Spatiotemporal correlates of cognitive control: proactive and reactive control of response inhibition and associations with resting state activity.

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General summary

Cognitive control refers to the ability to regulate thought and action in a goal-directed manner and is essential for optimal daily life functioning. Cognitive control can be partitioned into specific functions facilitating efficient control, such as working memory, set-shifting and response inhibition, as well as in the temporal domain into proactive and reactive control. While proactive control refers to the preparation in expectation of an upcoming interfering event, reactive control refers to the processes elicited by the interfering event itself. The preferred control strategy might vary between individuals and task settings. The neural mechanisms underlying reactive control have been investigated extensively over the last two decades, but how these mechanisms interact with proactive control is less known. The current thesis seeks to investigate these control processes by looking at the neural mechanisms underlying proactive and reactive control of response inhibition, a core sub-function of cognitive control. We focused specifically on activity in regions associated with reactive response inhibition, as well as frontal-midline theta (FM-theta) activity measured at the scalp. Further, as resting state activity has been associated with cognitive control performance, it was investigated whether resting state FM-theta activity was associated with proactive and reactive control.

First, we found that proactive control of response inhibition leads to increased activity in some, but not all, of the regions traditionally involved in reactive response inhibition. Importantly, activity within sub-regions of the right inferior frontal gyrus, a proposed core region of the response inhibition network, show functional specialization in response to proactive control. Second, we show that a proposed marker of cognitive control, FM-theta activity, is rather a multidimensional feature, associated with several processes related to the preparation to stop, preparation to respond, as well as reflecting control adjustments across a range of cognitive control tasks beyond mere conflict and novelty. Finally, we did not find evidence for a relationship between resting state theta and proactive or reactive control. However, resting state theta was associated with reaction times in a working memory task, indicating that resting state dynamics may still mediate cognitive control performance. These findings expand the current understanding of cognitive control and are in line with more integrative, domain-general approaches. Importantly, the results of the current thesis have implications for our understanding of cognitive control in both healthy and clinical populations.

List of papers

Paper I

Messel, M. S., Raud, L., Hoff, P. K., Skaftnes, C. S., & Huster, R. J. (2019). Strategy switches in proactive inhibitory control and their association with task-general and stopping-specific networks. *Neuropsychologia*, 135, 107220.

Paper II

Messel, M. S., Raud, L., Hoff, P. K., Stubberud, J., & Huster, R. J. (2021). Frontal-midline theta reflects different mechanisms associated with proactive and reactive control of inhibition. *NeuroImage*, 241, 118400.

Paper III

Messel, M. S., Hussain, S. J., Stubberud, J, Nordvik, J. E., & Huster, R. J. (In preparation). Theta at rest and on task: associations with cognitive control performance.

1. Introduction

Cognitive control refers to the ability to regulate thought and action in a goal directed manner (Braver, 2012), and is essential for optimal daily life functioning. Cognitive control of behavior allows us to interpret changes in our environment and to adapt our behavior accordingly, like the driver stopping the car when the traffic light turns red, or the store clerk suppressing the urge to snap at an angry costumer. Cognitive control is also involved in more long-term adaptations, such as planning a well-deserved holiday after your doctoral thesis has been submitted, or saving money in case you end up unemployed after the same thesis. Thus, definitions of cognitive control include both higher-level functions such as planning, judgement, problem-solving and reasoning, as well as lower-level functions such as control of attention, inhibition and set shifting.

The term cognitive control is often used interchangeably with the term executive functions (EFs), which can be defined as "*general purpose control mechanisms that modulate the operation of various cognitive subprocesses and thereby regulate the dynamics of human cognition*" (Miyake et al., 2000, p. 50). While the term cognitive control is perhaps most common in the field of cognitive neuroscience, the term executive functions has a more widespread use in clinical psychology (Friedman & Robbins, 2021). The latter has traditionally been more focused on cognitive impairments and related activity in the prefrontal cortex (PFC), as measured by traditional neuropsychological tests such as the Stroop test, the digit span test, and the trail making test, just to name a few. The term cognitive control is predominantly used in the field of cognitive neuroscience, and has more commonly been used to describe healthy functioning associated with activity in the PFC and related networks. However, definitions of both cognitive control and EFs often assume some general abilities or processes that regulate and optimize goal-directed behavior, and will be used interchangeably in the current thesis, unless otherwise specified.

Impairments in cognitive control are seen in a wide variety of psychological and neurological disorders, such as depression, Attention Deficit/Hyperactivity Disorder (ADHD), schizophrenia, Parkinson's disease and substance abuse disorders (Barch & Sheffield, 2014; Fillmore & Rush, 2002; Hughes et al., 2012; Monterosso et al., 2005; van den Wildenberg et al., 2006; Wodka et al., 2007), to name a few. Thus, investigating the neural correlates of cognitive control is of utter importance for the understanding and treatment of these disorders (Braver, 2012; Lever et al., 2016). Furthermore, resting state activity measures, together with newer machine learning approaches and neuromodulation studies, have given new possibilities in the characterization and treatment of psychological disorders

(Eyler et al., 2019; Faiman et al., 2021; Nakano et al., 2020; Sundermann et al., 2014; F. Vecchio et al., 2013). However, the potential of such methods is dependent on a proper mapping of the relationship between resting state activity and cognitive control measures.

In the current thesis, the terms cognitive control and EFs are both used to refer to the higher-level processes that enable the regulation of thought and action in a goal-directed manner, through the regulation and coordination of lower-level processes such as sensory and motor functions (Friedman & Miyake, 2017). Cognitive control is understood in terms of two prominent frameworks in the field: the unity/diversity framework and the dual mechanisms of control framework, with a specific focus on response inhibition. Response inhibition is the ability to suppress or cancel a prepotent or already initiated response (Aron et al., 2014; Hampshire & Sharp, 2015) and is considered a core component of cognitive control (Miyake et al., 2000). Specifically, the current thesis seeks to investigate how proactive and reactive control facilitate efficient response inhibition at the behavioral level and at the neural level. Furthermore, whether cognitive control processes are associated with baseline characteristics of the brain such as resting state activity, and whether this relationship varies with temporal modes of control is investigated.

1.1 Frameworks for understanding cognitive control

During the cognitive revolution in the second half of the 1900s, an increased focus on then outdated terms such as mind, perception, and expectation slowly replaced the strict rules of behaviorism in the United States (G. A. Miller, 2003). Together with progress in linguistics, anthropology, philosophy, neuroscience and computer science, a new field of cognitive sciences, and later cognitive neuroscience was born. Frameworks of cognition were affected by information processing theories (Broadbent, 1958; G. A. Miller, 1956), and an increased focus on automatic and controlled processes (Schneider & Shiffrin, 1977; Shiffrin & Schneider, 1977). A conceptual shift from feedforward-based information processing mechanisms to a combination of feedforward and feedback mechanisms, including attentional filters or biases, led to a distinction between bottom-up and top-down information processing to allow for cognitive flexibility (Gratton et al., 2018). Early definitions of cognitive control included control over selective attention (Posner & Presti, 1987), working memory and attentional processes (Baddeley & Hitch, 1974; Engle & Kane, 2003), or defined cognitive control in the context of a supervisory attentional system (Norman & Shallice, 1986). The development and digitization of the electroencephalogram (EEG), together with major advances in brain imaging techniques in the 1970s and beyond allowed a

surge of new material to shape cognitive control frameworks, such as an increased focus on the brain and nervous system. Today, the field of cognitive neuroscience is in rapid expansion, taking advantage of newer brain imaging methods as well as machine learning approaches and artificial intelligence to bridge the gap between the brain and cognition.

Gratton (2018) proposes five general processing steps that are commonly represented in many frameworks for cognitive control: 1) Generation and representation of task goals and the ability to access these when needed, 2) goal selection or attention biasing, 3) task sets, 4) monitoring, and 5) inhibition and interference control. Others have argued for similar (Banich, 2009; Ullsperger et al., 2014) or more mechanistic accounts (Verbruggen et al., 2014b). Although many of these processing steps are commonly agreed upon, frameworks for cognitive control use different partitioning schemes and terminology to explain how such processing steps lead to flexible control. Specifically, frameworks may vary in their relative focus on working memory (Curtis & D'Esposito, 2003), attention (Corbetta & Shulman, 2002; Shulman et al., 2009) and conflict (Botvinick et al., 2001, 2004; J. D. Cohen et al., 2000). Others focus on the specific sub-functions itself that comprise cognitive control (Miyake et al., 2000), while other attempts have been made to partition cognitive control in the temporal domain (Braver, 2012). The difference in terminology and structure of such frameworks make it difficult to integrate them, although they might share some commonalities in the underlying processes they try to explain. However, such frameworks can be useful on their own by facilitating the understanding of complex control processes and their neurophysiological correlates, by anchoring them to theoretical construct of cognitive control.

Two prominent frameworks in the field of cognitive control today is the unity/diversity (UD) framework (Friedman & Miyake, 2017; Miyake et al., 2000; Miyake & Friedman, 2012) and the dual mechanisms of control (DMC) framework (Braver, 2012; Braver et al., 2008; Chiew & Braver, 2017). In the UD framework, cognitive control arises from a set of general-purpose control mechanisms, referred to as executive functions, that modulates lower-level cognitive sub-processes to facilitate and regulate human cognition. In a seminal study by Miyake et al. (2000), a latent-variable approach was used to investigate the relationship between different EFs. Specifically, the focus was on three main EFs: updating, shifting, and inhibition. Here, updating refers to monitoring and updating of working memory content, shifting refers to the flexible alternation between tasks, and inhibition refers to the deliberate override of a dominant or prepotent response (Miyake & Friedman, 2012). Different tasks targeting the same EF (e.g., the stop-signal task, the anti-saccade task and the Stroop task all target the EF inhibition)

are used to extract what is common across tasks to get a measure of the latent variable. In their original study (Miyake et al., 2000), it was found that these three latent variable EFs are all moderately correlated with each other, and that each contributed (albeit differently) to all the different cognitive tasks. This indicates that there is some unity, as well as diversity in the EFs, suggesting that cognitive control is not a completely unitary ability (Figure 1A).

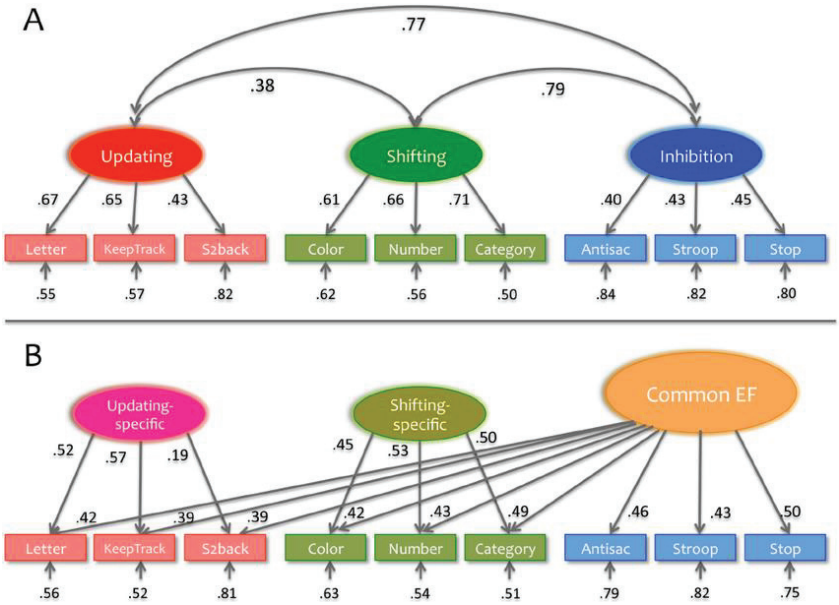

Figure 1. Overview of the factor analysis result underlying the Unity and Diversity framework. A) Unity and diversity in EFs as originally proposed in the UD framework in Miyake et al. (2000). B) Unity and diversity in EFs represented by a Common EF factor, and an updating- and shifting-specific factor. Reprinted with permission from Miyake, A., & Friedman, N. P. (2012). The nature and organization of individual differences in executive functions: Four general conclusions. Current directions in psychological science, 21(1), 8-14.

Individual differences in the performance on each EF task can be decomposed into what is common across all three EFs (updating, shifting and inhibition) and what is specific to that particular EF (Miyake & Friedman, 2012). More recent investigations have revealed that while there seems to be evidence for specific shifting and updating abilities, variance in inhibition can be explained entirely by the unity in these EFs, referred to as a Common EF factor (Figure 1B). The shifting-specific ability is thought to reflect flexibility in transitioning between task sets, and the updating-specific ability reflects gating of information and/or retrieval from long-term memory. It has been suggested that the common EF factor represents the ability to actively maintain task goals and goal-related information, and thereby

bias lower-level processing (Miyake & Friedman, 2012). Although this ability is important in a wide variety of different EFs, it might also be that the Common EF factor reflects abilities especially important for inhibition. However, whether this implies that inhibition can be reduced to the maintenance of goals and the biasing of lower-level processing to achieve such goals, or that inhibition is an ability in itself that just relies more heavily on these processes, is not certain (Miyake & Friedman, 2012).

Supporting evidence for the unity and diversity of EFs comes from genetic research, which has shown that overall, the heritability of the common EF is high, but the different EFs also show specific genetic contributions (Y. Chen et al., 2020; Engelhardt et al., 2015; Friedman et al., 2008). Further, the relationship between EFs and other neuropsychological measures as well as IQ differs between different EFs (Friedman et al., 2006). Further support comes from a recent study utilizing multivoxel pattern analysis which found that tasks targeting inhibition, updating and shifting were also associated with activity in common regions in the brain (He et al., 2021). Importantly, the approach also revealed that the EFs were encoded by distinct neural representations, supporting the diversity between them (He et al., 2021). Although the UD framework has gained a lot of support, it has also been criticized, both based on methodological grounds and replicability of factor analyses (Gignac & Kretzschmar, 2017; Karr et al., 2018) as well as the construct validity of EFs (Rey-Mermet et al., 2018, 2019).

Another functional decomposition of cognitive control is in terms of its temporal dynamics, which is the basis of the DMC framework (Braver, 2012). The DMC account was originally postulated to explain how control processes explain variation in working memory function (Braver et al., 2008), and how the distinction between proactive and reactive control processes could explain sources of working memory variation between task or situations, neural dysfunction, and individual differences. Proactive control refers to control processes initiated by the expectation of an upcoming cognitively demanding event, to bias lower-level processing such as attention, perception, and action systems in a goal-directed manner. Reactive control, on the other hand, is recruited after the detection of the event itself, and is thought to reflect a bottom-up recruitment of attentional processes. The implementation of cognitive control is thought to arise from the interplay between the two temporal modes of control, proactive and reactive control, which acts on a temporal continuum to facilitate efficient action control and goal-directed behavior.

Proactive and reactive control are thought to reflect two semi-independent systems that may be engaged simultaneously to facilitate efficient control. However, Braver (2012) suggests that the tendency to adopt one strategy over another is dependent on both intra-individual, inter-individual, as

well as showing between-group differences. Intra-individual variation is evident when situational or task demands lead to the preference of one strategy over the other. For example, reward motivation yields a more proactive task strategy (Qiao et al., 2018), although in some cases reward can also boost reactive task strategies (Boehler et al., 2014). Furthermore, strong expectations of an upcoming interfering event tend to lead to the recruitment of proactive control processes, while reactive control processes are more likely to be recruited when expectancy is low (Burgess & Braver, 2010). While such changes in context affect situational control mode preferences, individuals can also show more stable tendencies to rely on one strategy over another. Proactive control is thought to be dependent on the ability to actively maintain goal-related information in preparation for an upcoming task, as well as evaluating the cost/benefits of the chosen control strategy for optimal task performance. Thus, the tendency to adopt a proactive or reactive task strategy will also depend on more stable inter-individual differences related to working memory capacity, fluid intelligence, and affect-related traits (Braver, 2012), which could also be related to inter-individual differences at the neural level.

Importantly, the aforementioned frameworks are not necessarily mutually exclusive, although their partitioning schemes differ. Indeed, Friedman and Miyake (2017) suggests that both the Common EF and proactive control reflects the ability to actively maintain task goals and goal-related information, and that the Common EF is related to stable biases in the balance between proactive and reactive control. Another, perhaps more common way of thinking of the two frameworks in an integrated manner in the literature is to think of proactive and reactive control strategies as working on the specific sub-functions as suggested by Miyake et al. (2000). Thus, inhibition, updating and shifting can themselves be partitioned in the temporal domain, as governed by proactive and reactive control processes (Aron, 2011; Bugg & Braver, 2016; Wiemers & Redick, 2018).

Both the UD and the DMC frameworks have had a major influence on cognitive control research and serve as plausible conceptual starting points when investigating cognitive control. The partitioning of cognitive control in the temporal domain and at the level of sub-functions is an important step towards removing the need to refer to an overarching controller of cognitive functions, a so-called control homunculus, when studying cognitive control (Botvinick et al., 2001; Logie, 2016; Verbruggen et al., 2014b). However, the partitioning of cognitive control into sub-functions is only helpful if the substrates themselves are not treated as separate control homunculi (Verbruggen et al., 2014b). One important part of diminishing such homunculi is to discern how these control processes are recruited and facilitated at the neural level.

1.2 Neural correlates of cognitive control

In the 19th century, advances of the understanding of the cerebral cortex together with case lesion studies showing discrete cognitive deficits (although not always consistent) led to the idea that higher-order cognitive functions was functionally located to the frontal lobes (Benton, 1991). Indeed, for a long time these functions were simply referred to as frontal lobe functions. One striking example is that of Phineas Gage, who during a work accident got an iron bar thrusted through his head, leaving an over 6 mm large whole in the scull, most likely severing much of his left PFC. Gage survived, but with a significantly changed personality. The former dutiful and polite man was now described as somewhat flaky and with a tendency for profanities, he "was no longer Gage" (Harlow, 1869).

Models that anchored specific cognitive control functions to specific neural systems showed a rapid increase in number during the 1990s and the beginning of the 21st century, mostly focusing on how cognitive control processes enabling top-down bias were allocated to the active maintenance of activity patterns in the PFC, together with conflict detection in the anterior midcingulate cortex (aMCC)[1] (Barch et al., 1997; Botvinick et al., 2001; J. D. Cohen et al., 2000; E. K. Miller & Cohen, 2001). Even today, the PFC is central in many frameworks for cognitive control (Friedman & Robbins, 2021), and both the UD and the DMC framework have specific hypotheses about associated neural underpinnings in the PFC. Recently, more advanced neuroimaging and statistical methods have initiated a shift towards a domain-general systems and networks approach, shifting the focus from the PFC alone to the cortex and the brain as a whole (Hampshire & Sharp, 2015; Mirabella, 2014). However, a domain-general vs modular approach is not necessarily evidence for the unity and diversity of cognitive control, respectively, but rather reflects the idea that cognitive control and its sub-functions are broad constructs that might be more likely to emerge from the dynamic interaction between many different brain regions or networks (Eisenreich et al., 2016; Gratton et al., 2018). Nonetheless, the identification of neural correlates associated with core sub-functions of cognitive control is in no doubt important to understand the complex dynamics of cognitive control.

[1] The midcingulate cortex is a heterogenous structure consisting of the anterior cingulate cortex (ACC), the midcingulate cortex (MCC) and the posterior cortex. Although some studies of conflict monitoring and systems for action monitoring often refer to the ACC or the dorsal ACC (e.g., Botvinick et al., 2004), parcellations of the cingulate cortex rather suggests that these regions better corresponds to the (anterior) MCC (Ullsperger et al., 2014; Vogt, 2016; Vogt et al., 2003). The current thesis will use the terminology aMCC in line with current advances of the cingulate cortex function (Vogt, 2016).

1.2.1 The frontal lobe and PFC organization.

The frontal lobe constitutes about one third of the entire human cerebral cortex, and is separated from the parietal lobe by the central sulcus, and from the temporal lobes by the lateral fissure. The PFC is anatomically defined as the part of the frontal lobe in front of the primary and secondary motor areas, and consists of the lateral PFC, the ventromedial PFC, the frontal pole, and the medial frontal cortex. The human frontal lobe shows tremendous connections both to other cortical and sub-cortical regions of the brain (i.e., motor, visual, basal ganglia), as well as within the frontal lobe itself, with the largest portion of inputs coming from the thalamus, which relays inputs from the sensory domains (Fuster, 2015). Thus, the frontal lobe and the PFC seem well equipped to handle the complexity of cognitive control processes, in concert with other regions of the brain such as the parietal cortex, the cingulate cortex, as well as the basal ganglia. Today, there is increased focus on wide-spread networks spanning the entire human cortex (Barton & Venditti, 2013), and how such systems interact to facilitate efficient cognitive control (Duncan, 2010; Hampshire & Sharp, 2015; Menon & D'Esposito, 2021; Mirabella, 2014).

1.2.2 Neural correlates of cognitive control in the UD and DMC frameworks.

Both the UD and the DMC frameworks are associated with specific predictions about the neural activity underlying cognitive control. In both frameworks, cognitive control is implemented via PFC-basal ganglia networks, mediated by activity in the dopaminergic system, and with connections to the posterior cortex (Braver, 2012; Miyake & Friedman, 2012). In the UD framework, the goal-relevant information is maintained in the PFC to bias lower-level processes through the posterior cortex. Information in the PFC is dependent on a flexible-gating mechanism via the basal ganglia (BA) and the dopaminergic (DA) systems. Importantly, this PFC-BA-DA model entails different activity patterns for the different EFs (Miyake & Friedman, 2012). Specifically, the common EF would be associated with strong and sustained activation in the PFC, together with strong connections to the posterior cortex, to enable active maintenance of goal-related information and top-down biasing of lower-level processes. The shifting-specific ability would rather be associated with the persistence of these PFC representations after the goal-relevant information is no longer relevant, and the updating-specific ability might be associated with the dopamine-mediated flexible-gating mechanism in the basal ganglia, allowing new representations of task-relevant information to be accessed and maintained in the PFC (Miyake &

Friedman, 2012; O'Reilly & Frank, 2006). In the DMC framework, proactive control is associated with sustained activity in the lateral regions of the PFC to enable active maintenance of task-relevant information. The sustained activation of these task-relevant representations is enabled by a flexible gating-signal governed by the dopaminergic system during the detection and presentation of the cues signaling an upcoming likelihood of an interfering event. Reactive control is, on the other hand, associated with transient activity in the lateral PFC, together with contributions from a wide network of regions. Importantly, this transient activation of the PFC is triggered by bottom-up activation of task-goals (Braver, 2012), such as conflict-monitoring implemented by the aMCC (Botvinick et al., 2001, 2004) that conveys the detection of conflict to relevant control systems, which then modulates their influence on the current information processing stream (Botvinick et al., 2001).

Although both frameworks are based on specific predictions of the PFC-BA-DA models, the neuroanatomical support for such activation patterns are a bit more difficult to detangle. Evidence for the unity of EFs comes from research finding that some parts of the PFC are consistently activated during a wide range of executive functions (Cieslik et al., 2015; He et al., 2021). Indeed, if the Common EF represents abilities reflected in cognitive control in general, similar activations across tasks might reflect common neural correlates of the Common EF. Previous research has suggested that cognitive control indeed is associated with domain-general activation patterns, such that a wide variety of cognitive tasks activate the same regions (Hampshire & Sharp, 2015; Wu et al., 2020). Research has also consistently found that different tasks activate specific regions of the cortex (reviewed in Friedman & Robbins, 2021), indicating that also diversity in cognitive control is evident at the neural level. However, as cognitive control by definition biases lower-level processing such as sensory and motor processes, then both differences and similarities across task activations might be due to differences and similarities in these lower-level processes. Recent research has sought to resolve such problems using data-driven multivariate pattern analysis and multimodal imaging. Indeed, these studies find evidence for both distinct neural representations specific to the different cognitive tasks, as well as common activation patterns across tasks (He et al., 2021; Lerman-Sinkoff et al., 2017), indicating that unity and diversity are found at both the behavioral and neural level.

Several studies indicate that a broad range of cognitive tasks are supported by activity in several PFC regions, supporting the idea of a multiple demand cortex (MDC), where regions spanning the mid-dorsolateral and mid-ventrolateral cortex as well as the aMCC are recruited for many different cognitive demands (Duncan & Owen, 2000). Specifically, the activity in these regions reflects selective and

adaptive coding of information relevant to the task at hand (Duncan, 2010; Duncan & Owen, 2000). Different connectivity patterns between regions suggests both the existence of several distinct networks, as well as functional specialization within the MDC (Camilleri et al., 2018; Erika-Florence et al., 2014; Hampshire & Sharp, 2015). Others argue for a modular perspective, where specific regions in the PFC are associated with specific control processes (Aron, 2011; Botvinick et al., 2001). Then again, some have argued that there is no specific region or networks that enable cognitive control, but rather that cognitive control is an emergent property from widespread network processing in the brain (Eisenreich et al., 2016; Zink et al., 2021).

The MDC assumes that both proactive and reactive control modes are dependent on the same networks but involve different activity states and temporality. Specifically, when an interfering event is expected, MDC enters a stable state of low activation that enables top-down potentiation of relevant sensorimotor areas. When the interfering event is detected, reactive control is implemented via increased activity in both the MDC and the sensorimotor areas (Duncan, 2010; Hampshire & Sharp, 2015). Neuroimaging research indicates that proactive and reactive control are associated with both distinct regions of the brain as well as overlapping networks (van Belle et al., 2014; F. Zhang & Iwaki, 2019). The interpretation of such findings is complicated by the fast timescale such control processes act on at the single-trial level, which might not be accessible via fMRI alone. Evidence from EEG has shown that stimulus-locked event-related potentials (ERPs) such as the N2 and P3 are subjective to modulations of cognitive control (Huster et al., 2013). For example, the N2 has been shown to attenuate with increasing proactive control demands (Nieuwenhuis et al., 2003; Ramautar et al., 2004), indicating that proactive control facilitates processes occurring after the detection of the interfering event itself. Other lines of research have found distinct ERP signatures associated with proactive and reactive control modes (Langford et al., 2016; Schevernels et al., 2015). However, while fMRI research is limited in its ability to temporally dissociate proactive and reactive control processes at the single-trial level, EEG research is limited by a spatial resolution that cannot dissociate distinct nearby lying regions' contribution to cognitive control. Whether proactive and reactive control rely on the same or distinct underlying mechanisms is not yet certain. Furthermore, it seems likely that these two modes of control interact to facilitate efficient control, but how this interaction is facilitated at the neural level is not yet clear.

1.2.3 FM-theta as a neural marker of cognitive control.

Another electrophysiological feature associated with cognitive control is frontal-midline theta (FM-theta). FM-theta activity can be defined as oscillating activity with a frequency between 4-8 Hz measured at fronto-central scalp electrodes. Specifically, FM-theta activity has been associated with a system for action monitoring situated in the PFC and the aMCC (Huster et al., 2013; Myers et al., 2021). FM-theta activity is thought to reflect a general mechanism of cognitive control, and is associated with a wide variety of executive functions, such as working memory (Maurer et al., 2015; Zakrzewska & Brzezicka, 2014), task switching (Cooper et al., 2019), and response inhibition (Dippel et al., 2017; Huster et al., 2013). Often, FM-theta activity is associated with a reactive control process, and has been suggested to reflect a generic control mechanism during novelty, conflict, and error (Cavanagh et al., 2012; Cavanagh & Frank, 2014; M. X. Cohen & Donner, 2013). This has been supported by the fact that a large variety of stimulus- and response-locked event related potentials (ERPs), such as the mismatch and control-related N2, the error-related negativity and the feedback-related negativity, are all thought to be a reflection of underlying theta dynamics (Cavanagh et al., 2012). Indeed, the strong association between theta activity and cognitive processes in the PFC has led to FM-theta activity being coined a theta lingua franca for action monitoring processes (Cavanagh et al., 2012).

Recent research indicates that FM-theta activity is also associated with proactive control processes (Cooper et al., 2015; Dippel et al., 2017). For example, FM-theta activity elicited by an informative cue has been found to be associated with reaction times in a cued task-switching task (Cooper et al., 2019) and the probability of a stop-signal in a stop-signal task (Chang et al., 2017). Furthermore, FM-theta activity increases prior to difficult tasks compared to easy tasks (Cooper et al., 2017, 2019; Loof et al., 2019), indicating that FM-theta activity prior to a cognitively demanding event reflects preparation for the upcoming task.

The putative association between FM-theta activity and proactive control is supported by the fact that lower frequencies, such as theta band activity, reflect inter-regional communication in the brain necessary for functional integration of information, as is necessary for top-down processing (Cavanagh & Frank, 2014; Stein et al., 2000). How the control processes reflected in theta activations are biologically relayed to necessary motor and sensory systems is not yet certain. Some evidence suggest that neural populations oscillating at the same frequency with a given phase give rise to temporal windows of information transmission (Buzsáki & Draguhn, 2004; Fries, 2005). In this way, neuronal oscillations enable flexible and effective communication evident through coherence pattern among

groups of neurons (Fries, 2005). Hence, increase in FM-theta power (and phase synchronization) both in anticipation of, and after cognitively interfering events might provide a temporal window for organizing neuronal mechanisms or communicating neuronal responses to meet cognitive demands (Cavanagh & Frank, 2014).

1.3 Proactive and reactive control of response inhibition

Response inhibition can be defined as the ability to suppress or cancel a routine, prepotent, or already initiated motor action (Hampshire & Sharp, 2015), and might be especially important for efficient cognitive control (Miyake et al., 2000). Impairments in response inhibition are seen in a wide variety of psychological and neurological disorders, such as ADHD, substance abuse, schizophrenia, and Parkinson's disease (Fillmore & Rush, 2002; Hughes et al., 2012; Monterosso et al., 2005; van den Wildenberg et al., 2006; Wodka et al., 2007), indicating the importance of response inhibition for optimal daily life function. Response inhibition is often used as a proxy measure for other more covert or abstract forms of inhibition, such as inhibition of thoughts, emotions, and memories (Aron, 2007; Miyake et al., 2000). The temporal partitioning of cognitive control has also been extended to response inhibition (Aron, 2011; Braver, 2012). Here, proactive control of inhibition refers to the preparation to inhibit a response following the expectation of an upcoming signal to stop. Reactive control of response inhibition, on the other hand, refers to the transiently activated control processes elicited by the detection of the stop-signal itself. Thus, proactive and reactive control processes work on a temporal continuum to facilitate efficient response inhibition. In this respect, response inhibition in the present thesis is defined in a broader context than the often synonymously used term *outright stopping*, which is often used to describe the specific suppression or inhibition of an initiated action. Here, response inhibition is also defined in terms of the series of processes leading to such outright stopping, including signal detection, response preparation and interference control, and how such processes is governed by proactive and reactive control processes.

1.3.1. Measuring response inhibition.

Response inhibition is commonly measured by the stop-signal task (SST) and the go/no-go task (GNGT). In the GNGT, participants are presented with stimuli (e.g., a green arrow pointing left), and are instructed to respond with the corresponding hand (go trial). On a minority of trials, the arrow is

presented in a different color (e.g., blue), signaling to the participants that they are not supposed to make a response (no-go trial). Because the no-go trials are presented at a lower frequency than the go trials, participants develop a prepotent tendency to respond, and must inhibit this tendency when the arrow is blue instead of green. Response inhibition abilities can be measured as the percentage of accurately withheld responses on the no-go trials. As the GNGT does not require the inhibition of an already initiated response, some have argued that the GNGT rather reflects response selection more than response inhibition per se (Littman & Takács, 2017; Raud et al., 2020b). This is further supported by studies showing that response inhibition assessed by the GNGT and the SST show somewhat different neural network activity (Cieslik et al., 2015; Swick et al., 2011).

The SST is similar to the GNGT, but in the SST each trial requiring inhibition consists of a go stimulus (i.e., the green arrow) followed by a stop stimulus (the blue arrow). In this way, the response is already initiated (elicited by the go signal) when the participants are instructed to withhold their response (i.e., at the onset of the stop-signal). The delay between the go stimulus onset and the stop stimulus onset (stop-signal delay; SSD), is often varied dynamically, such that the delay decreases after an unsuccessful stop trial and increases after a successful one. As the difficulty of inhibiting a response increases with longer delays, this dynamical staircase tracking of the SSD normally ensures a stop-trial accuracy of about 50%. The SST enables calculating the stop-signal reaction time (SSRT), a measure of the stopping latency. This estimation is based on a conceptual horse race model (Band et al., 2003; Logan & Cowan, 1984). Here, the response inhibition process is conceptualized as a horse race between two independent runners: a go-runner, elicited at the go-signal onset, and a stop-runner, elicited at the stop-signal onset. If the go-runner finishes first, the response is executed (unsuccessful stop trial). If the stop-runner finishes first, the go response is successfully inhibited (successful stop trial). Varying the SSD thus varies the head start of the go-runner, making it more or less likely that the response will be successfully inhibited. The SSRT is estimated based on the relationship between the go trial reaction time (go-RT), the SSD, and the probability of responding on a stop trial.

The SST is easily adapted to explicitly modulate proactive control, for example by varying the frequency of the stop trials between blocks or experiments. An increasingly more common method is to add cues prior to the go-signal that explicitly tell the participant the probability of an upcoming stop-signal. The assumption is that participants will recruit more proactive strategies if the probability of an upcoming stop-trial is high, and likewise less proactive strategies if the probability of an upcoming stop-trial is low. This manipulation has the advantage that the degree of proactive control should vary as a

function of the probability of an upcoming stop-trial, and thus the proactive control engagement can be assessed by comparing conditions of high and low stop-trial probability. A variant of this approach is the stop-signal anticipation task (SSAT), which requires one to stop a moving bar before it reaches a set point (go trial) or when the bar is stopped on its own (stop trials). In this task as well, proactive control is modulated by informing the participants of the likelihood that the bar will stop on its own. Modulations of proactive control usually lead to increased reaction times in go trials (Albares et al., 2014; Verbruggen & Logan, 2009; Zandbelt & Vink, 2010), which is interpreted as a proactive adjustment of behavior.

1.3.2 Neural correlates of response inhibition: evidence from fMRI.

Response inhibition is commonly associated with activity in a right-lateralized network, including the right inferior frontal gyrus (IFG) and the pre-supplementary motor area (pre-SMA), as well as activity in the right inferior parietal cortex (IPC), right insula, and the aMCC (Aron et al., 2014; Cieslik et al., 2015; Levy & Wagner, 2011; van Belle et al., 2014). Assumingly, reactive response inhibition is implemented specifically by regions such as the rIFG and pre-SMA, which together modulate basal ganglia pathways through the so-called hyper-direct pathway (Aron et al., 2016; Cai et al., 2019; W. Chen et al., 2020). Although it has been speculated whether conditions of proactive control may lead to different pathways being utilized (i.e., the indirect pathway through both the subthalamic nucleus (STN) and the striatum) (Criaud et al., 2021; Jahfari et al., 2012; F. Zhang & Iwaki, 2019), research on the exact cortical contributions to proactive control remains inconclusive. Contrasting fMRI activations during conditions of go-trials where the probability of a stop-signal is high (uncertain go-trials) with go-trials where the probability of a stop-signal is zero (certain go-trials) has revealed that many of the same regions activated during reactive inhibition are also activated during conditions of proactive control. Since go-trials do not include a stop-signal, such activations have been interpreted as reflecting an early activation of the stopping network, perhaps to facilitate efficient inhibition (Chikazoe et al., 2009; Jaffard et al., 2008; Meyer & Bucci, 2016). However, a meta-analysis based on the SSAT revealed that proactive and reactive control of inhibition recruit both common and distinct neural networks across the cortex (van Belle et al., 2014), indicating that there is at least some functional dissociation of proactive and reactive control at the neural source level. Specifically, proactive control was uniquely associated with a network consisting of the superior parietal lobe, the dorsal premotor cortex, and the left putamen, while reactive control was uniquely associated with two right-lateralized fronto-parietal networks.

Networks common to both proactive and reactive control overlapped in the frontal lobe, and specifically in the left and right middle frontal gyrus (van Belle et al., 2014).

