINATION

Introduction

Inhibitory control, or the ability to inhibit thoughts and actions in accordance with internal and environmental demands, is an essential component to living a safe, well-adjusted life. For example, if you are planning to cross a street when you notice a car coming, the ability to halt your stride is critical to avoiding injury. Similarly, the ability to withhold inappropriate expressions of anger can be vital to maintaining interpersonal connections. In fact, mechanisms underlying motoric inhibition (such as inhibiting your stride into a busy street or inhibiting rageful vocalizations) are thought to underlie many forms of cognitive and behavioral control such as emotion regulation (Lewis et al., 2006), attentional control (Zavala et al., 2017), and impulse control (Schachar & Logan, 1990).

Mechanisms of inhibitory control are understood to be rooted in the cortical-basal ganglia circuitry, which is disrupted in Parkinson's Disease (PD). PD directly attacks the dopaminergic neurons of the basal ganglia, resulting in difficulty initiating a movement – a hallmark pathophysiological characteristic of PD– as well as difficulty inhibiting a movement (Obeso et al., 2011). Indeed, studies employing the stop signal task (SST; Logan & Cowan, 1984) – a standard motor inhibition paradigm in which participants must try to inhibit a prepotent response when cued to do so – have shown that PD patients are impaired in their ability to withhold an incipient action compared to healthy controls (Gauggel et al., 2004; Obeso et al., 2011).

PD-related disruptions in this circuitry are manifested electrophysiologically as excessive synchrony in the beta frequency band (13-30 Hz; Hammond et al., 2007). Beta activity is considered to be a domain general indicator of inhibitory control processes (Wessel & Anderson, 2024) and, in the context of PD, is closely associated with rigidity and akinesia (Hammond et al., 2007). Importantly, beta activity over different cortical regions appears to be involved in different aspects of the inhibitory control process. Specifically, evidence suggests that sensorimotor beta is causally related to the motoric component of stopping (Pogosyan et al., 2009) while prefrontal beta appears to be related to the cognitive aspects of stopping (Muralidharan et al., 2019; Schmidt et al., 2019; Wagner et al., 2018). In other words, sensorimotor beta may directly facilitate the actual termination of a movement while prefrontal beta may subserve detection of the need to stop and/or evaluation of the consequences of stopping.

How the cognitive and motoric components of stopping may be differentially affected by PD is as yet unknown. Much of our understanding of inhibitory control deficits in PD has been gleaned using the SST. As previously mentioned, this task requires participants to withhold a prepotent response when presented with a cue. Though the SST has been an effective tool for illuminating many mechanisms of motor control, its design does not allow for the disambiguation of the cognitive and motoric components of inhibitory control. That is, because participants are inhibiting a response they are preparing to make (in contrast to an ongoing response) it is not possible to precisely align the behavioral time of stopping with the associated electrophysiological recording. This creates ambiguity surrounding mechanisms involved in identifying the need to stop (cognitive component) and those involved in motor termination (motoric component). As cognitive deficits are common in PD (Aarsland et al., 2021), it is

important to understand the extent to which these deficits are related to perturbations in the inhibitory control circuitry that contribute to the motoric deficits observed in PD.

Previous work has related chronic administration of l-dopa, the dopaminergic medication commonly used by PD patients, to impulse control disorders often observed in people with PD (Antonelli et al., 2011 for review). Though the relationship has been inconsistently observed (Sharma, Markon, & Clark, 2014), it is suspected that impulse control disorders may be, at least in part, related to mechanisms underlying response inhibition (Bari & Robbins, 2013). Some researchers have suggested that impulse control may relate specifically to higher-order cognitive mechanisms that might not be reliably captured by the SST (Skippen et al., 2019). This possibility further highlights the imperative to parse the cognitive and motoric mechanisms underlying response inhibition.

Furthermore, it is unclear whether l-dopa separably influences beta dynamics in sensorimotor and prefrontal cortices associated with the cognitive and motoric components of stopping. Previous work suggests that administration of l-dopa modulates beta power over sensorimotor (Chung et al., 2018), motor (Cao et al., 2020), and prefrontal cortices (George et al., 2013). However, to what extent this modulation is specific to motor functions or might reflect cognitive functions as well has not yet been resolved.

Here, we aimed to investigate the effect of l-dopa on the cognitive and motoric aspects of motor termination and how these effects may be reflected in sensorimotor and prefrontal beta dynamics. To do this, we employed the continuous movement stop task (CMST; Schultz, Denning, et al., 2023) – a novel stop signal paradigm that allows for clear separation of the cognitive and motoric components of stopping. In this task, participants are instructed to move in a continuous, circular fashion while monitoring a countdown. On some trials, the countdown

reaches the end before the stop signal is presented. These trials allow the participant to anticipate precisely when they will be instructed to stop moving. On the remaining trials, the stop signal is presented pseudorandomly during the countdown. In this condition, participants are unable to anticipate when they will be instructed to stop moving. This design is beneficial in that it allows for the comparison of the same behavior (stopping) in conditions that elicit either planned or unplanned stops, which balances motor elements of the task so that cognitive aspects can be more precisely examined. Additionally, because stopping is directly observable on every trial, it allows for precise temporal alignment between the behavior and the electrophysiology.

Based on previous work, we predicted that stop signal presentation would elicit greater prefrontal beta on unplanned stop trials compared to planned stop trials. We also expected that the observed prefrontal and sensorimotor beta dynamics would be modulated by l-dopa. Furthermore, given the relationship between impulsivity and dopaminergic medication, we anticipated that stopping behavior may worsen when patients are on medication compared to off. Finally, considering the body of evidence suggesting that theta frequency activity (4-7 Hz) is both an important component of inhibitory control (Cavanagh & Frank, 2014; Parker et al., 2015) and may be a pathophysiological feature of PD (Parker et al., 2015; Singh et al., 2018), we also explored the possibility that l-dopa modulates theta dynamics.

Methods

Participants

Participants were 12 patients (9 males, 3 females) aged 48 – 74 years old (m = 62.67 years) who have been diagnosed with Parkinson's Disease (mean disease duration = 11.1 years) and were approved to undergo Deep Brain Stimulation Surgery. Participant demographic

information and clinical characteristics are included in **table 11**. All participants were recruited from Emory Movement Disorders Clinic and provided written informed consent. All procedures were approved by the Institutional Review Board of Emory University.

ID	Sex	Age	Handedness	More Symptomatic Side	MDS UPDRS-II (Off medication)	Disease Duration (years)
1	M	48	Right	Right	45	13
2	M	67	Right	Left	35	9
3	M	61	Right	Right	33.5	14
4	M	58	Right	Right	28.5	10
5	F	48	Right	Right	42	10
6	M	60	Right	Right	43.5	10
7	M	71	Left	Left	49	6
8	F	74	Right	Both	47	11
9	F	68	Right	Left	38	22
10	M	59	Right	Both	47.5	9
11	M	69	Right	Left	39	8
12	M	69	Right	Right	55.5	11

Table 11. Demographic and clinical information for participants

Task

Participants performed the Continuous Movement Stop Task (CMST; Schultz et al., 2023)(**Fig.18**) while electrophysiological activity was recorded using a 64-channel BioSemi ActiveTwo system (Amsterdam, Netherlands) at 2048 Hz sampling rate. Each participant performed this task twice in one day – once while off dopaminergic medication and once on medication. During this CMST, participants were seated in front of a computer monitor with a computer mouse in their dominant hand. They were instructed to begin moving the mouse in a circle after presented with a “go” cue (green circle) and to continue moving while monitoring a countdown until presented with a “stop” cue which indicated that they should cease movement as quickly as possible. The CMST consists of two trial types: planned and unplanned. On a planned stop trial, the countdown reaches 1 before the stop-signal is presented. On these trials,

participants are able to predict exactly when the stop-signal will arrive, allowing them to plan when to terminate their movement. On unplanned stop trials, the stop signal is presented pseudorandomly during the countdown. On these trials, participants are unable to predict when the stop-signal will arrive and must instead terminate their movement in response to the cue. Trials are randomly intermixed such that participants cannot predict which trial type they are performing. Movement in this task is identified as the change in location of the mouse cursor in pixel space. The task consisted of 120 trials, 50% of which were unplanned stop trials. The duration of each trial ranged from 7.5s to 2.0002s (m = 4.16s).

Behavioral analysis

We analyzed four behavioral metrics: go signal reaction time (goRT), speed, slowing, and stop completion time (SCT). GoRT is defined as the time between the presentation of the go signal and the onset of movement. Speed is defined as the change in the XY coordinates of the cursor over time and was analyzed as an average over time from the onset of movement until stop signal presentation. To evaluate slowing, we subtracted average speed in the last 500ms prior to stop signal

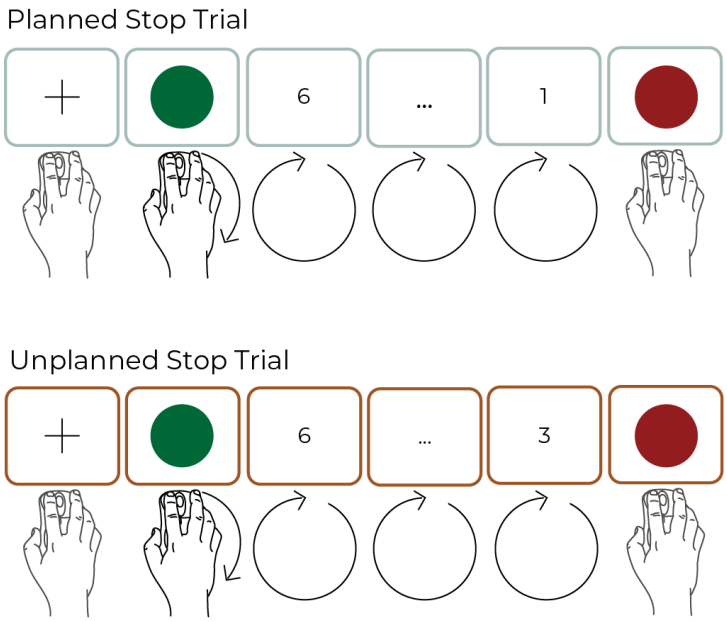

Figure 18. Depiction of task design. Each trial began with a fixation cross followed by a go signal (green circle) which occurred after a delay of 300ms, 500ms, or 700ms and was displayed for 500ms. The countdown began at either 6, 5, 4, or 3 with equal probability for every trial. Each number of the countdown was displayed for exactly 1 second. On planned stop trials, the stop signal occurred exactly 1 second after the countdown reached one (i.e. the stop signal arrived at Time 0 of the countdown). On unplanned stop trials, the stop signal was displayed at a pseudorandom time point.

arrival from speed averaged across a time window ranging from the onset of movement to 1000ms prior to stop signal arrival. Finally, SCT is defined as the time between the onset of the stop signal to the point of full motor arrest (change in cursor location = 0). Trials in which patients took longer than 1000ms to respond to the go signal were excluded from analysis. Similarly, trials in which patients took longer than 1000ms to stop after stop signal presentation or stopped more than 500ms before stop signal onset were also excluded from analysis. On average, 3.17 planned and 3.58 unplanned stop trials were removed from analysis for these reasons.

EEG recording and preprocessing

EEG data were recorded using a 64-channel BioSemi ActiveTwo system (Amsterdam, Netherlands) at a 2048 Hz sampling rate. Event triggers were used to synchronize on-screen events with EEG signals via the BioSemi USB trigger interface. To confirm the accuracy of the event triggers, a photodiode was affixed to the bottom corner of screen on the laptop delivering the task and was digitized with the EEG data.

Preprocessing of the data was performed using custom Matlab scripts and the EEGLAB toolbox (Delorme & Makeig, 2004). Data were first high-pass filtered at 1Hz and re-referenced to the common average. We then used the 'pop_runica' function in EEGLAB (Delorme et al., 2007) to decompose data into independent components. Components that were identified as eye blinks or saccades were removed. The remaining artifacts were identified using the EEGLAB functions 'pop_jointprob' and 'pop_rejkurt'. Epochs that were identified as containing absolute values and/or kurtosis values greater than 5 standard deviations above the mean were excluded from analysis. On average, 23.95% of planned stop trials and 24.2% of unplanned stop trials

were excluded from analysis for this reason. On average, 42.43 planned stop and 42.06 unplanned stop trials were included in the final analysis.

Electrophysiological analysis

Based on previous work which identified regions important for inhibitory control, we focused our analysis on 3 regions of interest (ROIs): right frontal (Fc6, F6, & F8), midfrontal (Fz, FCz, & Cz) and left sensorimotor (C3).

Data from each channel were filtered into separate analytic amplitudes at 60 different frequencies ranging from 2.5 to 60 Hz using a finite impulse response filter (EEGLAB function 'eegfilt'). A Hilbert transform was then applied to the filtered signal. Data were epoched from -1500 to +1500ms relative to four events of interest: go signal, goRT, stop signal, and SCT. Epochs were averaged across trials and compared to an average baseline of 500ms occurring within the inter-trial interval (-1000 to -500 ms prior to the start of the trial). Epochs for each event were then averaged across subjects.

We then averaged across both beta band (13-30 Hz) and theta band (4-7 Hz) to more clearly visualize event-related dynamics for each. We sought to evaluate the effect of medication status (On Vs Off meds) and trial type (planned vs unplanned) on beta and theta band activity by performing a Bayesian paired samples t-test ('bf.ttest'; Krekelberg, 2025) for each of the four events of interest and each of the three ROIs. Bayes factors (BFs) range from <.03, which indicates very strong evidence for the null hypothesis, to >30, which indicates very strong evidence for the alternative hypothesis. Here, we exclusively report BFs greater than 3 (moderate to very strong evidence for the alternative hypothesis). Though there is not a significance threshold in Bayesian statistics, we refer to BFs of 3 and above as 'significant' for simplicity.

As a post-hoc analysis, we explored variability of beta and theta dynamics to address a hypothesis that electrophysiological dynamics were generally more constrained off medication compared to on. To do this, we calculated the variance (Matlab function 'var') for each previously defined epoch of interest for each subject. We then performed a Bayesian paired samples t-test using JASP (JASP Team, 2021) to compare variances between medication status. Because our primary interest was exploring the possibility of medication-induced changes in frequency band dynamics, we combined across planned and unplanned trial types for this analysis.