At least two issues arise from comparing certain go-trials with uncertain go-trials when looking at proactive control of inhibition. First, one assumes that the certain go-trials are free of proactive control, and that certain and uncertain go-trials are equal except the involvement of proactive control, an assumption that might not be true. For example, it seems plausible that proactive processes interact with both response initiation as well as conflict monitoring and updating processes as a result of the unfulfilled expectation of an upcoming stop-signal. Indeed, Zandbelt and colleagues (2013) found that the effect of stop-signal probability on go-trial activity was in fact larger during the go-stimulus and response period than during the cue period in the right IPC, right IFG, and the right middle frontal gyrus (MFG), indicating that activity associated with proactive control can be functionally dissociated into several temporally distinct components (Zandbelt et al., 2013). Second, as there are no stop-trials in the certain go condition, these paradigms only allow the investigation of the effect of proactive control on go-trial activity, a trial type where no reactive inhibition is thought to take place. That is, the contrast of certain versus uncertain go-trials does not allow the investigation of the effect of proactive control on inhibition itself; i.e., how proactive control interacts with reactive processes elicited by the detection of the stop-signal.

By varying the *degree* of uncertainty, for example by including several conditions with different stop-signal probabilities, it is possible to investigate the effect of increasing proactive control on go-trial activity. Here, it has been found that when comparing go-trials with different levels of uncertainty, not all the regions implicated in response inhibition show similar activity modulations during increasing proactive control (Leunissen et al., 2016; Zandbelt et al., 2013). This indicates that there is some degree of functional specialization within the stopping network. Importantly, such parametric modulations of stop-signal probability also allow the investigation of proactive control on stop-trial activity directly, as the paradigm includes stop-trials with varying degrees of stop-signal probability. Contrasting conditions inducing high and low proactive control in the context of reactive stopping, Leunissen and colleagues (2016) found that activity in the caudate increased with higher levels of proactive control, while activity in the STN decreased. In another study, effective connectivity analyses revealed that higher proactive control, as induced by a probability cue (probability of an upcoming stop-signal was zero, low, or high), led to decreased reactive control processes and weaker fronto-subcortical projections (Jahfari et al., 2012). The difference in activity between stop trials with low and high degree of stop-signal probability

may reflect heightened proactive control, but also interaction effects between proactive and reactive control processes that can take place both prior to, and after the onset of the stop-signal. For example, research suggests that increased proactive control may facilitate more efficient inhibition by increasing response thresholds in advance (Verbruggen & Logan, 2009). Others have suggested that in certain contexts, much of the top-down control in response inhibition takes place before the stop-signal is presented (Elchlepp et al., 2016), which in extreme situations might even make reactive control of inhibition unnecessary for successful inhibition, in line with accounts of a prepared inhibitory reflex (Verbruggen et al., 2014a)

1.3.2.1 Modular and domain-general approaches. The exact functional contributions of the regions involved in response inhibition have been an issue of debate. Specifically, two main approaches seek to explain how response inhibition is facilitated at the cortical level. The modular view has given the rIFG a special role in response inhibition, proposing that this region is a core node in a stopping network together with the pre-SMA and the STN (Aron, 2006, 2007; Aron et al., 2004; Swann et al., 2012). Here, the rIFG is thought to facilitate outright stopping either by modulating basal ganglia pathways directly, or through the pre-SMA. Evidence for this theory originates from lesion studies, showing that lesions to the rIFG impaired response inhibition, and that the degree of impairment, as measured by the SSRT, was correlated with the magnitude of the lesion (Aron et al., 2003). Lesions to other regions did not impair response inhibition, indicating that the rIFG was the core node of the stopping network. Further evidence comes from fMRI studies, which consistently show rIFG activity during conditions requiring response inhibition (Chikazoe et al., 2007; Cieslik et al., 2015; van Belle et al., 2014). This activity has been associated with both the SSRT and the probability of successful inhibition (Aron, 2006; Hughes et al., 2012; Schaum et al., 2021). Although the pre-SMA has also been implicated in stopping (Cai et al., 2012; Nachev et al., 2007; Swann et al., 2012), the exact nature of the relationship between the pre-SMA and the rIFG has been debated (Obeso et al., 2013, 2017). Research suggests that pre-SMA activity can even precede that of the rIFG (Swann et al., 2012), thus questioning the hierarchical control of the rIFG – pre-SMA – basal ganglia network. According to the modular approach, other regions involved in response inhibition, such as the orbitofrontal cortex and the dorsolateral PFC (dlPFC), are important for efficient response inhibition, but do not reflect outright stopping per se. Rather, activity in these regions during response inhibition might reflect associated functions such as implementation of task rules and working memory (Aron et al., 2014).

Activity in the rIFG is also evident during proactive control (Swann et al., 2013; van Belle et al., 2014; Zandbelt et al., 2013). It has been suggested that the rIFG acts as a brake, such that during conditions of proactive control, rIFG activity contributes to both braking of prepotent response tendencies, as well as outright stopping (Aron, 2011; Wessel et al., 2013). Deep brain electrical stimulation of the rIFG was shown to slow down responding compared to sham stimulation, and this effect was larger during uncertain than certain go-trials (Wessel et al., 2013). Another study found that the rIFG, pre-SMA, and the STN were all activated by both proactive and reactive inhibition, and that the functional connectivity from the IFG to the pre-SMA was modulated by both control modes (F. Zhang & Iwaki, 2019). Importantly, proactive and reactive control were associated with distinct fronto-basal ganglia pathways (F. Zhang & Iwaki, 2019). However, the modular approach has received several lines of criticism, especially focused on the special role of the rIFG in inhibition. Although some argue that the rIFG is critical for response inhibition, others have shown that other regions are equally critical. For example, in one study, stimulation of the pre-SMA led to shorter SSRTs, while stimulation of the rIFG did not affect response inhibition performance (Obeso et al., 2017). Furthermore, lesions to the left IFG also seem to impair response inhibition performance (Swick et al., 2008), thus questioning the validity of the assumption of a right-lateralized stopping network. Another line of criticism pertains to whether rIFG activity actually reflects response inhibition per se. Indeed, rIFG activity is evident during a wide variety of cognitive tasks, and it has been suggested that activity in the rIFG during response inhibition rather reflects attentional processes associated with the detection of a stop-signal (Erika-Florence et al., 2014; Hampshire et al., 2009, 2010). Clearly, the rIFG is important for response inhibition, but whether this region is the sole critical region for response inhibition is an issue of recurrent debates (Aron et al., 2014; Hampshire, 2015; Swick & Chatham, 2014).

One reason for such controversy regarding the role of the rIFG in response inhibition might stem from the heterogeneous nature of the inferior frontal area and the rIFG itself. Indeed, research has found that also surrounding regions such as the anterior insula are associated with autonomic arousal related to stopping (Aron et al., 2014), or the detection of behaviorally salient events (Cai et al., 2014). Further, the IFJ has been consistently activated during different cognitive control processes (He et al., 2021; Levy & Wagner, 2011). Importantly, also sub-regions of the rIFG might have varying functional roles associated with response inhibition (Boen et al., 2020; Hartwigsen et al., 2019; Verbruggen et al., 2010), further complicating interpretation of the role of the rIFG in response inhibition.

Domain-general approaches in explaining the neural correlates of response inhibition rather assume that complex cognitive functions are a result of activity in wide-spread cortical networks, where different regions can flexibly adapt to facilitate the task at hand (Duncan, 2010; Hampshire & Sharp, 2015; Mirabella, 2014; R. Zhang et al., 2017; S. Zhang & Li, 2012), and response inhibition is only one task facilitated by such domain-general networks. The MDC consists of specific regions In the PFC and parietal cortex, such as the inferior frontal area, the pre-SMA and aMCC, as well as the frontal operculum and regions surrounding the intraparietal sulcus (Duncan, 2010). It has been proposed that the neural mechanisms enabling response inhibition in the MDC is that of local lateral inhibition and top-down potentiation (Hampshire & Sharp, 2015). In the stop-signal task, expectation of a stop-signal leads to neurons in the MDC entering a stable activity state that facilitate the relevant sensorimotor regions. Thus, this top-down biasing of the MDC leads to upregulation of stop-relevant processes, and down-regulation of non-relevant processes by lateral inhibition. As the go-signal becomes less relevant relative to the stop, this leads to slowing of the go trial reaction times. At the detection of the stop-signal, the MDC enters a high activity face leading to increased potentiation of relevant stop processes, which finally leads to the inhibition of a response (again through lateral inhibition) (Hampshire & Sharp, 2015). In this way, activity in MDC facilitates both proactive and reactive control of inhibition.

Both the modular and domain-general approaches have support in the literature and seem to suggest that proactive and reactive control of inhibition is reflected in activity in the same regions, but that the same regions may also belong to different functional networks associated with either proactive or reactive control. However, fMRI research on proactive and reactive control of response inhibition is undoubtedly limited by the temporal resolution of fMRI due to the relatively slow blood oxygen level dependent (BOLD) effect. Thus, activity in the same region as reflected in fMRI contrast images might not reflect the same processes, as these are temporally dissociated on a scale not accessible by fMRI. Indeed, response inhibition at the single trial level is assumed to occur within milliseconds from the onset of a stop-signal, and thus dissociating proactive and reactive control processes, as well as inhibitory processes from other cognitive processes such as attention, might not be feasible with fMRI.

1.3.3 Electrophysiological correlates.

Response inhibition is associated with several electrophysiological correlates, both in the time domain as well as in the frequency domain (reviewed in Huster et al., 2013). Specifically, response inhibition in

the stop-signal task usually elicits a fronto-central negativity peaking around 200 ms post stop-signal (stop-N2), as well as a larger positivity peaking around 300 ms post stop with a somewhat wider topography (stop-P3). The N2 is especially sensitive to proactive control modulations induced by stop-signal frequency as well as cueing. It is thought to originate from a midcingulate source and is related to oscillatory components in the theta frequency band. FM-theta activity in response inhibition is increased in stop-trials compared to go-trials (Lavallee et al., 2014; Nigbur et al., 2011; Yamanaka & Yamamoto, 2010), and higher activity again is seen in unsuccessful stop-trials (González-Villar et al., 2016). Furthermore, stop-trial theta activity is sensitive to both proactive modulations (Dippel et al., 2016, 2017) and task context beyond frequency manipulations such as stimulus-response mappings (Lavallee et al., 2014). The latter is important, as it indicates that theta activity is sensitive to the context of the stop-signal, beyond mere novelty.

Recent research also indicates that FM-theta activity is evident *prior* to the onset of a stop-signal, and that this activity has a functional role in proactive control of response inhibition. For example, one study found that theta activity prior to the onset of the stop-signal was positively correlated with the anticipation of an upcoming stop-signal (Chang et al., 2017), possibly indicating that heightened FM-theta activity indicates a proactive preparation of the same mechanisms associated with reactive theta. Another recent study investigated how pre-trial FM-theta activity was modulated by the nogo-signal frequency in a GNGT (Adelhöfer & Beste, 2020). They found no effect of no-go signal frequency on pre-trial theta activity, but pre-trial theta activity was higher before go than no-go trials (Adelhöfer & Beste, 2020). As the experimental tasks used in these studies did not include an explicit probability cue, such pre-trial effects are hard to interpret. While few studies have investigated the effect of cuing on proactive FM-theta activity in a stop-signal task specifically, together with results from cued task-switching paradigms (see section *1.2.3 FM-theta as a neural marker of cognitive control)* these findings indicate that FM-theta activity has an important functional role in both proactive and reactive control of inhibition. However, whether proactive FM-theta activity reflects the same underlying neural mechanisms as reactive FM-theta activity is not certain. Indeed, one may argue that if proactive and reactive inhibition processes are explained by a unitary mechanism, then the corresponding FM-theta activity should originate from the same neural generators (Sauseng et al., 2019).

Attempts to integrate the effects of proactive and reactive control of inhibition may be facilitated by the integration of EEG and fMRI data, as these two methods complement each other in their high temporal and spatial resolution, respectively. Simultaneous recordings of EEG and fMRI have

revealed that reactive inhibition, as reflected in FM-theta activity, is associated with activity in the pre-SMA, the rIFG, the left MFG and the cingulate gyrus (Ko et al., 2016; Lavallee et al., 2014). Another approach is to utilize high-density EEG in combination with source analysis. Such analyses have found that reactive FM-theta activity may originate in the superior frontal gyrus (Dippel et al., 2017), or the aMCC/ACC (Hong et al., 2020; Huster et al., 2013; Kaiser et al., 2019). Few studies have investigated the neural source of proactive FM-theta activity, although it seems as there are some overlapping associations between proactive and reactive control also at the neural source level (Adelhöfer & Beste, 2020). Interestingly, it also seems as though the activity at the neural source level and the FM-theta activity vary with no-go signal frequency in a GNGT (Adelhöfer & Beste, 2020; Dippel et al., 2017). Together, these results indicate that FM-theta is associated with both proactive and reactive control modes, and that the relationship between FM-theta activity and activity at the source level is dependent on the degree of proactive control.

1.4 Resting state activity and cognitive control

Research indicates that FM-theta activity measured at rest is also associated with cognitive control (Hermens et al., 2005; Karamacoska et al., 2018; Lansbergen et al., 2007; Pscherer et al., 2019, 2020). Resting state activity can be defined as the neural activity present in the absence of any experimental task, and is thought to reflect the spontaneous organization and facilitation of sensory, motor and cognitive processing (Mantini et al., 2007). Resting state activity is dependent on the underlying neuroanatomical structure (Hermundstad et al., 2013; Z. Wang et al., 2013), but could also reflect structure, neuronal dynamics, signal transmission delays and noise (Deco et al., 2011). Resting state brain activity measured with EEG have been shown to have high intra-individual stability (Näpflin et al., 2007; Põld et al., 2021), perhaps reflecting some characteristics of brain networks that are specific to the individual (Mennes et al., 2010). This is further supported by the fact that individual differences in resting EEG activity are associated with genetic factors (Smit et al., 2005) and with stable characteristics such as intelligence (Thatcher et al., 2005, 2007), risk-taking behavior (Balconi et al., 2017; Studer et al., 2013), and impulsivity (Rass et al., 2016). Resting state EEG has also been associated with personality traits such as agreeableness and neuroticism (Jach et al., 2020).

Research on resting state theta (RS-theta) activity and cognitive control has revealed that theta activity measured at rest is associated with better behavioral performance in tasks targeting response inhibition (Karamacoska et al., 2018; Lansbergen et al., 2007), working memory (Barkley et al., 2020), as

well as reaction times (Hermens et al., 2005; van Dongen-Boomsma et al., 2010). Furthermore, RS-theta activity has been associated with better self-reported executive functions (Basharpoor et al., 2019), and executive functions in elderly (Finnigan & Robertson, 2011). However, a study investigating the relationship between resting state dynamics across several frequency bands and cognitive control performance found low support for such a relationship (Gordon et al., 2018). Here, behavioral measures from a choice reaction time task, a switching task, an anti-saccade task, and a mental rotation task were investigated in relation to resting state power in the alpha, theta, and beta bands, as well as relative power ratios between the different bands. The results revealed that none of the resting state frequency band estimates were associated with the behavioral performance in the cognitive control tasks (Gordon et al., 2018).

The notion of a relationship between RS-theta and cognitive control performance warrants the idea that there might also be a relationship between RS-theta and task-elicited FM-theta activity. However, few studies have investigated this specifically. In a couple of studies by Pscherer and colleagues, it was found that RS-theta activity was negatively associated with higher conflict-induced FM-theta activity and poorer behavioral performance in a GNGT (Pscherer et al., 2019), as well as positively associated with conflict-related theta activity in a flanker task, an effect specific to the stimulus-related coding (Pscherer et al., 2020). This indicates that RS-theta activity is related to cognitive control through task-elicited FM-theta activity. RS-theta activity has also been associated with stimulus-locked ERPs during cognitive control, such as no-go anteriorization in a cued continuous performance task (Schiller et al., 2014) and the conflict-related N2 in response to internally guided decision-making (Nakao et al., 2013). As the N2 is thought to reflect the underlying phase-locked FM-theta activity (Cavanagh et al., 2012; Huster et al., 2013), this supports that there is a relationship between resting state theta and task-elicited FM-theta activity.

There seems to be even less research focused on the relationship between RS-theta and proactive control. In a study by Clements and colleagues (2021), RS-theta was associated with a higher congruency effect in a cued flanker task, indicating worse reactive control. Interestingly, RS-theta activity was not associated with proactive activity at all, which was rather associated with resting state alpha activity (Clements et al., 2021). Another study using neurofeedback (NF) training targeted at the upregulation of FM-theta activity found that increased FM-theta activity during the NF training sessions led to increased performance in tasks requiring proactive control, but not in tasks requiring more reactive control (Enriquez-Geppert et al., 2014), a finding recently replicated in a similar study

(Eschmann & Mecklinger, 2021). These NF studies used task theta to estimate an individual NF training frequency, as well as using resting state theta activity as a baseline for the NF training. Thus, the effects of NF-training on cognitive control might depend on a relationship between task theta and RS-theta. Although the evidence is scarce, the putative relationship between RS-theta and task-elicited FM-theta during both reactive and proactive control is supported by the associations between RS-theta and task performance, as well as the role of FM-theta activity in neural communication and top-down constraints of sensory or motor activity (Cavanagh & Frank, 2014; Stein et al., 2000).

What is the nature of resting state dynamics that might mediate task performance and task activity? One possibility is that resting state activity reflects individual differences in baseline activity of the underlying neural generators or of the dopaminergic system (Bellucci et al., 2019). During a task requiring cognitive control, task-elicited FM-theta activity might be affected by individual differences in the ability to modulate or upregulate the neural mechanisms relevant for efficient cognitive control. If FM-theta activity reflects surprise, conflict, or a more general need for control (Cavanagh et al., 2012; Dippel et al., 2017; Lavallee et al., 2014), high resting state theta activity might reflect a higher baseline level or an increased readiness for the task at hand, thus making alarm or control thresholds faster to reach. Such a relationship might not necessarily reflect a simple mapping of RS-theta to cognitive control but may to some degree reflect the functional capacity of the neural system reflected in FM-theta activity during tasks (Deco et al., 2011). Similarly, it has been suggested that resting state activity reflects the activity of a limited set of functional networks that are dynamically recruited and modulated during tasks (Mantini et al., 2007), such that task-elicited FM-theta activity is a result of a variety of resting state dynamics, including, but not limited to, RS-theta, that are recruited on demand. Nevertheless, these explanations warrant a putative relationship between resting state theta and task-elicited theta, which has not yet been fully investigated.

1.5 Summary

The reviewed literature indicates that proactive and reactive control is associated with both distinct neural networks, as well as common electrophysiological signatures. Specifically, it seems as reactive control of response inhibition is associated with activity in a right-lateralized network including the rIFG and the pre-SMA. However, how such activity is modulated by proactive control is not yet certain. Although research seems to suggest that there is some overlap in the regions associated with proactive and reactive control of inhibition, how the activity in these regions is modulated by different degrees of

proactive control, and how this shapes efficient response inhibition has remained equivocal. Furthermore, FM-theta has been suggested as a neural marker of cognitive control based on its association with cognitively interfering events and conflict-induced modulations. However, as a marker of cognitive control, FM-theta should also be associated with proactive modes of control. FM-theta activity might reflect a need for control both in expectation of, and triggered by, an interfering event, and act as a temporal window for communicating this need by top-down constraints on sensory-, motor- and cognitive processing. In this regard, FM-theta activity may be a biologically plausible marker of mechanisms implementing both proactive and reactive control at the neural level. Additionally, the tendency to adopt a proactive or reactive control mode might vary with stable characteristics of the individual, possibly reflected in resting state activity. Specifically, resting state theta activity might reflect a functional capacity of the underlying neural generator, such that increased RS-theta make control-processes, as reflected in FM-theta, more readily activated when needed. Although this is supported by evidence of a relationship between RS-theta and cognitive control performance, the relationship between RS-theta, task-elicited FM-theta, proactive and reactive control has remained equivocal. Thus, the current thesis fills a void in the investigation of the neural underpinnings of proactive and reactive control in general, with specific focus on response inhibition and FM-theta activity.

2. Research Questions

Based on the reviewed literature, three broad research questions were investigated in the present thesis.

2.1 Are the neural mechanisms enacting response inhibition affected by proactive control?

As suggested by the reviewed literature, the effect of proactive control seems to lead to increased activity in some of the regions of the stopping network, although this has mainly been investigated using comparisons of certain and uncertain go-trials. It has remained unclear if there is a differential effect of proactive control across the stopping network in general, and within sub-regions of the rIFG. The first objective of the present thesis was to investigate how activity in regions usually associated with response inhibition (i.e., the stopping network) is modulated by varying the degree of proactive control, and if different sub-regions of the rIFG are modulated to different degrees. The reason for this objective was to confirm that proactive control affects response inhibition processes at the neural level, and to pinpoint any functional dissociations in proactive and reactive control processes in the spatial domain.

2.2 Is FM-theta a neural marker of both proactive and reactive control of inhibition?

FM-theta activity has been coined a theta lingua franca due to its association with a wide variety of cognitive control processes. However, FM-theta activity in proactive control processes has only recently become a focus of investigation. In the present thesis, it is argued that if FM-theta activity reflects a mechanism signaling a general need for control, FM-theta activity should also be evident during, and should be modulated by, proactive control processes. The second objective of the thesis was therefore to investigate the effect of proactive control on FM-theta activity both during conditions with and without an explicit need for reactive inhibition, as well as temporally dissociating FM-theta activity associated with proactive control and reactive control. It was hypothesized that FM-theta activity associated with proactive and reactive control would rely on the same underlying neural generators as reflected in fMRI activity in the stopping network.

2.3 Is resting state theta activity associated with task-elicited FM-theta and cognitive control performance?

Proactive and reactive control show intra-individual variation related to personality and other stable traits. The focus on resting state, or intrinsic, brain activity for understanding task-elicited neural mechanisms is increasing. As resting state brain oscillations might reflect individual differences in the underlying anatomical structure and neuronal dynamics that may shape sensory, motor, and cognitive processing, there may be individual differences in resting state theta activity associated with cognitive control processes. The third research objective sought to investigate the possibility that theta activity during rest is associated with how cognitive control processes are implemented at the neural and behavioral level across proactive and reactive control modes.

3. Brief methodological overview

The current thesis consists of three research papers, which are based on two different experimental studies. In the first study (Paper I and Paper II), simultaneous EEG and fMRI data acquisition was utilized in combination with a cued stop-signal task to investigate the spatiotemporal correlates of proactive and reactive control of response inhibition. In the second study (Paper III), EEG data was recorded while participants performed four different cognitive tasks and a resting state measurement to assess the relationship between theta activity at rest and during different modes of control. An overview of the different study designs and relevant measures for the specific papers are listed in Table 1.

Table 1. Overview of the three papers included in the thesis.

		Sample	Tasks	Modality	Key variables
Study 1	Paper I	27 (39)	Cued stop-signal task	Behavior fMRI	Reaction times Accuracy fMRI whole-brain activity ROI activity PPI estimates Brain-behavior correlations
	Paper II	22 (39)	Cued stop-signal task	Behavior fMRI EEG	Reaction times Accuracy Average FM-theta Single-trial FM-theta EEG-fMRI joint ICA
Study 2	Paper III	21 (26)	N-back task Stroop task Standard stop-signal task Task-switching task Resting state measurement	Behavior EEG	Reaction times FM-theta RS-theta Brain-behavior correlations

Note. Overview of the two different studies conducted in the thesis and the different tasks, modalities and key variables used in the three different papers. Sample refers to number of participants included in the analyses, with total number of recruited participants in parentheses. fMRI = functional magnetic resonance imaging, ROI = region of interest, PPI = psycho-physiological interaction, EEG = electroencephalography, ICA = independent component analysis, FM-theta = Frontal-midline theta, RS-theta = resting state theta.

3.1 Participants

The study sample in both of the studies were healthy adults between 18-40 (study 1) or 18-60 (study 2) years old. Participants were recruited via social media, posters, and private networks. All participants were right-handed and reported no history of neurological or psychological disorders. Paper III is based on data collected from a larger neurofeedback (NF) study investigating the effect of EEG-NF targeted at the upregulation of FM-theta on cognitive control performance. This protocol included additional tests administered in Norwegian. Thus, the second study had an additional requirement of Norwegian as mother tongue, while in the first study all test instructions were administered in English and did not have such a requirement. Prior to participating in the study, all participants read and signed an informed consent form, and were informed that they could withdraw from the study at any time. Participants received a compensation of NOK 200 or NOK 500 for their participation in study 1 or study 2, respectively. The studies were conducted in accordance with the declaration of Helsinki, and received ethical approval from the local ethics committee at the Departments of Psychology, University of Oslo (study 1) or from the Regional Committee for Medical and Health Research Ethics in South-Eastern Norway (study 2).

3.2 Tasks and measures

The task used in study 1 was a cued stop-signal task (cues: 0%, 25%, 66%) that modulated the degree of proactive control of inhibition by explicitly giving the participants prior information about the likelihood of an upcoming stop-signal. While the participants performed this task, simultaneous recordings of EEG and fMRI were performed. The tasks used in study 2 were a standard stop-signal task, a Stroop task, an n-back task, and a task-switching task. These tasks were chosen to assess different sub-functions of cognitive control as suggested in the UD framework (Miyake et al., 2000). Further, study 2 also consisted of a resting state measurement, designed to assess the participants resting state activity. While the participants performed these tasks and measurements, EEG data was recorded. The analyses in all three papers were focused on behavioral measures from the different cognitive tasks utilized in the different studies, as well as either fMRI data (Paper I), EEG data (Paper III) or both (Paper II). In the following sections, the cognitive functions and the tasks used to assess them are described shortly. However, as response inhibition and the SST has already been described in detail (see section *1.3.1. Measuring response inhibition*), the focus is on working memory and the n-back task, interference control and the Stroop task, and set-shifting and the task-switching task.

3.2.1 Working memory and the N-back task

Working memory is the ability to maintain and update a (limited) amount of task-relevant information (Baddeley & Hitch, 1974; Shah & Miyake, 1999), and is important for a wide range of daily life functions and complex cognitive tasks (Diamond, 2013; Shah & Miyake, 1999). The n-back task is a popular task used to assess working memory. The n-back task is a continuous recognition task where the participant must decide whether the item presented on the screen is the same item presented *n* trials before. When *n* = 1, the participant must decide whether the item presented is equal to the item presented the trial before. When *n* increases, the working memory load increases accordingly. For example, when *n* = 3, the participant must decide whether the item presented is the same item as that presented 3 trials before. This requires maintaining three items in working memory, but also updating the contents of these three items at each new trial. Working memory has been associated with activity in the dlPFC (Curtis & D'Esposito, 2003; Funahashi, 2006), which seems to increase with increasing working memory load (Braver et al., 1997). Working memory has also been associated with FM-theta activity (Gevins et al., 1997; Jensen & Tesche, 2002), and this activity has been shown to stem from a midcingulate source (Onton et al., 2005). However, the interpretation of FM-theta effects during working memory tasks is complicated by the difficulty in separating the maintenance from the retention phase, in addition to large individual variability (Maurer et al., 2015) and trial to trial variability in working memory (Onton et al., 2005). Furthermore, working memory tasks likely also requires other control processes, such as sustained attention and inhibitory control of irrelevant new information (Diamond, 2013; Sauseng et al., 2010). It has been suggested that FM-theta activity during working memory might reflect the integration of information across different brain regions, important both for working memory as well as other control processes (Sauseng et al., 2010).

3.2.2 Interference control and the Stroop task

One of the most well-known and used tasks in psychology is the Stroop task (MacLeod, 1991; Stroop, 1936), consisting of congruent and incongruent color/word pairings. In the congruent conditions, the word and the color of the word matches (i.e., the word "red" written in red). In incongruent conditions, there is a mismatch between the word and the color of the word (i.e., the word "red" written in blue). The task of the participant is to respond to the color of the word, rather than the word itself. As there is a prepotent tendency to respond to the word, incongruent conditions cause interference, and requires the suppression of the automatic response to the word to allow for a response to the color instead

(Khng & Lee, 2014). Thus, interference control refers to the ability to suppress distracting stimuli from interfering with working memory or motor response operations (Jongen & Jonkman, 2008; Nigg, 2000). Such interference is commonly associated with decreased reaction times and associated activity in the rIFG, right anterior insula, the aMCC and pre-SMA, as well as FM-theta activity (Hanslmayr et al., 2008; Tafuro et al., 2019). Although both interference control and response inhibition rely on inhibitory control (Miyake et al., 2000), they seem to reflect two different types, or classes, of cognitive inhibition (Khng & Lee, 2014; Nigg, 2000), that rely on partly overlapping, but also distinct networks (Cieslik et al., 2015). However, the exact nature of the difference between the inhibition in the Stroop task and the SST is not yet clear, and may be caused by qualitatively different inhibitory mechanisms, or similar inhibitory mechanisms enacted at different levels of the task processing (Khng & Lee, 2014; Verbruggen et al., 2006).

3.2.3 Set-shifting and the task-switching task

Set-switching refers to the ability to alternate between different tasks presented sequentially without temporal overlap (Strobach et al., 2018). When the same task is repeated (i.e, respond to the shape of the stimulus) across several trials, there seems to be a priming effect facilitating task performance. However, when the task is switched (i.e, respond to the color of the stimulus) compared to the previous trial, the switch cost leads to increased reaction times and decreased performance (e.g., Hyafil et al., 2009). The ability to switch between tasks is thus dependent on cognitive control processes that regulates the task representations, updating of task goals, response selection and monitoring. The switch cost may reflect the reconfiguration of these control processes to the new task, although the exact nature of the switch cost is not clear. It has been suggested that it may reflect the priming from the previous tasks as well as task preparation and task set inhibition (Strobach et al., 2018). Indeed, it has been suggested that inhibition is necessary to inhibit the previous task set in favor of the new (Koch et al., 2010). Task-switching is associated with activity in the PFC and aMCC (Braver et al., 2003; Hyafil et al., 2009), as well as FM-theta activity during both preparation to switch and switching (Cooper et al., 2017, 2019; McKewen et al., 2020).

4. Summary of papers

4.1 Paper I: Strategy switches in proactive inhibitory control and their association with task-general and stopping-specific networks.

Background. Reactive control of inhibition is commonly associated with activity in a predominantly right-lateralized network, which for example includes the pre-SMA and the rIFG. However, how activity in this network is modulated by prior information about the probability of an upcoming stop-signal, presumably eliciting proactive control processes, is not yet known. While some research indicates a pre-activation of the stopping-network (also of the rIFG), others argue against a specific role of the rIFG in inhibition. One possible source of such disagreements is the discrepancy in the literature on which parts of the inferior frontal area that is involved in response inhibition processes, such as the pars triangularis, pars opercularis, or neighboring regions such as the anterior insula.

Methods. Simultaneous recordings of EEG and fMRI data were utilized together with a cued stop-signal task, and Paper I focused on the fMRI data and behavioral measures of response inhibition. Whole-brain contrast images as well as a region of interest (ROI) analyses (regions: left insula, pre-SMA, aMCC, right insula, right IPC, right MFG, pars opercularis, pars triangularis, striatum) were utilized to assess the effect of increasing stop-signal probability on activity in regions traditionally involved in stopping, in both go-trials and stop-trials. In addition, brain-behavior correlations were computed to assess the relationship between go-RT and ROI activity increases with increasing stop-signal probability. Finally, an exploratory psycho-physiological interaction (PPI) analysis was performed to assess the functional connectivity between rIFG pars opercularis and the rest of the brain when comparing high vs low stop-signal probability in go trials and stop trials.

Results. Increasing stop-signal probability led to increased RTs in the go trials as well as increased stop-trial accuracy, indicative of strategic proactive control adjustments. Regions traditionally associated with response inhibition, such as the pre-SMA and the rIFG pars opercularis, showed increased stop trial activity with increasing stop-signal probability, possibly indicating more efficient inhibition. However, this activity pattern was not specific to these two regions. Other regions, however, showed a different activity pattern, with some showing go trial activity modulations only, indicating a functional dissociation within the stopping network. An additional functional dissociation was evident within the rIFG itself: while the pars opercularis showed a general stop-activity modulation, the pars triangularis showed a more go-specific activity modulation, supported by a significant correlation between the go

trial activity difference in this region between the 25% and the 66% conditions and the corresponding go-RT difference.

Conclusion. The results indicate a functional dissociation within the stopping network in response to proactive control modulations that is associated with strategic behavioral task adaptions.

4.2 Paper II: Frontal-midline theta reflects different mechanisms associated with proactive and reactive control of inhibition.

Background. Reactive response inhibition is associated with activity in a right-lateralized network as well as FM-theta activity. Recent research indicates that FM-theta activity is modulated by proactive control, both after the stop-signal is presented, as well as prior to the stop-signal, as for example elicited by a probability cue. It is less clear how such cue-locked FM-theta activity is modulated by proactive control, and how both cue-locked and target-locked (i.e., go-/stop-locked) activity is associated with behavioral performance measures of inhibition. Furthermore, if proactive and reactive inhibition processes are explained by a unitary control mechanism, then the corresponding FM-theta activity should originate from the same neural generators. However, the relationship between FM-theta activity and activity at the source level, and how it is modulated by varying degrees of proactive control, is not yet known.

Methods. A cued stop-signal task (cues: 0%, 25% and 66%) in combination with simultaneous recordings of EEG and fMRI was utilized. FM-theta activity was investigated at three levels: At the trial-average level comparing cue-locked and target-locked theta activity in the different trial types, at the single-trial level investigating the association between single-trial FM-theta activity and behavioral measures; and at the neural source level using a joint ICA analysis to integrate the fMRI and EEG data. Further, FM-theta activity was investigated at two time points: during the proactive cue period, and after the target signal, which was either the go or stop signal.

Results. At the trial-average level, there was higher target-locked FM-theta activity in the stop trials than in the go trials, and in the 66% condition compared to the 25% condition. However, these differences were not evident in cue-locked FM-theta activity. At the single trial level, both higher cue-locked and go-locked FM-theta activity were associated with shorter reaction times in go trials, while higher stop-locked FM-theta activity was associated with a lower probability of successful response inhibition in the stop trials. This dissociation was also evident at the neural source level, where specific independent components related to going, stopping, and cue-associated proactive control were associated with

distinct cortical regions. Regarding the stop activity, a specific component emerged reflecting FM-theta and originating from a right-lateralized network. In contrast, go activity was associated with activity in the cingulate gyrus and the medial frontal gyrus, including the SMA.

Conclusion. The results indicate that FM-theta activity can be dissociated into several mechanisms associated with proactive control, response initiation, and response inhibition processes.

4.3 Paper III: Theta at rest and on task: associations with cognitive control performance.

Background. FM-theta activity is thought to reflect a general cognitive control process associated with a wide variety of cognitive control tasks. Recent research indicates that FM-theta activity measured at rest is also associated with cognitive control performance, because it reflects features of an individuals' cognitive control networks. This implies an association between resting state and task-elicited FM-theta activity, that could also extend to behavioral measures. However, it is not certain how such a relationship might vary between proactive and reactive modes of control and different cognitive control sub-functions.

Methods. Behavioural performance and FM-theta activity were measured during the completion of four different cognitive control tasks: the n-back task, the Stroop task, the SST, and the task-switching task. It was assumed that these tasks differ in their reliance on predominantly proactive or reactive task strategies, such that the SST and the Stroop task relies more on reactive control strategies, while the n-back task and the task-switching task relies more on proactive control strategies. The association between these task measures and resting state theta (RS-theta) activity was analysed with several repeated measures ANCOVAs in a Bayesian statistical framework.

Results. There was no evidence for higher FM-theta activity in conditions with high cognitive load compared to the conditions with low cognitive load in the n-back task, the Stroop task, and the task-switching task. Only in the SST did FM-theta activity show the expected load modulations with higher FM-theta activity in stop-trials compared to go-trials. Further, task theta was negatively correlated with RTs in the stay-condition in the task-switching task, and the three-back-condition in the n-back task. Lastly, there was no evidence for a relationship between RS-theta activity and task-elicited FM-theta activity in any of the cognitive control tasks. There was, however, evidence for a negative correlation between RS-theta activity and reaction times in the n-back task, such that higher resting state activity was associated with shorter reaction times in the three-back condition.

Conclusion. The results indicate that the relationship between RS-theta and task-elicited theta is weak. However, resting state dynamics may still be associated with task performance during cognitive control. Furthermore, the results indicate that although task FM-theta activity clearly is associated with task behaviour, the effects of increased cognitive load on behaviour is driven by processes not reflected in FM-theta activity.