Results

Behavior

As has been previously observed (Schultz et al., 2023) SCT was significantly longer for unplanned compared to planned stop trials for both the Off meds condition (Mplan = 629ms, sd = 167ms; Munplan = 726md, sd = 162ms; t(11) = -2.66, p = .022, d = -.767, ci = [-1.4, -.11]) and On meds condition (Mplan = 694ms, sd = 332ms; Munplan = 849ms, sd = 299ms; t(11) = .003, d = -1.12, ci = [-1.83, -.37]; **figure 19**). SCT did not differ by medication status for planned stop trials (t(11) = .961, p = .357) or unplanned stop trials (t(11) = 1.751, p = .108).

goRT did not differ by medication status (On mean = 322ms, sd = 113ms, Off mean = 344ms, sd = 108ms, t(11) = -1.018, p = .331). Slowing was also unaffected by medication status for both planned (Mon = .124, sd = .079; Moff = .098, sd = .129; t(11) = 1.234, p = .243) and unplanned stop trials (Mon = .033, sd = .256; Moff = -0.005, sd = .262; t(11) = .884, p = .396). Surprisingly, we found that patients did not slow down significantly more on planned than unplanned stop trials (a behavior observed in a previous study; Schultz et al., 2023) on

medication (t(11) = 1.166, p = .268) nor off medication (t(11) = 1.026, p = .327). Lastly, we found that overall speed of movement did not differ by medication status (Mon = 1.49, sd = .454; Moff = 1.988, sd = 2.38; t(11) = -0.731, p = .48).

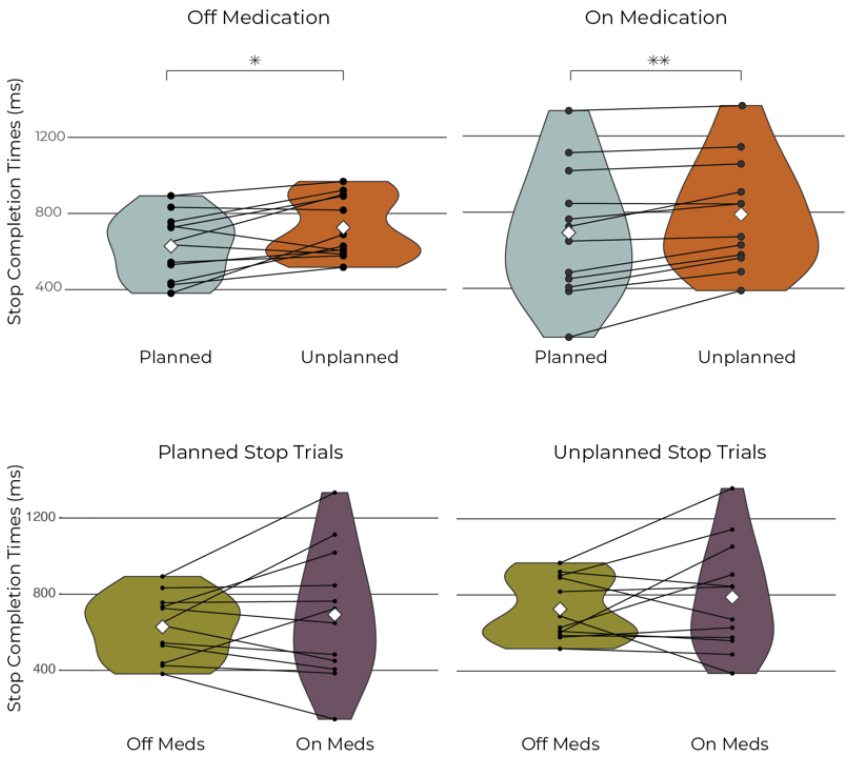

Figure 19. Stop Completion Times. SCT on planned stop trials was significantly faster than unplanned stop trials when patients were on medication and off medication. There were no significant differences in SCT between medication statuses. * indicated p<.05, ** indicates p<.01

Electrophysiology

Average Beta

Outcomes of average beta power analyses are shown in **figures 20 & 21**. All points at which the BF exceeded 3 are indicated with a light green square, with darker greens indicating a higher BF. Overall, beta power over right frontal cortex tended to be higher in the off-medication condition compared to on medication. However, this difference rarely reached significance (BF>3). We also did not find the anticipated differences in beta power in this ROI between planned and unplanned stop trials around the time of stop signal onset or stop completion. Some significant differences emerged between trial types around the time of go signal onset and goRT. However, given that planned and unplanned stop trials were identical at the start of the trial, we do not believe these differences are a consequence of trial type and more likely they just represent chance occurrences.

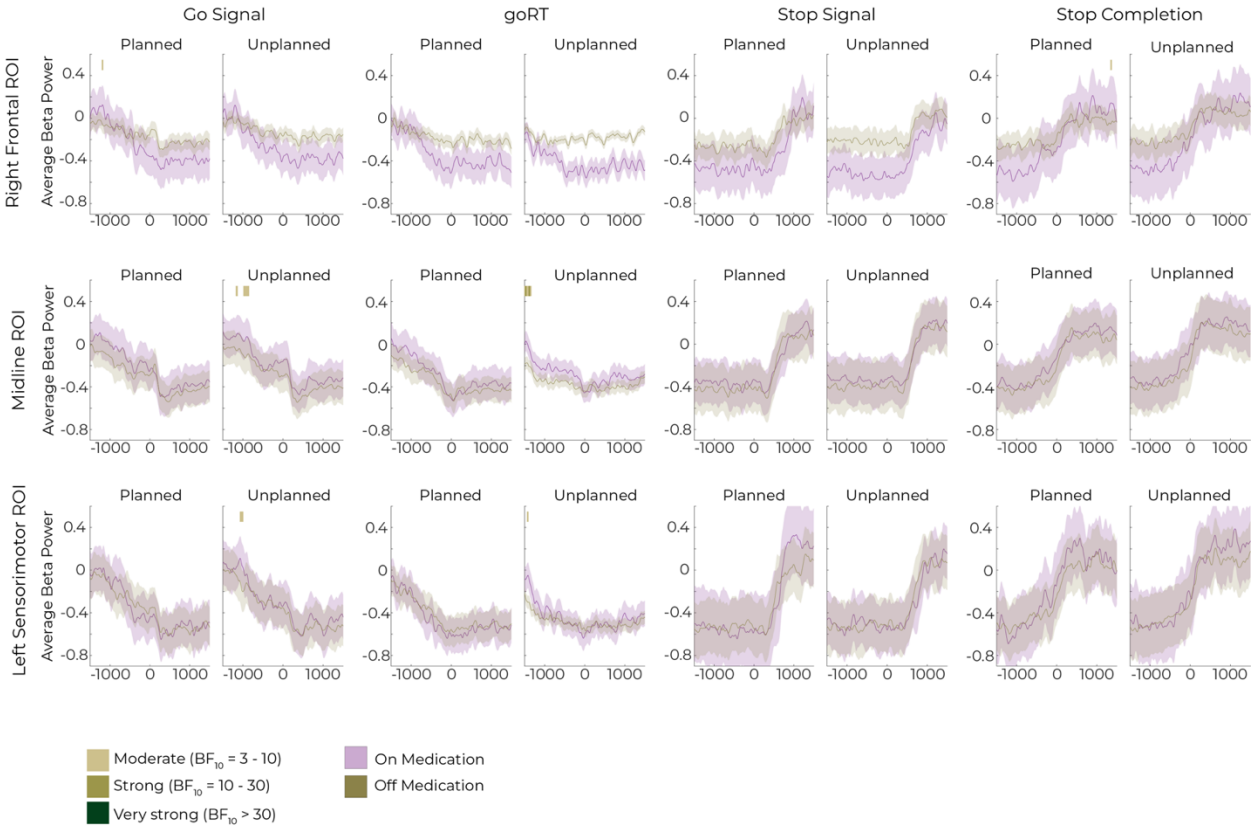

Figure 20. Average Beta Power during planned and unplanned stop trials comparing patients on and off medication. Each plot is aligned one of the 4 events of interest (i.e. time 0 = go signal onset). Periods of significance (BF >3) are marked with a green rectangle.

In contrast to our findings in the right frontal ROI, average beta over the midfrontal ROI tended to be slightly higher when patients were on medication than when they were off medication. However, these differences rarely reached significance. We also observed, brief, significant differences between trial types around the time of stop signal onset and stop completion, with beta power being higher for unplanned compared to planned stop trials. This was the case for both on and off medication conditions.

Analysis of average beta over left sensorimotor cortex revealed that beta power was similar between on and off medication for all events. We also did not observe differences in beta power between planned and unplanned stop trials, with the exception of a difference around the

time of go signal onset. However, as previously stated, this difference is likely not a consequence of trial type manipulation.

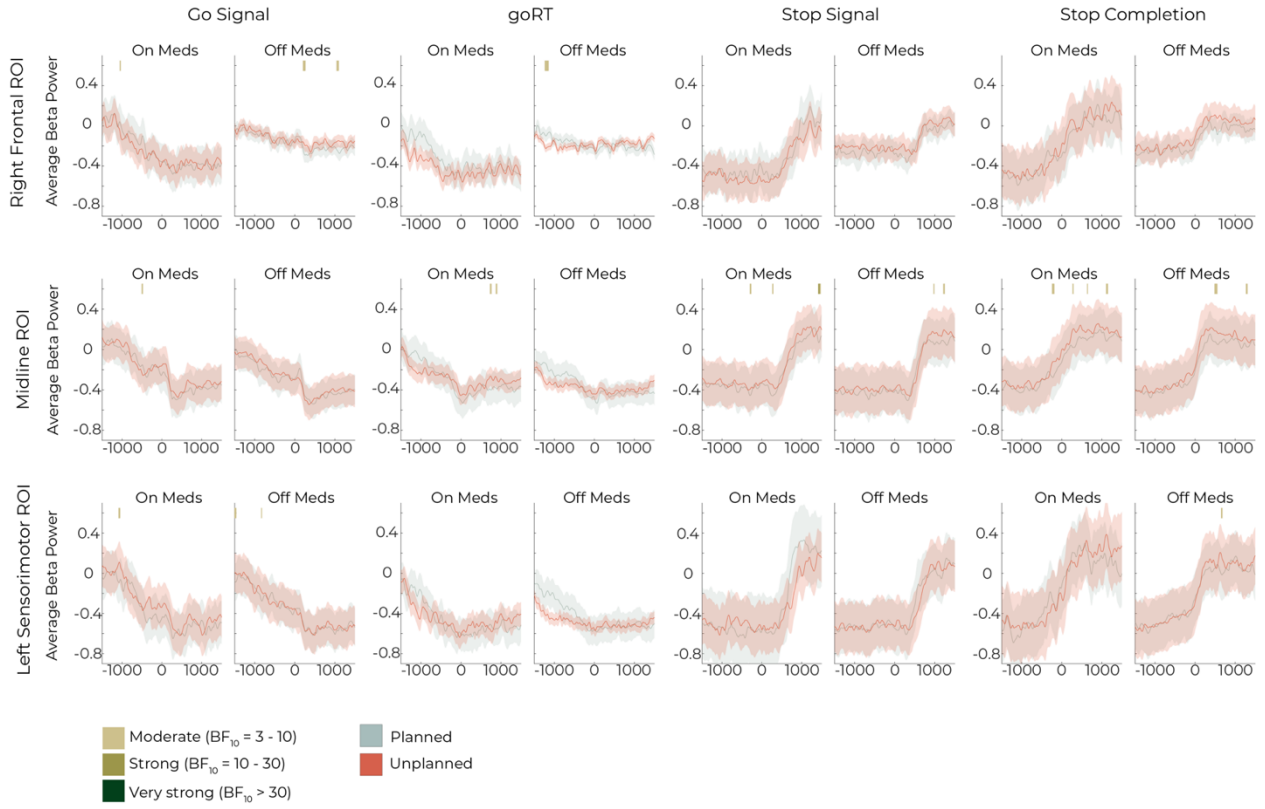

Figure 21. Average Beta Power comparing planned and unplanned stop trials while patients are on and off medication. Each plot is aligned one of the 4 events of interest (i.e. time 0 = go signal onset). Periods of significance (BF >3) are marked with a green rectangle.

Overall, we did not find compelling evidence that beta power is differentially modulated in any of the examined ROIs by acute administration of l-dopa. Additionally, because we did not observe differences in beta power between planned and unplanned stop trials, we are unable to assert that beta power may be differentially modulated by the cognitive and motoric demands of the task.

Average Theta

Outcomes of average theta power analyses are shown in **figures 22 & 23**. Analysis of average theta power over right frontal cortex revealed several epochs of significant differences between medication conditions with the off medications condition demonstrating higher power than when patients were on medication. These differences were especially pronounced around the time of stop signal presentation but were also present for brief periods in the epochs aligned to go signal onset, goRT, and stop completion. We did not observe differences in average theta between trial types, with the exception of a brief period of moderate significance around the time of goRT.

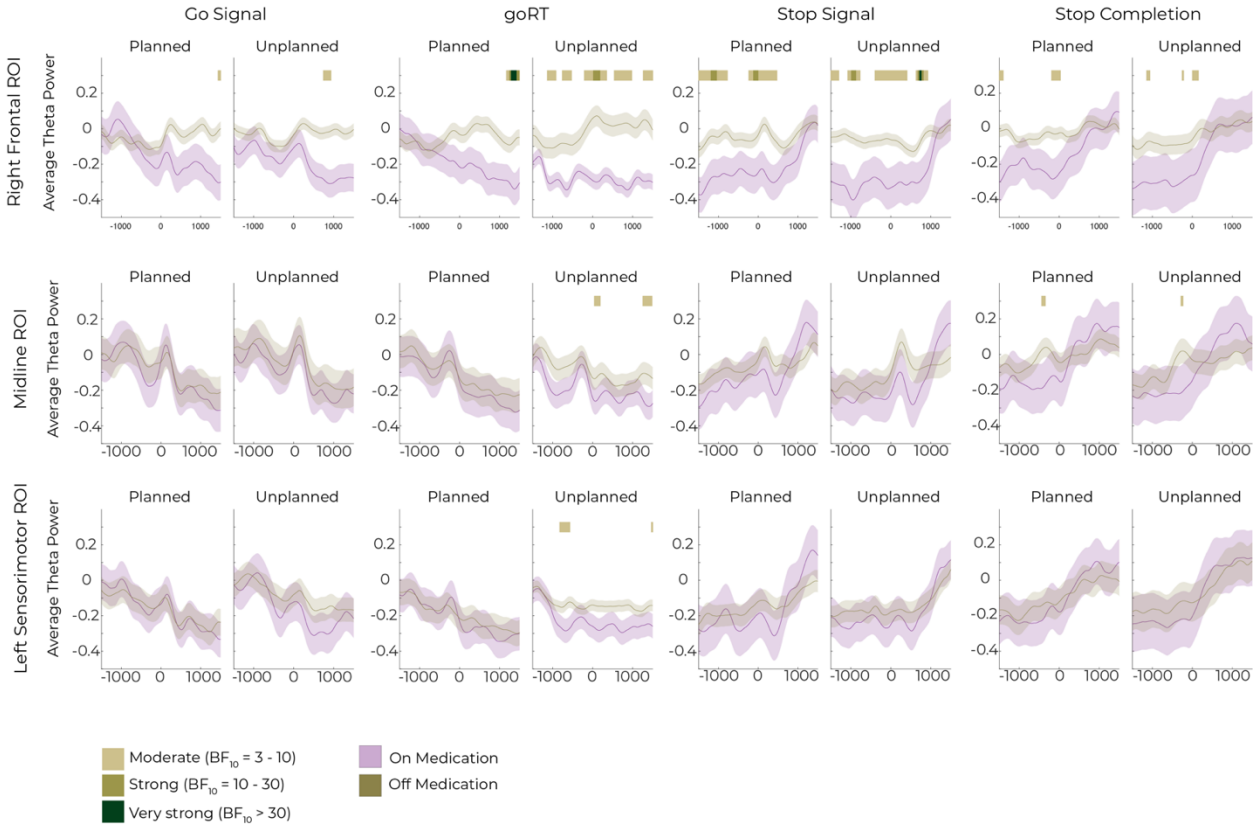

Figure 22. Average Theta Power during planned and unplanned stop trials comparing patients on and off medication. Each plot is aligned one of the 4 events of interest (i.e. time 0 = go signal onset). Periods of significance (BF >3) are marked with a green rectangle.