5. Discussion

The aim of the thesis was to investigate the neural correlates of cognitive control, focusing specifically on proactive and reactive control processes in response inhibition. In addition, it was investigated whether neural correlates of cognitive control were associated with resting state activity. To these means, EEG and fMRI data was recorded together with cognitive tasks measuring different sub-components of cognitive control. We found that proactive and reactive control of response inhibition were associated with distinct spatiotemporal neural correlates that were modulated by stop-signal probability (Paper I and Paper II). Increased stop-signal probability in a cued stop-signal task led to a proactive slowing of reaction times and increased stop trial accuracy, indicating that the stop-signal probability modulations increased proactive control. In Paper I, we showed that such reaction time slowing was associated with go-trial activity in specific regions of the stopping network, while other regions clearly showed more stopping-specific activity patterns, indicating functional specialization within the stopping network. In Paper II, integration of the EEG and fMRI data showed that FM-theta activity reflects different mechanisms associated with proactive and reactive control of inhibition. In Paper III, it was found that RS-theta activity was associated with specific task behaviour, but not with task-elicited FM-theta activity. We did not find support for our hypothesis of a specific relationship between RS-theta and proactive and reactive control modes. Overall, these results are summarised in three key findings, discussed next.

5.1 Functional heterogeneity of the rIFG during response inhibition

Two decades of research have consistently associated response inhibition with activity in the rIFG (Aron et al., 2004, 2014; Chikazoe et al., 2007, 2009; Yi & Kim, 2020), and the present results are in line with such findings. Furthermore, several lines of research have also pointed to the role of the rIFG in proactive control of inhibition, either facilitating braking in the likelihood of an upcoming stop-signal (Aron, 2011; Wessel et al., 2013), or by top-down control of the basal ganglia (Jahfari et al., 2012). Although such consistent findings seem to indicate a clear role of the rIFG in response inhibition, the present thesis offers a more nuanced interpretation. Specifically, an interpretation of the current findings in the context of both unimodal and multimodal EEG-fMRI assessments as presented here indicate that 1) rIFG is a functionally heterogenous region, 2) activity in the rIFG might not reflect outright stopping per se, and 3) regions beyond the rIFG are also involved in response inhibition. Thus,

the present results are in accordance with a more domain-general account of the rIFG in response inhibition.

5.1.1 Activity within rIFG sub-regions varies in response to proactive control modulations.

Previous reports show that there are dissociable regions within the inferior frontal area that show some degree of functional specialisation (Sebastian et al., 2016; Verbruggen et al., 2010), although the exact nature of this functional specialisation is unclear. In paper I, we found support for such a functional dissociation by showing different effects in the rIFG pars opercularis and pars triangularis during proactive control of response inhibition. Specifically, we found that while the pars opercularis showed higher activity in the 66% condition compared to the 25% condition in both the go- and stop-trials, the pars triangularis showed a more go-specific effect, with significantly higher go-trial activity in the 0% and the 66% condition than in the 25% condition, but no stop-trial modulations. Furthermore, the pars triangularis was associated with proactive modulations at the behavioural level in terms of correlations with go trial RTs, supporting such a dissociation. The results of Paper II are also in line with a functional dissociation of the rIFG during response inhibition: although both cue-associated and target-associated rIFG activity was evident in the stop component, inspection of the MNI coordinates revealed that the cue-associated rIFG activity was in close proximity to the pars opercularis ROI in Paper I, while the target-associated activity corresponded to more ventral regions of the rIFG. Overall, these results further confirm the role of the rIFG pars opercularis in response inhibition (Aron et al., 2014; Curley et al., 2018), here including the proactive preparation to stop. The pars triangularis showed a more go-specific activity in Paper I, and has been associated with the updating of responses according to current task goals or action plans (Lenartowicz et al., 2011). These results highlight the functional heterogeneity of the rIFG that should be taken into account when investigating response inhibition in the future.

5.1.2 The nature of rIFG activity during response inhibition.

A long-lasting debate in the response inhibition literature is whether rIFG activity reflects response inhibition per se (i.e., outright stopping), or rather a more general attentional mechanism (e.g., Aron et al., 2014; Hampshire, 2015; Swick & Chatham, 2014). For example, Hampshire and colleagues (2010) investigated the role of the rIFG in attention and response inhibition by contrasting trials that required no overt response, trials that only required a response to a behavioural cue, and trials requiring

response inhibition. The results showed that rIFG activity increased in all three of these conditions, indicating that the rIFG does not respond to response inhibition demands specifically, but perhaps rather to salient cues relevant for the task at hand (Hampshire et al., 2010). Furthermore, Erika-Florence and colleagues (2014) showed that rIFG sub-regions did not differ in their response to inhibitory demands, indicating that the attentional and inhibitory effects cannot be ascribed to different regions of the rIFG. However, as previously discussed (*5.1.1. Activity within rIFG-subregions vary in response to proactive control modulations)*, our data support a functional dissociation within the rIFG, at least in terms of proactive control of response inhibition.

Although the present thesis cannot dissociate between attentional and inhibitory effects, the results of Paper II do indicate that the rIFG is involved in response inhibition-related activity: the stop-component, and not the go-component was associated with rIFG activity. Furthermore, this was true for both cue-locked and target-locked activity. The added temporal information of the EEG in the joint-ICA also contributes to the interpretation of the ROI activity in Paper I: the pars opercularis and the anterior insula were the only regions in the right inferior frontal area that showed increased activity with increased stop-signal probability, which, together with the stop-component activation in the rIFG, indicates that these regions are involved in response inhibition. However, Paper II also showed that rIFG activity was evident in one of the proactive components, indicating that such activity does not reflect outright stopping, but rather other processes involved in response inhibition, such as proactive preparation. The single-trial analyses in Paper II further indicates that the stop-associated rIFG activity was not associated with outright stopping. Here, higher stop-locked FM-theta activity was associated with a higher probability of an unsuccessful stop-trial, while cue-locked theta activity in the stop-trials was not associated with stop-trial outcome. If the rIFG activity associated with FM-theta activity seen in the joint-ICA analysis would reflect outright stopping, then one would assume that this activity would also be associated with successful inhibition at the single-trial level, but this was not the case, neither for cue-locked, nor stop-locked theta activity.

It has been suggested that the similar activity patterns evident during stop-trials and ignore-trials do not reflect attention, but rather is evidence for inhibitory demands in all trials, also trials that do not require one to inhibit a response (Waller et al., 2021; Wessel & Aron, 2013, 2017). Indeed, recent research has suggested a two-stage model of response inhibition, where the rIFG implements an initial inhibitory “pause” response associated with a general attentional capture of all salient events, followed by a second stopping-specific “cancel” response that relies on activity in a broader network including the

pre-SMA, possibly also giving rise to the fronto-central ERPs and the stop-elicited FM-theta activity (Tatz et al., 2021).

Neither a pure attentional account, nor the two-stage model described above is entirely consistent with the present findings. The attentional account suggests that rIFG activity should be modulated by attention. In Paper I, it was found that the rIFG pars opercularis showed increased activity with increasing stop-signal probability. Importantly, the pars opercularis ROI used in Paper I closely corresponds to that of Hampshire (2015). If this activity would reflect salience or attentional processing, one would rather have expected the opposite effect: decreased rIFG activity with increasing stop-signal probability due to the stop-signal being relatively less infrequent and less novel. Although this seems to contradict the attentional hypothesis, the fMRI results in Paper I cannot dissociate the cue-related and stop-related activity during stop-trials. Thus, the increase in activity in the pars opercularis cannot be ascribed to stop-locked effects entirely. On the other hand, the two-stage model suggests that rIFG activity should be associated with inhibitory attentional demands regardless of trial type. However, this was not supported by the joint ICA results in paper II: rIFG activity was only evident during the stop-component and one of the proactive components, but not the go-component, indicating that rIFG activity does not respond to all salient events. Finally, the two-stage model implies that FM-theta activity would be a reflection of the cancel response specific to outright stopping. Here, on the other hand, we show that FM-theta activity elicited by the stop-signal does not reflect outright stopping per se, as increased theta was associated with stronger probability of an unsuccessful stop-trial, suggesting a reflection of more general control-related processes. Thus, it seems clear that such models cannot be interpreted without considering rIFG heterogeneity, FM-theta multidimensionality, and proactive control.

5.1.3 Response inhibition is not exclusively reflected in rIFG activity.

The long-standing focus on the rIFG in response inhibition has given this region a special role in successful inhibition. However, research has also consistently implicated regions such as the insula, left IFG, pre-SMA, the IPC and the aMCC in response inhibition, although their contribution to outright stopping has often been down-played, especially according to modular approaches focused on the rIFG (and to some extent also the pre-SMA). However, domain-general approaches have shifted the focus away from specific regions, and rather towards general networks. In Paper I, it was found that the pre-

SMA, the aMCC, and the right anterior insula, all showed higher stop-trial activity in the 66% condition compared to the 25% condition, in addition to the rIFG pars opercularis. This is in line with previous research, showing that the pre-SMA, insula and the aMCC are important regions in reactive control of inhibition, but also that these regions show modulations by proactive control (Chikazoe et al., 2009; Zandbelt et al., 2013). The involvement of many of these regions in response inhibition was further confirmed by the findings of Paper II. Specifically, we found that a single independent component seemed to capture the stopping-specific FM-theta activity, which was associated with activity in a right-lateralised network including the IFG, MFG, insula, and the SMA. Of note, the stop-associated activity in the insula and the SMA overlapped with the right insula and pre-SMA ROIs in Paper I, thus confirming that the increase in these regions from the 25% to the 66% condition is associated with stopping-associated processes.

The pre-SMA has been implicated in response inhibition (Cai et al., 2012; Nachev et al., 2007, 2008), although its exact functional role is debated. During conditions requiring reactive control (i.e., when the stop-signal probability is low), it has been suggested that the rIFG and the pre-SMA have dissociable effects on the basal ganglia (Jahfari et al., 2012). Specifically, while higher activity in the rIFG was associated with higher activity in the STN and the caudate, higher pre-SMA activity was associated with lower activity in the STN and the caudate. This indicates that when a stop-response is less prepared, connectivity between the preSMA and the STN/caudate serves to rapidly increase response thresholds in the basal ganglia (Forstmann et al., 2008, 2010; Jahfari et al., 2012). This fast modulation of basal ganglia activity is in line with findings of pre-SMA activity preceding that of the rIFG (Swann et al., 2012), and indicates an important role of the pre-SMA in conveying conflict detection to relevant regions. This is further supported by the close proximity and interconnectivity between the aMCC and the pre-SMA (Hoffstaedter et al., 2013; Nachev et al., 2008). In paper I, the pre-SMA showed specific stop-trial activity modulations to increased stop-signal probability, as well as being associated with stopping in the joint ICA analysis in Paper II. Considering the reviewed literature, this indicates that when stopping is expected, pre-SMA serves important implementation of control during response inhibition, perhaps via connections to the basal ganglia regions.

Some research also points to the right anterior insula as an important region for the detection of behaviourally salient events during response inhibition (Cai et al., 2014; Levy & Wagner, 2011). In Paper I, we found that the bilateral insula showed both go-related and stop-related effects in relation to stop-signal probability modulations. Indeed, these two regions also showed associations with behavioural

proactive adaptions. In Paper II, activity in both the left and right insula was associated with go-related FM-theta activity in one independent component, while activity in the right insula was associated with stopping in another component. This indicates a more general effect of the anterior insula in response inhibition tasks, beyond outright stopping per se. Of note, it is interesting that the rIFG, pre-SMA and the anterior insula all showed a similar activation pattern across stop-signal probability conditions in Paper I, and across several of the components in the joint ICA in Paper II. In fact, together with the aMCC, these regions have been proposed as core regions of a multiple demand network (Camilleri et al., 2018).

5.2 FM-theta activity is a non-unitary reflection of cognitive control

The present thesis investigated task FM-theta activity in two settings: 1) as a reflection of proactive and reactive control in response inhibition, and 2) as a reflection of different cognitive control sub-functions. Here, it was found that proactive FM-theta activity (as elicited by a probability cue) reflects both preparation to respond and (likely) preparation to stop, while target-locked theta activity seems to reflect control processes beyond outright stopping. Further, FM-theta activity does not show similar effects of cognitive load across different cognitive tasks, as well as dissociable relationships with behaviour between tasks. On the basis of these results, it is suggested that FM-theta is a heterogeneous feature associated with both response initiation and response inhibition, as well as reflecting control across a range of cognitive tasks. These findings are discussed in more detail next.

5.2.1 FM-theta activity during proactive control.

Recent research has suggested that cue-locked or pre-trial FM-theta activity is indicative of proactive control and is associated with behaviour (Adelhöfer & Beste, 2020; Chang et al., 2017; Cooper et al., 2019; Dippel et al., 2017), and the results of the present thesis are in line with such reports. In Paper II, the single-trial linear regression investigating the effect of FM-theta activity on go trial reaction times revealed that higher cue-locked and go-locked activity were significant predictors of faster reaction times. The relationship between cue-locked theta and reaction times has been shown using other tasks of cognitive control (M. X. Cohen & Cavanagh, 2011; M. X. Cohen & Donner, 2013; Cooper et al., 2017), and the present study is one of the first to show that both cue-locked and go-locked FM-theta activity are associated with go-trial reaction times in a cued stop-signal task on the single-trial level. Here, we suggest that such proactive FM-theta activity is reflecting a heightened preparation of the motor control

network in general, which leads to fast and correct responses in the go-trials but results in an error-prone strategy in the stop-trials. Although no association between cue-locked FM-theta activity and behaviour in the stop-trials was found at the single-trial level, the idea of proactive FM-theta activity as reflecting general response preparation may explain the unexpected higher cue-locked FM-theta activity in the unsuccessful stop-trials compared to the go-trials as revealed by the trial average analysis. According to assumptions of the horse race model, unsuccessful stop-trials are a result of reaction times faster than the SSRT + SSD, while in successful stop-trials the reaction times are slower, giving the stop-process enough time to win the race. Thus, the increased cue-locked FM-theta activity in the unsuccessful stop-trials compared to the go-trials might reflect increased preparation to respond in these trials, leading to fast reaction times and thus unsuccessful inhibition. Although this association was not tested specifically at the trial-average level, it is supported by findings of increased theta-beta cross-frequency coupling prior to unsuccessful compared to successful no-go trials in a cued spatial attention GNGT, interpreted as reflecting early response activation (Bengson et al., 2012).

It has been suggested that the relative success or failure to stop is dependent on the preparation or control adjustments of stopping before the stop-signal (Elchlepp et al., 2016; Knyazev et al., 2008). Indeed, it has been shown that when proactive control is high, the top-down effective connectivity between the PFC and the STN and striatum in the basal ganglia is weaker, indicating a lower need for reactive control (Jahfari et al., 2012). These results are not necessarily at odds with the results of Paper II, as the relationship between single-trial theta activity and behaviour was pooled across the different probability conditions. In the go-trials, this also included the 0% condition where participants clearly adopted a fast response strategy, which might lead to a stronger relationship between cue-locked theta and behaviour in the present results. Although it was somewhat surprising that the cue-locked theta activity was not associated with stop-trial outcome at the single-trial level, and was not modulated by stop-signal probability at the trial average level, the joint-ICA analysis did reveal a stop-related component that was associated with both cue-locked and stop-locked theta activity. This component also showed associations with rIFG activity. Although one needs to be careful of reverse inferences, the results do indicate that there is a role of cue-locked FM-theta activity in proactive control of inhibition, but that cue-locked FM-theta activity is also associated with other processes. Here we show that such cue-locked FM-theta activity also facilitates fast responding.

The dissociation between FM-theta activity as reflected in both response inhibition as well as response preparation was reflected at the neural source level. Here, it was found that FM-theta activity

in go- and stop-trials could be dissociated into components related to either going, stopping or proactive control. Furthermore, these components were associated with specific regions of the brain, confirming that FM-theta activity is indeed heterogeneous in nature. Specifically, the stop-component showed both stop- and cue-related theta activity, that was associated with activity in a clearly right-lateralised network. Go-related theta-activity activity was captured by another component, and was associated with activity in the MFG, the caudate, the bilateral IFG, as well as the SMA. Finally, additional cue-related activity was captured by two independent components, although with a somewhat more inconsistent fMRI activity pattern. The result of the independent component analysis together with the EEG data thus support the notion of functional heterogeneity of FM-theta activity.

5.2.2 Target-locked FM-theta activity.

The results of Paper II indicate that target-locked FM-theta activity is important for both response inhibition as well as response execution. It was found that after the presentation of a go- or stop-signal, FM-theta activity was on average higher in the 25% condition than in the 66% condition, and higher in the stop-trials than the go-trials. This is in line with previous reports of proactive modulations of FM-theta activity and ERPs (Dippel et al., 2016, 2017; Enriquez-Geppert et al., 2010; Nieuwenhuis et al., 2003; Ramautar et al., 2004), and might reflect conflict-induced modulations and an increased need for control (Cavanagh et al., 2012; Cavanagh & Frank, 2014). Specifically, when the probability of stopping is high, the relative conflict induced by the stop-signal is perceived as lower, and the associated FM-theta activity might be a reflection of a relatively lower need for control (Botvinick et al., 2001; Cavanagh et al., 2012).

Second, the fact that FM-theta activity reflects a need for control is supported by even higher FM-theta activity in the unsuccessful stop-trials than the successful stop-trials. At the single-trial level, higher FM-theta was associated with higher probability of an unsuccessful stop-trial. This is in line with previous reports of higher N2 amplitudes and FM-theta activity during unsuccessful compared to successful stop-trials (González-Villar et al., 2016; Knyazev et al., 2008), and is consistent with accounts of FM-theta activity as a generic control mechanism (Cavanagh et al., 2012). One possible explanation for such effects is that during unsuccessful stop-trials, the stop-signal is less expected, or the stop response less prepared. This leads to a relatively larger conflict induced by the detection of the stop-signal, and a larger need for control to be able to inhibit the response, that nevertheless is insufficient to

successfully inhibit the response. Such an account is in line with previous research finding that much of the control of response inhibition is enacted before the stop-signal is presented (Elchlepp et al., 2016). Importantly, this finding supports the notion that successful inhibition is not due to higher stop-locked FM-theta activity specifically, but that FM-theta rather reflects a general need for control recruited at the detection of conflict.

The importance of proactive preparation can also explain the result of Paper III. Interestingly, we found that the tasks relying more on proactive control (i.e., the n-back task and the task-switching task) did not show a difference in FM-theta activity between the high and low cognitive load conditions. Although proactive control was not modulated explicitly in Paper III, this may indicate that when the overall level of top-down control is high, the reliance on reactive control processes to facilitate efficient performance is lower. Thus, proactive control offers a putative explanation as to why there was a difference in reaction times between the low and high cognitive load conditions in these tasks, but not a difference in FM-theta activity. The role of proactive control in task-switching is supported by research on cued stop-signal tasks finding an effect of cue-locked theta activity on go-trial reaction times (Cooper et al., 2019), and that theta activity increases before difficult tasks (Loof et al., 2019). Furthermore, the relationship between proactive control and working memory (Braver, 2012; Redick, 2014), in addition to the role of FM-theta activity in working memory (Zakrzewska & Brzezicka, 2014), further suggests a putative role of proactive preparation in the task performance and task elicited FM-theta activity in these tasks. These findings indicate that during tasks relying more on proactive control across trials, there is less need for reactive control processes, as reflected in target-locked FM-theta activity, to facilitate efficient behaviour. In these instances, it has been suggested that FM-theta might rather reflect a common target-related control process (McKewen et al., 2020).

The SST was the only task in Paper III that showed increased FM-theta activity in the high cognitive load condition compared to the low cognitive load condition, in line with the findings from Paper II. In Paper II, we found a relationship between go-trial theta activity and reaction times, in that higher FM-theta activity was associated with shorter reaction times. Although the evidence for such an effect remained inconclusive in Paper III, a visual inspection of the data revealed similar relationships in both the go- and the stop-trials. The fact that the SST was the only task where there was a theta-difference between the high and low load condition, and that the stop-trial theta activity was higher than the high load conditions in any of the other tasks warrants the question of what separates response inhibition from the other executive functions targeted in Paper III. It has been suggested that

both the Stroop task, the task-switching task, as well as the n-back task may all require some degree of inhibition (Khng & Lee, 2014; Koch et al., 2010; Nigg, 2000), indicating that the difference between the SST and the other tasks is not a reflection of inhibition per se. However, these tasks are thought to target different forms of cognitive inhibition (Nigg, 2000), and the difference between these tasks might reflect a more control-demanding inhibition in the stop-signal task. This is supported by differences between the SST and the GNGT, which are thought to rely on different mechanisms for action suppression (Raud et al., 2020b). Comparisons of the stop trials in the SST to no-go trials in the GNGT have shown that the P3 is usually larger in stop trials compared to no-go trials (Cunillera et al., 2016; Enriquez-Geppert et al., 2010). Furthermore, research has shown that these tasks do not differ in the N2 (Enriquez-Geppert et al., 2010). As the N2 is thought to reflect conflict monitoring processes, these results indicate that the GNGT and the SST differ in their degree of control, and not in the degree of conflict. This is further supported by a study comparing the GNGT to other tasks requiring either a response or a change of response in a minority of the trials thus eliciting conflict, which found no difference between tasks in FM-theta activity (Kaiser et al., 2019). Overall, these results indicate that FM-theta activity is sensitive to degree of control.

Furthermore, the results of both Paper II and Paper III suggests that FM-theta activity during cognitive control reflects control-modulations beyond those of conflict and novelty. For example, one possible explanation of the difference in FM-theta activity in the go- and stop-trials in the SST in Paper III, that was not evident in the other tasks (i.e., n-back, Stroop, and task-switching), is that stop-signal FM-theta activity is increased due to the novelty of the stop-signal, which is presented on a minority of the trials in the SST. However, in Paper II we showed that FM-theta activity is modulated by effects beyond mere novelty. Furthermore, the task-switching task in Paper III also had less frequent presentations of the switch trials, compared to the stay trials, and no difference in FM-theta activity was found here, again indicating that FM-theta activity does not reflect novelty per se. Thus, although novelty might contribute to the increased FM-theta effect, it does not explain the full breadth of theta dynamics in the present thesis. Another possibility is that stop trials are associated with more conflict-related processing than the other high cognitive load conditions (i.e., incongruent trials in the Stroop task, three-back-targets in the n-back task, and switch-trials in the task-switching task). Although the three-back condition and the switch trials might not reflect conflict per se, there is clearly conflict induced by the incongruent trials in the Stroop-task (Entel et al., 2015; Heidlmayr et al., 2020). Thus, the FM-theta activity seen in both Paper II and Paper III together support the notion that FM-theta activity reflects control adjustments beyond those of conflict and novelty.

5.2.4 FM-theta as a multidimensional feature.

The notion of FM-theta activity as a multidimensional feature is in line with recent research (Eisma et al., 2021; McKewen et al., 2021; Zuure et al., 2020). For example, McKewen and colleagues (2021) used a cued task-switching task to dissociate theta networks associated with proactive and reactive control. By comparing theta coherence at FCz and Pz seed regions with associated switching and mixing costs, they showed that distinct frontoparietal theta networks were associated with proactive and reactive control (McKewen et al., 2021). Eisma and colleagues (2021) showed that FM-theta activity was evident during different tasks targeting response inhibition (GNGT), proactive and reactive control (AX-continuous performance task), and during response conflict (modified flanker task). Although all tasks elicited a higher FM-theta activity response during conditions requiring high compared to low conflict (i.e., no-go trials compared to go trials in the GNGT), there were also differences between tasks. Specifically, reactive control and inhibitory control did not differ in FM-theta activity, but both had higher theta than proactive control and response conflict. Proactive control was again higher than response conflict. Thus, although that study used a somewhat different cognitive control partitioning scheme than the current thesis, the results clearly indicate a dissociation of FM-theta activity between different sub-components of cognitive control. Finally, Zuure and colleagues (2021) used a multivariate source-separation approach to test whether FM-theta activity, as elicited during a conflict-inducing Simon task, reflects a multidimensional feature. They found support for this hypothesis by showing that at the subject-level, there were multiple FM-theta components that reflected unique features of the data and remained stable over time, thus indicating that the FM-theta signal consists of the aggregated activity of multiple, diverse theta generators. The present results are in accordance with such findings and demonstrate that FM-theta activity related to proactive and reactive control of inhibition reflects a multidimensional feature associated with different neural mechanisms and regions.

5.3 Proactive and reactive control is not reflected in resting state theta

The present thesis did not find support for an association between resting state theta activity and proactive and reactive control modes. Specifically, there was no evidence for a difference in the effect of RS-theta on FM-theta activity between the different tasks. It has been suggested that individual differences in abilities to actively maintain task goals and representations impacts the tendency to adopt a proactive control mode, and that this ability depends on working memory (Braver, 2012). Thus, the finding of a negative correlation between resting state theta and performance in the three-back task

indicates a relationship between resting state and working memory, that may represent a putative link to proactive control. The three-back task has a higher working memory load that the one-back task, indicating that resting state activity is associated with more complex working memory processes. However, the evidence for similar relationships in the other tasks was overall inconclusive, making interpretations about specific relationships between resting state activity and proactive/reactive control difficult. This finding was unexpected, considering the importance of inter-individual differences in proactive and reactive control processes in the DMC framework (Braver, 2012), as well as the relationship between resting state activity and stable traits such as personality and intelligence. Although the evidence remained inconclusive in either direction, there are several reasons grounded in the present design and analysis, as well conceptual issues that may explain this discrepancy. These reasons are discussed next.

First, the present thesis focused on FM-theta activity due to its associations with reactive control and putative relationship with proactive control. However, a relationship between resting state activity and task-elicited neural dynamics might not operate at such a predefined frequency band. Specifically, the stable characteristics evident in resting state activity may be a result of an emergent property across several frequency bands, regions, and networks. Thus, focusing on theta activity measured at a single channel might be a too narrow approach to capture these effects. However, the same might be true for cognitive control processes in general: efficient control is unlikely the result of activity in a single frequency band (see section *5.4.1 Cognitive control is not exclusively associated with FM-theta activity*). The assumption that FM-theta activity reflects some of the underlying control processes, as well as underlying neural source activity (such as aMCC function or structure), still holds for resting state theta activity. Thus, although the lack of support for an association between RS-theta and proactive and reactive control in the present thesis might be a result of the complex dynamics surely underlying resting state activity, the approach still gives valuable information about the specific relationship between resting state activity and cognitive control in the theta frequency band.

Second, in Paper II it was found that FM-theta activity is a multidimensional feature, possibly reflecting mechanisms related to both proactive control, response inhibition, as well as response preparation. Thus, it may be that such complexity in the FM-theta signal masks RS-theta associations with sub-functions reflected in the task-elicited theta activity. Thus, approaches more capable of handling such complexity, such as component-based or other signal decomposition methods, might be a more fruitful approach for investigating such relationships.

Third, although resting state activity might represent some stable characteristic of the individual, whether these characteristics are related to personality traits or individual cognitive differences relevant for proactive and reactive control is not certain. Braver (2012) states that both trait reward sensitivity, and threat sensitivity should be associated with proactive control, while trait and state anxiety have been associated with the tendency to adopt a more reactive control strategy. Further, individual differences in working memory capacity and intelligence should also affect the proactive control mode, as they affect the ability to actively maintain goal-relevant information in working memory. Thus, in the DMC framework, the putative relationship between resting state activity and proactive and reactive control might be dependent on an association between resting state activity and these trait characteristics.

Research has shown that that resting state fMRI activity and connectivity have been associated with trait impulsivity as measured by the behavioural inhibition system/ behavioural activation system (BIS/BAS) scale (Angelides et al., 2017; Krmpotich et al., 2013), trait anger (Fulwiler et al., 2012), and trait anxiety (Modi et al., 2015). However, in the EEG domain there seem to be somewhat more conflicting results. Although resting state EEG activity has been found to show trait-like individual differences (Erickson et al., 2018), and that the personality trait of agreeableness can be decoded from EEG resting state activity (Jach et al., 2020), others have not found similar results (Korjus et al., 2015). One study found that frontal resting state EEG activity was associated with individual differences in risk-taking behaviour (Studer et al., 2013), indicating that resting state EEG activity indeed can be related to differences in proactive and reactive control. However, a systematic review of over 50 studies could not conclude on any systematic relationships between resting state EEG activity and approach/avoidance behaviour (A. Vecchio & De Pascalis, 2020), which is related to anxiety and the tendency to adopt a more reactive control mode. Although a complete review of the literature on the relationship between EEG resting state activity and these traits are beyond the scope of this thesis, the results indicate that the relationship between EEG resting state activity and traits associated with proactive and reactive control is unclear. Thus, if such a relationship is not evident in the resting state theta activity, this might explain why the present thesis did not find such a relationship.

Finally, the exact nature of resting state activity and its role in cognitive control is not yet clear. Research has shown that activity resembling resting state dynamics is still evident during task performance, indicating that intrinsic brain activity affects and interacts with task-elicited processes (Fox et al., 2006, 2007). Indeed, in a study on resting state fMRI activity, it was found that up to 74% of the

relationship between task performance and task activity could be attributed to ongoing fluctuations in intrinsic activity in the somatosensory cortex (Fox et al., 2007). Furthermore, research has shown that drug-induced modulation of the dopaminergic system led to modulations of resting state activity, which again affected the participants evaluation of facial attractiveness (Bellucci et al., 2019). Considering the role of the dopaminergic system in cognitive control (Braver, 2012; Cools, 2015; Friedman & Miyake, 2017), and the reviewed relationship between resting state activity and cognitive control performance, the dopaminergic system offers a putative way in which such associations may be enacted. To summarize, whether resting state activity is associated with task performance through increased baseline activity levels, underlying neuroanatomy, or the dopaminergic system (or perhaps most likely: a combination of all these factors), yields exciting prospects for future research and our understanding of cognitive control.

5.4 Methodological considerations

5.4.1 Cognitive control is not exclusively associated with FM-theta activity.

Although the main focus of the present thesis in terms of oscillatory activity has been that of FM-theta activity, one has to acknowledge that efficient cognitive control is obviously dependent on additional processes that are not captured by FM-theta activity, such as sensory-, attentional- or motor control processes (Kaiser & Schütz-Bosbach, 2019; Salinas & Stanford, 2013; Verbruggen et al., 2014a). For example, proactive activity in the form of mu desynchronization (Raud et al., 2020a), central beta activity related to motor processing, and occipital alpha related to visual detection, are all modulated by proactive control (Kaiser & Schütz-Bosbach, 2019). Although the focus of the present thesis has been that of stimulus-locked FM-theta power, research also suggest that theta total power, phase coherence and frontoparietal connectivity also plays a part in efficient cognitive control. Further, recent years has seen an increased focus on the relevance of frontal beta bursts in successful response inhibition (Hannah et al., 2020; Jana et al., 2020; Sundby et al., 2021; Wagner et al., 2018; Wessel, 2020), although their causal effects for response inhibition has been questioned (Errington et al., 2020). Nevertheless, it seems likely that complex processes such as proactive and reactive control are reflected in a magnitude of frequency bands and other neural measures, beyond what is discussed in the present thesis.

5.4.2 Network dynamics.

Although the results of the current thesis points to a more domain general approach and functional dissociation within the stopping network, functional connectivity within this network was not investigated specifically (except from the whole-brain approaches of the PPI analysis in Paper I, and statistical dependence of regions in the joint ICA in Paper II). Thus, the term stopping network used in the current thesis is with reference to the regions commonly associated with response inhibition, without investigating the connectivity between them. However, previous research has shown that these regions show both structural and functional connectivity associated with response inhibition (Erika-Florence et al., 2014; Hampshire & Sharp, 2015; B. Wang et al., 2020; R. Zhang et al., 2017), indicating that these regions likely also operate as a network.

5.4.3 Resting state activity.

The nature of resting state activity is debated. Specifically, it seems clear that intrinsic brain activity reflects active processing (as opposed to idleness), and that a resting state measure with eyes open clearly includes processing of visual stimuli, as well as other sensory inputs. Although some, for this reason, advocate for eyes closed measurements, this still does not remove other sensory inputs. Not least, one must acknowledge that the task of doing nothing when instructed so during a resting state measurement is extremely difficult, if not impossible. However, as the brain will always be engaged in some sort of sensory processing, resting state activity is still a valid approach in estimating the brain's intrinsic activity. Thus, resting state measurements could rather be conceptualized as a cognitive state that is free of task manipulations. However, it seems that a clear-cut dissociation between resting state and task-elicited activity at the conceptual level might not be reflected at the neural level to a similar degree (Northoff et al., 2010).

5.4.4 Reliability and validity of cognitive control measures.

Recent debates regarding the reliability of behavioural measures of cognitive control have highlighted the issue of a reliability fallacy in cognitive psychology: tasks designed to assess between-group effects come at the expense of low reliability for individual differences (Hedge et al., 2018). Indeed, behavioural measures of cognitive tasks such as the Stroop task, the n-back task, the task-switching task, and the SST

have been shown to have low reliability, although with some variations between tasks (Enkavi et al., 2019). The measurement reliability is a valid concern, as low reliability might lead to biased parameter estimations and test statistics (Green et al., 2016; Nimon et al., 2012). Furthermore, as the effect of reliability increases with decreased sample size, these concerns are especially pressing in the field of neuroscience, where the sample sizes are often small based on both time and monetary constraints involved in neuroimaging methods. The importance of reliable measures has gained renewed interest in terms of investigating individual differences in cognitive control, and attempts to evaluate the reliability of measures of cognitive control and response inhibition are increasing (Enkavi et al., 2019). Thus, future research should investigate how to best assess individual differences in cognitive control, either by incorporating reliability estimates in their study design, or to seek to develop new approaches that better capture the effect of interest, either at the group or individual level.

As previously alluded to, cognitive control is a complex and general structure, that even at the level of sub-functions can be difficult to measure. For example, research has questioned the validity of the horse-race model underlying the SST and the SSRT as a valid measure of stopping latency (Bissett et al., 2021; Matzke et al., 2013; Verbruggen et al., 2013). Thus, recent approaches have tried to establish more objective and direct physiological measures of the stopping latency (Raud & Huster, 2017; van den Wildenberg et al., 2010; Wagner et al., 2018; Wessel & Aron, 2015), although so far no clear consensus has been achieved (Huster et al., 2020).

A similar issue is whether laboratory cognitive control tasks can be translated into “real life” cognitive control. Some researchers have advocated for, and conducted, experiments that are more ecologically valid (Ladouce et al., 2017; Reiser et al., 2019), for example, by using mobile EEG devices to measure proactive and reactive movement control in real life settings (Mustile et al., 2021). However, such real-world cognitive tasks come with their own drawbacks and issues, such as decreased signal-to-noise ratio, movement artefacts and interpretation issues. Nevertheless, the development of technologies such as mobile EEG devices and virtual reality equipment have huge potentials for the advancement of our understanding of cognitive control. However, this does not imply that laboratory tasks such as the cognitive control tasks used in the present thesis are uninformative about “real life” cognitive control. Cognitive tasks performed in a controlled environment have contributed to extensive knowledge about the neural dynamics and cognitive processes underlying cognitive control. These processes are likely also involved when the store clerk resists the urge to snap back at the costumer, or

when stopping the car as the traffic light turns red. How these processes are modified by the often unpredictable and ever-changing real life, however, remains to be discovered.

5.4.5 Multimodal designs and sample size.

Both of the experimental studies conducted for the present thesis had a relatively low sample size. Study 1 utilized a complex multimodal design involving simultaneous recordings of EEG, fMRI, and behavioural data. Although this design enabled the identification of precise spatiotemporal correlates of response inhibition, it has certain drawbacks. First, EEG recorded in an fMRI scanner enables less online control of the quality of the EEG signal, as well as massive artefacts in the raw EEG data due to the strong magnetic field imposed by the scanner. Although many of these artefacts can be removed offline (see methods, Paper II), there is still some detrimental effects on the quality of the data. Thus, several participants had to be excluded from further analysis based on insufficient EEG data quality. Second, exclusion criteria based on both behavioural data, EEG data and fMRI data separately leads to the exclusion of more participants in a study using multimodal designs, than for example a purely behavioural study. Third, data collection using such complex setups are time consuming in themselves, also affecting the final sample size. However, the results of Paper I and Paper II clearly show that such multimodal setups can lead to novel findings that enhance our understanding of the brain.