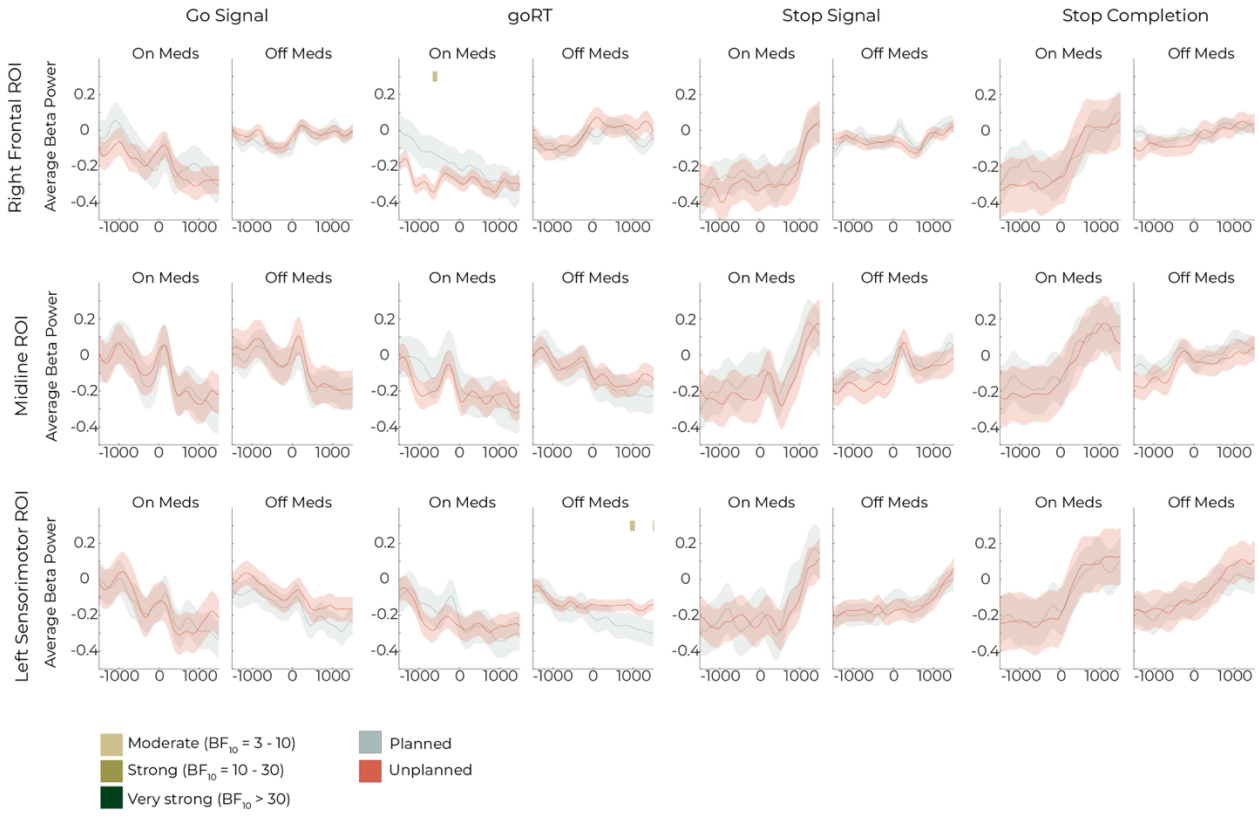

Figure 23. Average Theta Power comparing planned and unplanned stop trials while patients are on and off medication. Each plot is aligned one of the 4 events of interest (i.e. time 0 = go signal onset). Periods of significance (BF >3) are marked with a green rectangle.

Analysis of average theta over the midfrontal ROI revealed small differences between medication statuses around the time of goRT and SCT. We did not observe any differences between trial types for any event.

We found a small difference in average theta power between medication statuses around the time of goRT over left sensorimotor cortex, but not during any other event. A small difference was also observed in this ROI between trial types aligned to goRT, but no other differences were observed.

Overall, this analysis yielded compelling evidence that theta power over the right frontal region was meaningfully modulated by acute administration of l-dopa and that this effect was most pronounced around the time of stop signal presentation.

Variance

Bayes factors for all analyses are reported in **tables 12 and 13**. We found moderate evidence of a significant difference in average beta power variance aligned to goRT over the midfrontal ROI (BF_{10} = 4.322; $mean_{on}$ = .036 (sd = .027), $mean_{off}$ = .022 (sd_{off} = .023)). All other Bayes factors were within the anecdotal range.

Beta Variance					
Right Frontal ROI					
	BF_{10}	*M* (on)	*sd* (on)	*M* (off)	*sd* (off)
Go Signal	1.27	0.094	0.163	0.026	0.025
goRT	2.86	0.061	0.085	0.018	0.017
Stop Signal	0.54	0.154	0.424	0.029	0.027
SCT	1.01	0.226	0.497	0.033	0.036
Midfrontal ROI					
	BF_{10}	*M* (on)	*sd* (on)	*M* (off)	*sd* (off)
Go Signal	1.79	0.057	0.047	0.044	0.049
goRT	**4.32***	0.036	0.027	0.022	0.023
Stop Signal	0.22	0.079	0.079	0.082	0.076
SCT	0.23	0.091	0.084	0.085	0.076
Left Sensorimotor ROI					
	BF_{10}	*M* (on)	*sd* (on)	*M* (off)	*sd* (off)
Go Signal	0.22	0.085	0.088	0.079	0.144
goRT	0.33	0.051	0.046	0.039	0.079
Stop Signal	0.33	0.332	1.2	0.1	0.12
SCT	0.4	0.288	0.7	0.12	0.15

Table 12. Results of Bayesian paired-samples t-tests comparing variances of average beta power for on and off medication status aligned to each event of interest across each ROI. *M* = mean variance score; *sd* = standard deviation of variance score. A BF_{10} of 1-3 is considered anecdotal evidence for H_1; BF_{10} of 10 – 30 is considered strong evidence in favor of H1. * = moderate evidence, ** = strong evidence.

We found strong evidence of a difference in average theta power variance within the right frontal ROI aligned to the stop signal (BF_{10} = 9.939; $mean_{on}$ = .045 (sd = .045), $mean_{off}$ = .013 (*sd* = .017)) and moderate evidence of a difference aligned to SCT within the same ROI (BF_{10} = 4.654; $mean_{on}$ = .062 (sd = .077), $mean_{off}$ = .016 (*sd* = .02)).

Theta Variance					
Right Frontal ROI					
	BF_{10}	*M* (on)	*sd* (on)	*M* (off)	*sd* (off)
Go Signal	0.22	0.042	0.051	0.039	0.088
goRT	0.22	0.03	0.031	0.033	0.079
Stop Signal	**9.94****	0.045	0.045	0.013	0.017
SCT	**4.65***	0.062	0.077	0.018	0.02
Midfrontal ROI					
	BF_{10}	*M* (on)	*sd* (on)	*M* (off)	*sd* (off)
Go Signal	**12.35****	0.043	0.027	0.022	0.013
goRT	**10.97****	0.033	0.021	0.016	0.012
Stop Signal	**5.37***	0.049	0.053	0.016	0.01
SCT	**3.51***	0.062	0.075	0.02	0.013
Left Sensorimotor ROI					
	BF_{10}	*M* (on)	*sd* (on)	*M* (off)	*sd* (off)
Go Signal	**5.13***	0.029	0.021	0.016	0.025
goRT	**15.59****	0.02	0.017	0.01	0.013
Stop Signal	1.84	0.043	0.062	0.013	0.017
SCT	1.34	0.053	0.062	0.022	0.036

Table 13. Results of Bayesian paired-samples t-tests comparing variances of average theta power for on and off medication status aligned to each event of interest across each ROI. *M* = mean variance score; *sd* = standard deviation of variance scores. A BF_{10} of 1-3 is considered anecdotal evidence for H_1; BF_{10} of 10 – 30 is considered strong evidence in favor of H1. H1. * = moderate evidence, ** = strong evidence.

Strong evidence supporting a difference in variances was also found within the midfrontal ROI (**fig. 24**) aligned to the Go Signal (BF_{10} = 12.35; $mean_{on}$ = .043 (sd = .027), $mean_{off}$ = .022 (*sd* = .013)) and aligned to goRT (BF_{10} = 10.97; $mean_{on}$ = .033 (sd = .021), $mean_{off}$ = .016 (*sd* = .012)). Moderate evidence for a significant difference was also found within this ROI aligned to the Stop Signal (BF_{10} = 5.37; $mean_{on}$ = .044 (sd = .053), $mean_{off}$ = .016 (*sd* = .01)) and SCT (BF_{10} = 3.51; $mean_{on}$ = .062 (sd = .075), $mean_{off}$ = .02 (*sd* = .013)).

Finally, we found strong evidence for a difference in average theta variance between on and off medication within the left sensorimotor ROI aligned to goRT (BF_{10} = 15.59; $mean_{on}$ = .02 (sd = .017), $mean_{off}$ = .01 (*sd* = .01)) and moderate evidence for a difference aligned to the Go Signal (BF_{10} = 5.13; $mean_{on}$ = .029 (sd = .021), $mean_{off}$ = .016 (*sd* = .025)).

In sum, this analysis suggests that variance of beta power is not meaningfully affected by acute administration of l-dopa. However, variance of theta power does appear to be strongly, meaningfully influenced by dopaminergic medication and that this effect is most pronounced in the midfrontal region.

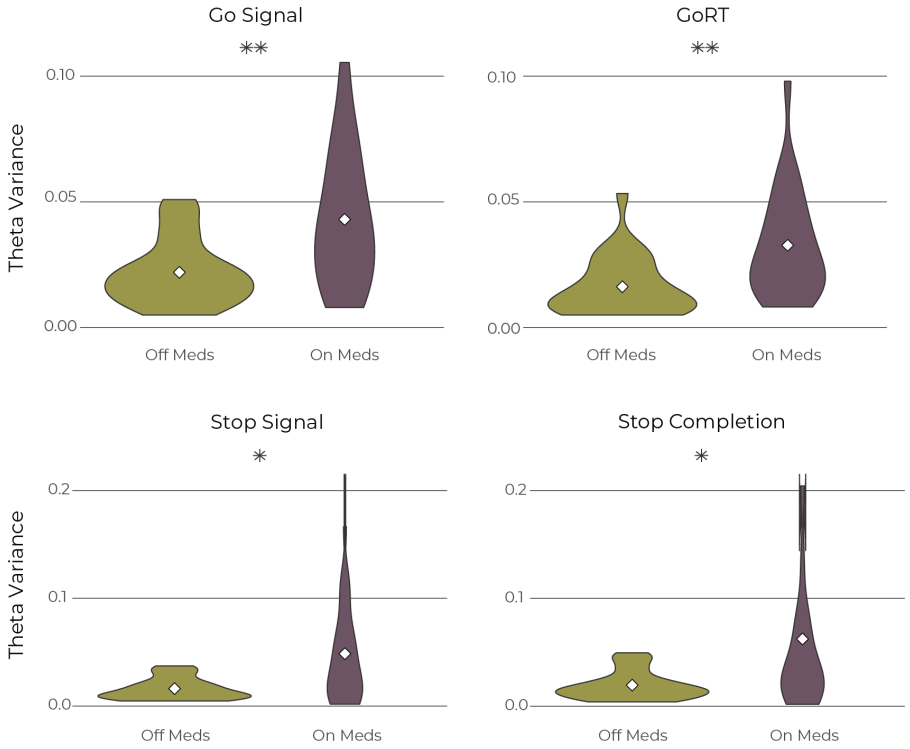

Figure 24. Midfrontal theta power variances. ** indicates BF_{10} >10. * indicates BF_{10} > 3

Discussion

Here, we employed the CMST to explore the possibility of separable stopping mechanisms that are differentially impacted by dopaminergic medication. We examined behavioral outcomes, explored oscillatory dynamics in the beta and theta frequency ranges, and evaluated the influence of medication on variability in average power across both frequency ranges.

We found that participants with PD stopped significantly slower on unplanned stop trials compared to planned, as has been previously observed in people without PD (Schultz et al., 2023). We did not observe any behavioral effects of medication status.

Though we did not find evidence to support our hypothesis that beta frequency over right frontal cortex activity would differ between trial types, we did find some moderate evidence of a distinction in the midfrontal ROI around the time of stop signal presentation and stop completion, with beta power being higher for unplanned compared to planned stop trials. Due to volume conduction issues inherent to scalp EEG, it is possible this activity could be associated with substrates located in prefrontal cortex. However, without employing source localization methods we are unable to discern the source of this signal.