Bayesian hypothesis testing in the field of neuroscience is increasing, perhaps somewhat because of the possibly to quantify evidence for the null hypothesis (as opposed to traditional null hypothesis significance testing, which only quantifies evidence *against* the null). As this evidence is based on the ratio of the likelihood of the alternative hypothesis relative to the null hypothesis (given the data), evidence against an alternative model can be equally interpreted as evidence for the null model. Furthermore, it has been shown that even in small samples, Bayesian evidence for the absence of an effect is reasonable (Keysers et al., 2020), and with increasing sample sizes inconclusive evidence become increasingly more rare. In Paper III we used a Bayesian analysis framework to quantify the evidence for or against our alternative hypothesis. Although some of the effects we investigated were associated with inconclusive evidence, the Bayesian framework enabled both interpretations of effects and lack of effects, even with a small sample size.

Overall, multimodal approaches and small sample sizes are important to consider when evaluating the results of the present thesis, and the findings of the present thesis should act as a springboard for future investigations using lager sample sizes.

5.5 Implications and future directions

The partitioning of cognitive control in the temporal domain and according to specific sub-functions is undoubtfully useful when navigating the complex and grand structure of cognitive control. Identifying the neural correlates of such control components have led to extensive knowledge about how cognitive control is enacted at the neural level, but has also been characterized by modular approaches, mapping specific sub-functions of control to specific regions of the brain. Recent advances have, on the other hand, shown an increased focus on the integration of such findings, as enacted by domain-general networks associated with a wide range of cognitive functions. The present thesis is in line with such approaches, although cognitive control was not investigated in terms of networks, but rather from a multimodal perspective and across cognitive control modes and sub-functions. Thus, the thesis joins recent advances in placing response inhibition within a wider system for cognitive control, which allows for a more nuanced understanding of response inhibition and cognitive control within the dynamic organization of the brain as a whole. Indeed, a prime goal of the cognitive revolution was to understand the brain as a dynamic entity, and not a sole input-output information processor. Over the years, such thinking has perhaps been downplayed in the quest to understand task-elicited activity patterns. However, recent years saw an increased focus on the intrinsic properties of the brain, both in terms of resting state activity and consciousness, as well as in the understanding of mind wandering during tasks. Thus, the present thesis joins recent efforts in trying to connect cognitive control to baseline characteristics and intrinsic properties of the brain.

The implications of the current thesis are thus manifold. First, it is highlighted how response inhibition should be viewed as a result of both proactive and reactive control processes, which may be difficult to detangle using unimodal approaches. Second, we show that the mapping of response inhibition in general to single features, be it a region or a frequency, might mask the intricate neural dynamics at the neural source level, either in form of rIFG heterogeneity, or FM-theta multidimensionality. Specifically, the findings contribute to recurrent debates regarding rIFG function in response inhibition. Third, the results indicate that the relationship between resting state and cognitive control is not restricted to single frequency bands (or at least not to the theta band). Overall, these

results indeed have implications for the field as a whole in how cognitive control and response inhibition is understood and investigated. Further, the thesis also has implications for the clinical field, where the relationship between proactive and reactive control might elucidate the impairments seen in cognitive control and response inhibition across a wide variety of psychological and neurological disorders. Moreover, psychological assessments and treatment protocols based on a relationship between resting state and cognitive performance should take note that such relationships might not be frequency-specific, and that the exact nature of such relationships can differ between individuals and task settings. This is an exciting approach to cognitive control that should be of prime concern for future research.

6. Conclusion

The cognitive control and response inhibition fields are buzzing, and our understanding of the neural mechanisms enacting these functions are advanced every day. The results of the present thesis are in line with recent advances in these fields. First, we show that response inhibition is associated with activity in the rIFG, but that this activity is not stopping-specific, is not unique in its association with outright stopping, and shows functional dissociation within rIFG sub-regions in response to proactive control modulations. Further, we show that a proposed neural marker of cognitive control, FM-theta activity, is a reflection of several mechanisms associated with both the preparation to stop, preparation to respond, as well as reflecting a need for control across a range of cognitive control tasks. These findings are in line with recent research of domain-general networks enacting cognitive control in the brain, and that neither cognitive control, nor response inhibition, are unitary functions. Indeed, the results of the present thesis support the notion that a simple mapping of a cognitive control function to a specific feature of the brain, be it the rIFG or FM-theta activity, is highly unlikely. Finally, the present thesis shows that proactive and reactive control are not reflected in resting state theta activity, but that resting state dynamics may still mediate cognitive control performance. Overall, the results of the present thesis indicate that cognitive control, as partitioned in the functional as well as temporal domain, is associated with heterogeneous spatiotemporal neural correlates. These findings have implications for our understanding of cognitive control both in healthy and in clinical populations.

References

Adelhöfer, N., & Beste, C. (2020). Pre-trial theta band activity in the ventromedial prefrontal cortex correlates with inhibition-related theta band activity in the right inferior frontal cortex. *NeuroImage*, *219*, 117052. https://doi.org/10.1016/j.neuroimage.2020.117052

Albares, M., Lio, G., Criaud, M., Anton, J.-L., Desmurget, M., & Boulinguez, P. (2014). The dorsal medial frontal cortex mediates automatic motor inhibition in uncertain contexts: Evidence from combined fMRI and EEG studies: Automatic Motor Inhibition. *Human Brain Mapping*, *35*(11), 5517–5531. https://doi.org/10.1002/hbm.22567

Angelides, N. H., Gupta, J., & Vickery, T. J. (2017). Associating resting-state connectivity with trait impulsivity. *Social Cognitive and Affective Neuroscience*, *12*(6), 1001–1008. https://doi.org/10.1093/scan/nsx031

Aron, A. R. (2006). Cortical and Subcortical Contributions to Stop Signal Response Inhibition: Role of the Subthalamic Nucleus. *Journal of Neuroscience*, *26*(9), 2424–2433. https://doi.org/10.1523/JNEUROSCI.4682-05.2006

Aron, A. R. (2007). The Neural Basis of Inhibition in Cognitive Control. *The Neuroscientist*, *13*(3), 214–228. https://doi.org/10.1177/1073858407299288

Aron, A. R. (2011). From Reactive to Proactive and Selective Control: Developing a Richer Model for Stopping Inappropriate Responses. *Biological Psychiatry*, *69*(12), e55–e68. https://doi.org/10.1016/j.biopsych.2010.07.024

Aron, A. R., Fletcher, P. C., Bullmore, E. T., Sahakian, B. J., & Robbins, T. W. (2003). Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. *Nature Neuroscience*, *6*(2), 115–116. https://doi.org/10.1038/nn1003

Aron, A. R., Herz, D. M., Brown, P., Forstmann, B. U., & Zaghloul, K. (2016). Frontosubthalamic Circuits for Control of Action and Cognition. *The Journal of Neuroscience*, *36*(45), 11489–11495. https://doi.org/10.1523/JNEUROSCI.2348-16.2016

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. *Trends in Cognitive Sciences*, *8*(4), 170–177. https://doi.org/10.1016/j.tics.2004.02.010

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2014). Inhibition and the right inferior frontal cortex: One decade on. *Trends in Cognitive Sciences*, *18*(4), 177–185. https://doi.org/10.1016/j.tics.2013.12.003

Baddeley, A. D., & Hitch, G. (1974). Working Memory. In G. H. Bower (Ed.), *Psychology of Learning and Motivation* (Vol. 8, pp. 47–89). Academic Press. https://doi.org/10.1016/S0079-7421(08)60452-1

Balconi, M., Vanutelli, M. E., & Grippa, E. (2017). Resting state and personality component (BIS/BAS) predict the brain activity (EEG and fNIRS measure) in response to emotional cues. *Brain and Behavior*, *7*(5), e00686. https://doi.org/10.1002/brb3.686

Band, G. P. H., van der Molen, M. W., & Logan, G. D. (2003). Horse-race model simulations of the stop-signal procedure. *Acta Psychologica*, *112*(2), 105–142. https://doi.org/10.1016/S0001-6918(02)00079-3

Banich, M. T. (2009). Executive Function: The Search for an Integrated Account. *Current Directions in Psychological Science*, *18*(2), 89–94. https://doi.org/10.1111/j.1467-8721.2009.01615.x

Barch, D. M., Braver, T. S., Nystrom, L. E., Forman, S. D., Noll, D. C., & Cohen, J. D. (1997). Dissociating working memory from task difficulty in human prefrontal cortex. *Neuropsychologia*, *35*(10), 1373–1380. https://doi.org/10.1016/S0028-3932(97)00072-9

Barch, D. M., & Sheffield, J. M. (2014). Cognitive impairments in psychotic disorders: Common mechanisms and measurement. *World Psychiatry*, *13*(3), 224–232. https://doi.org/10.1002/wps.20145

Barkley, C. M., Hu, Z., Fieberg, A. M., Eberly, L. E., Birnbaum, A. K., Leppik, I. E., & Marino, S. E. (2020). An association between resting state EEG parameters and the severity of topiramate-related cognitive impairment. *Epilepsy & Behavior*, 107598. https://doi.org/10.1016/j.yebeh.2020.107598

Barton, R. A., & Venditti, C. (2013). Human frontal lobes are not relatively large. *Proceedings of the National Academy of Sciences*, *110*(22), 9001–9006. https://doi.org/10.1073/pnas.1215723110

Basharpoor, S., Heidari, F., & Molavi, P. (2019). EEG coherence in theta, alpha, and beta bands in frontal regions and executive functions. *Applied Neuropsychology: Adult*, *0*(0), 1–8. https://doi.org/10.1080/23279095.2019.1632860

Bellucci, G., Münte, T. F., & Park, S. Q. (2019). Resting-state dynamics as a neuromarker of dopamine administration in healthy female adults. *Journal of Psychopharmacology*, *33*(8), 955–964. https://doi.org/10.1177/0269881119855983

Bengson, J. J., Mangun, G. R., & Mazaheri, A. (2012). The neural markers of an imminent failure of response inhibition. *NeuroImage*, *59*(2), 1534–1539. https://doi.org/10.1016/j.neuroimage.2011.08.034

Benton, A. L. (1991). The prefrontal region: Its early history. In *Frontal lobe function and dysfunction* (pp. 3–32). Oxford University Press.

Bissett, P. G., Jones, H. M., Poldrack, R. A., & Logan, G. D. (2021). Severe violations of independence in response inhibition tasks. *Science Advances*, *7*(12), eabf4355. https://doi.org/10.1126/sciadv.abf4355

Boehler, C. N., Schevernels, H., Hopf, J.-M., Stoppel, C. M., & Krebs, R. M. (2014). Reward prospect rapidly speeds up response inhibition via reactive control. *Cognitive, Affective, & Behavioral Neuroscience*, *14*(2), 593–609. https://doi.org/10.3758/s13415-014-0251-5

Boen, R., Raud, L., & Huster, R. J. (2020). *Inhibitory control and the structural parcellation of the right inferior frontal gyrus* [Preprint]. Neuroscience. https://doi.org/10.1101/2020.08.13.249516

Botvinick, M. M., Braver, T. S., Barch, D. M., Carter, C. S., & Cohen, J. D. (2001). Conflict monitoring and cognitive control. *Psychological Review*, *108*(3), 624–652. https://doi.org/10.1037/0033-295X.108.3.624

Botvinick, M. M., Cohen, J. D., & Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: An update. *Trends in Cognitive Sciences*, *8*(12), 539–546. https://doi.org/10.1016/j.tics.2004.10.003

Braver, T. S. (2012). The variable nature of cognitive control: A dual mechanisms framework. *Trends in Cognitive Sciences*, *16*(2), 106–113. https://doi.org/10.1016/j.tics.2011.12.010

Braver, T. S., Gray, J. R., & Burgess, G. C. (2008). Explaining the Many Varieties of Working Memory Variation: Dual Mechanisms of Cognitive Control. In A. Conway, C. Jarrold, M. Kane, A. Miyake, & J. Towse (Eds.), *Variation in Working Memory* (pp. 76–106). Oxford University Press. https://doi.org/10.1093/acprof:oso/9780195168648.003.0004

Broadbent, D. E. (Donald E. (1958). *Perception and communication*. 347.

Bugg, J. M., & Braver, T. S. (2016). Proactive control of irrelevant task rules during cued task switching. *Psychological Research*, *80*(5), 860–876. https://doi.org/10.1007/s00426-015-0686-5

Burgess, G. C., & Braver, T. S. (2010). Neural Mechanisms of Interference Control in Working Memory: Effects of Interference Expectancy and Fluid Intelligence. *PLOS ONE*, *5*(9), e12861. https://doi.org/10.1371/journal.pone.0012861

Buzsáki, G., & Draguhn, A. (2004). Neuronal Oscillations in Cortical Networks. *Science*, *304*(5679), 1926–1929. https://doi.org/10.1126/science.1099745

Cai, W., Duberg, K., Padmanabhan, A., Rehert, R., Bradley, T., Carrion, V., & Menon, V. (2019). Hyperdirect insula-basal-ganglia pathway and adult-like maturity of global brain responses predict inhibitory control in children. *Nature Communications*, *10*(1), 4798. https://doi.org/10.1038/s41467-019-12756-8

Cai, W., George, J. S., Verbruggen, F., Chambers, C. D., & Aron, A. R. (2012). The role of the right presupplementary motor area in stopping action: Two studies with event-related transcranial magnetic stimulation. *Journal of Neurophysiology*, *108*(2), 380–389. https://doi.org/10.1152/jn.00132.2012

Cai, W., Ryali, S., Chen, T., Li, C.-S. R., & Menon, V. (2014). Dissociable Roles of Right Inferior Frontal Cortex and Anterior Insula in Inhibitory Control: Evidence from Intrinsic and Task-Related Functional Parcellation, Connectivity, and Response Profile Analyses across Multiple Datasets. *Journal of Neuroscience*, *34*(44), 14652–14667. https://doi.org/10.1523/JNEUROSCI.3048-14.2014

Camilleri, J. A., Müller, V. I., Fox, P., Laird, A. R., Hoffstaedter, F., Kalenscher, T., & Eickhoff, S. B. (2018). Definition and characterization of an extended Multiple-Demand Network. *NeuroImage*, *165*, 138–147. https://doi.org/10.1016/j.neuroimage.2017.10.020

Cavanagh, J. F., & Frank, M. J. (2014). Frontal theta as a mechanism for cognitive control. *Trends in Cognitive Sciences*, *18*(8), 414–421. https://doi.org/10.1016/j.tics.2014.04.012

Cavanagh, J. F., Zambrano-Vazquez, L., & Allen, J. J. B. (2012). Theta lingua franca: A common mid-frontal substrate for action monitoring processes: Omnipresent theta. *Psychophysiology*, *49*(2), 220–238. https://doi.org/10.1111/j.1469-8986.2011.01293.x

Chang, A., Ide, J. S., Li, H.-H., Chen, C.-C., & Li, C.-S. R. (2017). Proactive Control: Neural Oscillatory Correlates of Conflict Anticipation and Response Slowing. *ENeuro*, *4*(3). https://doi.org/10.1523/ENEURO.0061-17.2017

Chen, W., de Hemptinne, C., Miller, A. M., Leibbrand, M., Little, S. J., Lim, D. A., Larson, P. S., & Starr, P. A. (2020). Prefrontal-Subthalamic Hyperdirect Pathway Modulates Movement Inhibition in Humans. *Neuron*, *106*(4), 579-588.e3. https://doi.org/10.1016/j.neuron.2020.02.012

Chen, Y., Chen, C., Wu, T., Qiu, B., Zhang, W., & Fan, J. (2020). Accessing the development and heritability of the capacity of cognitive control. *Neuropsychologia*, *139*, 107361. https://doi.org/10.1016/j.neuropsychologia.2020.107361

Chiew, K. S., & Braver, T. S. (2017). Context processing and cognitive control: From gating models to dual mechanisms. In *The Wiley handbook of cognitive control* (pp. 143–166). Wiley Blackwell. https://doi.org/10.1002/9781118920497.ch9

Chikazoe, J., Jimura, K., Hirose, S., Yamashita, K. -i., Miyashita, Y., & Konishi, S. (2009). Preparation to Inhibit a Response Complements Response Inhibition during Performance of a Stop-Signal Task. *Journal of Neuroscience*, *29*(50), 15870–15877. https://doi.org/10.1523/JNEUROSCI.3645-09.2009

Chikazoe, J., Konishi, S., Asari, T., Jimura, K., & Miyashita, Y. (2007). Activation of Right Inferior Frontal Gyrus during Response Inhibition across Response Modalities. *Journal of Cognitive Neuroscience*, *19*(1), 69–80. https://doi.org/10.1162/jocn.2007.19.1.69

Cieslik, E. C., Mueller, V. I., Eickhoff, C. R., Langner, R., & Eickhoff, S. B. (2015). Three key regions for supervisory attentional control: Evidence from neuroimaging meta-analyses. *Neuroscience & Biobehavioral Reviews*, *48*, 22–34. https://doi.org/10.1016/j.neubiorev.2014.11.003

Clements, G. M., Bowie, D. C., Gyurkovics, M., Low, K. A., Fabiani, M., & Gratton, G. (2021). Spontaneous Alpha and Theta Oscillations Are Related to Complementary Aspects of Cognitive Control in Younger and Older Adults. *Frontiers in Human Neuroscience*, *15*, 106. https://doi.org/10.3389/fnhum.2021.621620

Cohen, J. D., Botvinick, M., & Carter, C. S. (2000). Anterior cingulate and prefrontal cortex: Who's in control? *Nature Neuroscience*, *3*(5), 421–423. https://doi.org/10.1038/74783

Cohen, M. X., & Cavanagh, J. F. (2011). Single-Trial Regression Elucidates the Role of Prefrontal Theta Oscillations in Response Conflict. *Frontiers in Psychology*, *2*. https://doi.org/10.3389/fpsyg.2011.00030

Cohen, M. X., & Donner, T. H. (2013). Midfrontal conflict-related theta-band power reflects neural oscillations that predict behavior. *Journal of Neurophysiology*, *110*(12), 2752–2763. https://doi.org/10.1152/jn.00479.2013

Cools, R. (2015). The cost of dopamine for dynamic cognitive control. *Current Opinion in Behavioral Sciences*, *4*, 152–159. https://doi.org/10.1016/j.cobeha.2015.05.007

Cooper, P. S., Karayanidis, F., McKewen, M., McLellan-Hall, S., Wong, A. S. W., Skippen, P., & Cavanagh, J. F. (2019). Frontal theta predicts specific cognitive control-induced behavioural changes beyond general reaction time slowing. *NeuroImage*, *189*, 130–140. https://doi.org/10.1016/j.neuroimage.2019.01.022

Cooper, P. S., Wong, A. S. W., Fulham, W. R., Thienel, R., Mansfield, E., Michie, P. T., & Karayanidis, F. (2015). Theta frontoparietal connectivity associated with proactive and reactive cognitive control processes. *NeuroImage*, *108*, 354–363. https://doi.org/10.1016/j.neuroimage.2014.12.028

Cooper, P. S., Wong, A. S. W., McKewen, M., Michie, P. T., & Karayanidis, F. (2017). Frontoparietal theta oscillations during proactive control are associated with goal-updating and reduced behavioral variability. *Biological Psychology*, *129*, 253–264. https://doi.org/10.1016/j.biopsycho.2017.09.008

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews Neuroscience*, *3*(3), 201–215. https://doi.org/10.1038/nrn755

Criaud, M., Anton, J.-L., Nazarian, B., Longcamp, M., Metereau, E., Boulinguez, P., & Ballanger, B. (2021). The Human Basal Ganglia Mediate the Interplay between Reactive and Proactive Control of Response through Both Motor Inhibition and Sensory Modulation. *Brain Sciences*, *11*(5), 560. https://doi.org/10.3390/brainsci11050560

Cunillera, T., Brignani, D., Cucurell, D., Fuentemilla, L., & Miniussi, C. (2016). The right inferior frontal cortex in response inhibition: A tDCS–ERP co-registration study. *NeuroImage*, *140*, 66–75. https://doi.org/10.1016/j.neuroimage.2015.11.044

Curley, L. B., Newman, E., Thompson, W. K., Brown, T. T., Hagler, D. J., Akshoomoff, N., Reuter, C., Dale, A. M., & Jernigan, T. L. (2018). Cortical morphology of the pars opercularis and its relationship to motor-inhibitory performance in a longitudinal, developing cohort. *Brain Structure and Function*, *223*(1), 211–220. https://doi.org/10.1007/s00429-017-1480-5

Curtis, C. E., & D'Esposito, M. (2003). Persistent activity in the prefrontal cortex during working memory. *Trends in Cognitive Sciences*, *7*(9), 415–423. https://doi.org/10.1016/S1364-6613(03)00197-9

Deco, G., Jirsa, V. K., & McIntosh, A. R. (2011). Emerging concepts for the dynamical organization of resting-state activity in the brain. *Nature Reviews Neuroscience*, *12*(1), 43–56. https://doi.org/10.1038/nrn2961

Dippel, G., Chmielewski, W., Mückschel, M., & Beste, C. (2016). Response mode-dependent differences in neurofunctional networks during response inhibition: An EEG-beamforming study. *Brain Structure and Function*, *221*(8), 4091–4101. https://doi.org/10.1007/s00429-015-1148-y

Dippel, G., Mückschel, M., Ziemssen, T., & Beste, C. (2017). Demands on response inhibition processes determine modulations of theta band activity in superior frontal areas and correlations with pupillometry – Implications for the norepinephrine system during inhibitory control. *NeuroImage*, *157*, 575–585. https://doi.org/10.1016/j.neuroimage.2017.06.037

Duncan, J. (2010). The multiple-demand (MD) system of the primate brain: Mental programs for intelligent behaviour. *Trends in Cognitive Sciences*, *14*(4), 172–179. https://doi.org/10.1016/j.tics.2010.01.004

Duncan, J., & Owen, A. M. (2000). Common regions of the human frontal lobe recruited by diverse cognitive demands. *Trends in Neurosciences*, *23*(10), 475–483. https://doi.org/10.1016/S0166-2236(00)01633-7

Eisenreich, B. R., Akaishi, R., & Hayden, B. Y. (2016). *Control without controllers: Towards a distributed neuroscience of executive control* (p. 077685). https://doi.org/10.1101/077685

Eisma, J., Rawls, E., Long, S., Mach, R., & Lamm, C. (2021). Frontal midline theta differentiates separate cognitive control strategies while still generalizing the need for cognitive control. *Scientific Reports*, *11*(1), 14641. https://doi.org/10.1038/s41598-021-94162-z

Elchlepp, H., Lavric, A., Chambers, C. D., & Verbruggen, F. (2016). Proactive inhibitory control: A general biasing account. *Cognitive Psychology*, *86*, 27–61. https://doi.org/10.1016/j.cogpsych.2016.01.004

Engelhardt, L. E., Briley, D. A., Mann, F. D., Harden, K. P., & Tucker-Drob, E. M. (2015). Genes Unite Executive Functions in Childhood. *Psychological Science*, *26*(8), 1151–1163. https://doi.org/10.1177/0956797615577209

Engle, R. W., & Kane, M. J. (2003). Executive Attention, Working Memory Capacity, and a Two-Factor Theory of Cognitive Control. In *Psychology of Learning and Motivation* (Vol. 44, pp. 145–199). Academic Press. https://doi.org/10.1016/S0079-7421(03)44005-X

Enkavi, A. Z., Eisenberg, I. W., Bissett, P. G., Mazza, G. L., MacKinnon, D. P., Marsch, L. A., & Poldrack, R. A. (2019). Large-scale analysis of test–retest reliabilities of self-regulation measures. *Proceedings of the National Academy of Sciences*, *116*(12), 5472–5477. https://doi.org/10.1073/pnas.1818430116

Enriquez-Geppert, Huster, R. J., Figge, C., & Herrmann, C. S. (2014). Self-regulation of frontal-midline theta facilitates memory updating and mental set shifting. *Frontiers in Behavioral Neuroscience*, *8*. https://doi.org/10.3389/fnbeh.2014.00420

Enriquez-Geppert, S., Konrad, C., Pantev, C., & Huster, R. J. (2010). Conflict and inhibition differentially affect the N200/P300 complex in a combined go/nogo and stop-signal task. *NeuroImage*, *51*(2), 877–887. https://doi.org/10.1016/j.neuroimage.2010.02.043

Entel, O., Tzelgov, J., Bereby-Meyer, Y., & Shahar, N. (2015). Exploring relations between task conflict and informational conflict in the Stroop task. *Psychological Research*, *79*(6), 913–927. https://doi.org/10.1007/s00426-014-0630-0

Erickson, B., Truelove-Hill, M., Oh, Y., Anderson, J., Zhang, F. (Zoe), & Kounios, J. (2018). Resting-state brain oscillations predict trait-like cognitive styles. *Neuropsychologia*, *120*, 1–8. https://doi.org/10.1016/j.neuropsychologia.2018.09.014

Erika-Florence, M., Leech, R., & Hampshire, A. (2014). A functional network perspective on response inhibition and attentional control. *Nature Communications*, *5*(1). https://doi.org/10.1038/ncomms5073

Errington, S. P., Woodman, G. F., & Schall, J. D. (2020). Dissociation of Medial Frontal β-Bursts and Executive Control. *Journal of Neuroscience*, *40*(48), 9272–9282. https://doi.org/10.1523/JNEUROSCI.2072-20.2020

Eschmann, K. C. J., & Mecklinger, A. (2021). Improving cognitive control: Is theta neurofeedback training associated with proactive rather than reactive control enhancement? *Psychophysiology*, *n/a*(n/a), e13873. https://doi.org/10.1111/psyp.13873

Eyler, L. T., Elman, J. A., Hatton, S. N., Gough, S., Mischel, A. K., Hagler, D. J., Franz, C. E., Docherty, A., Fennema-Notestine, C., Gillespie, N., Gustavson, D., Lyons, M. J., Neale, M. C., Panizzon, M. S., Dale, A. M., & Kremen, W. S. (2019). Resting State Abnormalities of the Default Mode Network in Mild Cognitive Impairment: A Systematic Review and Meta-Analysis. *Journal of Alzheimer's Disease*, *70*(1), 107–120. https://doi.org/10.3233/JAD-180847

Faiman, I., Smith, S., Hodsoll, J., Young, A. H., & Shotbolt, P. (2021). Resting-state EEG for the diagnosis of idiopathic epilepsy and psychogenic nonepileptic seizures: A systematic review. *Epilepsy & Behavior*, *121*, 108047. https://doi.org/10.1016/j.yebeh.2021.108047

Fillmore, M. T., & Rush, C. R. (2002). Impaired inhibitory control of behavior in chronic cocaine users. *Drug and Alcohol Dependence*, *66*(3), 265–273. https://doi.org/10.1016/S0376-8716(01)00206-X

Finnigan, S., & Robertson, I. H. (2011). Resting EEG theta power correlates with cognitive performance in healthy older adults. *Psychophysiology*, *48*(8), 1083–1087. https://doi.org/10.1111/j.1469-8986.2010.01173.x

Forstmann, B. U., Anwander, A., Schafer, A., Neumann, J., Brown, S., Wagenmakers, E.-J., Bogacz, R., & Turner, R. (2010). Cortico-striatal connections predict control over speed and accuracy in perceptual decision making. *Proceedings of the National Academy of Sciences*, *107*(36), 15916–15920. https://doi.org/10.1073/pnas.1004932107

Forstmann, B. U., Dutilh, G., Brown, S., Neumann, J., von Cramon, D. Y., Ridderinkhof, K. R., & Wagenmakers, E.-J. (2008). Striatum and pre-SMA facilitate decision-making under time pressure. *Proceedings of the National Academy of Sciences*, *105*(45), 17538–17542. https://doi.org/10.1073/pnas.0805903105

Fox, M. D., Corbetta, M., Snyder, A. Z., Vincent, J. L., & Raichle, M. E. (2006). Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. *Proceedings of the National Academy of Sciences*, *103*(26), 10046–10051. https://doi.org/10.1073/pnas.0604187103

Fox, M. D., Snyder, A. Z., Vincent, J. L., & Raichle, M. E. (2007). Intrinsic Fluctuations within Cortical Systems Account for Intertrial Variability in Human Behavior. *Neuron*, *56*(1), 171–184. https://doi.org/10.1016/j.neuron.2007.08.023

Friedman, N. P., & Miyake, A. (2017). Unity and diversity of executive functions: Individual differences as a window on cognitive structure. *Cortex*, *86*, 186–204. https://doi.org/10.1016/j.cortex.2016.04.023

Friedman, N. P., Miyake, A., Corley, R. P., Young, S. E., DeFries, J. C., & Hewitt, J. K. (2006). Not All Executive Functions Are Related to Intelligence. *Psychological Science*, *17*(2), 172–179. https://doi.org/10.1111/j.1467-9280.2006.01681.x

Friedman, N. P., Miyake, A., Young, S. E., DeFries, J. C., Corley, R. P., & Hewitt, J. K. (2008). Individual Differences in Executive Functions Are Almost Entirely Genetic in Origin. *Journal of Experimental Psychology. General*, *137*(2), 201–225. https://doi.org/10.1037/0096-3445.137.2.201

Friedman, N. P., & Robbins, T. W. (2021). The role of prefrontal cortex in cognitive control and executive function. *Neuropsychopharmacology*, 1–18. https://doi.org/10.1038/s41386-021-01132-0

Fries, P. (2005). A mechanism for cognitive dynamics: Neuronal communication through neuronal coherence. *Trends in Cognitive Sciences*, *9*(10), 474–480. https://doi.org/10.1016/j.tics.2005.08.011

Fulwiler, C. E., King, J. A., & Zhang, N. (2012). Amygdala-Orbitofrontal Resting State Functional Connectivity is Associated with Trait Anger. *Neuroreport*, *23*(10), 606–610. https://doi.org/10.1097/WNR.0b013e3283551cfc

Fuster, J. (2015). *The Prefrontal Cortex*. Academic Press.

Gignac, G. E., & Kretzschmar, A. (2017). Evaluating dimensional distinctness with correlated-factor models: Limitations and suggestions. *Intelligence*, *62*, 138–147. https://doi.org/10.1016/j.intell.2017.04.001

González-Villar, A. J., Bonilla, F. M., & Carrillo-de-la-Peña, M. T. (2016). When the brain simulates stopping: Neural activity recorded during real and imagined stop-signal tasks. *Cognitive, Affective, & Behavioral Neuroscience*, *16*(5), 825–835. https://doi.org/10.3758/s13415-016-0434-3

Gordon, S., Todder, D., Deutsch, I., Garbi, D., Getter, N., & Meiran, N. (2018). Are resting state spectral power measures related to executive functions in healthy young adults? *Neuropsychologia*, *108*, 61–72. https://doi.org/10.1016/j.neuropsychologia.2017.10.031

Gratton, G., Cooper, P., Fabiani, M., Carter, C. S., & Karayanidis, F. (2018). Dynamics of cognitive control: Theoretical bases, paradigms, and a view for the future. *Psychophysiology*, *55*(3), e13016. https://doi.org/10.1111/psyp.13016

Green, S. B., Yang, Y., Alt, M., Brinkley, S., Gray, S., Hogan, T., & Cowan, N. (2016). Use of internal consistency coefficients for estimating reliability of experimental task scores. *Psychonomic Bulletin & Review*, *23*(3), 750–763. https://doi.org/10.3758/s13423-015-0968-3

Hampshire, A. (2015). Putting the brakes on inhibitory models of frontal lobe function. *NeuroImage*, *113*, 340–355. https://doi.org/10.1016/j.neuroimage.2015.03.053

Hampshire, A., Chamberlain, S. R., Monti, M. M., Duncan, J., & Owen, A. M. (2010). The role of the right inferior frontal gyrus: Inhibition and attentional control. *NeuroImage*, *50*(3), 1313–1319. https://doi.org/10.1016/j.neuroimage.2009.12.109

Hampshire, A., & Sharp, D. J. (2015). Contrasting network and modular perspectives on inhibitory control. *Trends in Cognitive Sciences*, *19*(8), 445–452. https://doi.org/10.1016/j.tics.2015.06.006

Hampshire, A., Thompson, R., Duncan, J., & Owen, A. M. (2009). Selective tuning of the right inferior frontal gyrus during target detection. *Cognitive, Affective & Behavioral Neuroscience*, *9*(1), 103–112. https://doi.org/10.3758/CABN.9.1.103

Hannah, R., Muralidharan, V., Sundby, K. K., & Aron, A. R. (2020). Temporally-precise disruption of prefrontal cortex informed by the timing of beta bursts impairs human action-stopping. *NeuroImage*, *222*, 117222. https://doi.org/10.1016/j.neuroimage.2020.117222

Harlow, J. M. (1869). Recovery from the passage of an iron bar through the head. *History of Psychiatry*, *4*(14), 274–281. https://doi.org/10.1177/0957154X9300401407

Hartwigsen, G., Neef, N. E., Camilleri, J. A., Margulies, D. S., & Eickhoff, S. B. (2019). Functional Segregation of the Right Inferior Frontal Gyrus: Evidence From Coactivation-Based Parcellation. *Cerebral Cortex*, *29*(4), 1532–1546. https://doi.org/10.1093/cercor/bhy049

He, L., Zhuang, K., Chen, Q., Wei, D., Chen, X., Fan, J., & Qiu, J. (2021). Unity and diversity of neural representation in executive functions. *Journal of Experimental Psychology. General*. https://doi.org/10.1037/xge0001047

Hedge, C., Powell, G., & Sumner, P. (2018). The reliability paradox: Why robust cognitive tasks do not produce reliable individual differences. *Behavior Research Methods*, *50*(3), 1166–1186. https://doi.org/10.3758/s13428-017-0935-1

Heidlmayr, K., Kihlstedt, M., & Isel, F. (2020). A review on the electroencephalography markers of Stroop executive control processes. *Brain and Cognition*, *146*, 105637. https://doi.org/10.1016/j.bandc.2020.105637

Hermens, D. F., Soei, E. X. C., Clarke, S. D., Kohn, M. R., Gordon, E., & Williams, L. M. (2005). Resting EEG theta activity predicts cognitive performance in attention-deficit hyperactivity disorder. *Pediatric Neurology*, *32*(4), 248–256. https://doi.org/10.1016/j.pediatrneurol.2004.11.009

Hermundstad, A. M., Bassett, D. S., Brown, K. S., Aminoff, E. M., Clewett, D., Freeman, S., Frithsen, A., Johnson, A., Tipper, C. M., Miller, M. B., Grafton, S. T., & Carlson, J. M. (2013). Structural foundations of resting-state and task-based functional connectivity in the human brain. *Proceedings of the National Academy of Sciences*, *110*(15), 6169–6174. https://doi.org/10.1073/pnas.1219562110

Hoffstaedter, F., Grefkes, C., Caspers, S., Roski, C., Palomero-Gallagher, N., Laird, A. R., Fox, P. T., & Eickhoff, S. B. (2013). The role of anterior midcingulate cortex in cognitive motor control. *Human Brain Mapping*, *35*(6), 2741–2753. https://doi.org/10.1002/hbm.22363

Hong, X., Sun, J., Wang, J., Li, C., & Tong, S. (2020). Attention-related modulation of frontal midline theta oscillations in cingulate cortex during a spatial cueing Go/NoGo task. *International Journal of Psychophysiology*, *148*, 1–12. https://doi.org/10.1016/j.ijpsycho.2019.11.011

Hughes, M. E., Fulham, W. R., Johnston, P. J., & Michie, P. T. (2012). Stop-signal response inhibition in schizophrenia: Behavioural, event-related potential and functional neuroimaging data. *Biological Psychology*, *89*(1), 220–231. https://doi.org/10.1016/j.biopsycho.2011.10.013

Huster, R. J., Enriquez-Geppert, S., Lavallee, C. F., Falkenstein, M., & Herrmann, C. S. (2013). Electroencephalography of response inhibition tasks: Functional networks and cognitive contributions. *International Journal of Psychophysiology*, *87*(3), 217–233. https://doi.org/10.1016/j.ijpsycho.2012.08.001