Overall, although we observed some periods in which beta power appeared to be significantly different between conditions (i.e. off meds vs on and unplanned vs planned stop trials), our findings do not provide compelling support for the hypothesis that average beta power is meaningfully influenced by trial type or medication status with respect to our 4 events of interest (Go signal, goRT, Stop signal & SCT). As a general trend, we observed that average beta power over right frontal cortex was higher overall in the off-medication condition than in the on-medication condition. The lack of a statistically meaningful difference between on and off medications is somewhat surprising given that previous work has demonstrated an observable effect of dopaminergic medication on beta band activity in sensorimotor cortex (Cao et al., 2020; Chung et al., 2018) and right frontal cortex (George et al., 2013). However, the effect of levodopa on beta band activity appears to be modulated by task demands (George et al., 2013). It is possible that the demands of the CMST do not drive medication-related beta differences in the same way other tasks, such as the SST, do. Alternatively, we may simply be underpowered to observe this effect.

Interestingly, though we did observe an increase in prefrontal beta power around the time of stopping (as previously observed in other studies; Schmidt et al., 2019), this increase occurred

much later than expected. Based on previous work, many researchers suspect beta activity is causally related to stopping. However, it appears that, when aligned to the actual time of stopping, increases in prefrontal beta occur too late to be causal. Increases in sensorimotor beta, on the other hand, are well-documented to occur after movement termination (Barone & Rossiter, 2021 for review). Thus, it is possible that large amplitude sensorimotor post-movement beta increases could be dominating the EEG and obscuring the potentially lower amplitude prefrontal beta increases.

Our analysis of average theta power suggests that theta in the right frontal ROI is meaningfully influenced by dopaminergic medication. Specifically, we observed that average power around the time of goRT, stop signal onset, and stop completion was significantly higher for the off-medication condition compared to on medication in this ROI. Similar to beta, average theta power over right frontal cortex appears to be higher in general when participants were off medication compared to on.

We also observed that average theta power was significantly higher in the midfrontal ROI around the time of stop completion when participants were off medication compared to on. Plots showing average theta traces in this ROI (**figs. 22 & 23**) demonstrate a peak in theta shortly before stop completion time that is evident when participants are off medication but not when they are on medication.

Previous work has related midfrontal theta activity to cognitive aspects of inhibition (van Noordt et al., 2022) as well as cognition more generally (Cavanagh & Frank, 2014; Kelley et al., 2018; Singh et al., 2018)and has shown that theta power is attenuated in PD (Kelley et al., 2018; Parker et al., 2015; Singh et al., 2018). Based on the existing literature, it is possible that the midfrontal theta dynamics we observed are related to cognitive aspects of the task – perhaps

playing a role in indicating the need for cognitive control (Cavanagh & Frank, 2014). However, the role that right frontal theta activity plays in inhibitory control is not yet understood. Additionally, though animal research has demonstrated the importance of dopamine on midfrontal theta activity (Kim et al. 2017; Parker et al., 2014, 2015a, 2015b), the effects of levodopa administration and the possible modulatory influence of task demands require further investigation.

Plots of average power traces (**figs 20-23**), particularly those that show average beta band activity in the right frontal ROI and average theta band activity in all ROIs, seem to reveal a difference between on and off medication conditions in oscillatory dynamics (i.e. how power changes over time) that were not captured by our initial analysis. Specifically, it appears that right frontal beta and theta power remain relatively consistent over time while participants are off medication and that power in these frequency bands is more variable (perhaps more modulated by task demands) when participants are on medication. We were intrigued that such a finding could suggest that the excessive synchrony associated with PD (Hammond et al., 2007) may be constraining these normally dynamic changes into a more inflexible pattern – perhaps explaining some of the motor and cognitive inflexibility observed in PD clinically (Uhlhaas & Singer, 2006). As an attempt to quantify this observation, we calculated the variance of average beta and theta power and compared variances on and off medication for each event of interest. This analysis revealed statistically higher theta variance when participants were on medication compared to off in all three ROIs. Theta variance in the midfrontal ROI was higher on medication across all 4 events while variance in right frontal and left sensorimotor was higher on medication for 2 of the 4 events of interest. This finding suggests that dopaminergic medication exerts a meaningful influence on theta power dynamics, particularly in the midfrontal region.

Given that we did not observe behavioral differences when participants were on medication compared to off, we cannot posit how these variance differences might relate to cognitive or behavioral characteristics of PD. However, these findings leave open the possibility that muted theta dynamics are a clinically relevant pathological feature of PD.

Similar to theta variance, average beta variances tended to be higher on medication than off. However, these differences were not associated with statistically meaningful Bayesian statistics.

Limitations and future research

The current study includes several limitations that should be considered in the evaluation of the evidence provided. One of the primary limitations is sample size. With a sample size of only 12, it is possible that we were underpowered to observe some effects of medication status or trial type manipulation on our variables of interest. For instance, with our sample size, to find a significant effect with a two tailed significance of 0.05, given a power of .8, an effect size of at least 0.91 would be required. This is generally considered a large or very large effect size. So here we were only able to calculate very notable differences. In other words, though we did not find support for our hypothesis that right frontal beta would dissociate planned and unplanned stop trials, and that beta would be modulated by medication, we cannot conclude that these effects do not exist. Rather, we are only able to determine with certainty that we did not observe these effects in our current sample. Future research would benefit from a larger sample size from which stronger conclusions can be drawn.

An additional possible limitation is our decision to include 50% of each trial type. This decision was driven by previous work, which suggested that behavior did not change based on

percentage of unplanned stop trials (Schultz et al., 2023). However, it may be the case that the equal probability of an unplanned stop on every trial could have impacted the extent to which the unplanned trials were 'surprising' and encouraged participants to adopt a strategy that was consistent across every trial, which ultimately obscured any effect of trial type manipulation. This limitation could be addressed in future research by including a smaller percentage of unplanned stop trials. Alternatively, future research could include a cue at the beginning of the trial indicating trial type. Informing the participant about whether the stop signal would arrive when expected or not may encourage participants to adopt different strategies on each trial. For example, on an unplanned stop trial, a participant would likely engage some proactive inhibitory control mechanisms to facilitate the need to stop when the stop signal arrives at an unanticipated time. However, on a planned stop trial, these mechanisms would not be needed, as the participant would know from the outset when the stop signal would arrive.

Conclusion

Here, we aimed to explore the mechanisms of planned and unplanned stopping and to investigate potential modulatory effects of dopaminergic medication on the electrophysiology and behavioral outcomes. We found that participants stopped faster on planned stop trials than unplanned stop trials, both when they were on and off medications (as previously observed in non-patient populations; Schultz et al., 2023a, 2023b). Medication did not appear to have any effect on task behavior. We did, however, find some possible medication-related effects on the EEG data. Specifically, we found evidence that right frontal theta power may be modulated by medication, with power being higher when participants were off compared to on medication. Additionally, we found that theta power variance was greater when participants were on medication. This difference in variance seemed to be the most consistent in the midline ROI but

was present in both the right frontal and left sensorimotor ROIs. Though we did not find support for our hypothesis that right frontal beta would be greater on unplanned than planned stop trials, or that trial type differences would be modulated by dopaminergic medication, we did uncover an intriguing possibility that right frontal theta power and theta variance is meaningfully influenced by medication in Parkinson's patients.

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CHAPTER 5

INVESTIGATING COGNITIVE AND MOTORIC SIGNATURES OF INHIBITORY CONTROL WITH STEREO-EEG

Introduction

Inhibitory control, or the ability to stop unwanted thoughts and actions, is an essential aspect of daily life. However, the mechanisms by which the brain implements inhibitory processes are unclear.

The majority of studies investigating motor inhibition have utilized the stop signal task (SST), in which participants must respond rapidly to a "go" cue (typically with a button press) but inhibit their response on a subset of trials when presented with a "stop" cue (Logan & Cowan, 1984; Aron et al., 2014). Despite the valuable insights into inhibitory control provided by the SST, there are inherent limitations to this paradigm that must be addressed to achieve a more comprehensive understanding of motor inhibition.

One key limitation of the SST is its reliance on the inhibition of an intended but not yet executed movement, creating a temporal ambiguity with respect to the moment of movement termination. This ambiguity arises because the exact moment of movement termination is not directly observable, complicating efforts to accurately identify neural correlates associated with

different components of inhibition (Aron et al., 2014; Hannah & Aron, 2021). Specifically, it is unresolved whether neural activity observed during standard response inhibition paradigms relates to the cognitive recognition of the need to implement control, the actual termination of motor commands, or sensory feedback following successful inhibition.

Previous neuroimaging and electrophysiological studies have consistently implicated a right-lateralized cortico-basal ganglia network in implementing inhibitory control, notably through beta frequency (13-30 Hz) oscillations (Swann et al., 2009; Wessel, 2020). Theta frequency (4-7 Hz) activity has also been identified as critical, both in signaling the need for inhibitory control and directly mediating the inhibitory process (Cavanagh & Frank, 2014; Zavala et al., 2018). However, conventional methodologies each have limitations: fMRI provides broad spatial coverage but poor temporal resolution, whereas scalp electroencephalography (EEG) and magnetoencephalography (MEG) offer excellent temporal resolution but limited spatial specificity (Makeig et al., 2004; Hämäläinen et al., 1993). Although invasive techniques like electrocorticography (ECoG) and deep brain stimulation (DBS) recordings offer superior spatial and temporal resolution, their coverage is limited to specific brain areas (Rosenow & Lüders, 2001). Stereoelectroencephalography (SEEG), an invasive intracranial recording method, provides exceptional temporal and spatial resolution and can simultaneously sample both superficial and deep brain structures, overcoming many of these limitations (Kahane et al., 2003; Gonzalez-Martinez et al., 2014).

Here, we adopt an exploratory approach to elucidating the neural mechanisms underlying motor inhibition using a novel motor inhibition task—the Continuous Movement Stop Task (CMST)—which enables direct observation of actual movement termination on each trial (Schultz, Denning, et al., 2023). Leveraging the superior spatial and temporal resolution of

SEEG, we specifically investigated the dynamics of beta and theta oscillations around the onset of the stop signal and actual movement termination. By clarifying the precise timing and frequency characteristics of these neural activities, we aim to better delineate their roles in inhibitory control mechanisms.

Methods

Participants

Data were collected from 13 patients with drug-resistant epilepsy who were undergoing evaluation and monitoring at the Oregon Health and Science University (Portland, OR). Patients in this study underwent stereoelectroencephalography (sEEG) implantation with depth electrodes. Electrodes had an inter-contact spacing (pitch) ranging from 3-7 mm, depending on the electrode used (Kahane et al., 2003; Gonzalez-Martinez et al., 2014).

Participants were included in this study if they (1) had medically refractory epilepsy that required clinical (sEEG) implantation for seizure localization, (2) were between 6 and 89 years old, and (3) were able to perform the experimental task. Participants were excluded from the study if they had: (1) the presence of substantial brain malformations which could confound anatomical landmarks, (2) severe visual impairment(s), (3) global intelligence quotient (IQ) with standard score (SS) <70, (4) psychiatric history of active suicidal ideation, schizophrenia, or bipolar depression type 1, (5) Neurodegenerative or metabolic disorders that affect global cerebral function. All participants provided informed consent and all procedures and were approved by the Oregon Health & Science University Institutional Review Board (STUDY00018870).

Of the initial 13 participants (9 males, 4 females, age range 25-41 years, mean age 32.7 years) who completed the Continuous Movement Stop Task (CMST), one was excluded from subsequent analysis due to poor SEEG data quality (electrical artifacts overwhelming signal for all channels). Thus, data from 12 participants were included in the final analysis. Channels identified as pathological by clinical epileptologists or exhibiting significant pathological or artifactual activity upon inspection by the authors were excluded from further analysis. Out of the initial 1498 channels implanted, 832 were ultimately analyzed, with each participant contributing an average of 69 channels (SD = 13.16). Demographic details for each participant are summarized in **Table 13**.

Sbj #	Age	Sex	# of Electrodes Implanted	# of Electrodes Analyzed	# of Electrodes Responsive
1	29	M	119	35	35
2	39	M	126	68	61
3	31	F	126	66	38
4	30	M	126	68	64
5	25	M	128	82	59
6	34	M	127	81	72
7	41	F	113	69	64
8	41	M	128	75	71
9	35	M	128	74	74
10	39	F	126	74	70
11	29	F	124	55	55
12	26	M	127	81	79

Table 13. Demographic information and summary of electrode implantation, analysis, and responsiveness for each subject

Task

Patients performed the Continuous Movement Stop Task (CMST; **Chapter 1 Figure 1**) as previously described in Schultz, Denning et al. (2023). In this task, participants were instructed

to move their hand continuously in circular motion while monitoring a countdown that appeared on the screen in front of them. They were asked to begin moving when presented with a go signal ("Go") and to continue moving until presented with a stop signal ("Stop"). On 50% of trials, the countdown reached 1 before the stop signal was displayed. On these trials, termed 'planned stop trials', participants were able to predict exactly when the stop signal would be displayed, thus allowing them to plan the termination of their movement. On the other 50% of trials, the stop signal was displayed pseudorandomly during the countdown. On these trials, termed 'unplanned stop trials', participants were unable to predict when the stop signal would be presented.

We analyzed three behavioral metrics from this task: (1) goRT, or the amount of time between the onset of the go signal and the onset of movement; (2) stop completion time (SCT), defined as the time between the onset of the stop signal and full motor termination; and (3) the coefficient of variation ($SCT_{C.V.}$) for SCT.

The task was presented using the Matlab Psychophysics Toolbox (Brainard, 1997) and completed on a laptop which was placed on a table situated over the hospital bed. The table was adjusted to a height that allowed the participants to comfortably use the trackpad. The task consisted of 120 trials (60 planned stop trials) each of which lasted between approximately 2 and 7 seconds each.

sEEG Data

All signals were recorded using Cadwell Arc Zenith system. To synchronize task events with EEG signals, we used a photodiode which was affixed to the top corner of the task laptop and recorded on the same Cadwell Arc Zenith system as the EEG data. The photodiode square appeared immediately before the start of every trial and the presentation time was recorded with

the behavioral data. The photodiode signal was recorded on two channels of the EEG recording and a bipolar reference was applied to produce a clearly discernable square wave. Using the recorded timestamps of the photodiode presentation and the recorded timing of the signal presentation and behavior, we were able to precisely synchronize the EEG data with task events.

Data Preprocessing

Data were high-pass filtered at 1Hz and re-referenced to the common average. Electrodes identified by the clinical epileptology team as containing epileptiform activity were excluded from analysis. The remaining electrodes were visually inspected for signal quality. All electrodes that contained artifacts or epileptiform activity were also excluded from analysis. After removal of electrodes deemed unfit for analysis, data were then re-referenced to the common average of the remaining electrodes. Visual inspection was performed again to identify epochs that contained noise or epileptiform activity. Any such epochs were marked and these time periods were excluded from analysis.

Analysis

Data from each channel were filtered into separate analytic amplitudes at 180 different frequencies (ranging from 4 to 250 Hz) using a finite impulse response filter (eegfilt, fir1) and a hilbert transform was applied (Matlab *hilbert*). The analytic amplitudes for each frequency were aligned to 4 separate events of interest: (1) onset of the Go Signal, (2) goRT – the time at which participants began moving, (3) onset of the Stop Signal, and (4) SCT – the time at which participants ceased movement. All epochs were 3000ms long with the event of interest at the center (i.e. event of interest -/+ 1500ms). Epochs were averaged across trials and compared to an average baseline of 500ms occurring within the inter-trial interval (-1000 to -500 ms prior to the

start of the trial). We then created a distribution by repeating this procedure 1000 times with each iteration time-locking to random points within the epoch. Specifically, a random number was added to each event, offsetting it by a random amount while keeping the relative spacing of the epochs the same. This distribution was used to convert the averaged (event-locked) analytic amplitudes to z-scores by comparing them to the null distribution derived from values aligned to random time points, allowing us to determine how much each event-locked value deviates from what would be expected by chance.

To compare between planned and unplanned trials (henceforth referred to as the *context difference*), average analytic amplitudes for each trial type were directly subtracted (without employing the baseline correction technique just described). Z-scores for context differences were derived using a similar permutation method in which we employed a label-swapping technique – i.e. randomly shuffling trials and taking the difference, also repeated 1000 times.

Next, we evaluated the responsiveness of each channel to each of the four events of interest in the beta (13-30Hz) and theta (4-7Hz) frequency bands. A channel was deemed *responsive* if the absolute value of the z-scores for that channel within a given epoch exceeded 1.96 for a total of at least 50ms (non-consecutively). Channels that responded to either the go signal or stop signal are referred to as *signal-responsive*, those that responded to either goRT or SCT are referred to as *behavior-responsive*, and those that responded to the context difference are referred to as *context-responsive*.

To determine the timing of a channels responsive period with respect to an event of interest, we examined the timepoints in which the z-scores exceeded the 1.96 threshold (termed significant epochs). When 70% of the significant timepoints occurred prior to the event, this

channel was labeled as an *early responder*. Similarly, when 70% of the significant timepoints occurred after the event, the channel was labeled as a *late responder*. When the significant timepoints were distributed such that less than 70% of the significant timepoints occurred either before or after the event, the channel was labeled as responding to *both*. For example, if 40% of the significant timepoints occurred before the event and 60% occurred after, this channel would be identified as responding to *both.* These analyses were performed on channels that were signal-responsive, behavior-responsive, and context-responsive with respect to the stop signal and stop completion. Results from these analyses were then compared between beta and theta frequency bands.

Results

Behavior

Participants took 677ms on average (sd=237) to respond to the go signal. We found that participants stopped significantly faster on planned (m=568ms, sd=192ms) compared to unplanned stop trials (m=735ms, sd=231); t(11) = -2.441, p=.033, d=-.705, ci=[-1.328, -0.056](**fig.25**), in line with what has been previously observed (Schultz, Denning, et al., 2023; Schultz, Mantell, et al., 2023). Stop completion time (SCT) was also significantly more variable for planned (m=610ms, sd = 412) compared to unplanned (m=331ms, sd=128) stop trials; t(11) = 2.599, p=0.025, d=.34, ci=[0.092,1.382].

Electrophysiology

Summary of Channel Responses

A summary of electrodes analyzed and their response properties across all 12 subjects are represented in **Figures 26 and 27**. Here, we show that 832 of 1498 (55.5%) were analyzed. Of these 832 channels, 742 (89.2%) showed a response to one of the 4 events of interest (Go signal – 66.35%, goRT – 68.15%, Stop signal – 71.39% & SCT – 69.23%) in either the beta band, theta band, or both.

Of the 832 total channels analyzed, 22% were responsive exclusively to the stop signal in the beta frequency band, 5.3% were exclusively context-responsive, and 10.9% responded to both the stop signal and the context. In the theta frequency band, 26.6% were stop signal-responsive, 10.2% were context-responsive, and 21.8% responded to both the signal and the context. With respect to stop completion, 22.2% were behavior-responsive in the beta frequency band, 5.4% responded to the context, and 11.3% responded to both the behavior and the context. In the theta band, 29.2% responded to stop completion, 10.8% responded to the context, and

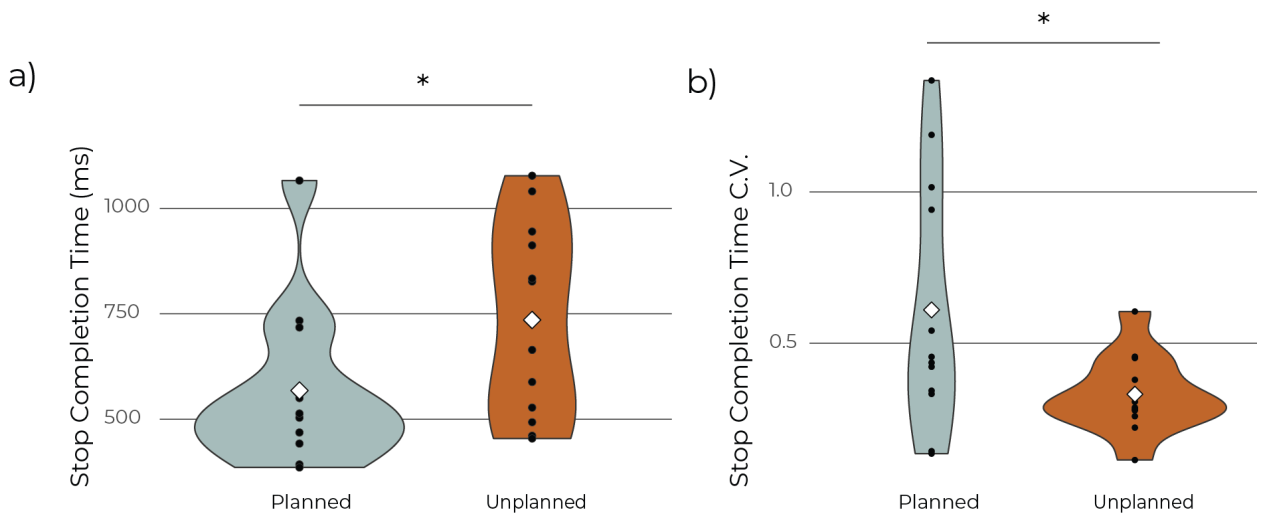

Figure 25. Behavioral Results. A) SCT for planned and unplanned stop trials. Participants stopped significantly faster on planned (m=568ms) compared to unplanned stop trials (m=735ms) p=.033**.** b) Variability of SCT for planned and unplanned stop trials. SCT was significantly more variable for planned (m=610ms) compared to unplanned (m=331ms) stop trials, p=0.025. * indicates p < .05

18.9% responded to both. A breakdown of the number of electrodes implanted, analyzed, and responsive for each participant are also presented in **Table 13.**

Responsive channels were distributed broadly across the brain, including both deep and more superficial areas, for both frequency bands (**fig. 28**). The locations of the electrodes presented in this figure are approximately accurate, but precise localizations are still forthcoming.

Timing of Responses

To better elucidate when these channels were responding to the event and how this varied across trial types and frequency bands, we compared the response time category (i.e. early or late) for channels responding to the stop signal and stop completion (**fig. 29**).

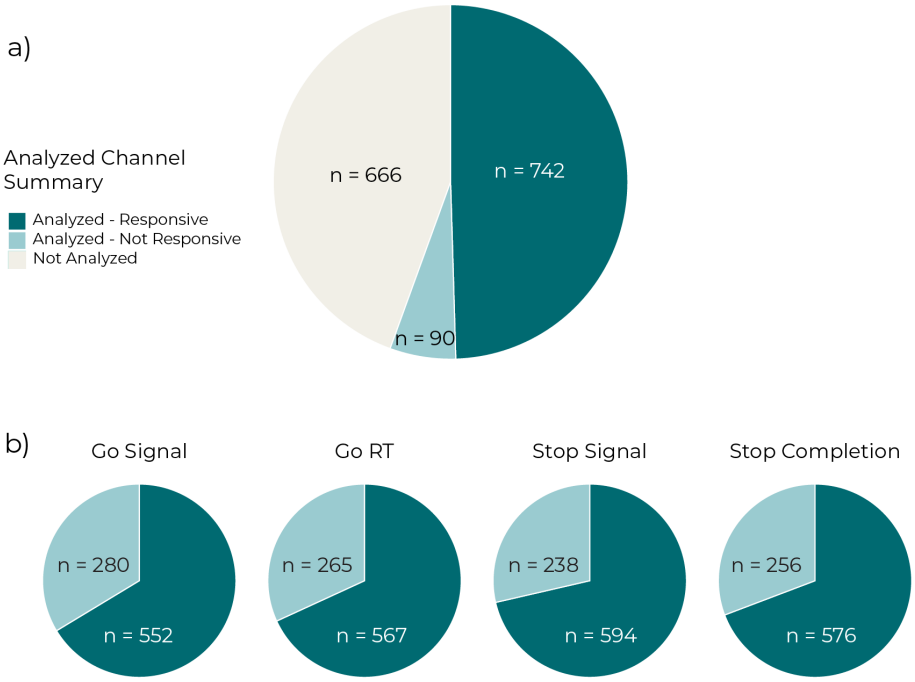

Figure 26. Summary of channel analysis. A) Proportion of all responsive channels. Of 1492 channels implanted across 12 subjects, 832 were analyzed and 742 were responsive to at least 1 of the 4 events of interest in the theta or beta frequency bands. B) Proportion of analyzed channels responding to each event of interest. 66.35% of analyzed channels responded to the go signal (in theta, beta, or both), 68.15% responded to goRT, 71.39% responded to the stop signal, and 69.23% responded to stop completion.

Stop Signal – Signal-Responsive

For channels responding to the stop signal on planned stop trials in the beta frequency band, we did not find any significant differences between the probability of early responses (m =

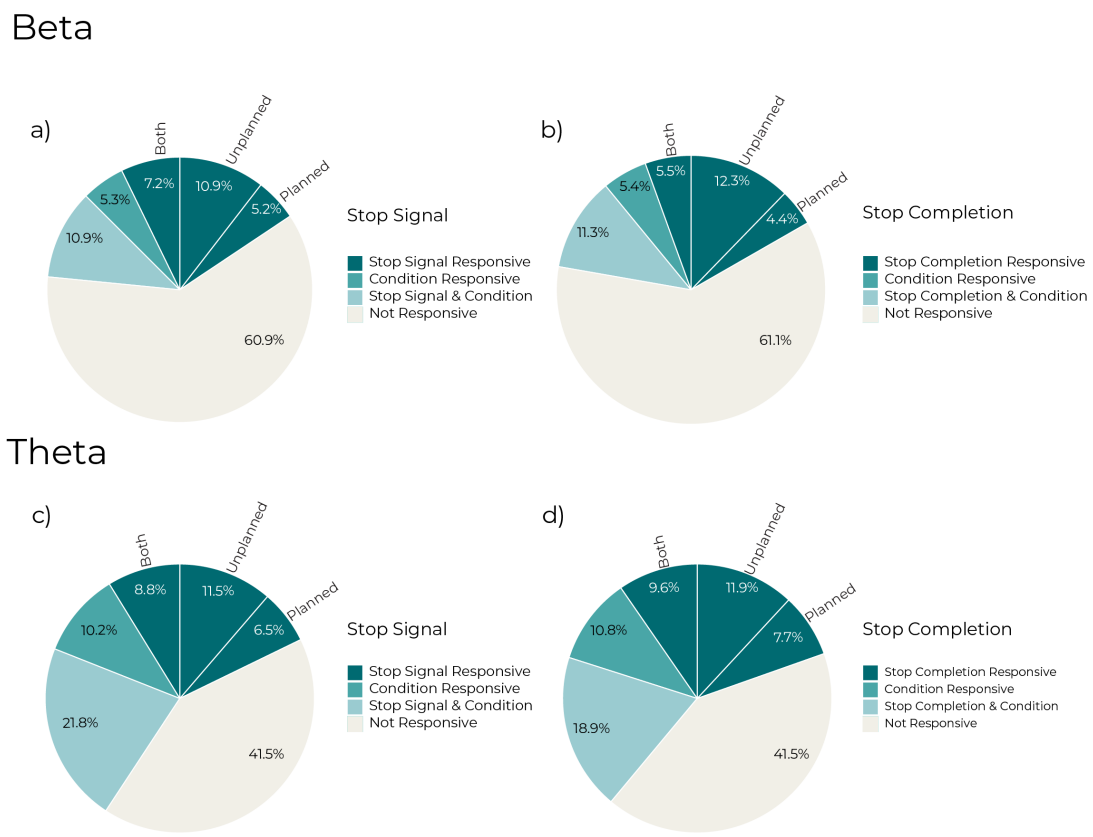

Figure 27. Breakdown of stop signal and stop completion responsive channels. (a) Stop Signal – Beta. 60.9% of channels did not exhibit a significant response to the stop signal in the beta frequency range. 5.2% responded exclusively to planned stop trials, 10.9% responded exclusively to unplanned stop trials, 7.2% responded to both planned and unplanned stop trials. 5.3% responded only to the context difference and 10.9% were both signal and context responsive. B) Stop Completion – Beta. 61.1% of channels did not exhibit a significant response to stop completion in the beta frequency range. 4.4% were exclusively behavior-responsive for planned stop trials, 12.3% were behavior-responsive for unplanned stop trials, and 5.5% responded to both planned and unplanned stop trials. 5.4% of channels were context-responsive and 11.3% were both behavior- and context-responsive. C) Stop signal – Theta. 41.5% of analyzed channels did not respond in the theta band to the stop signal. 6.5% were signal-responsive exclusively for planned stop trials, 11.5% were responsive for unplanned stop trials, and 8.8% responded to both planned and unplanned trials. 10.2% of channels were context-responsive and 21.8% were both behavior- and context-responsive. D) Stop completion – Theta. 41.5% of channels did not respond to stop completion in the theta band. 7.7% of channels exclusively responded to planned stop trials, 11.9% responded to unplanned stop trials, and 9.6% responded to both planned and unplanned stop trials. 10.8% of channels were context-responsive and 18.9% responded to both behavior and context.