Huster, R. J., Messel, M. S., Thunberg, C., & Raud, L. (2020). The P300 as marker of inhibitory control – Fact or fiction? *Cortex*, *132*, 334–348. https://doi.org/10.1016/j.cortex.2020.05.021

Hyafil, A., Summerfield, C., & Koechlin, E. (2009). Two Mechanisms for Task Switching in the Prefrontal Cortex. *The Journal of Neuroscience*, *29*(16), 5135–5142. https://doi.org/10.1523/JNEUROSCI.2828-08.2009

Jach, H. K., Feuerriegel, D., & Smillie, L. D. (2020). Decoding personality trait measures from resting EEG: An exploratory report. *Cortex*, *130*, 158–171. https://doi.org/10.1016/j.cortex.2020.05.013

Jaffard, M., Longcamp, M., Velay, J.-L., Anton, J.-L., Roth, M., Nazarian, B., & Boulinguez, P. (2008). Proactive inhibitory control of movement assessed by event-related fMRI. *NeuroImage*, *42*(3), 1196–1206. https://doi.org/10.1016/j.neuroimage.2008.05.041

Jahfari, S., Verbruggen, F., Frank, M. J., Waldorp, L. J., Colzato, L., Ridderinkhof, K. R., & Forstmann, B. U. (2012). How Preparation Changes the Need for Top-Down Control of the Basal Ganglia When Inhibiting

Premature Actions. *Journal of Neuroscience*, *32*(32), 10870–10878. https://doi.org/10.1523/JNEUROSCI.0902-12.2012

Jana, S., Hannah, R., Muralidharan, V., & Aron, A. R. (2020). Temporal cascade of frontal, motor and muscle processes underlying human action-stopping. *ELife*, *9*, e50371. https://doi.org/10.7554/eLife.50371

Jongen, E. M., & Jonkman, L. M. (2008). The developmental pattern of stimulus and response interference in a color-object Stroop task: An ERP study. *BMC Neuroscience*, *9*(1), 82. https://doi.org/10.1186/1471-2202-9-82

Kaiser, J., & Schütz-Bosbach, S. (2019). Proactive control without midfrontal control signals? The role of midfrontal oscillations in preparatory conflict adjustments. *Biological Psychology*, *148*, 107747. https://doi.org/10.1016/j.biopsycho.2019.107747

Kaiser, J., Simon, N. A., Sauseng, P., & Schütz-Bosbach, S. (2019). Midfrontal neural dynamics distinguish between general control and inhibition-specific processes in the stopping of motor actions. *Scientific Reports*, *9*(1), 13054. https://doi.org/10.1038/s41598-019-49476-4

Karamacoska, D., Barry, R. J., Steiner, G. Z., Coleman, E. P., & Wilson, E. J. (2018). Intrinsic EEG and task-related changes in EEG affect Go/NoGo task performance. *International Journal of Psychophysiology*, *125*, 17–28. https://doi.org/10.1016/j.ijpsycho.2018.01.015

Karr, J. E., Areshenkoff, C. N., Rast, P., Hofer, S. M., Iverson, G. L., & Garcia-Barrera, M. A. (2018). The unity and diversity of executive functions: A systematic review and re-analysis of latent variable studies. *Psychological Bulletin*, *144*(11), 1147. https://doi.org/10.1037/bul0000160

Keysers, C., Gazzola, V., & Wagenmakers, E.-J. (2020). Using Bayes factor hypothesis testing in neuroscience to establish evidence of absence. *Nature Neuroscience*, *23*(7), 788–799. https://doi.org/10.1038/s41593-020-0660-4

Khng, K. H., & Lee, K. (2014). The Relationship between Stroop and Stop-Signal Measures of Inhibition in Adolescents: Influences from Variations in Context and Measure Estimation. *PLOS ONE*, *9*(7), e101356. https://doi.org/10.1371/journal.pone.0101356

Knyazev, G. G., Levin, E. A., & Savostyanov, A. N. (2008). A failure to stop and attention fluctuations: An evoked oscillations study of the stop-signal paradigm. *Clinical Neurophysiology*, *119*(3), 556–567. https://doi.org/10.1016/j.clinph.2007.11.041

Ko, L.-W., Shih, Y.-C., Chikara, R. K., Chuang, Y.-T., & Chang, E. C. (2016). Neural Mechanisms of Inhibitory Response in a Battlefield Scenario: A Simultaneous fMRI-EEG Study. *Frontiers in Human Neuroscience*, *10*. https://doi.org/10.3389/fnhum.2016.00185

Koch, I., Gade, M., Schuch, S., & Philipp, A. M. (2010). The role of inhibition in task switching: A review. *Psychonomic Bulletin & Review*, *17*(1), 1–14. https://doi.org/10.3758/PBR.17.1.1

Korjus, K., Uusberg, A., Uusberg, H., Kuldkepp, N., Kreegipuu, K., Allik, J., Vicente, R., & Aru, J. (2015). Personality cannot be predicted from the power of resting state EEG. *Frontiers in Human Neuroscience*, *9*, 63. https://doi.org/10.3389/fnhum.2015.00063

Krmpotich, T. D., Tregellas, J. R., Thompson, L. L., Banich, M. T., Klenk, A. M., & Tanabe, J. L. (2013). Resting-state activity in the left executive control network is associated with behavioral approach and is increased in substance dependence. *Drug and Alcohol Dependence*, *129*(1), 1–7. https://doi.org/10.1016/j.drugalcdep.2013.01.021

Ladouce, S., Donaldson, D. I., Dudchenko, P. A., & Ietswaart, M. (2017). Understanding Minds in Real-World Environments: Toward a Mobile Cognition Approach. *Frontiers in Human Neuroscience*, *10*, 694. https://doi.org/10.3389/fnhum.2016.00694

Langford, Z. D., Schevernels, H., & Boehler, C. N. (2016). Motivational context for response inhibition influences proactive involvement of attention. *Scientific Reports*, *6*(1), 1–11. https://doi.org/10.1038/srep35122

Lansbergen, M. M., Schutter, D. J. L. G., & Kenemans, J. L. (2007). Subjective impulsivity and baseline EEG in relation to stopping performance. *Brain Research*, *1148*, 161–169. https://doi.org/10.1016/j.brainres.2007.02.034

Lavallee, C. F., Herrmann, C. S., Weerda, R., & Huster, R. J. (2014). Stimulus-Response Mappings Shape Inhibition Processes: A Combined EEG-fMRI Study of Contextual Stopping. *PLoS ONE*, *9*(4), e96159. https://doi.org/10.1371/journal.pone.0096159

Lenartowicz, A., Verbruggen, F., Logan, G. D., & Poldrack, R. A. (2011). Inhibition-related Activation in the Right Inferior Frontal Gyrus in the Absence of Inhibitory Cues. *Journal of Cognitive Neuroscience*, *23*(11), 3388–3399. https://doi.org/10.1162/jocn_a_00031

Lerman-Sinkoff, D. B., Sui, J., Rachakonda, S., Kandala, S., Calhoun, V. D., & Barch, D. M. (2017). Multimodal neural correlates of cognitive control in the Human Connectome Project. *NeuroImage*, *163*, 41–54. https://doi.org/10.1016/j.neuroimage.2017.08.081

Leunissen, I., Coxon, J. P., & Swinnen, S. P. (2016). A proactive task set influences how response inhibition is implemented in the basal ganglia: Basal Ganglia in Proactive and Reactive Inhibition. *Human Brain Mapping*, *37*(12), 4706–4717. https://doi.org/10.1002/hbm.23338

Lever, A., Ridderinkhof, K., Marsman, M., & Geurts, H. (2016). Reactive and Proactive Interference Control in Adults With Autism Spectrum Disorder Across the Lifespan. *Developmental Psychology*, *53*. https://doi.org/10.1037/dev0000219

Levy, B. J., & Wagner, A. D. (2011). Cognitive control and right ventrolateral prefrontal cortex: Reflexive reorienting, motor inhibition, and action updating: Cognitive control and right ventrolateral PFC. *Annals of the New York Academy of Sciences*, *1224*(1), 40–62. https://doi.org/10.1111/j.1749-6632.2011.05958.x

Littman, R., & Takács, Á. (2017). Do all inhibitions act alike? A study of go/no-go and stop-signal paradigms. *PLoS ONE*, *12*(10), e0186774. https://doi.org/10.1371/journal.pone.0186774

Logan, G. D., & Cowan, W. B. (1984). On the ability to inhibit thought and action: A theory of an act of control. *Psychological Review*, *91*(3), 295–327. https://doi.org/10.1037/0033-295X.91.3.295

Logie, R. H. (2016). Retiring the Central Executive. *Quarterly Journal of Experimental Psychology*, *69*(10), 2093–2109. https://doi.org/10.1080/17470218.2015.1136657

Loof, E. D., Vassena, E., Janssens, C., Taeye, L. D., Meurs, A., Roost, D. V., Boon, P., Raedt, R., & Verguts, T. (2019). Preparing for hard times: Scalp and intracranial physiological signatures of proactive cognitive control. *Psychophysiology*, *56*(10), e13417. https://doi.org/10.1111/psyp.13417

Mantini, D., Perrucci, M. G., Gratta, C. D., Romani, G. L., & Corbetta, M. (2007). Electrophysiological signatures of resting state networks in the human brain. *Proceedings of the National Academy of Sciences*, *104*(32), 13170–13175. https://doi.org/10.1073/pnas.0700668104

Matzke, D., Love, J., Wiecki, T., Brown, S., Logan, G., & Wagenmakers, E.-J. (2013). Release the BEESTS: Bayesian Estimation of Ex-Gaussian STop-Signal Reaction Time Distributions. *Frontiers in Psychology*, *4*, 918. https://doi.org/10.3389/fpsyg.2013.00918

Maurer, U., Brem, S., Liechti, M., Maurizio, S., Michels, L., & Brandeis, D. (2015). Frontal Midline Theta Reflects Individual Task Performance in a Working Memory Task. *Brain Topography*, *28*(1), 127–134. https://doi.org/10.1007/s10548-014-0361-y

McKewen, M., Cooper, P. S., Skippen, P., Wong, A. S. W., Michie, P. T., & Karayanidis, F. (2021). Dissociable theta networks underlie the switch and mixing costs during task switching. *Human Brain Mapping*, *n/a*(n/a). https://doi.org/10.1002/hbm.25573

McKewen, M., Cooper, P. S., Wong, A. S. W., Michie, P. T., Sauseng, P., & Karayanidis, F. (2020). Task-switching costs have distinct phase-locked and nonphase-locked EEG power effects. *Psychophysiology*, *57*(5), e13533. https://doi.org/10.1111/psyp.13533

Mennes, M., Kelly, C., Zuo, X.-N., Di Martino, A., Biswal, B. B., Castellanos, F. X., & Milham, M. P. (2010). Inter-individual differences in resting-state functional connectivity predict task-induced BOLD activity. *NeuroImage*, *50*(4), 1690–1701. https://doi.org/10.1016/j.neuroimage.2010.01.002

Menon, V., & D'Esposito, M. (2021). The role of PFC networks in cognitive control and executive function. *Neuropsychopharmacology*, 1–14. https://doi.org/10.1038/s41386-021-01152-w

Meyer, H. C., & Bucci, D. J. (2016). Neural and behavioral mechanisms of proactive and reactive inhibition. *Learning & Memory*, *23*(10), 504–514. https://doi.org/10.1101/lm.040501.115

Miller, E. K., & Cohen, J. D. (2001). An Integrative Theory of Prefrontal Cortex Function. *Annual Review of Neuroscience*, *24*(1), 167–202. https://doi.org/10.1146/annurev.neuro.24.1.167

Miller, G. A. (1956). The magical number seven, plus or minus two: Some limits on our capacity for processing information. *Psychological Review*, *63*(2), 81. https://doi.org/10.1037/h0043158

Miller, G. A. (2003). The cognitive revolution: A historical perspective. *Trends in Cognitive Sciences*, *7*(3), 141–144. https://doi.org/10.1016/S1364-6613(03)00029-9

Mirabella, G. (2014). Should I stay or should I go? Conceptual underpinnings of goal-directed actions. *Frontiers in Systems Neuroscience*, *8*. https://doi.org/10.3389/fnsys.2014.00206

Miyake, A., & Friedman, N. P. (2012). The Nature and Organization of Individual Differences in Executive Functions: Four General Conclusions. *Current Directions in Psychological Science*, *21*(1), 8–14. https://doi.org/10.1177/0963721411429458

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The Unity and Diversity of Executive Functions and Their Contributions to Complex "Frontal Lobe" Tasks: A Latent Variable Analysis. *Cognitive Psychology*, *41*(1), 49–100. https://doi.org/10.1006/cogp.1999.0734

Modi, S., Kumar, M., Kumar, P., & Khushu, S. (2015). Aberrant functional connectivity of resting state networks associated with trait anxiety. *Psychiatry Research: Neuroimaging*, *234*(1), 25–34. https://doi.org/10.1016/j.pscychresns.2015.07.006

Monterosso, J. R., Aron, A. R., Cordova, X., Xu, J., & London, E. D. (2005). Deficits in response inhibition associated with chronic methamphetamine abuse. *Drug and Alcohol Dependence*, *79*(2), 273–277. https://doi.org/10.1016/j.drugalcdep.2005.02.002

Mustile, M., Kourtis, D., Ladouce, S., Learmonth, G., Edwards, M. G., Donaldson, D. I., & Ietswaart, M. (2021). Mobile EEG reveals functionally dissociable dynamic processes supporting real-world ambulatory obstacle avoidance: Evidence for early proactive control. *The European Journal of Neuroscience*. https://doi.org/10.1111/ejn.15120

Myers, J. C., Chinn, L. K., Sur, S., & Golob, E. J. (2021). Widespread theta coherence during spatial cognitive control. *Neuropsychologia*, *160*, 107979. https://doi.org/10.1016/j.neuropsychologia.2021.107979

Nachev, P., Kennard, C., & Husain, M. (2008). Functional role of the supplementary and pre-supplementary motor areas. *Nature Reviews Neuroscience*, *9*(11), 856–869. https://doi.org/10.1038/nrn2478

Nachev, P., Wydell, H., O'Neill, K., Husain, M., & Kennard, C. (2007). The role of the pre-supplementary motor area in the control of action. *NeuroImage*, *36*, T155–T163. https://doi.org/10.1016/j.neuroimage.2007.03.034

Nakano, T., Takamura, M., Ichikawa, N., Okada, G., Okamoto, Y., Yamada, M., Suhara, T., Yamawaki, S., & Yoshimoto, J. (2020). Enhancing Multi-Center Generalization of Machine Learning-Based Depression Diagnosis From Resting-State fMRI. *Frontiers in Psychiatry*, *11*, 400. https://doi.org/10.3389/fpsyt.2020.00400

Nakao, T., Bai, Y., Nashiwa, H., & Northoff, G. (2013). Resting-state EEG power predicts conflict-related brain activity in internally guided but not in externally guided decision-making. *NeuroImage*, *66*, 9–21. https://doi.org/10.1016/j.neuroimage.2012.10.034

Näpflin, M., Wildi, M., & Sarnthein, J. (2007). Test–retest reliability of resting EEG spectra validates a statistical signature of persons. *Clinical Neurophysiology*, *118*(11), 2519–2524. https://doi.org/10.1016/j.clinph.2007.07.022

Nieuwenhuis, S., Yeung, N., van den Wildenberg, W., & Ridderinkhof, K. R. (2003). Electrophysiological correlates of anterior cingulate function in a go/no-go task: Effects of response conflict and trial type frequency. *Cognitive, Affective, & Behavioral Neuroscience*, *3*(1), 17–26. https://doi.org/10.3758/CABN.3.1.17

Nigbur, R., Ivanova, G., & Stürmer, B. (2011). Theta power as a marker for cognitive interference. *Clinical Neurophysiology*, *122*(11), 2185–2194. https://doi.org/10.1016/j.clinph.2011.03.030

Nigg, J. T. (2000). On inhibition/disinhibition in developmental psychopathology: Views from cognitive and personality psychology and a working inhibition taxonomy. *Psychological Bulletin*, *126*(2), 220. https://doi.org/10.1037/0033-2909.126.2.220

Nimon, K., Zientek, L. R., & Henson, R. K. (2012). The Assumption of a Reliable Instrument and Other Pitfalls to Avoid When Considering the Reliability of Data. *Frontiers in Psychology*, *3*, 102. https://doi.org/10.3389/fpsyg.2012.00102

Norman, D. A., & Shallice, T. (1986). Attention to Action. In R. J. Davidson, G. E. Schwartz, & D. Shapiro (Eds.), *Consciousness and Self-Regulation: Advances in Research and Theory Volume 4* (pp. 1–18). Springer US. https://doi.org/10.1007/978-1-4757-0629-1_1

Northoff, G., Duncan, N. W., & Hayes, D. J. (2010). The brain and its resting state activity—Experimental and methodological implications. *Progress in Neurobiology*, *92*(4), 593–600. https://doi.org/10.1016/j.pneurobio.2010.09.002

Obeso, I., Robles, N., Marrón, E. M., & Redolar-Ripoll, D. (2013). Dissociating the Role of the pre-SMA in Response Inhibition and Switching: A Combined Online and Offline TMS Approach. *Frontiers in Human Neuroscience*, *7*. https://doi.org/10.3389/fnhum.2013.00150

Obeso, I., Wilkinson, L., Teo, J. T., Talelli, P., Rothwell, J. C., & Jahanshahi, M. (2017). Theta burst magnetic stimulation over the pre-supplementary motor area improves motor inhibition. *Brain Stimulation*, *10*(5), 944–951. https://doi.org/10.1016/j.brs.2017.05.008

O'Reilly, R. C., & Frank, M. J. (2006). Making Working Memory Work: A Computational Model of Learning in the Prefrontal Cortex and Basal Ganglia. *Neural Computation*, *18*(2), 283–328. https://doi.org/10.1162/089976606775093909

Põld, T., Päeske, L., Hinrikus, H., Lass, J., & Bachmann, M. (2021). Long-term stability of resting state EEG-based linear and nonlinear measures. *International Journal of Psychophysiology*, *159*, 83–87. https://doi.org/10.1016/j.ijpsycho.2020.11.013

Posner, M. I., & Presti, D. E. (1987). Selective attention and cognitive control. *Trends in Neurosciences*, *10*(1), 13–17. https://doi.org/10.1016/0166-2236(87)90116-0

Pscherer, C., Bluschke, A., Prochnow, A., Eggert, E., Mückschel, M., & Beste, C. (2020). Resting theta activity is associated with specific coding levels in event-related theta activity during conflict monitoring. *Human Brain Mapping*, *41*(18), 5114–5127. https://doi.org/10.1002/hbm.25178

Pscherer, C., Mückschel, M., Summerer, L., Bluschke, A., & Beste, C. (2019). On the relevance of EEG resting theta activity for the neurophysiological dynamics underlying motor inhibitory control. *Human Brain Mapping*, *40*(14), 4253–4265. https://doi.org/10.1002/hbm.24699

Qiao, L., Xu, L., Che, X., Zhang, L., Li, Y., Xue, G., Li, H., & Chen, A. (2018). The Motivation-Based Promotion of Proactive Control: The Role of Salience Network. *Frontiers in Human Neuroscience*, *12*, 328. https://doi.org/10.3389/fnhum.2018.00328

Ramautar, J. R., Kok, A., & Ridderinkhof, K. R. (2004). Effects of stop-signal probability in the stop-signal paradigm: The N2/P3 complex further validated. *Brain and Cognition*, *56*(2), 234–252. https://doi.org/10.1016/j.bandc.2004.07.002

Rass, O., Ahn, W.-Y., & O'Donnell, B. F. (2016). Resting-state EEG, impulsiveness, and personality in daily and nondaily smokers. *Clinical Neurophysiology*, *127*(1), 409–418. https://doi.org/10.1016/j.clinph.2015.05.007

Raud, L., & Huster, R. J. (2017). The Temporal Dynamics of Response Inhibition and their Modulation by Cognitive Control. *Brain Topography*, *30*(4), 486–501. https://doi.org/10.1007/s10548-017-0566-y

Raud, L., Huster, R. J., Ivry, R. B., Labruna, L., Messel, M. S., & Greenhouse, I. (2020a). A Single Mechanism for Global and Selective Response Inhibition under the Influence of Motor Preparation. *Journal of Neuroscience*, *40*(41), 7921–7935. https://doi.org/10.1523/JNEUROSCI.0607-20.2020

Raud, L., Westerhausen, R., Dooley, N., & Huster, R. J. (2020b). Differences in unity: The go/no-go and stop signal tasks rely on different mechanisms. *NeuroImage*, *210*, 116582. https://doi.org/10.1016/j.neuroimage.2020.116582

Redick, T. S. (2014). Cognitive control in context: Working memory capacity and proactive control. *Acta Psychologica*, *145*, 1–9. https://doi.org/10.1016/j.actpsy.2013.10.010

Reiser, J. E., Wascher, E., & Arnau, S. (2019). Recording mobile EEG in an outdoor environment reveals cognitive-motor interference dependent on movement complexity. *Scientific Reports*, *9*(1), 13086. https://doi.org/10.1038/s41598-019-49503-4

Rey-Mermet, A., Gade, M., & Oberauer, K. (2018). Should we stop thinking about inhibition? Searching for individual and age differences in inhibition ability. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *44*(4), 501–526. https://doi.org/10.1037/xlm0000450

Rey-Mermet, A., Gade, M., Souza, A. S., von Bastian, C. C., & Oberauer, K. (2019). Is executive control related to working memory capacity and fluid intelligence? *Journal of Experimental Psychology: General*, *148*(8), 1335. https://doi.org/10.1037/xge0000593

Salinas, E., & Stanford, T. R. (2013). The Countermanding Task Revisited: Fast Stimulus Detection Is a Key Determinant of Psychophysical Performance. *The Journal of Neuroscience*, *33*(13), 5668–5685. https://doi.org/10.1523/JNEUROSCI.3977-12.2013

Sauseng, P., Tschentscher, N., & Biel, A. L. (2019). Be Prepared: Tune to FM-Theta for Cognitive Control. *Trends in Neurosciences*, *42*(5), 307–309. https://doi.org/10.1016/j.tins.2019.02.006

Schaum, M., Pinzuti, E., Sebastian, A., Lieb, K., Fries, P., Mobascher, A., Jung, P., Wibral, M., & Tüscher, O. (2021). Right inferior frontal gyrus implements motor inhibitory control via beta-band oscillations in humans. *ELife*, *10*, e61679. https://doi.org/10.7554/eLife.61679

Schevernels, H., Bombeke, K., Van der Borght, L., Hopf, J.-M., Krebs, R. M., & Boehler, C. N. (2015). Electrophysiological evidence for the involvement of proactive and reactive control in a rewarded stop-signal task. *NeuroImage*, *121*, 115–125. https://doi.org/10.1016/j.neuroimage.2015.07.023

Schiller, B., Gianotti, L. R. R., Nash, K., & Knoch, D. (2014). Individual Differences in Inhibitory Control—Relationship Between Baseline Activation in Lateral PFC and an Electrophysiological Index of Response Inhibition. *Cerebral Cortex*, *24*(9), 2430–2435. https://doi.org/10.1093/cercor/bht095

Schneider, W., & Shiffrin, R. M. (1977). Controlled and automatic human information processing: I. Detection, search, and attention. *Psychological Review*, *84*(1), 1–66. https://doi.org/10.1037/0033-295X.84.1.1

Sebastian, A., Jung, P., Neuhoff, J., Wibral, M., Fox, P. T., Lieb, K., Fries, P., Eickhoff, S. B., Tüscher, O., & Mobascher, A. (2016). Dissociable attentional and inhibitory networks of dorsal and ventral areas of the right inferior frontal cortex: A combined task-specific and coordinate-based meta-analytic fMRI study. *Brain Structure and Function*, *221*(3), 1635–1651. https://doi.org/10.1007/s00429-015-0994-y

Shiffrin, R. M., & Schneider, W. (1977). Controlled and automatic human information processing: II. Perceptual learning, automatic attending and a general theory. *Psychological Review*, *84*(2), 127–190. https://doi.org/10.1037/0033-295X.84.2.127

Shulman, G. L., Astafiev, S. V., Franke, D., Pope, D. L. W., Snyder, A. Z., McAvoy, M. P., & Corbetta, M. (2009). Interaction of Stimulus-Driven Reorienting and Expectation in Ventral and Dorsal Frontoparietal and Basal Ganglia-Cortical Networks. *Journal of Neuroscience*, *29*(14), 4392–4407. https://doi.org/10.1523/JNEUROSCI.5609-08.2009

Smit, D. J. A., Posthuma, D., Boomsma, D. I., & Geus, E. J. C. D. (2005). Heritability of background EEG across the power spectrum. *Psychophysiology*, *42*(6), 691–697. https://doi.org/10.1111/j.1469-8986.2005.00352.x

Stein, A. von, Chiang, C., & König, P. (2000). Top-down processing mediated by interareal synchronization. *Proceedings of the National Academy of Sciences*, *97*(26), 14748–14753. https://doi.org/10.1073/pnas.97.26.14748

Strobach, T., Wendt, M., & Janczyk, M. (2018). Editorial: Multitasking: Executive Functioning in Dual-Task and Task Switching Situations. *Frontiers in Psychology*, *9*, 108. https://doi.org/10.3389/fpsyg.2018.00108

Studer, B., Pedroni, A., & Rieskamp, J. (2013). Predicting risk-taking behavior from prefrontal resting-state activity and personality. *PloS One*, *8*(10), e76861. https://doi.org/10.1371/journal.pone.0076861

Sundby, K. K., Jana, S., & Aron, A. R. (2021). Double-blind disruption of right inferior frontal cortex with TMS reduces right frontal beta power for action stopping. *Journal of Neurophysiology*, *125*(1), 140–153. https://doi.org/10.1152/jn.00459.2020

Sundermann, B., Olde lütke Beverborg, M., & Pfleiderer, B. (2014). Toward literature-based feature selection for diagnostic classification: A meta-analysis of resting-state fMRI in depression. *Frontiers in Human Neuroscience*, *8*, 692. https://doi.org/10.3389/fnhum.2014.00692

Swann, N. C., Cai, W., Conner, C. R., Pieters, T. A., Claffey, M. P., George, J. S., Aron, A. R., & Tandon, N. (2012). Roles for the pre-supplementary motor area and the right inferior frontal gyrus in stopping action: Electrophysiological responses and functional and structural connectivity. *NeuroImage*, *59*(3), 2860–2870. https://doi.org/10.1016/j.neuroimage.2011.09.049

Swann, N. C., Tandon, N., Pieters, T. A., & Aron, A. R. (2013). Intracranial Electroencephalography Reveals Different Temporal Profiles for Dorsal- and Ventro-lateral Prefrontal Cortex in Preparing to Stop Action. *Cerebral Cortex*, *23*(10), 2479–2488. https://doi.org/10.1093/cercor/bhs245

Swick, D., Ashley, V., & Turken, A. U. (2008). Left inferior frontal gyrus is critical for response inhibition. *BMC Neuroscience*, *9*(1). https://doi.org/10.1186/1471-2202-9-102

Swick, D., Ashley, V., & Turken, U. (2011). Are the neural correlates of stopping and not going identical? Quantitative meta-analysis of two response inhibition tasks. *NeuroImage*, *56*(3), 1655–1665. https://doi.org/10.1016/j.neuroimage.2011.02.070

Swick, D., & Chatham, C. H. (2014). Ten years of inhibition revisited. *Frontiers in Human Neuroscience*, *8*. https://doi.org/10.3389/fnhum.2014.00329

Tatz, J. R., Soh, C., & Wessel, J. R. (2021). Common and Unique Inhibitory Control Signatures of Action-Stopping and Attentional Capture Suggest That Actions Are Stopped in Two Stages. *Journal of Neuroscience*, *41*(42), 8826–8838. https://doi.org/10.1523/JNEUROSCI.1105-21.2021

Thatcher, R. W., North, D., & Biver, C. (2005). EEG and intelligence: Relations between EEG coherence, EEG phase delay and power. *Clinical Neurophysiology*, *116*(9), 2129–2141. https://doi.org/10.1016/j.clinph.2005.04.026

Thatcher, R. W., North, D., & Biver, C. (2007). Intelligence and EEG current density using low-resolution electromagnetic tomography (LORETA). *Human Brain Mapping*, *28*(2), 118–133. https://doi.org/10.1002/hbm.20260

Ullsperger, M., Danielmeier, C., & Jocham, G. (2014). Neurophysiology of Performance Monitoring and Adaptive Behavior. *Physiological Reviews*, *94*(1), 35–79. https://doi.org/10.1152/physrev.00041.2012

van Belle, J., Vink, M., Durston, S., & Zandbelt, B. B. (2014). Common and unique neural networks for proactive and reactive response inhibition revealed by independent component analysis of functional MRI data. *NeuroImage*, *103*, 65–74. https://doi.org/10.1016/j.neuroimage.2014.09.014

van den Wildenberg, W. P. M., Burle, B., Vidal, F., van der Molen, M. W., Ridderinkhof, K. R., & Hasbroucq, T. (2010). Mechanisms and Dynamics of Cortical Motor Inhibition in the Stop-signal Paradigm: A TMS Study. *Journal of Cognitive Neuroscience*, *22*(2), 225–239. https://doi.org/10.1162/jocn.2009.21248

van den Wildenberg, W. P. M., van Boxtel, G. J. M., van der Molen, M. W., Bosch, D. A., Speelman, J. D., & Brunia, C. H. M. (2006). Stimulation of the Subthalamic Region Facilitates the Selection and Inhibition of Motor Responses in Parkinson's Disease. *Journal of Cognitive Neuroscience*, *18*(4), 626–636. https://doi.org/10.1162/jocn.2006.18.4.626

van Dongen-Boomsma, M., Lansbergen, M. M., Bekker, E. M., Sandra Kooij, J. J., van der Molen, M., Kenemans, J. L., & Buitelaar, J. K. (2010). Relation between resting EEG to cognitive performance and clinical symptoms in adults with attention-deficit/hyperactivity disorder. *Neuroscience Letters*, *469*(1), 102–106. https://doi.org/10.1016/j.neulet.2009.11.053

Vecchio, A., & De Pascalis, V. (2020). EEG Resting Asymmetries and Frequency Oscillations in Approach/Avoidance Personality Traits: A Systematic Review. *Symmetry*, *12*(10), 1712. https://doi.org/10.3390/sym12101712

Vecchio, F., Babiloni, C., Lizio, R., De Vico Fallani, F., Blinowska, K., Verrienti, G., Frisoni, G., & Rossini, P. M. (2013). Chapter 15 - Resting state cortical EEG rhythms in Alzheimer's disease: Toward EEG markers

for clinical applications: a review. In E. Başar, C. Başar-Eroğlu, A. Özerdem, P. M. Rossini, & G. G. Yener (Eds.), *Supplements to Clinical Neurophysiology* (Vol. 62, pp. 223–236). Elsevier. https://doi.org/10.1016/B978-0-7020-5307-8.00015-6

Verbruggen, F., Aron, A. R., Stevens, M. A., & Chambers, C. D. (2010). Theta burst stimulation dissociates attention and action updating in human inferior frontal cortex. *Proceedings of the National Academy of Sciences*, *107*(31), 13966–13971. https://doi.org/10.1073/pnas.1001957107

Verbruggen, F., Best, M., Bowditch, W. A., Stevens, T., & McLaren, I. P. L. (2014a). The inhibitory control reflex. *Neuropsychologia*, *65*, 263–278. https://doi.org/10.1016/j.neuropsychologia.2014.08.014

Verbruggen, F., Chambers, C. D., & Logan, G. D. (2013). Fictitious Inhibitory Differences: How Skewness and Slowing Distort the Estimation of Stopping Latencies. *Psychological Science*, *24*(3), 352–362. https://doi.org/10.1177/0956797612457390

Verbruggen, F., & Logan, G. D. (2009). Proactive adjustments of response strategies in the stop-signal paradigm. *Journal of Experimental Psychology: Human Perception and Performance*, *35*(3), 835–854. https://doi.org/10.1037/a0012726

Verbruggen, F., McLaren, I. P. L., & Chambers, C. D. (2014b). Banishing the Control Homunculi in Studies of Action Control and Behavior Change. *Perspectives on Psychological Science*, *9*(5), 497–524. https://doi.org/10.1177/1745691614526414

Vogt, B. A. (2016). Midcingulate cortex: Structure, connections, homologies, functions and diseases. *Journal of Chemical Neuroanatomy*, *74*, 28–46. https://doi.org/10.1016/j.jchemneu.2016.01.010

Vogt, B. A., Berger, G. R., & Derbyshire, S. W. G. (2003). Structural and functional dichotomy of human midcingulate cortex. *European Journal of Neuroscience*, *18*(11), 3134–3144. https://doi.org/10.1111/j.1460-9568.2003.03034.x

Wagner, J., Wessel, J. R., Ghahremani, A., & Aron, A. R. (2018). Establishing a right frontal beta signature for stopping action in scalp EEG: Implications for testing inhibitory control in other task contexts. *Journal of Cognitive Neuroscience*, *30*(1), 107–118. https://doi.org/10.1162/jocn_a_01183

Waller, D. A., Hazeltine, E., & Wessel, J. R. (2021). Common neural processes during action-stopping and infrequent stimulus detection: The frontocentral P3 as an index of generic motor inhibition. *International Journal of Psychophysiology*, *163*, 11–21. https://doi.org/10.1016/j.ijpsycho.2019.01.004

Wang, B., Hao, Y., Zhan, Q., Zhao, S., Li, D., Imtiaz, S., Xiang, J., Wu, J., Fukuyama, H., & Yan, T. (2020). Dynamic reconfiguration of functional brain networks supporting response inhibition in a stop-signal task. *Brain Imaging and Behavior*, *14*(6), 2500–2511. https://doi.org/10.1007/s11682-019-00203-7

Wang, Z., Chen, L. M., Négyessy, L., Friedman, R. M., Mishra, A., Gore, J. C., & Roe, A. W. (2013). The relationship of anatomical and functional connectivity to resting state connectivity in primate somatosensory cortex. *Neuron*, *78*(6), 1116–1126. https://doi.org/10.1016/j.neuron.2013.04.023

Wessel, J. R. (2020). β-Bursts Reveal the Trial-to-Trial Dynamics of Movement Initiation and Cancellation. *Journal of Neuroscience*, *40*(2), 411–423. https://doi.org/10.1523/JNEUROSCI.1887-19.2019

Wessel, J. R., & Aron, A. R. (2013). Unexpected Events Induce Motor Slowing via a Brain Mechanism for Action-Stopping with Global Suppressive Effects. *Journal of Neuroscience*, *33*(47), 18481–18491. https://doi.org/10.1523/JNEUROSCI.3456-13.2013

Wessel, J. R., & Aron, A. R. (2015). It's not too late: The onset of the fronto-central P3 indexes successful response inhibition in the stop-signal paradigm. *Psychophysiology*, *52*(4), 472–480. https://doi.org/10.1111/psyp.12374

Wessel, J. R., & Aron, A. R. (2017). On the Globality of Motor Suppression: Unexpected Events and Their Influence on Behavior and Cognition. *Neuron*, *93*(2), 259–280. https://doi.org/10.1016/j.neuron.2016.12.013

Wessel, J. R., Conner, C. R., Aron, A. R., & Tandon, N. (2013). Chronometric Electrical Stimulation of Right Inferior Frontal Cortex Increases Motor Braking. *Journal of Neuroscience*, *33*(50), 19611–19619. https://doi.org/10.1523/JNEUROSCI.3468-13.2013

Wiemers, E. A., & Redick, T. S. (2018). Working memory capacity and intra-individual variability of proactive control. *Acta Psychologica*, *182*, 21–31. https://doi.org/10.1016/j.actpsy.2017.11.002

Wodka, E. L., Mark Mahone, E., Blankner, J. G., Gidley Larson, J. C., Fotedar, S., Denckla, M. B., & Mostofsky, S. H. (2007). Evidence that response inhibition is a primary deficit in ADHD. *Journal of Clinical and Experimental Neuropsychology*, *29*(4), 345–356. https://doi.org/10.1080/13803390600678046

Wu, T., Chen, C., Spagna, A., Wu, X., Mackie, M.-A., Russell-Giller, S., Xu, P., Luo, Y., Liu, X., Hof, P. R., & Fan, J. (2020). The functional anatomy of cognitive control: A domain-general brain network for uncertainty processing. *Journal of Comparative Neurology*, *528*(8), 1265–1292. https://doi.org/10.1002/cne.24804

Yamanaka, K., & Yamamoto, Y. (2010). Single-trial EEG Power and Phase Dynamics Associated with Voluntary Response Inhibition. *Journal of Cognitive Neuroscience*, *22*(4), 714–727. https://doi.org/10.1162/jocn.2009.21258

Yi, K., & Kim, C. (2020). Dissociable neural correlates of spatial attention and response inhibition in spatially driven interference. *Neuroscience Letters*, *731*, 135111. https://doi.org/10.1016/j.neulet.2020.135111

Zakrzewska, M. Z., & Brzezicka, A. (2014). Working memory capacity as a moderator of load-related frontal midline theta variability in Sternberg task. *Frontiers in Human Neuroscience*, *8*. https://doi.org/10.3389/fnhum.2014.00399

Zandbelt, B. B., Bloemendaal, M., Neggers, S. F. W., Kahn, R. S., & Vink, M. (2013). Expectations and violations: Delineating the neural network of proactive inhibitory control: Neural Network of Proactive Inhibition. *Human Brain Mapping*, *34*(9), 2015–2024. https://doi.org/10.1002/hbm.22047

Zandbelt, B. B., & Vink, M. (2010). On the Role of the Striatum in Response Inhibition. *PLoS ONE*, *5*(11), e13848. https://doi.org/10.1371/journal.pone.0013848

Zhang, F., & Iwaki, S. (2019). Common Neural Network for Different Functions: An Investigation of Proactive and Reactive Inhibition. *Frontiers in Behavioral Neuroscience*, *13*. https://doi.org/10.3389/fnbeh.2019.00124

Zhang, R., Geng, X., & Lee, T. M. C. (2017). Large-scale functional neural network correlates of response inhibition: An fMRI meta-analysis. *Brain Structure & Function*, *222*(9), 3973–3990. https://doi.org/10.1007/s00429-017-1443-x

Zhang, S., & Li, C. R. (2012). Functional networks for cognitive control in a stop signal task: Independent component analysis. *Human Brain Mapping*, *33*(1), 89–104. https://doi.org/10.1002/hbm.21197

Zink, N., Lenartowicz, A., & Markett, S. (2021). A new era for executive function research: On the transition from centralized to distributed executive functioning. *Neuroscience & Biobehavioral Reviews*, *124*, 235–244. https://doi.org/10.1016/j.neubiorev.2021.02.011

Zuure, M. B., Hinkley, L. B., Tiesinga, P. H. E., Nagarajan, S. S., & Cohen, M. X. (2020). Multiple Midfrontal Thetas Revealed by Source Separation of Simultaneous MEG and EEG. *Journal of Neuroscience*, *40*(40), 7702–7713. https://doi.org/10.1523/JNEUROSCI.0321-20.2020

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Strategy switches in proactive inhibitory control and their association with task-general and stopping-specific networks

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ABSTRACT

Prior information about the likelihood of a stop-signal pre-activates networks associated with response inhibition in both go- and stop-trials. How such prior information modulates the neural mechanisms enacting response inhibition is only poorly understood. To investigate this, a cued stop-signal task (with cues indicating stopping probabilities of 0%, 25% or 66%) was implemented in combination with functional magnetic resonance imaging (fMRI) data acquisition. Specifically, we focused on the effect of proactive inhibitory control as reflected in the activity of regions known to regulate response inhibition. Further, modulatory activity profiles in three different sub-regions of the right inferior frontal area were investigated. Behavioural results revealed an adaptation of task strategies through proactive control, with a possible gain for efficient inhibition at high stopping probabilities. The imaging data indicate that this adaption was supported by different regions traditionally involved in the stopping network. While the right inferior parietal cortex (IPC), right middle frontal gyrus (MFG), right inferior frontal gyrus (rIFG) pars triangularis, and left anterior insula all showed increased go-trial activity in the 0% condition compared to the 25% condition, the pre-supplementary motor area (pre-SMA), anterior midcingulate cortex (aMCC), right anterior insula, and the rIFG pars opercularis showed a more stopping-specific pattern, with stronger stop-trial activity in the 66% condition than in the 25% condition. Furthermore, activity in inferior frontal sub-regions correlated with behavioural changes, where more pronounced response slowing was associated with stronger activity increases from low to high stopping probabilities. Notably, the different right inferior frontal sub-regions showed different activity patterns in response to proactive inhibitory control modulations, supporting the idea of a functional dissociation within this area. Specifically, while the pars opercularis and the right insula showed stopping-related modulations of activity, the rIFG pars triangularis exhibited modulations only in go-trials with strong adaptions to fast responding or proactive slowing. Overall, the results indicate that proactive inhibitory control results in the switching of task or strategy modes, either favouring fast responding or stopping, and that these strategical adaptations are governed by an interplay of different regions of the stopping network.