47.86, sd = 28.74) and late responses (m = 40.1, sd = 31.94; p =.662). Similarly, we did not find a early (m = 52.07, sd = 26.66) and late (m = 32.2, sd = 23.71) responses for unplanned stop trials. Additionally, we did not find a difference between planned and unplanned trials in early responses (p=.655) or late responses (p=.414).

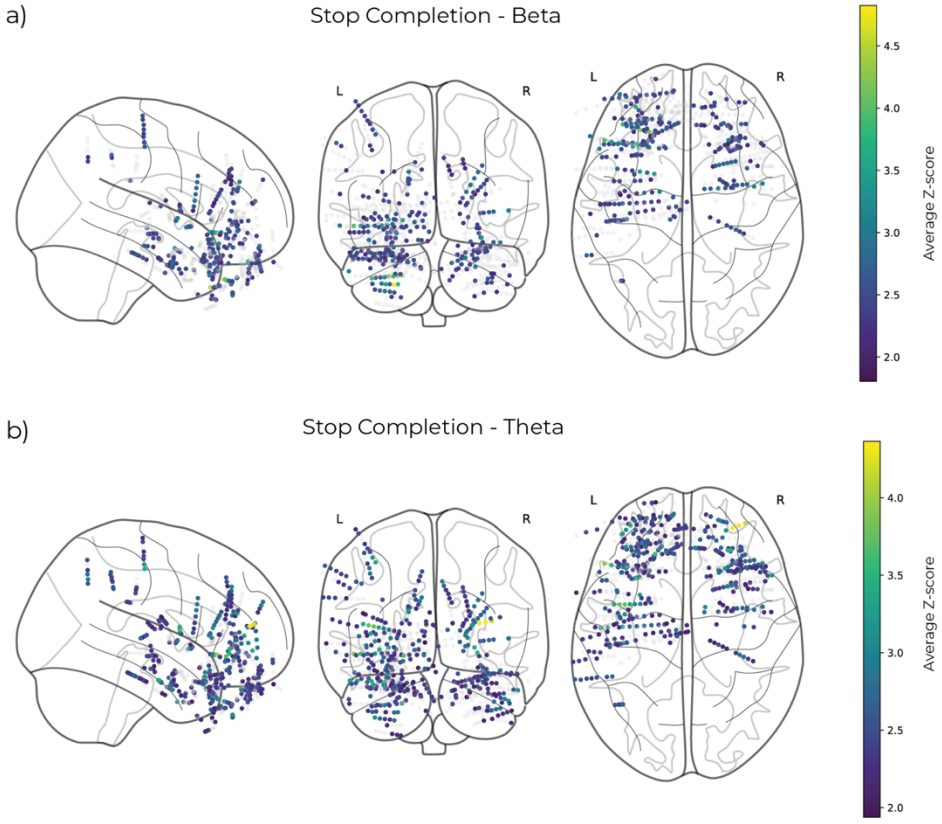

Figure 28. Depiction of locations of channels responding to stop completion. A) Channels responsive to stop completion in the beta frequency range. Color indicates average z-score for each channel. B) Channels responsive to stop completion in the theta frequency range. Color indicates average z-score for each channel.

Channels that responded in the theta range to the stop signal on planned stop trials were significantly more likely to respond before the stop signal (m = 64.98, sd = 19.29) than after the stop signal (m = 20.45, sd = 17.91); t(11) = 4.42, p = .001, d = 1.28, ci = [.49,2.03]. Channels

that responded to unplanned stop trials were also significantly more likely to respond prior to the stop signal (m = 62.65, sd = 18.52) than after (m = 16.79, sd = 17.1); (t(11) = 4.65, p <.001,d = 1.34, ci = [0.54,2.12]. There were no significant differences between planned and unplanned trials with respect to early responses (p = .71) or late responses (p = .57).

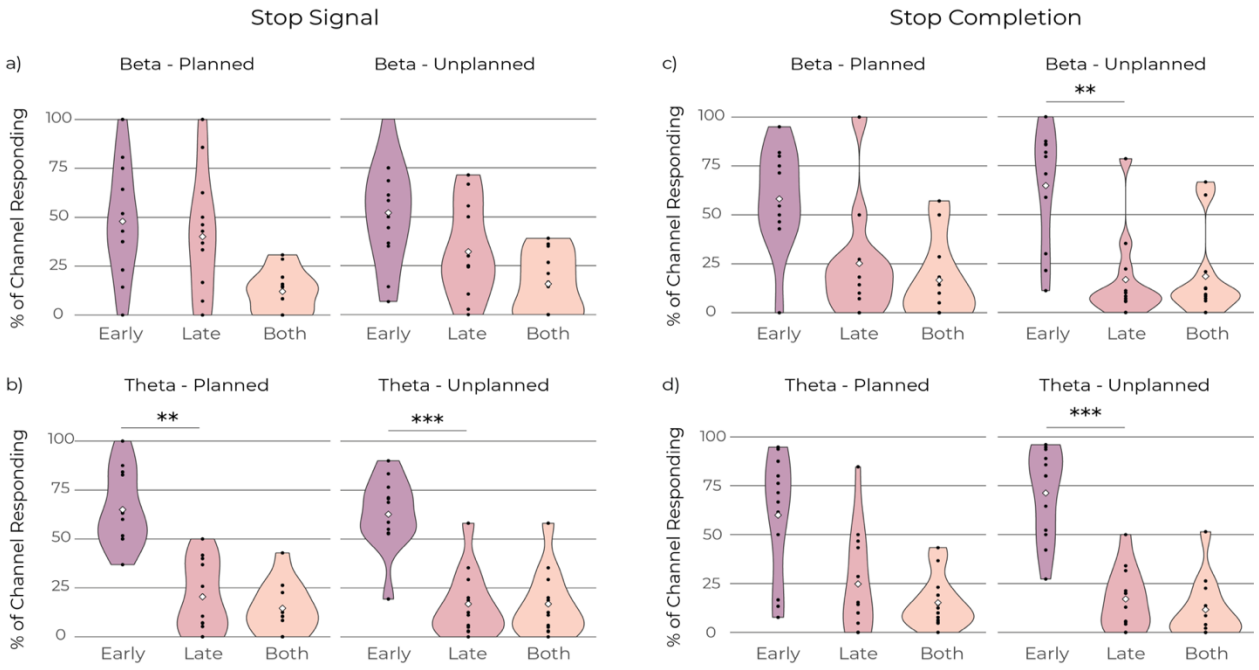

Figure 29. Beta and theta response timing with respect to stop signal presentation and stop completion for planned and unplanned stop trials. a) Beta response timing with respect to stop signal presentation for planned and unplanned stop trials. b) Theta response timing with respect to stop signal presentation for planned and unplanned stop trials. Early responses are significantly more likely than late responses on both planned (p = .001) and unplanned trials (p < .001). Early theta responses to the difference between trial types for stop completion are significantly more likely to occur in the theta band than beta band (p = .002). Responses occurring both before and after stop completion are significantly more likely to occur in the beta band than in the theta band (p < .001). c) Beta response timing with respect to stop completion for planned and unplanned stop trials. Responses occurring before stop completion are significantly more likely than those occurring after stop completion for unplanned stop trials (p = 008) but not for planned stop trials. d) Theta response timing with respect to stop completion for planned and unplanned stop trials. Responses occurring before stop completion are significantly more likely than those occurring after stop completion for unplanned stop trials (p < .001) but not for planned stop trials. *=p<.05; **=p<.01;***=p<.001

Stop Completion – Behavior-Responsive

Analysis of channels responding in the beta range to stop completion on planned stop trials, did not reveal any significant differences between the probability of early responses (m = 58.18, sd = 26.31) and late responses (m = 25.17, sd = 28.65; p =.058). We did, however, find a difference between early (m = 64.82, sd = 30.34) and late (m = 16.8, sd = 22.88) responses for unplanned stop trials. There were no significant differences

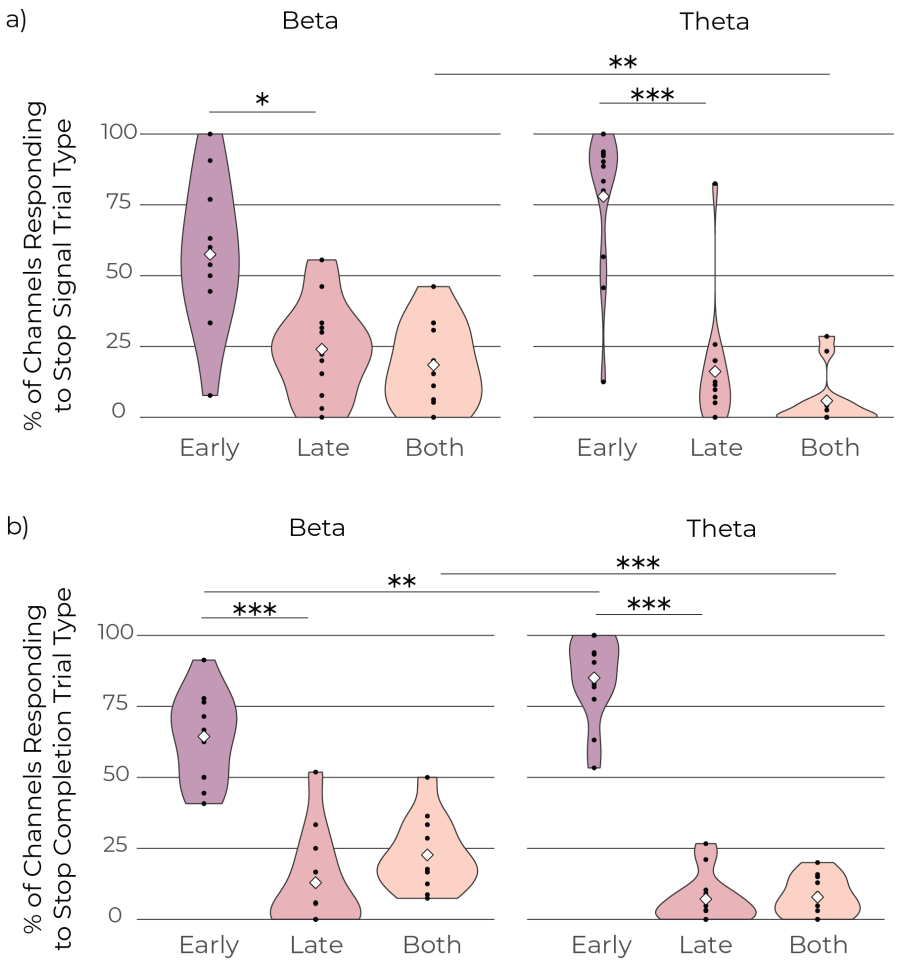

Figure 30. Beta and theta trial type response timing with respect to stop signal presentation and stop completion context-differences. a). Beta and theta response timing with respect to stop signal presentation. Channels responding in the beta frequency range to the context-difference are significantly more likely to occur prior to stop signal presentation than after (p = .017). Theta responses are also significantly more likely to occur prior to the stop signal than after (p < .001). Responses occurring both before and after the stop signal are significantly more likely to occur in the beta frequency range than in theta (p = .006). b) Beta and theta response timing with respect to stop completion. Early responses are significantly more likely than late responses in both the beta (p < .001) and theta (p < .001) frequency ranges. Early theta responses to the context-difference for stop completion are significantly more likely to occur in the theta band than beta band (p = .002). Responses occurring both before and after stop completion are significantly more likely to occur in the beta band than in the theta band (p < .001). * =p<. 05; **= <.01;***= p<.001

between planned and unplanned trials in early responses (p=.606) or late responses (p=.199).

Lastly, channels that responded in the theta band to stop completion on planned stop trials did not show a difference in response time category (m early = 59.96, sd = 31.38; m late = 24.8, sd = 26.48; p = .054). Responses on unplanned stop trials, however, were significantly more likely to occur before stop completion (m = 71.26, sd = 23.31), than after (m = 17.09, sd = 15.53); t(11) = 5.15, p <.001, d = 1.5, ci = [.64,2.3]. We did not find a difference between planned and unplanned stop trials in probability of early responses (p = .183) or late responses (p = .292).

Stop Signal – Context-Responsive

These analyses were repeated for context-responsive channels and results are shown in **Figure 30**.

Analysis of channels that were context-responsive with respect to the stop signal in the beta frequency range were significantly more likely to respond before the stop signal (m = 57.52, sd = 26.26) than after (m = 24.01, sd = 16.62); (11) = 2.81, p = .017, d = .81, ci = [.14, 1.45]. Similarly, channels that responded in the theta range were also significantly more like to respond prior to stop signal presentation (m = 77.99, sd = 26.5) than after (m = 16.18, sd = 22.53); t(11) = 4.44, p <.001, d = 1.28, ci = [.49, 2.04].

Stop Completion – Context-Responsive

Analysis of channels that were context-responsive with respect to stop completion in the beta frequency range were significantly more likely to respond before stop completion (m = 64.4, sd = 15.55) than after (m = 24.01, sd = 16.62); t(11) = 2.81, p = .017, d = .81, ci = [.14, 1.45].

Analysis of channels that were context-responsive with respect to stop completion in the theta frequency range were also significantly more likely to respond before stop completion (m = 85.02, sd = 14.79) than after (m = 7.14, sd = 8.69); t(11) = 11.58, p <.001, d=3.34, ci = [1.85, 4.82].

Comparing Theta and Beta

To better explore the functional role beta and theta frequency activity plays in the stopping process, we compared the channel response timing for context-responsive channel with respect to the stop signal and stop completion (**fig. 30**). In comparing response timing for stop signal context-responsive channels, we found that channels with a beta frequency response were significantly more likely to respond both before and after the stop signal (m = 18.47, sd = 14.88) than channels with a theta response (m = 5.82, sd = 9.73); t(11) = -3.44, p = .006, d = -.99, ci = [-1.68,-0.28]. We did not find significant differences in probability of early (p = .072) or late (p = .348) responses between the two frequency bands.

Our comparison of beta and theta response timing for context-responsive channels with respect to stop completion revealed that early responses were significantly more likely in the theta frequency band than beta: t(11) = 4.03, p = .002, d = 1.16, ci = [.41,1.89]. Similar to the stop signal comparison, we found that responding both before and after stop completion occurred more often for beta responsive channels (m = 22.69, sd = 12.48) than theta (m = 7.85, sd = 6.8); t(11) = -4.94, p <.001, d = -1.43, ci = [-2.23, -.6].

Lastly, we compared response timing for theta and beta responsive channels with respect to stop signal presentation for planned and unplanned stop trials (**fig. 31**). When examining planned stop trials, we found significantly greater percentage of early-response channels for theta

than for beta: t(11) = -2.56, p = .027, d=-.739, ci = [-1.37,-0.08]. Additionally, we found that beta-responsive channels were significantly more likely to respond after the stop signal than theta-responsive channels: t(11) = 2.29, p = .043, d = .661, ci = [.021, 1.28].