1. Introduction

Response inhibition refers to the ability to suppress or cancel a routine, prepotent or already initiated action (Hampshire and Sharp, 2015). This ability is critical for the adaption of thoughts and behaviour to a rapidly changing environment, and is one of the hallmarks of cognitive control (Miyake et al., 2000). While response inhibition traditionally has been investigated as the process triggered by the sudden onset of a stop-signal, so-called reactive inhibition, research has indicated that how much one prepares to stop, so-called proactive control of inhibition, may affect the neural mechanisms enacting response inhibition (Aron, 2011; Verbruggen and Logan, 2009b). While reactive inhibitory control is a bottom-up process related to the detection of a stop-signal, the modulation of inhibition through proactive control, henceforth referred to as proactive inhibitory control, is a top-down, working-memory dependent process associated with goal-directed behaviour (Braver, 2012). These two modes of inhibitory control supposedly interact through neural systems to facilitate and balance fast and effective inhibition according to environmental demands (Aron, 2011). Here, we investigated the parametric effect of

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proactive inhibitory control on conditions requiring reactive inhibitory control (i.e., stop-trials) and conditions without an explicit need for stopping (i.e., go-trials). In addition, we identified brain regions associated with proactive inhibitory control by correlation analysis with behavioural indices, and further investigated connectivity changes associated with modulations of proactive inhibitory control. Not least, based on debates regarding the neural correlates of response inhibition in the right inferior frontal area, we considered a putative functional dissociation of this area. Specifically, we investigated the modulatory effects of proactive inhibitory control on three different regions of the inferior frontal area, namely the right inferior frontal gyrus (rIFG) pars opercularis, rIFG pars triangularis, and the right anterior insula.

The stop-signal task (SST) is probably the most widely used paradigm to study response inhibition, not least because of the possibility to derive an estimate of the stopping latency from it. This stopping latency is approximated by the stop-signal reaction time (SSRT), computed as a difference measure of a go-trial reaction time distribution parameter (e.g., mean or median) and the stop-signal delay (SSD; Band et al., 2003; Verbruggen and Logan, 2009a). The use of the SST in combination with fMRI has consistently revealed activity associated with reactive inhibitory control in the bilateral IFG, the bilateral insula, the bilateral middle frontal gyrus (MFG), the dorsal anterior cingulate cortex (dACC) or midcingulate cortex (MCC) and the pre-supplementary motor area (pre-SMA), in addition to more posterior activations in the parietal cortex (reviewed in Aron et al., 2014; van Belle et al., 2014; Levy and Wagner, 2011). However, the different functional contributions of these regions in context of reactive inhibitory control have remained equivocal. Some research has pointed to the rIFG as an important region for inhibitory control in the brain (reviewed in Aron, 2007; Aron et al., 2014), supposedly modulating the basal ganglia directly or via the pre-SMA in a right-lateralised network. Alternatively, it has been suggested that the rIFG and pre-SMA are part of a wider cortical network, in which each region has flexible functional roles contributing to a wide variety of cognitive tasks beyond mere inhibitory control (reviewed in Hampshire and Sharp, 2015; Mirabella, 2014).

In the stop-signal paradigm, inhibitory control can be modulated proactively by explicitly informing the participant about the likelihood of an upcoming stop-signal. Thus, while reactive response inhibition is triggered by a somewhat surprising stop-signal, proactive inhibitory control is elicited by a probability cue indicating the likely occurrence of a stop-signal. Increased stop-signal probability has been associated with increased go-trial reaction times (go-RTs; Albares et al., 2014; Verbruggen and Logan, 2009b; Zandbelt and Vink, 2010). This behavioural adjustment is in line with adaptions of the speed-accuracy trade-off as a consequence of higher proactive control, where speed in go-trials is traded for successful inhibition in stop-trials (Forstmann et al., 2010; Verbruggen and Logan, 2008). Further, contrasting fMRI activations of go-trials where the probability of a stop-signal is high (uncertain go-trials), and go-trials where the probability of a stop-signal is zero (certain go-trials) has revealed increased activity in several regions associated with reactive inhibitory control, such as the dorsolateral prefrontal cortex (DLPFC; Chikazoe et al., 2009; Swann et al., 2013), insula (Jahfari et al., 2012), pre-SMA (Albares et al., 2014; Chikazoe et al., 2009; Jahfari et al., 2012; Swann et al., 2012) and the rIFG (Jahfari et al., 2012; Swann et al., 2012). Since go-trials do not include a stop-signal, and thus should not elicit reactive inhibitory control, this activity has been interpreted as reflecting an early, proactive activation of the otherwise reactive inhibitory network (Jaffard et al., 2008).

In addition to the comparison of uncertain and certain go-trials, recent research has also looked at the parametric effects of increasing stop-signal probability on the activity in the stopping network. Such a manipulation yields the possibility to investigate whether increasing stop-signal probability leads to a corresponding increase in activity across the stopping network. Interestingly, manipulating the degree of go-uncertainty has revealed that not all regions implicated in response inhibition show the same modulation of activity (Leunissen et al., 2016; Zandbelt et al., 2013). It may be that the activity modulations seen in response to such parametric manipulations depend on whether the activity is associated with outright stopping tied to the stop-signal, or to the proactive inhibitory control processes as elicited by the probability cue (Zandbelt et al., 2013), although no consensus has been reached. This may partly be because there has only recently been a shift towards the investigation of modulatory effects of varying stop-signal probability beyond the mere binary comparison of certain and uncertain go-trials. One has to note that activity changes in any brain region may thus reflect the engagement of task-general processes, task-specific (here stopping-specific) processes, or a mixture of the two, and broader parametric manipulations may be necessary to disentangle these effects.

The effect of proactive inhibitory control on response inhibition can putatively manifest itself in a number of ways. First, proactive inhibitory control may modulate the inhibition network already before the presentation of a stop signal, for example by heightening response thresholds (Jahfari et al., 2010). Secondly, it may facilitate the detection of the stop signal, e.g. through the adaptation of attentional processes associated with the novelty or unexpectedness of the stop-signal (Gur et al., 2007; Shulman et al., 2009; Zandbelt et al., 2013). Thirdly, proactive inhibitory control processes may be manifested by regulating the reactive inhibition network after the stop signal has been detected, possibly via direct effects on the fronto-basal ganglia connections (Aron, 2011; Aron and Poldrack, 2006; Jahfari et al., 2012). It has been suggested that while reactive inhibitory control might be implemented via a hyperdirect pathway through the subthalamic nucleus (STN) of the basal ganglia, conditions of proactive inhibitory control may rather invoke pathways via a more indirect, slower route through the caudate (Aron, 2011). Activity in basal ganglia regions may thus also be differentially affected in accordance with the degree of proactive inhibitory control (Leunissen et al., 2016).

Another debate relates to the functional unity of the rIFG and adjacent regions (e.g., Aron, 2011; Erika-Florence et al., 2014; Hampshire et al., 2010; Swick and Chatham, 2014; Verbruggen et al., 2010). First, analyses using a rIFG region of interest (ROI) located in medial parts of the rIFG might overlap with the anterior insula, and results may thus be contaminated by insular activity. This is problematic as it has been noted that insular activity during stop-trials might reflect autonomic arousal related to stopping (Aron et al., 2014), or the detection of behaviourally salient events (Cai et al., 2014). Second, whether the rIFG activity during response inhibition tasks reflects attentional processes tied to the detection of the stop-signal (Hampshire et al., 2010), inhibition related processes beyond mere attentional capture (Sebastian et al., 2016), or whether the rIFG sub-regions are part of different cortical networks supporting inhibition as well as other, more general cognitive control functions (Erika-Florence et al., 2014), is still unresolved. Recently, Hartwigsen et al. (2018) proposed a further functional segregation of the rIFG across the anterior-posterior axis, with the posterior parts being associated with action and inhibition-related functions, whereas the anterior parts were rather associated with cognition-related functions. Whether the neural correlates of response inhibition are indeed stronger associated with posterior and lateral structural parts of the rIFG (Aron et al., 2007; Swann et al., 2012; Wessel et al., 2013) needs further investigation.

Although previous research suggests that at least part of the stopping network is recruited during conditions of proactive inhibition, the effects of the modulation of proactive inhibitory control on the activity of this network still remains equivocal on at least two aspects. First, how is the stopping network associated with reactive inhibitory control and its parametric modulation by stop-signal probabilities (as opposed to an only binary comparison of uncertain go-trials and certain go-trials)? Second, does this modulation differentially affect sub-regions of the right inferior frontal area? To this means, a cued stop-signal task was implemented in combination with fMRI data acquisition. The cued stop-signal task included three stop-signal probabilities: 0%, 25% and 66%. To investigate the modulatory effects of proactive inhibitory control on

regions supposedly involved in inhibition, nine ROIs were defined: left and right insula, pre-SMA, anterior midcingulate cortex (aMCC), right IPC, right MFG, right IFG pars opercularis (hereby referred to as pars opercularis), right IFG pars triangularis (hereby referred to as pars triangularis), and the left caudate of the striatum. These regions were chosen in accordance with a meta-analysis of Cieslik et al. (2015). While the pars opercularis is the region traditionally implicated in response inhibition, including the pars triangularis makes it possible to investigate whether rIFG sub-regions are modulated differently by varying degrees of proactive control. Further, because of the aforementioned possible confounding effect of insula activity when investigating the rIFG (Aron et al., 2014), insula was included as a separate ROI. Thus, three regions (right anterior insula, pars opercularis, and pars triangularis) were chosen to investigate the functional specificity of the right inferior frontal area.

Although cued stop-signal tasks make it possible to elicit proactive inhibitory control processes, it becomes more difficult to temporally dissociate cue-related activity from activity elicited by the subsequent go- and stop-signals. Thus, the hypotheses regarding go- and stop-trial activity will rely on the expected observed net effect of cue- and signal-associated activity. In go-trials, we expected an increase in cue- and go-signal activity with increasing stop-signal probability in regions associated with the top-down allocation of attention, working memory and task rules as well as the regions involved in stopping, thus reflecting the engagement of proactive inhibitory control as a top-down goal-directed process (Braver, 2012). This increase should therefore be evident in the IFG, MFG and IPC, as well as in the pre-SMA, as a result of the proactive preparation of stopping. Behaviourally, this activity increase was expected to be paralleled by an increase in go-trial reaction times.

In stop-trials, the observed net activity would reflect the proactive inhibitory control processes elicited by the cue, as well as reactive inhibitory control processes elicited by the stop-signal. It was thus hypothesized that in the 25% condition, the cue-related activity would reflect a middle-ground between low and high proactive inhibitory processes, while the reactive inhibitory processes would be relatively high. In the 66% stop condition, on the other hand, proactive inhibitory control as elicited by the cue would be high, while the reactive inhibitory control as elicited by the stop-signal would be relatively low, as a result of altered response or inhibition thresholds via the basal ganglia (Jahfari et al., 2010, 2012). Thus, regions more closely related to outright stopping, such as the IFG and the pre-SMA would in sum show mid-level elevated stop-related activity in both the 25% and 66% condition due to the differential and partly countermanding effects of proactive and reactive inhibitory control. Regions, on the other hand, that are not directly involved in reactive stopping but that have rather been associated with general attentional control (top-down or proactive), such as the MFG and IPC, would be expected to exhibit an increase in net activity with increasing stop-signal probability. Regarding the three sub-regions in the right inferior frontal area (i.e., pars triangularis, pars opercularis, and right anterior insula), any differential effect of the modulation of stop-signal probability on these regions would indicate functional specificity within the right inferior frontal area.

2. Materials and methods

2.1. Participants

A total of 39 participants were recruited for the study. All participants reported normal or corrected-to-normal vision and no neurological or psychiatric disorders. Eleven participants were excluded from further data analysis; five due to excessive movement in the scanner, one aborted the experiment due to discomfort during scanning, and one participant reported left-handedness that was not noticed until after the completion of the experiment. Four participants were excluded based on behavioural results showing a stop-trial accuracy below 20% (one participant) or above 80% (three participants). This left a final sample of twenty-eight healthy, right-handed participants (age: *range* = 20–39 years, $M = 24.68$, $SD = 4.03$; 20 female). The experiment was approved by the local ethics committee at the Department of Psychology, University of Oslo. Prior to participating in the study, all participants read and signed an informed consent form, and were informed that they could withdraw from the study at any time. Participants received a compensation of 200 NOK each for their participation.

2.2. Task

A cued stop-signal task with three levels of stop-signal probabilities was implemented in combination with fMRI data acquisition. The cued stop-signal task had a jittered, event-related design optimised for fMRI scanning. A visual representation of the task is presented in Fig. 1. The task consisted of 600 task-trials in total. These were divided over three different cue conditions: 0%, 25% and 66%. Specifically, the 0% condition consisted of 50 go-trials, the 25% condition of 300 go-trials and 100 stop-trials, and the 66% condition of 50 go-trials and 100 stop-trials. The overall percentage of go- relative to stop-trials thus was 2/1 (~33% stop trials); this ratio was chosen to still guarantee a prepotent tendency towards fast responding, and correspondingly a high load on motor inhibition. In addition to the 600 task-trials (i.e., go- and stop-trials), 150 null-event trials were added to the design. These events consisted of a 1500 ms presentation of the fixation cross.

Each task-trial started with a fixation cross with a duration jittered randomly between 500 and 2400 ms. The fixation cross was followed by a cue indicating the stop-signal probability of a given trial (i.e., 0%, 25% or 66%), with a cue duration jittered randomly between 1000 and 2000 ms. After the presentation of the cue, the go-signal was presented for 100 ms. In go-trials, the go stimulus offset was followed by a fixation cross for another 1400 ms, during which the responses were collected. Responses outside this timeframe were logged as no-responses. Go-signals consisted of either a left- or right-ward pointing green arrow, indicating the response-hand to be used (left or right, respectively).

The stop-trials were identical to the go-trials with one exception; in stop-trials, a blue arrow (i.e., the stop-signal) pointing in the same direction as the preceding go-signal was presented for 100 ms with varying delays with respect to the go signal (SSD). For each participant, the SSD started at 300 ms and was then dynamically adjusted using a staircase procedure to ensure a 50% stop-trial accuracy. That is, the SSD was *increased* by 50 ms (adjusted to the screen refresh rate) if the previous stop-trial resulted in successful inhibition (i.e., no response), and *decreased* by 50 ms if the previous stop-trial resulted in unsuccessful inhibition (i.e., a response). The SSD was adjusted separately for each cue-condition, but collapsed for the right and left hand.

The 750 trials (task trials and null-event trials) were divided into 10 experimental blocks, with a randomised presentation of trials regarding left- and right-ward pointing arrows, cue-condition, go- and stop-conditions, and null-events. Each block lasted for approximately 6 min. After each block, participants were given feedback on their behavioural performance. If the average go-RT for that block was above 600 ms, participants were presented the feedback “be faster”, and if the average go-RT was below 600 ms the participants were presented the feedback “well done”. The overall duration of the task was approximately 1 h.

2.3. Image acquisition

Structural and functional MR data were acquired from a 3.0 T Philips Ingenia whole body MR scanner, equipped with a 32-channel Philips SENSE head coil (Philips Medical Systems, Best, the Netherlands). Each session started with a structural high resolution image using a T1-weighted sequence of 184 sagittal slices with a voxel size of $1 \times 1 \times 1$ mm, (field of view: 256×256 mm^2, acquisition matrix: 256×256, TE: 2.2 ms, TR: 4.5 ms, flip angle: 8°, no slice gap). The fMRI

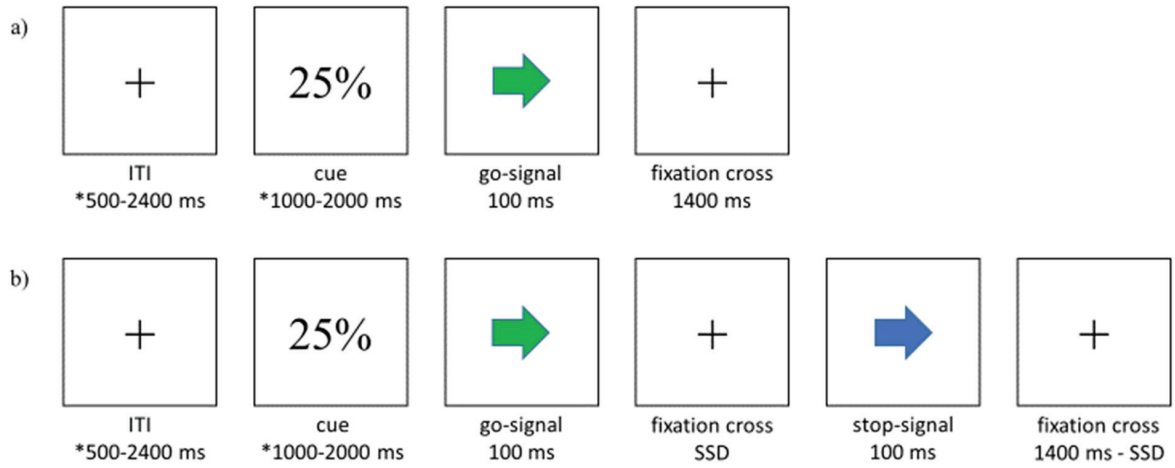

Fig. 1. Visual representation of the cued stop-signal task. This figure illustrates an example of a go-trial (a) and stop-trial (b) with 25% stop-signal probability and rightwards pointing arrows. ITI = inter-trial interval, ms = milliseconds, * indicates that the duration was jittered randomly within the specified time interval.

sequence was a BOLD-sensitive T2* weighted echo-planar imaging (EPI) sequence of 34 axial slices with a voxel size of 2.625 × 2.625 × 3.0 mm (field of view: 210 × 210 mm^2, acquisition matrix: 80 × 80, TE: 30 ms, TR: 2000 ms, flip angle: 80°, slice gap: 0.3 mm, interleaved acquisition). At the beginning of the fMRI sequence, three dummy scans were acquired and then discarded to allow for the stabilization of the magnetic field. The whole MRI session, including calibration, structural and functional sequences, took approximately 1 h and 10 min. EEG data were recorded concurrently, but the analyses reported here exclusively focus on the fMRI analyses.

2.4. Analysis

2.4.1. Behavioural data

For each participant, go-RT, go accuracy, SSRT, unsuccessful stop-trial reaction time (USRT; i.e., the response time of stop-trial errors of commission), SSD, and stop accuracy, were calculated separately for all cue conditions. The SSRT was estimated using the integration method (Verbruggen et al., 2013), with replacement of go omissions, as suggested in a recent consensus paper regarding the stop-signal task (Verbruggen et al., 2019). Specifically, go omission trials (i.e., go-trials without a response) was replaced with the maximum go-RT for the specific cue-condition. Thus, the go-trial distribution included valid go-trials, erroneous go-trials (i.e., trials with a choice error) and the go omission replacement trials. The full go-RT distribution were rank ordered, and the nth RT was selected by determining *n* as the product of multiplying the probability of responding in stop-trials with the number of all go-trials. Finally, the SSRT was estimated by subtracting the mean SSD from the nth RT.

Not all data sets of behavioural performance measures were normally distributed. The behavioural measures related to go-trials (i.e., go-RT and go accuracy) were analysed using a one-way repeated measures ANOVA, which has been found to be quite robust against deviations from normality (Schmider et al., 2010). All measures related to stop-trials (i.e., SSRT, USRT, SSD and stop accuracy) were compared using Wilcoxon Signed rank tests for dependent samples. All behavioural data were analysed in IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp.).

2.4.2. fMRI data: pre-processing

All pre-processing steps were performed with SPM12 (Wellcome Trust Centre for NeuroImaging, Institute of Neurology at University College London, UK), running under MATLAB r2016a (The MathWorks Inc., Natick, MA). Functional images were realigned to the first image and resliced using a 5th degree B-spline interpolation. Slice timing correction to adjust for time acquisition delays was performed using the central slice as reference. Functional images were co-registered to the structural image, and normalised to the Montreal Neurological Institute (MNI) standard space, using linear and non-linear deformations, written with a final resolution of 3 × 3 × 3 mm. Lastly, functional images were smoothed using a 6 mm full-width-at-half-maximum (FWHM) Gaussian kernel. The estimated motion parameters were inspected to ensure that relative motion (between adjacent time points) did not exceed half the voxel size.

2.4.3. fMRI data: analysis

First-level statistical analyses were performed in SPM12 in an event-related design using the general linear model (GLM) framework. The following events were included in the model: cues, successful go-trials, erroneous go-trials, successful stop-trials, unsuccessful stop-trials, null-events and feedback. All task conditions were modelled according to their corresponding stop-signal probability. Go- and stop-trials were modelled at go-signal onset and stop-signal onset, respectively, while unsuccessful stop-trials were modelled at response onset. In addition, six regressors coding the participant's motion parameters estimated during the realignment procedure were included to correct for head movement. Task events were modelled as zero-duration events, with the exception of feedback, which was modelled with a 20-s duration. All modelled events were convolved with a canonical hemodynamic response function (HRF). To account for slow-frequency drifts, a high-pass filter with cut-off at 128 s was implemented.

The conditions of interest were the successful stop-trials in the 25% condition and the 66% condition (hereby referred to as stop25 and stop66), and the successful go-trials in the 0%, 25% and 66% condition (hereby referred to as go0, go25, and go66). To explore the global activity evoked during reactive inhibition, a stop > go t-contrast was created for each participant; i.e., the collapsed activity in the stop25 and stop66 conditions were compared against the collapsed activity in the go25 and go66 condition (hereby referred to as global whole-brain analysis). The resulting t-maps from all participants were then subjected to a group-level random effects analysis, where a one-sample *t*-test was used on the sample contrast images. To further explore the activity evoked during reactive inhibition, this procedure was also performed separately for a stop25 > go25 contrast and for a stop66 > go66 contrast. As the main aim of the study was the investigation of activity within specific ROIs, the global whole-brain analysis was performed as a validity check of the paradigm. Thus, resulting t-value maps were analysed using the more lenient cluster-level inference,

with a height threshold of $p < .001$, and cluster probability of $p < .05$ (family wise error corrected; FWE).

ROIs were defined using the MarsBaR ROI toolbox version 0.44 for SPM (Brett et al., 2002). Nine ROIs were defined as spheres with a 6-mm radius centred at coordinates of local maxima extracted from a meta-analysis conducted by Cieslik et al. (2015; see Table 1 and Fig. 2). This meta-analysis was chosen because all studies included were studies using the standard stop-signal task, and coordinates were inferred from the contrast stop > go. We know of no more recent meta-analysis meeting these requirements. Furthermore, it included differential regions of the right inferior frontal area (i.e., the pars opercularis and the pars triangularis, as well as the right anterior insula). The regions used within the present study therefore represent a selection of those regions detected in the meta-analysis that is based on the specified a priori hypotheses. Thus, not all regions of the meta-analysis were included in the present study. For each participant, mean beta values were extracted from each ROI for the go0, go25, go66, stop25 and stop66 conditions. The extracted mean beta values were exported to IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp.) for statistical analysis.

As the main interest of the present study was the effect of stop-signal probability on go-trial and stop-trial activity, rather than the difference between go and stop, the following ROI analyses were performed. To see how stop-signal probability affects go-trial brain activity, a 3 (*stop-signal probability*; 0, 25, 66) x 9 (*ROI*; left insula, pre-SMA, aMCC, right insula, right IPC, right MFG, pars opercularis, pars triangularis, striatum) repeated-measures ANOVA was performed on the corresponding beta values. To see how stop-signal probability affected the brain activity in the stop-trials, a 2 (*stop-signal probability*; 25, 66) x 9 (*ROI*; left insula, pre-SMA, aMCC, right insula, right IPC, right MFG, pars opercularis, pars triangularis, striatum) repeated measures ANOVA was set up. All post-hoc tests related to the ANOVAs investigating the effect of stop-signal probability on ROI beta values are reported with Bonferroni-adjusted p-values as implemented in SPSS. For all statistics, Greenhouse-Geisser corrected estimates are reported when the assumption of sphericity was violated.

In contrast to the previous analyses, which focused on the effects of proactive inhibitory control on specific regions of interest, two whole-brain analyses were performed with SSRT as covariate of interest (one for each stop-signal probability), to investigate the relationship between the behavioural performance of reactive inhibitory control and brain activity. That is, for the 25% condition, first level contrast images of stop25 > go25 from all participants were subjected to a random effects multiple regression analysis with the SSRT in the 25% condition from each participant as a covariate of interest. This was then repeated for the 66% condition. Resulting t-value maps were analysed using voxel-wise inference with $p < .05$ (FWE). Similarly, to investigate which cortical regions might correlate with the behavioural indices of proactive inhibitory control induced by increased stop-signal probability, three difference scores were calculated: between go-RT in the go25 and the go0 condition (go-RT25 – go-RT0), as was the difference between go-RT in the go66 and go0 condition (go-RT66 – go-RT0), and in the go66 and go25 condition (go-RT66 – go-RT25). These estimated differences were then subjected as covariates of interest to three random effects multiple regression analyses, using first level contrast images of go25 > go0, go66 > go0 and go66 > go25, respectively. Group-level t-value maps were analysed using voxel-wise inference with $p < .05$ (FWE).

Table 1
Peak local maxima coordinates of ROIs.

Region	MNI Coordinates (x, y, z)
Right anterior insula	34, 22, −4
Right IFG (pars opercularis)	50, 12, 28
Right IFG (pars triangularis)	56, 20, 4
Left anterior insula	−40, 16, −4
Pre-SMA	4, 16, 48
Right MFG	36, 2, 54
aMCC	6, 30, 32
Right IPC	62, −42, 26
Striatum	−4, 12, −2

Note. IFG = inferior frontal gyrus, pre-SMA = pre-supplementary motor area, MFG = middle frontal gyrus, aMCC = anterior cingulate cortex, IPC = inferior parietal cortex.

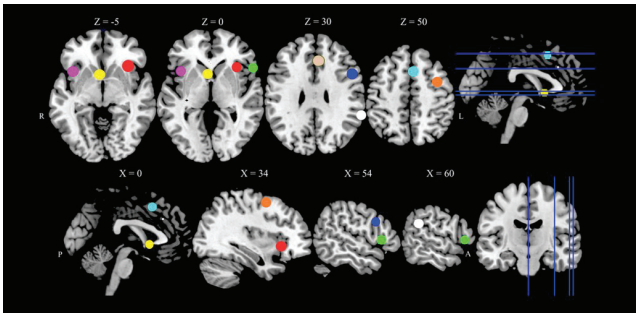

Fig. 2. Graphical depiction of the ROI locations. Left insula in pink, striatum in yellow, right insula in red, pars triangularis in bright green, aMCC in beige, pars opercularis in dark blue, right IPC in white, pre-SMA in turquoise, right MFG in orange. R = right, L = left, P = posterior, A = anterior. Note: For accurate locations of the ROIs see Table 1. ROIs are projected onto the template ch2better of MRIcroN (https://people.cas.sc.edu/rorden/mricron/index.html). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article).

Because of the specific hypotheses regarding the relationships of the pre-selected ROIs with both proactive and reactive inhibitory control, bivariate two-tailed correlations between the SSRT and ROI beta values for the 25% and 66% conditions, and one-tailed bivariate correlations between the go-RT difference estimates and the corresponding differences between ROI beta values were computed. The alpha level was Bonferroni-corrected for number of tests ($\alpha = 0.05/(9 \times 2) = 0.0028$).

Lastly, an exploratory psycho-physiological interaction (PPI) analysis was performed. PPI is a method that aims to determine which regions in the brain change their connectivity with a seed region when manipulating task context (Friston et al., 1997; O'Reilly et al., 2012). Three first level analyses were set up using the SPM toolbox for MATLAB. For all analyses, the rIFG pars opercularis (*center*: 50, 12, 28; *radius*: 6 mm) was chosen as the seed region. Although there are some indications that specifying the region individually for each subject within some constrained area is the most sensitive approach (e.g., O'Reilly et al., 2012), the seed region was kept constant for all subjects for better correspondence with the ROI analysis. First, the region's time series was extracted for each subject, which represented the eigenvariate of the pre-whitened, high-pass filtered time series, adjusted for effects of interest. The PPI analysis was then conducted by using the predetermined region of interest and the contrast go66 > go25. The resulting PPI interaction term, the eigenvariate time series and the experimental task vector was then subjected to a GLM analysis, and a t-contrast image for the interaction term was computed. The resulting t-maps of all participants were then subjected to a group-level random effects analysis, where a one-sample *t*-test was used on the sample of contrast images. These steps were repeated for the contrast stop66 > stop25, and go66 > go0. The resulting whole-brain t-value maps were analysed using voxel-wise inference with $p < .05$ (FWE).

3. Results

3.1. Behavioural results

A summary of the behavioural measures is presented in Table 2. Overall, the participants performed well in all three cue-conditions, as evidenced by high go-trial accuracies of 95.7%, 97.9% and 97.5% for the 0%, 25% and 66% conditions, respectively. There was a significant

Table 2
Behavioural data.

	Stop-signal probability condition		
	0%	25%	66%
Go-trial RT (ms)**	438.58 (57.44)	592.73 (64.74)	685.15 (115.44)
Go-trial accuracy (%)*	95.71 (4.38)	97.89 (2.68)	97.49 (2.70)
SSRT (ms)	–	250.91 (53.45)	227.29 (51.07)
SSD (ms)**	–	337.21 (89.34)	435.83 (112.03)
USRT (ms)**	–	524.04 (56.14)	598.14 (80.57)
Stop-trial accuracy (%)**	–	48.86 (6.07)	52.53 (5.36)

Note. Table shows means of behavioural measures for each probability condition. Standard deviations are presented in the parentheses. RT = reaction time, SSRT = stop-signal reaction time, SSD = stop-signal delay, USRT = unsuccessful stop-trial reaction time, ms = milliseconds. Significant differences marked with ** ($p < .001$) and * ($p < .05$).

effect of stop-signal probability on go-trial accuracies (F (1.33, 35.81) = 6.62, $p = .009$, $\eta_p^2 = 0.20$), caused by a significantly higher accuracy in the 25% condition than in the 0% condition ($p = .006$). The difference between the 25% and the 66% condition did not reach significance, nor did the difference between 0% and 66% ($p > .05$). There was also a significant effect of stop-signal probability on go-RT (F (1.32, 35.61) = 104.74, $p < .001$, $\eta_p^2 = 0.80$). Bonferroni-corrected post-hoc tests revealed that go-RT increased as a function of stop-signal probability. The go-RT in the 25% condition was significantly higher than in the 0% condition and in the 66% condition as compared the 25% condition (all $p < .001$).

The participants' accuracy in the stop-trials was close to 50%, although the accuracy was higher in the 66% condition than in the 25% condition ($z = 4.14$, $p < .001$). USRT increased with increasing stop-signal probability ($z = 4.60$, $p < .001$). Further, in line with assumption of the horse race model, the USRT was significantly shorter than the go-RT in both the 25% condition ($z = -4.62$, $p < .001$), and in the 66% condition ($z = -4.62$, $p < .001$). Lastly, the SSD increased significantly with increasing stop-signal probability ($z = 4.62$, $p < .001$). The difference between the SSRT in the 25% and in the 66% condition did not reach significance ($z = -1.62$, $p = .106$).