Discussion

Existing literature strongly suggests the involvement of beta and theta frequency activity as critical mechanisms of inhibitory control. Though previous work has unlocked a wealth of information through use of standard motor inhibition paradigms, like the stop signal task, limitations inherent in the task design left open questions regarding the timing of beta and theta oscillations with respect to suppression of motor output. Here, we sought to begin resolving these questions by employing a novel stop signal paradigm in conjunction with stereo EEG (sEEG). sEEG is an especially beneficial methodology for our purposes given that it provides excellent spatial and temporal resolution and provides a broad sampling of both cortical and subcortical structures. Additionally, by employing a task that permits direct observation of movement

termination, our approach significantly reduces the temporal ambiguity inherent to traditional SST paradigms (Schultz, Denning, et al., 2023), enabling clearer identification of beta and theta oscillatory mechanisms related to distinct inhibitory processes.

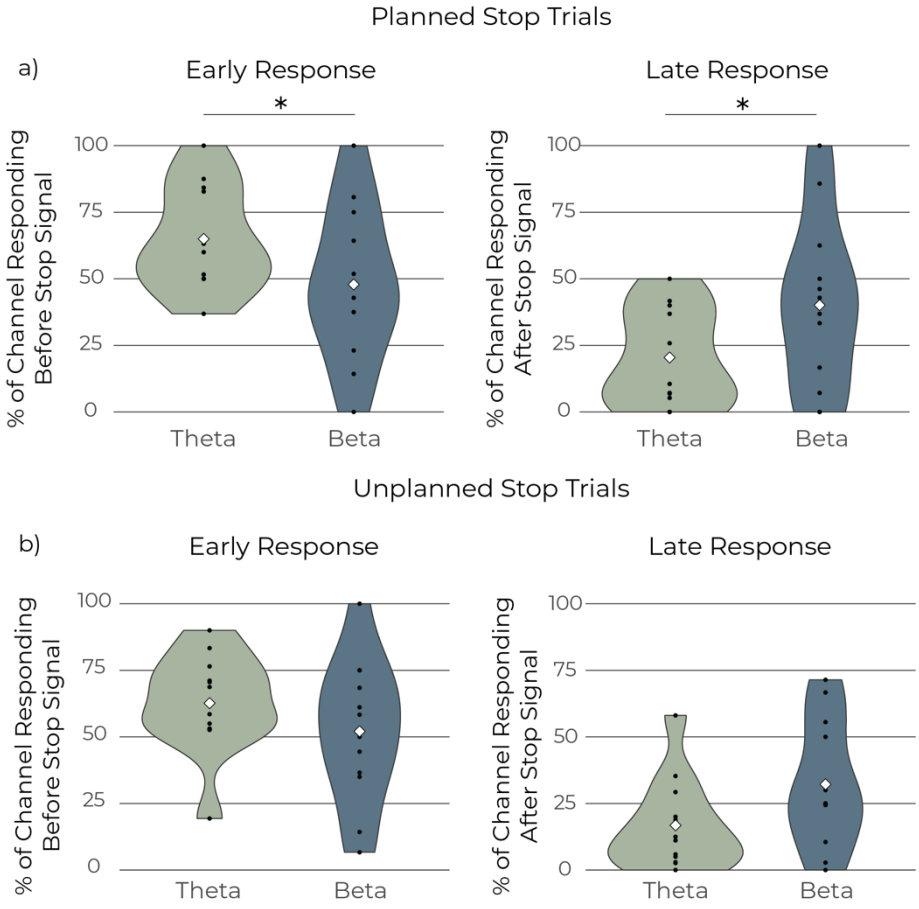

Figure 31. Comparing beta and theta response timing with respect to stop signal presentation for planned and unplanned stop trials. a) Response timing before and after stop signal presentation for planned stop trials. Theta exhibited significantly more early responses than beta ($p = .027$). Beta exhibited significantly more late responses than theta ($p = .043$) b) Response timing before and after stop signal presentation for unplanned stop trials. * =p<.05; **=p<.01; ***=p<.001

Our examination of behavioral outcomes revealed that participants stopped significantly faster on planned stop compared to unplanned stop trials, in line with previous research (Schultz, Denning, et al., 2023; Schultz, Mantell, et al., 2023). Additionally, we found that stop completion times were significantly more variable for planned compared to unplanned stop trials, which has also been previously observed (Schultz, Denning, et al., 2023; Schultz, Mantell, et al., 2023). The increased variability in stop completion times on planned stop trials may reflect participants'

strategic adjustments and varying levels of motor readiness influenced by anticipatory cognitive processes (Aron, 2011).

Analysis of the electrophysiological data revealed a response rate of 89.2% of the examined channels, suggesting that the task robustly engaged a variety of electrodes that were distributed throughout many regions of the brain. A more detailed assessment of the response properties of the analyzed electrodes revealed that 66.35% responded to the go signal, 68.15% responded to goRT, 71.39% responded to the stop signal (including context-responsive channels), and 69.23% responded to SCT (also including context-responsive channels). Additionally, our finding that some channels responded specifically to the context difference (i.e. differences between the predictability of the stop signal on planned and unplanned stop trials) highlights the distinct anticipatory and reactive processes elicited by the task.

Next, we evaluated the timing of beta and theta responses with respect to the stop signal and SCT. Overall, we found that beta and theta exhibited responses both before and after each event. This observation of both pre- and post-event neural responses could reflect distinct preparatory and reactive phases within inhibitory control mechanisms, potentially suggesting separate networks or processing stages within the inhibitory pathway (Wessel & Aron, 2017). Moreover, our observation of beta and theta responses prior to stop completion suggests that each band could play a causal role in motor termination as has been previously suggested (Cavanagh & Frank, 2014; Wessel & Anderson, 2024)

Though we observed responses before and after each event for both frequency bands, the probability of when a response would occur varied across trial types and frequencies, providing important information about potential functions of each frequency band. For example, we found

that beta responses on unplanned stop trials were significantly more likely to occur before stop completion than after. However, this difference was not significant for planned stop trials. It is possible that this distinction reflects motor termination mechanisms that are employed for unplanned stop trials that may differ from those employed for planned stop trials. This possibility is supported by the analysis of the context-responsive channels which demonstrated a preference for responding prior to stop completion compared to after (**fig. 30**). Though additional research will be necessary to determine the accuracy of this interpretation, this finding provides some support to the current model of inhibitory control which suggests that planned and unplanned stopping may be carried out by anatomically and functionally distinct pathways (Meyer & Bucci, 2016).

Exploration of response timing for the theta frequency band revealed an overall preference for responding prior to the event being examined. For example, theta was significantly more likely to exhibit a response prior to the stop signal for both planned and unplanned stop trials. This pattern held when examining context-responsive channels, revealing that theta responses were significantly more common prior to the stop signal. This observation could reflect a previously described monitoring function of theta (Cavanagh et al., 2012). If theta activity serves to monitor task progress and predict when the stop signal will be presented, we would expect to see theta activity prior to the stop signal. Additionally, we would expect that this activity might differ when the stop signal is predictable compared to when it is random (as seen in the context-responsive channels). Theta activity was also observed more often before SCT than after. This could reflect a functional role in motor termination as has been previously suggested (Cavanagh & Frank, 2014), however additional research will be needed to parse this potential function of theta from its purported role in monitoring task demands.

When comparing beta and theta responses, we found that theta is significantly more likely to respond prior to the stop signal than beta and that beta is more likely to respond after the stop signal than theta on planned stop trials. This suggests that theta may play more of a role in monitoring the countdown and anticipating presentation of the stop signal while beta may play more of a role in actively suppressing or updating motor commands, as previously suggested (Swann et al., 2009; Wessel, 2020). These differences, however, were not present when examining unplanned stop trials, possibly indicating a functional difference between trial types.

Limitations and Future Research

As previously mentioned, though sEEG offers exquisite spatial and temporal resolution it is not without limitations. Most notably, SEEG is exclusively conducted in patients with medically refractory epilepsy, potentially limiting the generalizability of findings to healthy populations (Kahane et al., 2003; Gonzalez-Martinez et al., 2014). Nevertheless, because patients undergoing neurosurgical monitoring often maintain otherwise healthy, high-functioning lifestyles post-surgery, it is reasonable to assume that neural abnormalities are typically focal, and activity recorded from non-pathological regions may closely resemble that of healthy brains (Parvizi & Kastner, 2018; Jobst et al., 2020). Additionally, electrode coverage is inherently sparse and patient-specific, as placements are restricted to clinically relevant regions for seizure localization (Rosenow & Lüders, 2001). Furthermore, the use of analgesic medications during neurosurgical monitoring could induce fatigue or impact task performance.

Despite these limitations, the present experiment represents a valuable addition to the current literature concerning mechanisms of inhibitory control. Specifically, we were able to characterize the timing of beta and theta activity with respect to the stop signal and the time of

actual motor arrest – an achievement that has not been accessible with the standard motor inhibition paradigms. Moreover, the SEEG methodology enabled us to record task-related oscillatory activity across diverse cortical and subcortical regions typically inaccessible by non-invasive or less invasive approaches. However, additional work is needed to better characterize the findings presented here and to further elucidate the functional significance of beta and theta activity. Currently, we are endeavoring to identify the precise anatomical location of each electrode (which will be completed prior to publication). This will allow us to identify region specific contributions of the electrophysiological signals observed during the task, which facilitate establishing neural substrates critical for response inhibition. Furthermore, we plan to directly compare neurophysiological signals associated with the CMST (presented here) with those associated with the stop signal task. This comparison will help ascertain physiological similarities between the two tasks and may help rectify the absence of a behavioral correlation previously observed (Schultz, Denning, et al., 2023).

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CHAPTER 6:

SUMMARY AND CONCLUSIONS

Summary Of Chapters

Chapter 1

Previous work has yielded substantial insight into mechanisms underlying inhibitory control. However, limitations in the design of the standard paradigms typically used to probe these mechanisms have left several important aspects of inhibitory control unexplored. Most notably, the timing of oscillatory activity with respect to cognitive and motoric component of inhibition is as yet unresolved. Parsing the physiological signatures associated with each component is an important step toward a comprehensive understanding of inhibitory control mechanisms and, given the apparent role of inhibitory control in a variety of neurological and psychiatric disorders, an important contribution to the wider field of neuroscience.

To address this critical gap in the literature and to resolve additional outstanding questions such as the generalizability of stopping an incipient movement and mechanisms underlying planned suppression of motor output, I created the continuous movement stop task (CMST). This task (1) balances motor elements of the task so that cognitive aspects can be more precisely examined; (2) provides a direct measure of stopping on every trial, allowing for greater temporal precision of inhibition-related spectral activity; and (3) requires termination of a continuous movement, promoting generalizability. Throughout this thesis, I engaged in an in-depth exploration of this new task and the electrophysiological correlates of task behavior in health subjects (behavior) and patient populations (behavior and electrophysiology).

Chapter 2

In Chapter 2, I validated the CMST and explored the wealth of behavioral outcome measures it provides. Critically, I found a behavioral distinction between trial types, with the time required to stop a movement (Stop Completion Time or SCT) being faster for planned compared to unplanned stop trials. This finding suggests that people are engaging different inhibitory strategies to facilitate stopping in these different contexts, in line with the context effect hypothesis. This hypothesis predicts strategic changes in motor programs for identical movements to optimize movement for the context in which it occurs (Mirabella et al., 2008). Context effects have been observed as an increase in response time on trials in which a stop signal may be presented compared to response time on simple go trials (Mirabella, 2020; Mirabella et al., 2008, 2019). In other words, people appear to be engaging proactive inhibitory mechanisms in the context in which they are preparing to withhold a movement.

These data also revealed that the variability of stop initiation and stop completion was greater for planned than unplanned stop trials. It is possible that this difference in SCT variability between trial types is driven by the inhibitory processes underlying unplanned motor termination being more stereotyped than those underlying planned motor termination. Additionally, the finding that stop initiation time was more variable for planned than unplanned stop trials could be interpreted as reflecting aspects of motor planning similar to those observed in previous work showing that reaction time variability during a go/no-go task was greater when go-signal onset was predictable than when it was not predictable (Wodka et al., 2009).

In this chapter, I also explored the relationship between task performance on the CMST to that on the SST. This comparison did not find any significant correlations, suggesting that there may be important differences between termination of a prepared, discrete movement and

termination of an ongoing movement. This possibility is currently being explored in more depth by comparing task performance and invasive electrophysiology between the CMST and SST in epilepsy patients.

Chapter 3

In Chapter 3, I further validated the CMST by evaluating behavioral outcomes in a population previously observed to exhibit inhibitory control deficits – people with a nicotine addiction. This experiment revealed diminished inhibitory control in this population as evidenced by the increased time required to stop a movement compared to controls. This suggests that, although it is possible that there are important differences between the SST and the CMST (as the experiment in Chapter 2 illustrates), the mechanisms involved in stopping a continuous movement are disrupted in a similar fashion to those involved in stopping a ballistic movement in this population.

Additionally, this experiment replicated the finding that variability in SCT is greater for planned than for unplanned trials seen in Chapter 2. This provides further support for the hypothesis that reactive inhibitory control mechanisms may be more stereotyped than those underlying proactive control. I also found greater variability in SCT for planned stop trials in smokers compared to non-smokers, suggesting that proactive inhibitory mechanisms may be differentially affected by nicotine addiction – a possibility which should be explored in future research. Overall, this experiment provided further support for the efficacy of the CMST and illuminated additional avenues for future inquiry.

Collectively, Chapters 2 and 3 provided the necessary foundation for continued exploration of inhibitory control mechanisms using the CMST. In the final two chapters, I explored electrophysiological mechanisms associated with CMST task performance.

Chapter 4

In Chapter 4, we employed the CMST to explore the possibility of separable stopping mechanisms that could be differentially impacted by dopaminergic medication. We examined behavioral outcomes, explored oscillatory dynamics in the beta and theta frequency ranges, and evaluated the influence of medication on variability of average power across both frequency ranges.