3.2. Imaging results

3.2.1. Whole-brain

Global stop vs go effects in brain activity. Contrasting stop > go, cluster-level inference revealed significant activity in bilateral IFG pars orbitalis and bilateral MFG (all $p < .05$), which is in line with the previous literature (Aron and Poldrack, 2006; Jahfari et al., 2010). The additional contrasts investigating stop-related brain activity in the 25% and 66% conditions separately seem to suggest differences between the two conditions, although no direct comparisons was performed on whole-brain data. See Table 3 for all significantly activated clusters, visually displayed in Fig. 3.

3.2.2. ROI analyses

Go-related changes in brain activity. To investigate the effect of proactive control on go-trial activity, a 3 (*stop-signal probability*; 0%, 25%, 66%) x 9 (*ROI*; left insula, pre-SMA, aMCC, right insula, right IPC, right MFG, pars opercularis, pars triangularis, striatum) repeated-measures ANOVA was performed with go-related beta values as the dependent variable. The ANOVA revealed a significant main effect of *stop-signal probability* (F (2, 54) = 5.45, $p = .007$, $\eta_p^2 = 0.17$), and *ROI* (F (8, 216) = 14.32, $p < .001$, $\eta_p^2 = 0.35$), as well as a significant interaction between *stop-signal probability* and *ROI* (F (7.67, 207.19) = 4.07, $p < .001$, $\eta_p^2 = 0.13$). As evident from Fig. 4A, Bonferroni-corrected post-hoc tests revealed that the bilateral insula, the pars opercularis, and the pars triangularis all showed a significant increase in activity from the 25% to the 66% condition (all $p < .05$). Furthermore, left insula, right IPC, right MFG, and the pars triangularis all exhibited a significant decrease in activity from the 0% to the 25% ($p < .05$). The right insula was the only region showing higher activity in the 66% condition than in the 0% condition ($p = .002$). Interestingly, the pre-SMA, aMCC and striatum did not show these probability-specific modulations.

Stop-related changes in brain activity. To investigate the effect of proactive inhibitory control and its interaction with the reactive stop-trial activity, a 2 (*stop-signal probability*; 25%, 66%) x 9 (*ROI*; left insula, pre-SMA, aMCC, right insula, right IPC, right MFG, pars opercularis, pars triangularis, striatum) repeated measures ANOVA was performed. The interaction effect between *stop-signal probability* and *ROI* was significant (F (8, 216) = 2.78, $p = .006$, $\eta_p^2 = 0.09$), as were the main effects of both *stop-signal probability* (F (1, 27) = 8.11, $p = .008$,

Table 3
Activated clusters contrasting stop > go.

Region	X (mm)	Y (mm)	Z (mm)	T	Cluster extent
stop > go.					
L Middle Occipital Gyrus	−42	−79	8	6.99	141
R Middle Occipital Gyrus	45	−79	5	6.79	687
L Angular Gyrus	−57	−61	29	6.02	120
R Middle Frontal Gyrus	45	29	44	5.36	118
L Middle Frontal Gyrus	−39	20	50	4.88	46
R IFG (p. orbitalis)	36	17	−19	4.70	58
L IFG (p. orbitalis)	−30	23	−16	4.47	52
R Angular Gyrus	30	−58	53	4.43	90
stop25 > go25					
L Inferior Parietal Lobule	−57	−55	38	6.49	113
R Angular Gyrus	51	−55	35	5.96	201
R Middle Occipital Gyrus	45	−79	5	5.60	140
R Inferior Temporal Gyrus	45	−49	−13	5.48	62
R Middle Temporal Gyrus	54	−40	5	4.85	85
L Insula Lobe	−30	20	−7	4.74	51
R Middle Frontal Gyrus	42	11	44	4.68	66
stop66 > go66					
L Middle Occipital Gyrus	−45	−79	8	7.04	175
R Middle Temporal Gyrus	48	−73	2	6.34	342
R Superior Parietal Lobe	33	−49	56	4.92	48

Note. Locations are reported as MNI coordinates. Anatomical labelling was performed using the SPM Anatomy toolbox (Eickhoff et al., 2005). Height threshold of $p < .001$, cluster probability of $p < .05$ (FWE). R = right, L = left. IFG = Inferior frontal gyrus. X, Y, Z coordinates listed are the location of the peak T value in each cluster.

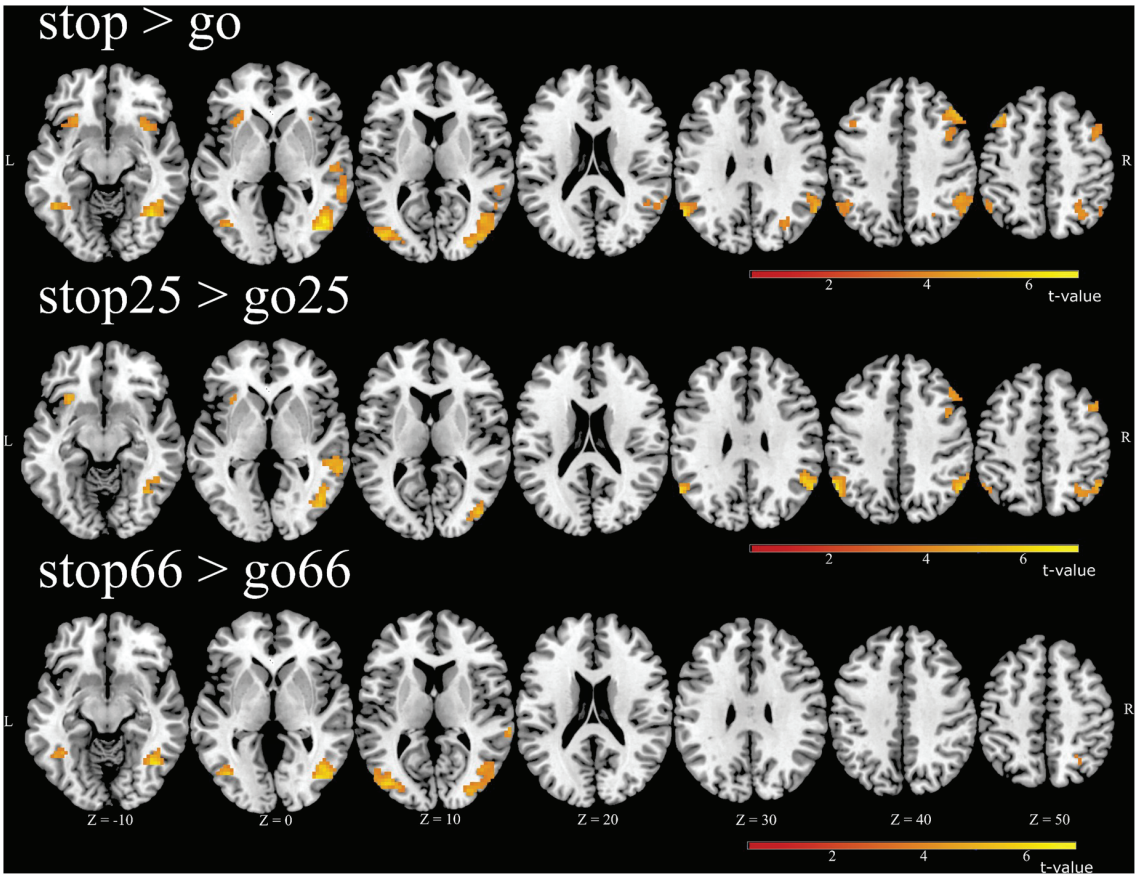

Fig. 3. Whole brain analysis overlaid on single-subject template brain. Height threshold of $p < .001$, cluster probability of $p < .05$ (FWE). Colour scale in t-value units. R = right, L = left. Activation maps were projected onto the template ch2better of MRIcroN (https://people.cas.sc.edu/rorden/mricron/index.html). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

$\eta_p^2 = 0.23$), and *ROI* (F (5.46, 147.50) = 15.64, $p < .001$, $\eta_p^2 = 0.37$). The main effect of stop-signal probability indicated generally higher activity in the 66% condition than the 25% condition. However, with respect to the interaction of *stop-signal probability* and *ROI*, follow-up Bonferroni-corrected post-hoc tests revealed some regional specificity with higher activity in the 66% condition than in the 25% condition in the bilateral insula, pre-SMA, aMCC, and the pars opercularis, while no significant differences between conditions were found for the right IPC, right MFG, the pars triangularis, and the striatum (Fig. 4B).

3.2.3. Brain-behaviour correlations

Whole brain analyses testing for correlations between the SSRTs and stop-trial related brain activity revealed a significant negative correlation between the right thalamus and the SSRT in the 66% condition, although the cluster only contained one voxel, and thus was quite small (Table 4). No significant activity was evident for the 25% condition.

Two-tailed bivariate correlations between SSRTs and ROI stop-trial beta values for both the 25% and the 66% condition did not reach significance (all $p > .0028$).

The whole-brain analysis investigating whether there was a relationship between the increase in go-RT and an increase in brain activity between the different stop-signal probability conditions did not reveal significant activations for the increase from 0% to 25%, 0% to66%, nor from 25% to 66%.

There was a significant bivariate correlation between the difference of ROI beta values in the 66% and 25% conditions and the corresponding difference in go-RT, with stronger increase in activity being associated with more pronounced RT slowing (Fig. 5). This was true for the left insula ($r = 0.517$, $p = .002$), aMCC ($r = 0.534$, $p = .002$), right insula ($r = 0.532$, $p = .002$), and the pars triangularis ($r = 0.624$, $p < .001$).The pre-SMA exhibited a relationship of similar strength ($r = 0.468$, $p = .006$), that nevertheless did not cross the Bonferroni corrected significance level. No significant bivariate correlations were found for the differencesof go66 > go0 or go25 > go0.

3.2.4. PPI analysis

PPI analyses of the go-trials revealed a significant increase in connectivity between the pars opercularis and the left putamen as well as the right fusiform gyrus in the 66% condition relative to the 25% condition (Table 5). However, the significant clusters were rather small. Neither the corresponding effects for stop-signal trials, nor the go66 > go0 analysis revealed any significant changes in connectivity.

4. Discussion

A cued stop-signal task was used to investigate the effects of proactive inhibitory control on response initiation and inhibition processes. As was expected based on previous research, whole-brain analyses revealed that inhibitory control was associated with activity in the bilateral IFG, MFG and IPC (e.g., Aron and Poldrack, 2006; Chikazoe et al., 2009). More importantly though, behavioural and imaging results indicate that the participants adjusted their performance proactively with increasing stop-signal probability. That is, go-RT and stop-trial accuracy increased with increasing stop-signal probability, while the SSRT remained unaltered. Thus, participants used the probability cues to switch between task strategies, from a go-oriented mode with short

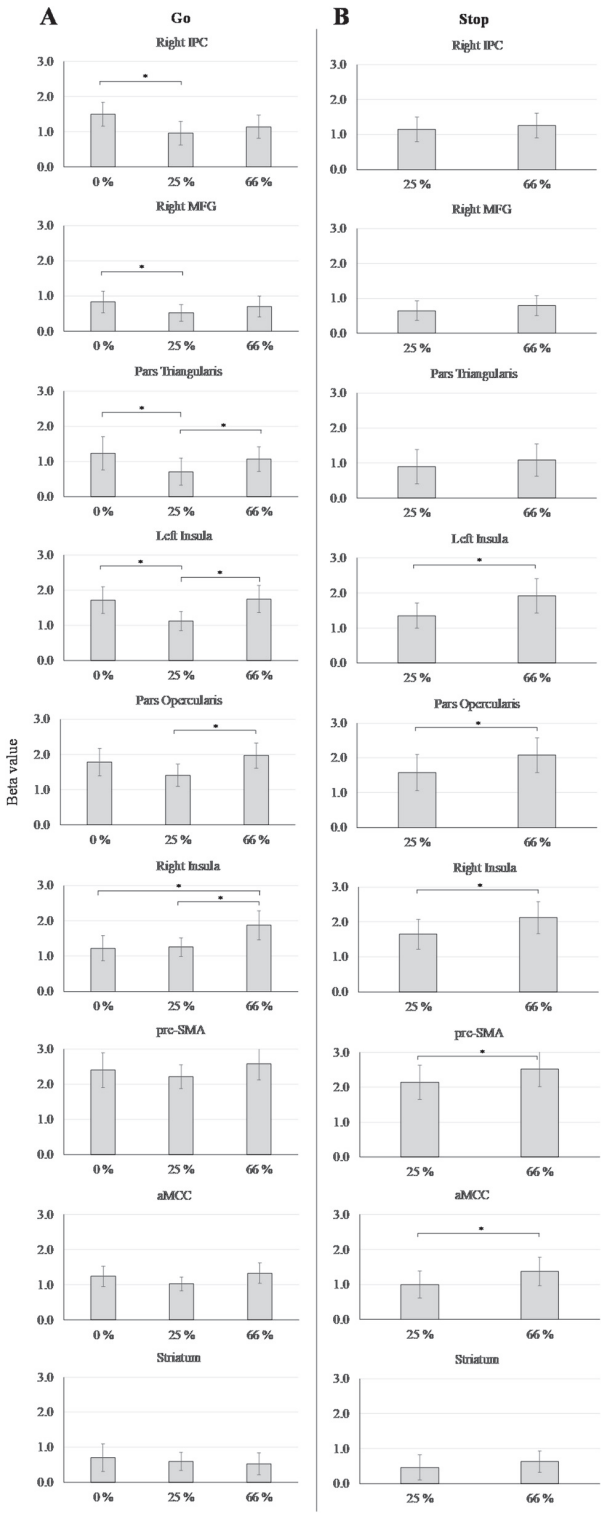

Fig. 4. Effect of stop-signal probability on A) go-trial activity and B) stop-trial activity. The figure exhibits the pairwise comparisons underlying the interaction effect between ROI and stop-signal probability. Significant differences are marked with * ($p < .05$, Bonferroni-corrected). Error bars represent 95% confidence intervals. aMCC = anterior midcingulate cortex, pre-SMA = pre-supplementary motor area, IPC = inferior parietal cortex, MFG = middle frontal gyrus.

Table 4
Correlation of the SSRT and stop-related activity in the whole-brain analysis.

Region	X (mm)	Y (mm)	Z (mm)	T	Cluster extent
R Thalamus	9	−19	17	6.68	1

Note. Results of the whole brain analyses testing for correlations between the SSRTs and stop-trial related brain activity in the 66% condition. Locations are reported as MNI coordinates. Anatomical labelling was performed by the SPM Anatomy toolbox (Eickhoff et al., 2005). Voxel-wise inference with $p < .05$ (FWE). R = right, L = left. X, Y, Z coordinates listed are the location of the peak T value in each cluster.

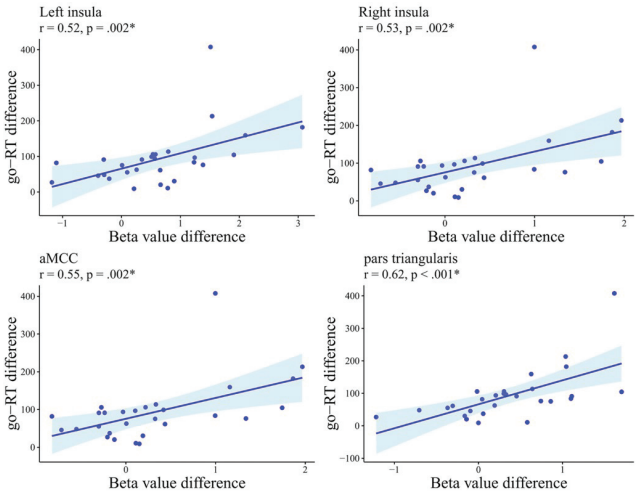

Fig. 5. Bivariate one-tailed correlations revealed a significant correlation between go-RT difference and ROI beta value difference between the 66% and 25% conditions. Significant effects are marked with * ($p < .0028$).

Table 5
PPI analysis.

Go66 > go25					
Region	X (mm)	Y (mm)	Z (mm)	T	Cluster extent
L Putamen	−12	11	−7	6.42	1
R Fusiform Gyrus	39	−43	−19	6.07	1

Note. Results of the PPI analysis using the rIFG pars opercularis as seed region. Locations are reported as MNI coordinates. Anatomical labelling was performed using the SPM Anatomy toolbox (Eickhoff et al., 2005). Voxel-wise inference with $p < .05$ (FWE). R = right, L = left. X, Y, Z coordinates listed are the location of the peak T value in each cluster.

response times, to a stopping mode with slow responses but higher stop-trial accuracy. The behavioural effects of mode switches were also reflected in the imaging data, where regions traditionally involved in outright stopping, such as the pre-SMA, pars opercularis, and the insula all showed stronger stop-trial activations in the 66% condition than in the 25% condition. Interestingly, go-trial activity was significantly higher in the 0% condition than the 25% condition in the left insula, pars triangularis, right MFG and right IPC. However, while the left insula and pars triangularis showed a significant increase in go-trial activity from the 25% to the 66% condition, this was not true for the MFG and IPC. This indicates that the mode-switching evident in the behavioural data is associated with different regions of the stopping network, where some regions may be more associated with the facilitation of fast responses in the 0% condition, and other regions with efficient inhibition in the 66% condition. Furthermore, the results indicate that sub-regions in the inferior frontal area exhibit different activity patterns in response to proactive inhibitory control modulations, with the pars opercularis and

right insula being more responsive to outright stopping, and the pars triangularis possibly being more associated with go-related processes during clear stimulus-response mappings.

4.1. Mode-switching of task-strategies

The increase in go-RT with increasing stop-signal probability is in line with previous research (Albares et al., 2014; Zandbelt and Vink, 2010), and has been attributed to an increase in proactive inhibitory control (e.g., Verbruggen and Logan, 2009b). Although it was expected that the SSRT would decrease with increasing stop-signal probability as a result of the increase in proactive inhibitory control, no such effect was found in the present study. The lack of a decrease in the SSRT has also been found in previous research (e.g., Lavallee et al., 2014; Leunissen et al., 2016), and has been attributed to a response-strategy adjustment where speed in the go-trials are traded for accuracy in the stop-trials (Verbruggen and Logan, 2009b). This was supported by the stop-trial accuracy, which was significantly higher in the 66% condition than in the 25% condition. Thus, the behavioural data indicate a shift from a predominately "go-mode" in the 0% condition to a predominately "stop-mode" in the 66% condition. Furthermore, the behavioural pattern observed in the 25% condition clearly indicates that participants tried to balance response speed and stopping accuracy (Verbruggen and Logan, 2008). In the 0% condition, participants do not have to proactively prepare for upcoming inhibition, and this certainty of a motor execution facilitates processes supporting fast responses. The added uncertainty in the 25% condition urges participants to apply a more balanced strategy, as evident in higher go-RTs compared to the 0% condition. In the 66% condition, participants clearly engage in efficient stopping. This is indicated by increased stopping accuracy, coming at the expense of prolonged go-RTs. This pattern further supports previous research that has found that people switch task strategies in accordance with the frequency and relevance of stop-trials (Bissett and Logan, 2014).

4.1.1. Regions facilitating fast responding in go-trials

The mode-switching of task-strategies evident in the behavioural data is mirrored in the neural data. That is, the facilitation of fast responses in the 0% condition and the facilitation of efficient stopping in the 66% condition may be associated with distinct regions of the stopping network. The right IPC, right MFG, pars triangularis and the left insula all showed a significantly increased go-trial activity in the 0% condition compared to the 25% condition. It is somewhat surprising that certain regions of the stopping network showed this elevated go-trial activity in the 0% condition compared to the 25% condition. Although speculative, this effect may reflect the certainty of an upcoming motor response and the allocation of attentional resources to the detection of the go-signal. That is, during conditions when the need for a response to the go-signal is certain (i.e., the 0% condition), attentional processes allocated to the detection of the target as well as facilitation of the fast response are recruited. A recent attempt to investigate the interaction between attentional resources and response inhibition did indeed find a down-modulation of go-stimulus processing in conditions when the probability of stopping is high, reflected in a relationship between attenuated EEG N1 amplitudes (a marker for early visual-sensory processing) and go-RTs (Langford et al., 2016). The opposite pattern (i.e., up-modulation of go-stimulus processing in conditions of low proactive inhibitory control) thus seems plausible. Since the N1 amplitude decreased with go-RT slowing, it is likely that these processes are under proactive control (Langford et al., 2016). As the rIPC has been associated with attentional processes during stop-signal tasks (Gur et al., 2007; Hampshire et al., 2010; Shulman et al., 2009; Zandbelt et al., 2013), an effect that seems to be independent of the task-relevance of the stop-signal (Boehler et al., 2011), it may be that the attentional processes related to the N1 modulation indeed are related to IPC activity. The reported associations of the IPC with both the maintenance of attentional control (Singh-Curry and Husain, 2009) and the bottom-up detection of salient stimuli (Corbetta and Shulman, 2002) further support this interpretation.

Both the pars triangularis and the left insula showed a more task-general pattern, with higher go-trial activity both in the 0% condition and in the 66% condition, than in the 25% condition. Thus, it may be that the activity in these regions is associated with general processes induced by the clear stimulus-response mappings of these two conditions. That is, during the 0% condition, these regions may help to facilitate the fast responding as evident by the short go-RTs. In the 66% condition however, the activity in these regions may be associated with a general response slowing, as a result of the increased proactive inhibitory control induced by the increased stop-signal probability. This is supported by the correlation between the behavioural slowing from the 25% condition to the 66% condition and the activity difference between these conditions in both the pars triangularis and the left insula.

4.1.2. Mechanisms of efficient stopping during proactive inhibitory control

The bilateral insula, pars opercularis, pre-SMA and aMCC all showed a significant increase in stop-trial activity from the 25% condition to the 66% condition. Thus, during increased proactive control there is an increase in activity in regions traditionally involved in reactive inhibitory control. This indicates that there is an interaction between the processes governing the two modes of inhibitory control.

Interestingly, for the pre-SMA and the aMCC, the increase in activity from the 25% condition to the 66% condition was not evident in go-trial activity. This may indicate that the inhibition-related processes associated with pre-SMA activity are occurring after, or related to, the detection of the stop-signal, such as connectivity with the basal ganglia to modulate response or inhibition thresholds. In fact, pre-SMA connections to the basal ganglia have been found to be modulated by stop-signal probability and trial outcome certainty (Forstmann et al., 2010; Jahfari et al., 2012). Although no significant difference between aMCC go-trial activity in the 25% and the 66% condition was found, this difference was nevertheless correlated with behavioural adaptions in the go-RT between these two probability conditions. The aMCC has also been implicated in response preparation and working memory (reviewed in Vogt, 2016). Thus, it may be that the activity pattern seen here indicates that the aMCC is involved in processes related to proactive inhibitory control, and processes beyond those introduced by the stop-signal. Future studies need to investigate this further.

4.2. Dissociable functional roles of inferior frontal sub-regions

Despite the association of the (right) IFG with response inhibition, its exact functional role has become the center of discussion. Indeed, our results indicate such a functional dissociation of the right inferior frontal area. The pars opercularis and the right insula showed the expected stopping activity, with higher activity in the 66% condition than in the 25% condition, in both go- and stop-trials. This is consistent with the idea that the rIFG acts as a brake during conditions of high proactive inhibitory control (Aron et al., 2014). Here, we show that this braking mechanism is not specific to the pars opercularis, but that the right insula also exhibits a similar response profile. It has been argued that the insula activity during stop-signal tasks rather reflects autonomic arousal related to stopping (Aron et al., 2014) or the detection of behaviourally salient events (Cai et al., 2014), instead of inhibition per se. Here, we show that insula activity is susceptible to proactive modulations of stopping, which may indicate more than pure autonomic arousal. If the insula activity was dependent on the saliency of the stop-signal, then a decrease in activity with increasing stop probability would be more likely, reflecting the increased expectancy of the stop-signal. Furthermore, the activity difference from the 25% to the 66% condition in the right insula was correlated with the corresponding go-RT difference, a correlation not evident for the pars opercularis. These findings further support the notion that the insula's function extends beyond mere

autonomic arousal or attentional mechanisms.

Interestingly, the pars triangularis showed a somewhat different activity pattern than the two other inferior frontal regions. While the pars triangularis did show a significant increase in activity from the 25% to the 66% condition, this was only true for go-trials. Furthermore, this was accompanied by a significant correlation with the behavioral RT difference between these two conditions. In the stop-trials, no significant modulations were evident in this region. Interestingly, the pars triangularis, as the only inferior frontal sub-region, showed a significant decrease in go-trial activity from the 0% to the 25% condition. Thus, while the pars opercularis and right insula may be more susceptible to proactive modulations of outright stopping, the pars triangularis activity pattern rather indicates an association with conditions favoring task modes with clear stimulus-response mappings. The present results further support previous research showing that more posterior parts of the inferior frontal area are indeed related to stopping and inhibition (Hartwigsen et al., 2018).

The PPI analysis revealed that go-trials during conditions of high compared to low proactive inhibitory control exhibited significantly higher connectivity between the pars opercularis and the left putamen as well as the right fusiform gyrus. No such connectivity patterns were evident in the stop-trials. These results support the notion that the pars opercularis is implicated in proactive inhibitory control, possibly as a braking mechanism (Aron et al., 2014), and further suggests that this braking mechanism may involve the striatum of the basal ganglia. The results of the PPI analysis open up for a dissociation of the functional roles of the pars opercularis and the right insula, as no connectivity between these regions was evident. However, some important limitations of the PPI analyses need to be addressed. First, PPI analyses usually suffer from a lack of power, owing to the modeling of changes of connectivity as an interaction term to exploit the residual variance of other regressors (O'Reilly et al., 2012). Further, and perhaps as a consequence of low power and sensitivity, the significant clusters evident in go-trials were small, and should be interpretated with some caution. The PPI results thus await further replication, not least through the use of alternative methods for the detection of connectivity patterns.

4.3. Future directions and limitations

To our surprise, the expectation that activity in go-trials would increase concurrently with the augmentation of stopping probability from 0% to 25% in regions associated with proactive inhibitory control was not met. Although lack of increase in go-trial activity from low to high stop-signal probability in regions such as the rIFG have been reported earlier (Jahfari et al., 2012; Leunissen et al., 2016), we speculate that such outcomes are based in specifics of the task design. As the distance between the probabilities chosen for the current design is larger than what has been used in previous research varying stop-signal probabilities, it may have triggered more pronounced strategic adaptations in the 0% and the 66% condition, leaving the 25% condition to be the most uncertain condition. This suggests that specific care has to be taken when using stopping probabilities as experimental factors, and future research is needed to further dissociate strategic adaptations from genuine inhibitory and attentional processes.

The ROIs chosen in the present study was inferred form a meta-analysis using the standard stop-signal task, and the contrast stop > go (Cieslik et al., 2015). It is interesting then that regions traditionally involved in stopping, such as the striatum, do not show activity modulations as an effect of increased proactive inhibitory control. Although the present results may indicate that the striatum rather exhibits proactive modulations through connectivity changes, this notion needs to be cross-validated with alternative analysis schemes. The striatum ROI used here was located to the left caudate, and it may be that proactive inhibitory control recruits other regions of the basal ganglia, as it has previously been shown that activity in the caudate varies in response to proactive inhibitory control modulations (Leunissen et al., 2016) Further, correlational analysis in the present study did reveal an association between the SSRT and the right thalamus that was only evident in the 66% condition. Although speculative considering the cluster size of this result, it does support the notion that proactive inhibitory control affects basal ganglia pathways (Aron, 2011; Leunissen et al., 2016). It may be that choosing a striatal ROI based on local maxima coordinates from research on proactive inhibitory control (as opposed to the standard SST) would have yielded different results, and future research should investigate this further.

It needs to be noted that the contributions of proactive and reactive inhibitory control to the net effects discussed here cannot be dissociated in this study because of the temporal proximity of the cue and the target stimulus. Thus, we assume that proactive inhibitory control increases with increasing stop-signal probability as we see a corresponding increase in go-RT. However, as we do not see the corresponding activity increase in the regions associated with proactive inhibitory control from the 0% to the 25% condition, we can only hypothesize that the different conditions trigger distinct strategy modes as reflected in different activity patterns. In addition, the exact neural mechanisms through which proactive inhibitory control exerts its influence, e.g., how proactive inhibitory control interacts with reactive inhibitory processes, is not known. Future studies should test the interaction between proactive and reactive inhibitory processes specifically.

5. Conclusion

The present study is the first to report how varying proactive inhibitory control results in the switching of task or strategy modes, either favouring fast responding or efficient stopping, and how this process is governed by different regions of the stopping network. Furthermore, using a parametric design, as opposed to only binary comparisons of certain to uncertain trials, helped to elucidate the net effects of the interaction of proactive and reactive mechanisms on regional activity. Lastly, the present study suggests a functional dissociation of the right inferior frontal area, where the pars opercularis and right insula seem to be more associated with outright stopping, while the pars triangularis rather is associated with clear stimulus-response mappings in go-trials.

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Declaration of competing interest

None.

References

Albares, M., Lio, G., Criaud, M., Anton, J., Desmurget, M., Boulinguez, P., 2014. The dorsal medial frontal cortex mediates automatic motor inhibition in uncertain contexts: evidence from combined fMRI and EEG studies. Hum. Brain Mapp. 35 (11), 5517–5531. https://doi.org/10.1002/hbm.22567.

Aron, A.R., 2007. The neural basis of inhibition in cognitive control. The Neuroscientist 13 (3), 214–228. https://doi.org/10.1177/1073858407299288.

Aron, A.R., 2011. From reactive to proactive and selective control: developing a richer model for stopping inappropriate responses. Biol. Psychiatry 69 (12), e55–e68. https://doi.org/10.1016/j.biopsych.2010.07.024.

Aron, A.R., Behrens, T.E., Smith, S., Frank, M.J., Poldrack, R.A., 2007. Triangulating a cognitive control network using diffusion-weighted magnetic resonance imaging (MRI) and functional MRI. J. Neurosci. 27 (14), 3743–3752. https://doi.org/10.1523/JNEUROSCI.0519-07.2007.

Aron, A.R., Poldrack, R.A., 2006. Cortical and subcortical contributions to stop signal response inhibition: role of the subthalamic nucleus. J. Neurosci. 26 (9), 2424–2433. https://doi.org/10.1523/JNEUROSCI.4682-05.2006.

Aron, A.R., Robbins, T.W., Poldrack, R.A., 2014. Inhibition and the right inferior frontal cortex: one decade on. Trends Cogn. Sci. 18 (4), 177–185. https://doi.org/10.1016/j.tics.2013.12.003.