In line with observations detailed in Chapters 2 and 3 (Schultz, Denning, et al., 2023; Schultz, Mantell, et al., 2023), we found that participants with PD stopped significantly slower on unplanned stop trials compared to planned. This behavioral outcome was not, however, significantly modulated by dopaminergic medication. Though this result may reflect a true lack of effect of medication on behavior, it is also possible that this experiment was underpowered to observe effects that were indeed present. Additionally, for this experiment, we chose to include 50% unplanned stop trials to reduce the total number of trials patients were asked to complete. Given that participants were asked to complete the task twice in one session (once off medication and once on medication), we aimed to reduce the total time they were required to be participate the experiment by as much as possible while retaining enough trials for each condition. However, it is possible that an equal probability of a planned or unplanned stop on every trial may have diminished the prepotency of the movement continuation, since a stop prior to the end of the countdown may have been anticipated. Future research will explore this possibility by reducing the percentage of unplanned stop trials.

In contrast to previous research showing a medication-induced modulation of beta power (Cao et al., 2020; Chung et al., 2018; George et al., 2013), our results did not indicate that task-related beta power was meaningfully influenced by administration of l-dopa. We did observe a few, brief, statistically different periods of beta power in the midline ROI around the time of the go signal and goRT. However, given the brevity of these epochs, I cannot confidently assert that these did not occur simply by chance.

Similarly, medication did not appear to meaningfully influence variability of beta power. We did find moderate evidence ($BF_{10} = 4.32$) for a difference in variability in the midfrontal ROI aligned to goRT when participants were on compared to off medication. However, this finding does not provide compelling evidence that dopaminergic medication meaningfully modulates beta power variability. Previous work suggests that an important component of PD pathology is excessive synchrony of beta frequency activity (Hammond et al., 2007) and that the efficacy of medication may be due to its mitigating effects on this pathological synchronization (Hammond et al., 2007). If this is the case, one might expect that dynamic changes in beta power would be constrained when off medication and that this constraint would be reduced or abolished when on medication, resulting in greater variability when on compared to off medication. Our data, however, do not support this possibility. Importantly, given the limitations described in Chapter 4, we do not assert that we have provided evidence against this hypothesis.

Finally, we found limited evidence that beta dynamics were affected by differences in the cognitive demands associated with each trial type. Theoretically, unplanned stop trials should create greater cognitive demands around the time of the stop signal than planned stop trials. This is because the presentation of stop signal is unanticipated on these trials, requiring participants to reactively respond to the change in environmental demands. Given this difference, we expected

to see greater prefrontal beta power on unplanned compared to planned stop trials after stop signal presentation (Muralidharan et al., 2019; Wagner et al., 2018). Though we did not find evidence to support this distinction in the prefrontal ROI, we did observe moderate differences in beta power between trial types in the midfrontal ROI. It is possible that, due to volume conduction, beta activity observed in the midline ROI actually originated in prefrontal sources, but this is not a conclusion we are able to draw presently. Future research will be need to better characterize the source and function of the beta differences observed here.

One important observation this experiment yielded is the timing of beta with respect to movement termination. Given the consistent association between beta activity and response inhibition, it is generally assumed that beta power increases are causally related to stopping (Schmidt et al., 2019). If this is accurate, we would expect to see beta increases prior to stop completion time. However, the beta power increases we observed occurred after stopping, suggesting that increases in beta power could not have played a causal role in motor termination. However, it is possible that increases in beta power prior to movement termination were present but were sufficiently small (or sufficiently deep) so as to not be readily detectable. Furthermore, these signals could have been obscured by larger amplitude post-movement beta increases thought to be generated by sensorimotor cortex (Barone & Rossiter, 2021).

The analysis of theta frequency activity presented in this chapter suggests that theta is meaningfully modulated by administration of dopaminergic medication. For example, we found several epochs in which theta power over right frontal cortex was greater when participants were off medication compared to when they were on medication. These differences were most prominent around the time of goRT and stop signal presentation but were also present at the time of stop completion. Previous work has shown an effect of dopaminergic medication on

midfrontal theta activity (Parker et al., 2015; Singh et al., 2018), however, to my knowledge, this represents the first example of a medication-induced modulation of right prefrontal theta. Though midfrontal theta power did not appear to be as substantially modulated by l-dopa in this experiment, we did find greater theta power at the time of stop completion in the midfrontal ROI when participants were off medication compared to on. Specifically, we observed a brief period immediately before stop completion at which theta power transiently, but noticeably, increased when participants were off medication that was not present when they were on medication. This difference could reflect a compensatory mechanism that is required when off medication but not when on. That is, if theta functions to coordinate disparate neural populations to implement control, it may be the case that an increase in theta power is required to overcome the pathological hypersynchrony that is a characteristic of PD and that this need is abolished when dopaminergic medication reduces the pathological synchronization. The presence of a compensatory mechanism of this nature could help explain the absence of behavioral differences we observed between medication states. Further investigation of this possibility may yield important information regarding the role of midfrontal theta in the termination of motor output.

Finally, we found that variability of theta power was meaningfully modulated by administration of l-dopa. This effect was present in all three ROIs but was consistent across all events (Go signal, goRT, Stop signal, & SCT) in the midfrontal ROI. It is possible that this increase in theta power variability when participants were on medication reflects part of the therapeutic effect of dopaminergic medication. That is, if dynamic changes in theta power (as opposed to the relative presence or absence of theta) are important for its ability to effectively implement cognitive control, then diminishing the range of theta power would reduce its efficacy, possibly contributing some of the symptoms associate with PD. Increasing the range of

dynamic theta changes via l-dopa, then, would improve these symptoms. Additional research is needed to address this possibility.

Overall, we did not find compelling support for our hypothesis that beta power in right frontal and sensorimotor areas would be modulated by trial type or medication status. We did, however, observe that increases in beta power appeared to be too late to play a causal role in movement termination. Theta power, on the other hand, does appear to be meaningfully modulated by dopaminergic medication as evidence by significant differences between power over right prefrontal cortex when on compare to off medication and significant differences in variability (most prominently in the midfrontal region). We did not find differences in theta power between trial types. However, given the limitations previously described in Chapter 4, further inquiry is required to better elucidate the association of these frequency bands with the cognitive and motoric elements of the task.

Chapter 5

In chapter 5, we explored the electrophysiological correlates of task behavior using the superior temporal and spatial resolution of intracranial EEG (sEEG). sEEG offers a unique opportunity to evaluate task-related oscillatory activity occurring in a variety of cortical and subcortical areas. Additionally, because signals are being recorded directly from the brain, sEEG has a superior signal-to-noise ratio compared to that of scalp EEG.

Analysis of behavior was in line with that observed in the previous three chapters with participants requiring more time to stop on unplanned compared to planned stop trials. Additionally, we found that stop completion time (SCT) was more variable for planned than for

unplanned trials, as observed in previous experiments (Schultz, Denning, et al., 2023; Schultz, Mantell, et al., 2023).

Evaluation of the electrophysiology revealed considerable engagement of a broad sample of neural populations with 89.2% of electrodes responding to at least one component of the task (Go signal, goRT, Stop signal, and SCT). We also were able to identify channels that responded exclusively to the distinction between planned and unplanned stop trials (termed 'context-responsive'), supporting our assertion that behavioral differences between planned and unplanned stop trials are the consequence of separable mechanisms facilitating stopping in each context.

Our primary analyses involved examining the timing of beta and theta responses (defined as a significant change from baseline) with respect to the onset of the stop signal and the completion of movement termination (stop completion time or SCT). One critical outcome of these analysis is our observation of beta responses occurring prior to SCT, which suggests that beta frequency activity could play a causal role in movement termination as suspected. Additionally, we found that theta activity also preceded SCT, supporting the assertion that theta could play a causal role in the termination of motor output as well (Cavanagh & Frank, 2014).

Further exploration of the timing of beta and theta responses yielded additional critical insights regarding possible functional roles of oscillatory activity in each frequency band. For example, we found that beta responses on unplanned stop trials were significantly more likely to occur before stop completion than after. However, this difference was not significant for planned stop trials, possibly reflecting a distinction between motor termination mechanisms that are employed for unplanned stop trials and those employed for planned stop trials. This possibility is supported by the analysis of the context-responsive electrodes, which demonstrated a preference

for responding prior to stop completion compared to after. This finding provides some support to the current model of inhibitory control which suggests that planned and unplanned stopping may be carried out by anatomically and functionally distinct pathways (Meyer & Bucci, n.d.).

Our investigation of response timing for the theta frequency band demonstrated a general preference for responding prior to the event being examined. For example, theta was significantly more likely to exhibit a response prior to the stop signal for both planned and unplanned stop trials – a pattern which held when examining context-responsive channels. This observation could reflect a previously described monitoring function of theta (Cavanagh et al., 2012). That is, if theta activity serves to monitor task progress and predict when the stop signal will be presented, we would expect to see theta activity prior to the stop signal. Additionally, we would expect that this activity might differ when the stop signal is predictable compared to when it is random (as seen in the context-responsive channels). However, further research will be necessary to better parse the potential functional roles of theta oscillations.

To better understand the relative contributions of theta and beta activity to each part of the stopping process (signal detection and motor termination), we compared the timing of activity in the two frequency bands with respect to stop signal presentation. We found that theta is significantly more likely to respond prior to the stop signal than beta and that beta is more likely to respond after the stop signal than theta on planned stop trials. This supports our interpretation that theta plays more of a role in monitoring the countdown and anticipating presentation of the stop signal while beta may play more of a role in responding to the stop signal.

In summary, we found that oscillatory activity in both theta and beta bands are strongly associated with both signal detection and motor termination processes. Activity in both

frequency bands occurs early enough to potentially play a causal role in motor termination and both occur early enough to be involved in the cognitive component. However, given that theta more commonly occurs before presentation of the stop signal than beta, theta may be more involved in anticipatory/predictive processes than beta.

Conclusions

Overall, this thesis represents a unique attempt to resolve existing questions concerning the cognitive and motoric mechanisms of inhibitory control. Previous work has established oscillatory activity in the theta and beta frequency ranges as important signatures of inhibitory processes, but limitations inherent in the design of standard motor inhibition tasks left ambiguities surrounding the timing of this oscillatory activity with respect to the different processes involved in motor inhibition. Specifically, it is unclear how beta and theta activity relate to the cognitive and motoric components of inhibitory control. Here, we employed the CMST – a novel motor inhibition task that provides an unambiguous measure of motor termination on every trial. Use of this task in combination with neuroscientific methodologies allowed us to begin unraveling neural mechanisms underlying inhibitory control and offered an opportunity to assess the previously assumed generalizability of the predominant inhibitory control paradigms.

Generalizability of Standard Motor Inhibition Tasks

Our current understanding of inhibitory control is based largely on studies which employed standard motor inhibition tasks such as the stop signal task (SST) and the Go/No-Go task. Though the efficacy of these tasks for elucidating mechanisms underlying inhibitory control is unquestionable, it has long been assumed that mechanisms elicited by these tasks are the same

as those we employ in our daily lives (Wessel & Anderson, 2024). That is, it is assumed that the mechanisms employed to facilitate response suppression on the SST are the same as those employed to prevent you from stepping on a Lego. This assumption, however reasonable, has not yet been adequately vetted. Here, we directly compared the CMST to the SST. We also evaluated CMST task performance in a population previously observed to exhibit deficits in performance on the standard motor inhibition tasks. Our results demonstrate that, although there are likely important differences between the tasks – as evidenced in chapter 2 by the lack of correlation found between the outcome measures of the CMST and the SST – there is also evidently substantial overlap in the processes underlying performance of each task. This conclusion is supported in part by our observation of deficits in task performance on the CMST in a population of people with a nicotine addiction – who demonstrate diminished performance on the SST and Go/No-Go in previous research (Billieux et al., 2010; Galván et al., 2011). Furthermore, we identified oscillatory activity associated with stop signal detection and motor termination that has been consistently observed during the other standard inhibition paradigms. Though, additional research is needed to determine the extent of the similarities (and dissimilarities) between the cognitive and motoric mechanisms elicited by these tasks the work presented here supports the proposition that mechanisms of inhibitory control may be domain general (Wessel & Anderson, 2024).

Beta timing

Another important outstanding question is the functional role of beta band oscillations in motor termination. Beta frequency activity is strongly and consistently associated with response inhibition (Wessel & Anderson, 2024) and some research employing non-invasive brain stimulation techniques suggest it could play a causal role in the suppression of movement

(Pogosyan et al., 2009). However, the ability to precisely lock electrophysiological activity to the time of movement termination is critical to resolving this question. Here, we present two studies with apparently contradictory outcomes. In chapter 4, scalp EEG data revealed an increase in beta occurring after the time of stopping – suggesting that beta is not causally linked. Conversely, our sEEG data clearly show significant changes in beta activity before the time of stopping. However, it is possible that the prefrontal sources of beta activity hypothesized to implement suppression of motor output were too deep to be readily detectable with scalp EEG but were easily observable with sEEG. Future research is needed to better reconcile these two findings. For example, a scalp EEG study with sufficient electrode density to perform source localization may be an important next step. It may also be the case that scalp EEG is not an ideal methodology for detecting prefrontal sources of beta associated with initiating response inhibition and that future research may be better served using methodologies such as magnetoencephalography, which has demonstrated utility in identifying these sources of beta (Schaum et al., 2021).

Separating Cognitive and Motoric Components of Inhibition

Our primary aim was to parse the electrophysiological correlates of the cognitive and motoric components of the inhibitory control process. Toward this goal, we compared activity during planned and unplanned stop trials recorded with scalp EEG and sEEG. Because the stop signal was predictable on planned stop trials, participants were able to plan the termination of their movement (at least 1 second in advance) rather than stopping as a reaction to the stop signal. This effectively diminishes the cognitive component of stopping that occurs when participants must implement motor termination as a reaction to the stop signal. We hypothesized that this difference between planning to stop and reacting to a stop signal would elicit distinct

mechanisms. Again, our two electrophysiology studies seem to contradict each other. We did not find a distinction between planned and unplanned stop trials in our experiment presented in Chapter 4, but we found several channels that responded this difference in chapter 5. This discrepancy may again be explained by the depth at which we were able to record with sEEG. Additionally, our small sample size and the relatively higher signal-to-noise ratio of scalp EEG could also account for this difference.

Importantly, with respect to the sEEG data, it does appear that our trial type manipulation effectively elicits distinct neural processes around the time of stop signal presentation and stop completion. We found that both theta and beta appear to be involved in preparatory/ anticipatory activity – as evidenced by our observation of responses prior to the stop signal – and outcome monitoring/ updating processes – as evidenced by activity observed after stop completion. However, our results suggest that theta activity may be more heavily involved in predictive and anticipatory processes while beta might play a bigger role in implementation of motor termination processes and the subsequent updating of the motor set. Additional research is currently underway to more precisely localize the source of the observed activity and to more clearly parse the possible roles of stopping-related oscillatory dynamics.

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