Band, G.P.H., Molen, M.W., Logan, G.D., 2003. Horse-race model simulations of the stop-signal procedure. Acta Psychol. 112, 105–142. https://doi.org/10.1016/S0001-6918(02)00079-3.
Bissett, P.G., Logan, G.D., 2014. Selective stopping? Maybe not. J. Exp. Psychol. Gen. 143 (1), 455–472. https://doi.org/10.1037/a0032122.
Boehler, C.N., Appelbaum, L.G., Krebs, R.M., Chen, L., Woldorff, M.G., 2011. The role of stimulus salience and attentional capture across the neural hierarchy in a stop-signal task. PLoS One 6 (10). https://doi.org/10.1371/journal.pone.0026386 e26386.
Braver, T.S., 2012. The variable nature of cognitive control: a dual-mechanisms framework. Trends Cogn. Sci. 16 (2), 106–113. https://doi.org/10.1016/j.tics.2011.12.010.
Brett, M., Anton, J., Valabregue, R., Poline, J., 2002. Region of interest analysis using an SPM toolbox [abstract]. Presented at the 8th international conference on functional mapping of the human brain, june 2-6, 2002, sendai, Japan. Neuroimage 16 (2). Available on CD-ROM in.
Cai, W., Ryali, S., Chen, T., Li, C.R., Menon, V., 2014. Dissociable roles of right inferior frontal cortex and anterior insula in inhibitory control: evidence from intrinsic and task-related functional parcellation, connectivity, and response profile Analyses across multiple datasets. J. Neurosci. 34 (44), 14652–14667. https://doi.org/10.1523/JNEUROSCI.3048-14.2014.
Chikazoe, J., Jimura, K., Hirose, K., Yamashito, K., Miyashita, Y., Konishi, S., 2009. Preparation to inhibit a response complements response inhibition during performance on a stop-signal task. J. Neurosci. 29 (50), 15870–15877. https://doi.org/10.1523/JNEUROSCI.3645-09.2009.
Cieslik, E.C., Mueller, V.I., Eickhoff, C.R., Langner, R., Eickhoff, S.B., 2015. Three key regions for supervisory attentional control: evidence from neuroimaging meta-analyses. Neurosci. Biobehav. Rev. 48, 22–34.
Corbetta, M., Shulman, G.L., 2002. Control of goal-directed and stimulus-driven attention in the brain. Nat. Rev. 3, 201–215. https://doi.org/10.1038/nrn755.
Eickhoff, S., Stephan, K.E., Mohlberg, H., Grefkes, C., Fink, G.R., Amunts, K., Zilles, K., 2005. A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. Neuroimage 25 (4), 1325–1335.
Erika-Florence, M., Leech, R., Hampshire, A., 2014. A functional network perspective on response inhibition and attentional control. Nat. Commun. 5, 4073. https://doi.org/10.1038/ncomms5073.
Forstmann, B.U., Anwander, A., Schäfer, A., Neumann, J., Brown, S., Wagenmakers, E., et al., 2010. Cortico-striatal connections predict control over speed and accuracy in perceptual decision making. Proc. Natl. Acad. Sci. 107 (36), 15916–15920. https://doi.org/10.1073/pnas.1004932107.
Friston, K.J., Buechel, C., Fink, G.R., Morris, J., Rolls, E., Dolan, R.J., 1997. Psychophysiological and modulatory interactions in neuroimaging. Neuroimage 6 (3), 218–229.
Gur, R.C., Turetsky, B.I., Loughead, J., Waxman, J., Snyder, W., Ragland, J.D., et al., 2007. Hemodynamic responses in neural circuitries for detection of visual target and novelty: an event-related fMRI study. Hum. Brain Mapp. 28, 263–274. https://doi.org/10.1002/hbm.20319.
Hartwigsen, G., Neef, N.E., Camilleri, J.A., Margulies, D.S., Eickhoff, S.B., 2018. Functional segregation of the right inferior frontal cyrus: evidence from coactivation-based parcellation. Cerebr. Cortex bhy049, 1–15. https://doi.org/10.1093/cercor/bhy049.
Hampshire, A., Chamberlain, S.R., Monti, M.M., Duncan, J., Owen, A.M., 2010. The role of the right inferior frontal gyrus: inhibition and attentional control. Neuroimage 50, 1313–1319. https://doi.org/10.1016/j.neuroimage.2009.12.109.
Hampshire, A., Sharp, D.J., 2015. Contrasting network and modular perspectives on inhibitory control. Trends Cogn. Sci. 19 (8), 445–452. https://doi.org/10.1016/j.tics.2015.06.006.
Jaffard, M., Longcamp, M., Velay, J., Anton, J., Roth, M., Nazarian, B., Boulinguez, P., 2008. Proactive inhibitory control of movement assessed by event-related fMRI. Neuroimage 42, 1196–1206. https://doi.org/10.1016/j.neuroimage.2008.05.041.
Jahfari, S., Stinear, C.M., Claffey, M., Verbruggen, F., Aron, A.R., 2010. Responding with restraint: what are the neurocognitive mechanisms? J. Cogn. Neurosci. 22 (7), 1479–1492. https://doi.org/10.1162/jocn.2009.21307.
Jahfari, S., Verbruggen, F., Frank, M.J., Waldorp, L.J., Colzato, L., Ridderinkhof, K.R., Forstmann, B.U., 2012. How preparation changes the need for top-down control of the basal ganglia when inhibiting premature actions. J. Neurosci. 32 (32), 10870–10878. https://doi.org/10.1523/JNEUROSCI.0902-12.2012.
Langford, Z.D., Krebs, R.M., Talsma, D., Woldorff, M.G., Boehler, C.N., 2016. Strategic down-regulation of attentional resources as a mechanism of proactive response inhibition. Eur. J. Neurosci. 44 (4), 2095–2103. https://doi.org/10.1111/ejn.13303.
Lavallee, C.F., Herrmann, C.S., Weerda, R., Huster, R.J., 2014. Stimulus-response mappings shape inhibition processes: a combined EEG-fMRI study of contextual stopping. PLoS One 9 (4), e96159. https://doi.org/10.1371/journal.pone.0096159.
Leunissen, I., Coxon, J.P., Swinnnen, S.P., 2016. A proactive task set influences how response inhibition is implemented in the basal ganglia. Hum. Brain Mapp. 37 (12), 4706–4717. https://doi.org/10.1002/hbm.23338.
Levy, B.J., Wagner, A.D., 2011. Cognitive control and right ventrolateral prefrontal cortex: reflexive reorienting, motor inhibition, and action updating. Ann. N. Y. Acad. Sci. 1224, 40–62. https://doi.org/10.1111/j.1749-6632.2011.05958.x.
Mirabella, G., 2014. Should I stay or should I go? Conceptual underpinnings of goal-directed actions. Front. Syst. Neurosci. 8, 1–21. https://doi.org/10.3389/fnsys.2014.00206.
Miyake, A., Friedman, N.P., Emerson, M.J., Witzki, A.H., Howerter, A., 2000. The unity and diversity of executive functions and their contributions to complex "Frontal lobe'' tasks: a latent variable analysis. Cogn. Psychol. 41, 49–100. https://doi.org/10.1006/cogp.1999.0734.
O'Reilly, J.X., Woolrich, M.W., Behrens, T.E., Smith, S.M., Johansen-Berg, H., 2012. Tools of the trade: psychophysiological interactions and functional connectivity. Soc. Cogn. Affect. Neurosci. 7 (5), 604–609.
Schmider, E., Ziegler, M., Danay, E., Beyer, L., Bühner, M., 2010. Is it really robust? Reinvestigating the robustness of ANOVA against violations of the normal distribution assumption. Methodology 6 (4), 147–151. https://doi.org/10.1027/1614- 2241/a000016.
Sebastian, A., Jung, P., Neuhoff, J., Wibral, M., Fox, P.T., Lieb, K., et al., 2016. Dissociable attentional and inhibitory networks of dorsal and ventral areas of the right inferior frontal cortex: a combined task-specific and coordinate-based meta-analytic fMRI study. Brain Struct. Funct. 221 (3), 1635–1651. https://doi.org/10.1007/s00429-015-0994-y.
Shulman, G.L., Astafiev, S.V., Franke, D., Pope, D.L.W., Snyder, A.Z., McAvoy, M.P., Corbetta, M., 2009. Interaction of stimulus-driven reorienting and expectation in ventral and dorsal fronto-parietal and basal ganglia-cortical networks. J. Neurosci. 29 (14), 4392–4407. https://doi.org/10.1523/JNEUROSCI.5609-08.2009.
Singh-Curry, V., Husain, M., 2009. The functional role of the inferior parietal lobe in the dorsal and ventral stream dichotomy. Neuropsychologia 47, 1434–1448. https://doi.org/10.1016/j.neuropsychologia.2008.11.033.
Swann, N.C., Cai, W., Conner, C.R., Pieters, T.A., Claffey, M.P., George, J.S., et al., 2012. Roles for the pre-supplementary motor area and the right inferior frontal gyrus in stopping action: electrophysiological responses and functional and structural connectivity. Neuroimage 59, 2860–2870. https://doi.org/10.1016/j.neuroimage.2011.09.049.
Swann, N.C., Tandon, N., Pieters, T.A., Aron, A.R., 2013. Intracranial electroencephalography reveals different temporal profiles for dorsal- and ventro-lateral prefrontal cortex in preparing to stop action. Cerebr. Cortex 23, 2479–2488. https://doi.org/10.1093/cercor/bhs245.
Swick, D., Chatham, C.H., 2014. Ten years of inhibition revisited. Front. Hum. Neurosci. 8 https://doi.org/10.3389/fnhum.2014.00329.
van Belle, J., Vink, M., Durston, S., Zandbelt, B.B., 2014. Common and unique neural networks for proactive and reactive response inhibition revealed by independent component analysis of functional MRI data. Neuroimage 103, 65–74. https://doi.org/10.1016/j.neuroimage.2014.09.014.
Verbruggen, F., Aron, A.R., Band, G.P., Beste, C., Bissett, P.G., Brockett, A.T., et al., 2019. A consensus guide to capturing the ability to inhibit actions and impulsive behaviors in the stop-signal task. Elife 8, e46323.
Verbruggen, F., Aron, A.R., Stevens, M.A., Chambers, C.D., 2010. Theta burst stimulation dissociates attention and action updating in human inferior frontal cortex. Proc. Natl. Acad. Sci. 107 (31), 13966–13971. https://doi.org/10.1073/pnas.1001957107.
Verbruggen, F., Chambers, C.D., Logan, G.D., 2013. Fictitious inhibitory differences: how skewness and slowing distort the estimation of stopping latencies. Psychol. Sci. 24 (3), 352–362. https://doi.org/10.1177/0956797612457390.
Verbruggen, F., Logan, G.D., 2008. Response inhibition in the stop-signal paradigm. Trends Cogn. Sci. 12 (11), 418–424. https://doi.org/10.1016/j.tics.2008.07.005.
Verbruggen, F., Logan, G.D., 2009. Models of response inhibition in the stop-signal and stop-change paradigms. Neurosci. Rev. Biobehavioural Rev. 33 (5), 647–661. https://doi.org/10.1016/j.neubiorev.2008.08.014.
Verbruggen, F., Logan, G.D., 2009. Proactive adjustments of response strategies in the stop-signal paradigm. J. Exp. Psychol. Hum. Percept. Perform. 35 (3), 835–854. https://doi.org/10.1037/a0012726.
Vogt, B.A., 2016. Midcingulate cortex: structure, connections, homologies, functions and diseases. J. Chem. Neuroanat. 74, 28–46.
Wessel, J.R., Conner, C.R., Aron, A.R., Tandon, N., 2013. Chronometric electrical stimulation of right inferior frontal cortex increases motor braking. J. Neurosci. 33 (50), 19611–19619. https://doi.org/10.1523/JNEUROSCI.3468-13.2013.
Zandbelt, B.B., Bloemendaal, M., Neggers, S.F.W., Kahn, R.S., Vink, M., 2013. Expectations and violations: delineating the neural network of proactive inhibitory control. Hum. Brain Mapp. 34, 2015–2024. https://doi.org/10.1002/hbm.22047.
Zandbelt, B.B., Vink, M., 2010. On the role of the striatum in response inhibition. PLoS One 5 (11), e13848. https://doi.org/10.1371/journal.pone.0013848.

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Frontal-midline theta reflects different mechanisms associated with proactive and reactive control of inhibition

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ABSTRACT

Reactive control of response inhibition is associated with a right-lateralised cortical network, as well as frontal-midline theta (FM-theta) activity measured at the scalp. However, response inhibition is also governed by proactive control processes, and how such proactive control is reflected in FM-theta activity and associated neural source activity remains unclear. To investigate this, simultaneous recordings of electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) data was performed while participants performed a cued stop-signal task. The cues (0%, 25% or 66%) indicated the likelihood of an upcoming stop-signal in the following trial. Results indicated that participants adjusted their behaviour proactively, with increasing go-trial reaction times following increasing stop-signal probability, as well as modulations of both go-trial and stop-trial accuracies. Target-locked theta activity was higher in stop-trials than go-trials and modulated by probability. At the single-trial level, cue-locked theta was associated with shorter reaction-times, while target-locked theta was associated with both faster reaction times and higher probability of an unsuccessful stop-trial. This dissociation was also evident at the neural source level, where a joint ICA revealed independent components related to going, stopping and proactive preparation. Overall, the results indicate that FM-theta activity can be dissociated into several mechanisms associated with proactive control, response initiation and response inhibition processes. We propose that FM-theta activity reflects both heightened preparation of the motor control network, as well as stopping-related processes associated with a right lateralized cortical network.

1. Introduction

Response inhibition is the ability to suppress or cancel a routine, prepotent or already initiated action (Hampshire and Sharp, 2015). As conceptualised in the dual mechanisms of control (DMC) framework (Braver, 2012), response inhibition is governed by proactive and reactive control (Aron, 2011). Here, proactive control of inhibition is the preparation in expectation of an upcoming stop-signal and relies on top-down control and working memory. Reactive control of inhibition (hereby referred to as reactive inhibition) is transiently elicited by the stop-signal itself, and is a bottom-up process relying on sensory and attentional mechanisms. Impaired inhibition is seen in a variety of disorders, such as attention deficit/hyperactivity disorder (Wodka et al., 2007), schizophrenia (Hughes et al., 2012), Parkinson's disease (van den Wildenberg et al., 2006) and drug abuse (Fillmore and Rush, 2002; Monterosso et al., 2005). Understanding the dynamics and mechanisms of proactive and reactive control of inhibition is therefore of utter importance, as such impairments may result from disturbance in either of the two domains. However, the neural mechanisms underlying proactive and reactive control of inhibition as well as their interplay remain elusive, not least due to the difficulty of unimodal approaches to concurrently specify neural activity at a high spatial and temporal resolution.

Response inhibition is commonly investigated using the stop-signal task. Here, a go-signal probes the participant to make a rapid response, while on a minority of the trials, the go-signal is followed by a stop-signal after a variable delay (stop-signal delay; SSD), which instructs the participants to withhold their initiated response. The latency of inhibition, the stop-signal reaction time (SSRT), can be estimated as a difference measure of the go-trial reaction time and the SSD (Band

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et al., 2003; Verbruggen and Logan, 2008). By adding cues that indicate the likelihood of an upcoming stop-signal, the stop-signal task can assess proactive inhibition. In the behavioural domain, cues that signal a higher stop signal probability lead to increased go-trial reaction times, which is usually interpreted as a proactive adjustment of behaviour (Boulinguez et al., 2009; S. Jahfari et al., 2012; Verbruggen and Logan, 2009a; Zandbelt and Vink, 2010).

Successful response inhibition relies on a right-dominant network that includes the right inferior frontal gyrus (rIFG), pre-supplementary motor area (pre-SMA), right inferior parietal cortex (rIPC), insula, middle frontal gyrus (MFG), as well as the cingulate cortex (Aron et al., 2014; Cieslik et al., 2015; Levy and Wagner, 2011; van Belle et al., 2014). Some evidence suggests that networks associated with reactive inhibition are also active during proactive inhibition (Chikazoe et al., 2009; Jahfari et al., 2010; Zandbelt et al., 2013), indicating a pre-activation of the stopping network in preparation for inhibition (Aron, 2011). However, not all regions of the stopping network show such similar activity across the two modes of control (Criaud et al., 2017; Leunissen et al., 2016; Messel et al., 2019). Indeed, a large meta-analysis (van Belle et al., 2014) revealed both common and unique networks supporting proactive and reactive control of response inhibition, which may interact to facilitate efficient and accurate inhibition. However, the interpretation of these findings is complicated by the inability of fMRI analyses to temporarily dissociate processes that happen before and after the stop-signal.

Electroencephalography (EEG) research has revealed frontal midline theta (FM-theta) activity reflecting a generic, reactive mechanism associated with response inhibition (Cavanagh et al., 2012; Huster et al., 2013). Such theta activity is thought to originate from a neural generator in the midcingulate cortex (MCC), a core node of a performance monitoring system that helps to optimize behaviour during uncertainty (Cavanagh and Shackman, 2015; Ullsperger et al., 2014). During response inhibition specifically, stop-trials usually elicit a stronger FM-theta response than go-trials (Lavallee et al., 2014; Nigbur et al., 2011; Yamanaka and Yamamoto, 2010), while lower theta activity during successful compared to unsuccessful stop-trials has been reported (González-Villar et al., 2016; Knyazev et al., 2008). Further, task manipulations of proactive control have revealed higher FM-theta activity in conditions with low stop-signal frequency (Dippel et al., 2016; Dippel et al., 2017), indicating that theta activity might reflect the novelty of the stop-signal itself (Cavanagh et al., 2012; Cavanagh and Frank, 2014). However, theta activity also seems to be sensitive to task context beyond mere frequency manipulations, such as the current stimulus-response contingencies (Lavallee et al., 2014), and may potentially reflect a more general need for control during uncertain conditions (Cavanagh and Frank, 2014; Cooper et al., 2019; Kaiser et al., 2019).

FM-theta activity *prior* to the onset of the stop-signal (as elicited by a probability cue) has been associated with stop-signal anticipation (Chang et al., 2017). However, other studies have not found similar relationships (Bengson et al., 2012; Kaiser and Schütz-Bosbach, 2019). Studies using other cognitive tasks have found increased cue-locked FM-theta activity prior to difficult tasks, compared to easy tasks (Cooper et al., 2017; Cooper et al., 2019; Loof et al., 2019), in addition to associations with faster reaction times (Cooper et al., 2019) and less reaction time variability (Cooper et al., 2017). It seems somewhat contradictory that cue-locked theta activity may be beneficial for response inhibition as well as response initiation, unless cue-locked theta reflects a more general need for control than inhibition-specific preparation (Cavanagh et al., 2012; Cavanagh and Frank, 2014).

Although FM-theta activity has been suggested as a neural mechanism underlying both proactive and reactive control (Cooper et al., 2019), one can argue that this necessitates a common underlying neural generator (Sauseng et al., 2019). These interacting processes can be difficult to disentangle by low-resolution EEG or fMRI alone. Hence, a multimodal approach taking advantage of the temporal and spatial resolution of EEG and fMRI, respectively, might be more advantageous. Previous research using multimodal EEG-fMRI has mostly focused on reactive inhibition processes. Here, simultaneous recordings of EEG and fMRI have revealed reactive FM-theta to be associated with activity in the pre-SMA (Ko et al., 2016), the rIFG, the left MFG and the cingulate gyrus (Lavallee et al., 2014). Source analyses have revealed that stop-locked FM-theta activity may originate in the superior frontal gyrus (SFG) (Dippel et al., 2017), the MCC or other regions of the cingulate cortex (Hong et al., 2020; Huster et al., 2013), and that the source of FM-theta activity may vary with varying demands of proactive control (Dippel et al., 2016). A recent study demonstrated that pre-trial FM-theta activity was associated with activity in the rIFG in the go/no-go task, and this relationship was modulated by no-go signal frequency (Adelhöfer and Beste, 2020). These findings indicate that FM-theta reflect different processes during different degrees of expectancy and proactive control.

1.1. Summary and hypotheses

In sum, the exact dynamics of how proactive control modulates response inhibition efficiency is not altogether clear. Due to its associations with cognitive control, FM-theta activity is an ideal candidate for investigating such dynamics, as well as its modulations by proactive control both prior to the target onset, and following the stop-signal. Further, the advantages of using combined EEG and fMRI yields the optimal solution for investigating the complex interplay of response inhibition processes.

The present study utilized a cued stop-signal task in combination with simultaneous EEG and fMRI data acquisition. First, it was expected that reactive FM-theta activity (i.e., elicited after the stop-signal) would decrease with increasing stop-signal probability according to the conflict monitoring account, while cue-locked FM-theta activity would increase with increasing stop-signal probability and the increasing need for control. While it was expected that reactive FM-theta activity would be associated with activity in the MCC, and perhaps also the rIFG and pre-SMA, the association between cue-locked FM-theta and specific brain regions is less clear. At the single-trial level, it was expected that higher cue-locked FM-theta activity would be associated with faster reaction times in go-trials and successful stopping.

2. Materials and methods

2.1. Participants

A total of 39 participants were recruited for the study. All participants reported normal or corrected-to-normal vision and no neurological or psychiatric disorders. 17 participants were excluded from further data analysis; five due to excessive movement in the scanner, and additional six due to poor EEG data quality. Of the resulting participant pool, four additional participants were excluded based on behavioural results. Specifically, these participants were excluded based on stop-trial accuracies below 20% or above 80%, where one participant additionally displayed go-trial omissions above 10%. Lastly, one left-handed participant and one participant who did not finish the whole experiment were excluded. This left a final sample of twenty-two healthy, right-handed participants (age: *range* = 20–39 years, $M = 25.14$, $SD = 4.37$; 14 female). The experiment was approved by the local ethics committee at the Department of Psychology, University of Oslo. Prior to participating in the study, all participants read and signed an informed consent form, and were informed that they could withdraw from the study at any time. Participants received a compensation of 200 NOK each. The experimental paradigm and participant pool are the same as described in Messel et al. (2019), where unimodal fMRI and behavioural results have been published previously. Therefore, the description of setup, participants and fMRI data acquisition has been described previously in Messel et al. (2019). However, the sample differs slightly due to further EEG data exclusion criteria used in the present study.

2.2. Setup

The experimental task was implemented using E-Prime 2.0 stimulus presentation software (Psychology Software Tools, Pittsburgh, PA), carried out on a Dell Precision T7160 machine and presented on a 40″ MR-compatible fibre optic screen (NordicNeuroLab, Bergen, Norway). The screen was located behind the scanner bore, and the participants viewed the screen through a mirror placed on the head coil, resulting in a viewing distance of approximately 1.2 m. Screen resolution was 1920 × 1080 with a 60 Hz refresh rate. Responses were made with MR compatible response grips in each hand (NordicNeuroLab, Bergen, Norway).

2.3. Task

A cued stop-signal task with three levels of stop-signal probabilities was implemented in combination with fMRI and EEG data acquisition. The cued stop-signal task had a jittered, event-related design optimized for fMRI scanning. A visual representation of the task is presented in Fig. 1. The task consisted of 600 trials in total, divided over three different cue conditions: 0%, 25% and 66%. Each trial started with the presentation of a fixation cross (duration jittered randomly between 500 and 2400 milliseconds), followed by a probability cue that indicated the stop-signal probability of a given trial (i.e., 0%, 25% or 66%). The cue duration was jittered randomly between 1000 and 2000 milliseconds. The go-signal consisted of either a left- or right-ward pointing green arrow that signalled the response-hand to be used (left or right, respectively), and was presented for 100 milliseconds after the cue. In go-trials, the go-signal offset was followed by a fixation cross for another 1400 milliseconds, during which the responses were collected. In stop-trials, a blue arrow (i.e., the stop-signal) pointing in the same direction as the preceding go-signal was presented for 100 milliseconds with varying delays with respect to the go signal (the stop signal delay, SSD). The SSD was tracked using a staircase algorithm. It started at 300 milliseconds and *increased* with 50 milliseconds (adjusted to the screen refresh rate) if the previous stop-trial resulted in successful inhibition (i.e., no response), and *decreased* by 50 milliseconds if the previous stop-trial resulted in unsuccessful inhibition (i.e., a response). The SSD was adjusted separately for each cue-condition, but collapsed for the right and left hand.

The 0% condition consisted of 50 go-trials, the 25% condition of 300 go-trials and 100 stop-trials, and the 66% condition of 50 go-trials and 100 stop-trials. The overall percentage of go- relative to stop-trials thus was 2/1 (~33% stop trials); this ratio was chosen to still guarantee a prepotent tendency towards fast responding, and correspondingly a high load on motor inhibition. In addition to the 600 task-trials (i.e., go- and stop-trials), 150 null-event trials were added to the design. These events consisted of a 1500 millisecond presentation of the fixation cross.

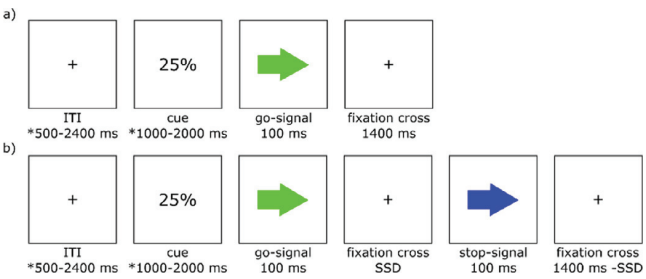

Fig. 1. Visual representation of the cued stop-signal task. This figure illustrates an example of a go-trial (a) and stop-trial (b) with 25% stop-signal probability and rightwards pointing arrows. ITI = inter-trial interval, ms = milliseconds, SSD = stop-signal delay, * indicates that the duration was jittered randomly within the specified time interval.

The 750 trials (task trials and null-event trials) were divided into 10 experimental blocks, with a randomized presentation of trials regarding left- and right-ward pointing arrows, cue-condition, go- and stop- conditions, and null-events. Each block lasted for approximately six minutes. After each block, participants were given feedback on their behavioural performance. If the average go-RT for that block was above 600 milliseconds, participants were presented the feedback "be faster", and if the average go-RT was below 600 milliseconds the participants were presented the feedback "well done". The overall duration of the task was approximately one hour.

2.4. EEG data acquisition

EEG data was recorded using the MRI compatible BrainAmp system (Brain Products GmbH, Gilching, Germany), using 32 channels mounted on a flexible lycra-eletrocap (easycap, Falk Minow Services, Munich, Germany) according to the 10–20 system. In addition to the scalp EEG electrodes, an electrocardiogram (ECG) electrode was placed on the mid-lower back for recording of cardiac activity. The data was recorded continuously using the BrainVision Recorder (Brain Products GmbH, Germany) software (online high cutoff of 1000 Hz, sampling rate of 5000 Hz, online reference at FCz). Impedances were kept below 14k Ω. The EEG data was synced to the MRI scanner using the BrainVision SyncBox to prevent drift of the repetition time (TR) in relation to the sampling rate.

2.5. Image acquisition

Structural and functional MR images were acquired from a 3.0 Tesla Philips Ingenia whole body MR scanner, equipped with a 32-channel Philips SENSE head coil (Philips Medical Systems, Best, the Netherlands). Each session started with a structural high resolution image using a T1-weighted sequence of 184 sagittal slices with a voxel size of 1 × 1 × 1 mm, (field of view: 256 × 256 $mm^{2,}$ acquisition matrix: 256 × 256, TE: 2.2 ms, TR: 4.5 ms, flip angle: 8°, no slice gap). The fMRI sequence was a BOLD-sensitive $T2^*$ weighted echo-planar imaging (EPI) sequence of 34 axial slices with a voxel size of 2.625 × 2.625 × 3.0 mm (field of view: 210 × 210 mm^2, acquisition matrix: 80 × 80, TE: 30 ms, TR: 2000 ms, flip angle: 80°, slice gap: 0.3 mm). At the beginning of the fMRI sequence, three dummy scans were acquired and then discarded to allow for the stabilization of the magnetic field. The whole MRI session, including calibration, structural and functional sequences, took approximately one hour and ten minutes.

2.6. Analysis

2.6.1. Behavioural data

The behavioural data were analysed separately for all three cue-conditions, and in accordance with up-to-date stop-signal task guidelines (Congdon et al., 2012; Verbruggen et al., 2019). Mean go-trial reaction times (go-RT) were estimated based on go-trials with a correct response (Go-trial choice errors and go trial omissions were excluded). The go-trial response window was set to 1400 ms after go-signal offset. Go-trial accuracies were calculated as the percent correct go-trials relative to all go-trials.

The average SSD was based on all stop-trials (i.e., successful stops, unsuccessful stops, stop-trials with a choice error response as well as stop-trials with a response before the onset of the stop-signal). SSRT was estimated using the integration method (Logan and Cowan, 1984; Verbruggen and Logan, 2009b) with replacement of go-omissions (Verbruggen et al., 2019). The integration method entails subtracting the mean SSD from the n'th RT of an ordered go-RT distribution. Specifically, all go-trials (correct go-trials, go-trials with a choice error, as well as go-omissions replaced with the maximum go-RT) were sorted in ascending order. N was determined by multiplying the number of all

go-trials with the probability of an unsuccessful inhibition. Unsuccessful stop-trial RT (US-RT) was estimated based on all stop-trials with a response, but excluding the trials with a choice error or a premature response.

Average behavioural estimates for all cue conditions and participants were inspected, and participants were excluded if any of the following exclusion criteria were met: 1) a stop-trial accuracy above 80% or below 20%, 3) Go-trial accuracies below 75%, 4) go-trial omissions above 10%, 5) US-RT > go-RT.

Some of the behavioural analyses were performed using non-parametric approaches. Specifically, the effect of stop-signal probability on go-RT and accuracy was tested using the Friedmans test. Differences between the 25% and 66% condition for stop-trial accuracy and SSRTs, as well as the difference between go-RT and USRT were tested using the Wilcoxon signed rank tests. All other comparisons were done using paired sample t-tests. Statistical behavioural analyses were performed in R (R Foundation for Statistical Computing, Vienna, Austria) using Rstudio (RStudio, PBC, Boston, MA) and the package rstatix (Kassambara, 2020).

2.6.2. EEG data: Pre-processing

Gradient and cardioballistic artefacts were removed from the data using BrainVision analyzer (v. 2.1; Brain Products GmbH, Germany). First, the gradient artefact was removed using an average artefact subtraction method based on a moving average of 11 gradient intervals. In addition, template drift detection was used to adjust for minor drifts in the data that may occur due to mismatch of the EEG sampling rate and the TR of the scanner. In one of the datasets, the EEG recordings were not synced to the TR of the scanner, thus making the volume onset trigger in the EEG recordings unreliable. In this dataset, the volume onset trigger was adapted manually. The data was subsequently low-pass filtered at 40 Hz and down-sampled to 500 Hz.

The removal of the cardioballistic artefact was a three-step procedure using a moving average template. First, a 12 Hz low pass filter was applied to the ECG channel data to better be able to detect the peak of the QRS-complex. Then, an automatic search for a QRS template was performed within the first 30 to 60 s following the onset of the fMRI sequence. If no good template was found automatically, the template was set manually. Subsequent pulses were identified based on a pulse rate of 40–100 beats per second, and a template correlation and amplitude threshold, which were set manually for each data set. The time-delay from the R-peak to the blood flow reaching the brain was estimated based on the whole dataset, and a channel-specific artefact was calculated based on a moving average of 21 pulses and removed from each channel. To remove residual pulse artefacts, an independent component analysis (ICA) excluding the ECG electrode was performed. Components were identified as cardioballistic activity and subsequently removed from the data by a combination of the correlation with the ECG electrode, visual inspection of component topography and time course, as well as visual inspection of activity time-locked to the stop signal to avoid the removal of activity associated with response inhibition.

The subsequent preprocessing steps were performed in MATLAB R2018b (The MathWorks, Inc., Massachusetts, USA) using the EEGLAB toolbox (v. 14.1.1b; Delorme and Makeig, 2004). The data was high-pass filtered at 0.1 Hz and re-referenced to the average reference. Pauses were removed from the dataset, before an additional ICA was performed. For each participant, the number of channels entered into the ICA was reduced by the number of components previously removed from the data when correcting for the pulse artefact. Components reflecting eye blinks and movement artefacts were identified by visual inspection and removed. The EEG markers were recoded according to the event of interest, which included the stop trials in the 25% condition and the 66% condition (hereby referred to as stop25 and stop66, respectively), the go trials with a correct response in the 0% condition, 25% condition and 66% condition (hereby referred to as go0, go25, and go66, respectively), and the unsuccessful stop (US) trials in the 25% condition and the 66% condition (hereby referred to as US25 and US66, respectively).

For the analysis of trial averages, the cleaned data were segmented into epochs of −1500 to 1500 ms centred at the event of interest. For single-trial analyses, cue-locked data were segmented into epochs from −1500 to 2800 ms time-locked to the cue, while target-locked data were segmented into epochs of −1500 to 1500 ms centred at the target event of interest. Due to the long cue-locked single-trial epochs, some trial epochs at the beginning or the end of a block could not be extracted (go0: 1.31% on average, go25: 0.17% on average, go66: 0.27% on average). These trials were removed from the single-trial analyses. All epochs were baseline corrected using the whole pre-stimulus period. Noisy epochs were removed by visual inspection.

2.6.3. EEG data: Trial average analysis

To investigate the effect of stop-signal probability on trial-averaged FM-theta activity, the stop-locked (for stop-trials and US-trials) and go-locked (go-trials) data for the 25% and 66% condition (i.e., stop25, stop66, US25, US66, go25 and go66) was subjected to a time-frequency transformation using the newtimef function in EEGLAB. Based on previous research, all analyses were performed on channel FCz (Cavanagh et al., 2012; Chang et al., 2017; Pinner and Cavanagh, 2017). Event-related spectral perturbations (ERSPs) were calculated for the frequency window between 1 and 30 Hz in 120 frequency steps, using 200 output times. An increasing amount of cycles in each Morlet wavelet was used, from 1 to 15 in steps of 0.25. The averaged data was normalized to the spectral baseline by dividing by the average power across trials at each frequency from the time period −400 to −100 ms before go/stop-signal onset and log-transformed. The estimation of each subject's individual theta activity (ITA) was implemented such that for each subject, the theta frequency (i.e., frequency between 4 and 8 Hz) with the highest power within a time window of 200–450 ms post go/stop-signal onset was detected, and then the power of this individual peak frequency was averaged across a frequency band of peak frequency +/- 1 Hz, and for a time window of +/- 50 ms from the peak frequency latency. The final ITA values were then subjected to a 2 × 3 rm-ANOVA with the factors *stop-signal probability* (25, 66) and *trial type* (go, stop, US).

To investigate the effect of stop-signal probability on activity prior to the go-signal, but after the cue, the same time-frequency transformation as described above was applied to cue-locked epochs of go-trials, stop-trials and US-trials for the 25% and 66% condition. The ITA was estimated similarly to that of the go/stop-locked activity, although the time window for finding the peak frequency was set at 200–600 ms post cue. This time interval was chosen based on previous findings of a cue-locked theta peak within this interval (Cooper et al., 2017; Kaiser and Schütz-Bosbach, 2019). A 2 × 3 rm-ANOVA was performed with *stop-signal probability* (25, 66) and *trial type* (go, stop, US) as independent variables, and the ITA as the dependant variable.

Although no specific hypothesis was made about how go-trial FM-theta activity would differ between cue-locked and go-locked activity, as well as potential modulations by stop-signal probability, visual inspection of the data led to the unexpected finding that FM-theta activity seemed to be largest in the 0% condition. To formally investigate this further, an exploratory post-hoc 2 × 3 rm-ANOVA with the factors *time* (cue-locked, go-locked) and *probability* (0, 25, 66) was run on the go-trial ITAs.

Statistical analyses on the trial-averages were performed using the R package rstatix (Kassambara, 2020).

2.6.4. EEG data: Single-trial analysis

To investigate the effect of proactive control on FM-theta activity at the single-trial level, time-frequency transformations adapted for single-

trial analysis were performed on cue-locked and target-locked activity in the stop-trials, go-trials and US-trials of the 25% condition and the 66% condition, as well as the 0% condition for the go-trials.. ERSPs were calculated via the *newtimef* function in MATLAB, adapted for single-trial analysis, for electrode FCz for the frequency window between 1 and 30 Hz in 120 frequency steps, using 200 output times. An increasing amount of cycles in each Morlet wavelet was used, from 1 to 15 in steps of 0.25. Single-trial time-frequency decompositions were normalized by dividing by the mean baseline power per frequency for each trial (Grandchamp and Delorme, 2011), and then converted to decibel (dB) by using a log-transformation of the baseline-corrected trial data (dB = 10 x log10(power/baseline). The baseline power was extracted from −400 to 100 ms before target onset. The ITA was calculated similarly to that of the trial-averaged cue-locked and target-locked FM-theta activity, only individually for each trial. Overall, this resulted in data extracted from two different time periods (cue-locked and target-locked) from three different trial types (go-trials, stop-trials, US-trials), extracted separately from the different probability conditions.

First, to assess possible associations of cue-locked and stop-locked theta activity with stop-trial outcome, a single-trial mixed model logistic regression was run (using the R package lme4; Bates et al., 2015). Specifically, cue-locked and stop-locked ITAs was entered as fixed effects, while participants were entered as random effects. The resulting coefficients were standardized by dividing by the SD, and deemed significant if $p|z| > 0.05$.

Second, to assess possible associations of cue-locked and go-locked FM-theta activity with go-trial reaction times, a single-trial mixed model linear regression was run (using the R package lme4; Bates et al., 2015). Specifically, cue-locked and go-locked ITAs were entered as fixed effects, while participants were entered as random effects. The resulting coefficients were deemed significant by the Satterthwaite approximation using the lmerTest R package (Kuznetsova et al., 2017), thresholded at $p < .05$ (Luke, 2017).

2.6.5. fMRI data: Pre-processing

All pre-processing steps were performed with SPM12 (Wellcome Trust Centre for NeuroImaging, Institute of Neurology at University College London, UK), running under MATLAB r2016a (The MathWorks Inc., Natick, MA). Functional images were realigned to the first image and resliced using a 5th degree B-spline interpolation. Slice timing correction to adjust for time acquisition delays was performed using the central slice as reference. Functional images were co-registered to the structural image, and normalized to the Montreal Neurological Institute (MNI) standard space, using linear and non-linear deformations, written with a final resolution of 3 × 3 × 3 mm. Lastly, functional images were smoothed using a 6 mm full-width-at-half-maximum (FWHM) Gaussian kernel. The estimated motion parameters were inspected to ensure that relative motion (between adjacent time points) did not exceed half the voxel size.

2.6.6. fMRI data: First level analysis

First-level statistical analyses were performed in SPM12 using the general linear model (GLM) framework and an event-related design. Due to the temporal proximity of cue and target onsets, two first-level models were set up for each participant, one for events modelled at target or response onset, and another for events modelled at the cue onset.

The first model included all target events modelled at target or response onset (hereby referred to as the target-model for simplicity). The following events were included in the target-model: cues, successful go-trials, erroneous go-trials, successful stop-trials, unsuccessful stop-trials, choice error stop-trials, null-events and feedback. All task conditions were modelled according to their corresponding stop-signal probability. Go- and stop-trials were modelled at go-signal onset and stop-signal onset, respectively, while unsuccessful stop-trials were modelled at response onset. Additional six regressors coding the participant's motion parameters, estimated during the realignment procedure, were included to correct for head movement. Task events were modelled as zero-duration events, with the exception of cues, which were modelled according to the corresponding cue duration. All modelled events were convolved with a canonical hemodynamic response function (HRF). To account for slow-frequency drifts, a high-pass filter with a cut-off at 128 s was implemented. Four t-contrasts were set up for each participant, stop25>0, stop66>0, go25>0, and go66>0.

The second model (hereby referred to as the cue-model), was identical to the target-model, except that it included only cues as events of interest, as well as null-events and pauses. Cues where modelled in accordance with their stimulus duration, their corresponding stop-signal probability, and the upcoming trial type (go, stop etc.). For example, a 25% cue preceding a go-trial was modelled as a cue25_go regressor, modelled at cue onset. Again, four t-contrasts were created for each participant: cue25_stop>0, cue66_stop>0, cue25_go>0 and cue66_go>0.

2.6.7. Joint ICA analysis

A joint ICA concurrently run on the EEG data and the fMRI data was performed to further investigate the associations between proactive and reactive response inhibition. Such a joint ICA yields a spatiotemporal decomposition where the fMRI-derived component coefficients indicate where, and the EEG-derived component coefficients when, the signal is changing (Calhoun et al., 2006). We expand this framework to include several conditions. The joint ICA analysis was performed using the Fusion ICA Toolbox (FIT) for MATLAB (Calhoun et al., 2006; https://trendscenter.org/software/fit/).

For the EEG data, the FCz peak frequency time course (i.e., the peak frequency within a window of 200 and 450 ms after stop-signal onset, averaged across peak frequency +/- 1 Hz) was extracted from the trial average ERSPs (calculated as described in *Section 2.6.3 EEG data: trial average analysis)* for the go25, go66, stop25 and stop66 conditions for each participant. Furthermore, the cue-locked FCz theta time course (here, the peak frequency within a window of 200 and 600 ms after cue onset) was extracted from the trial average ERSPs from the cue_go25, cue_go66, cue_stop25 and cue_stop66 conditions. For the fMRI data, the first level contrast images of go25>0, go66>0, stop25>0 and stop66>0 from the target-model, as well as the first level contrast images of cue_go25>0, cue_go66>0, cue_stop25>0 and cue_stop66 >0 from the cue-model were used. The FCz theta time course ranging from −400 ms relative to the target/cue onset to the end of the epoch as well as grey matter data from the contrast images representing both cue-locked and target-locked activity for both conditions (i.e., 25% and 66% conditions) were concurrently included in the joint ICA. This resulted in a data matrix that for column-wise contained the four "modalities" (cue-locked fMRI activity, target-locked fMRI activity, cue-locked theta activity and target-locked theta activity) with each of the four conditions (go25, go66, stop25 and stop66) entered as separate rows for each subject (4 × 22). The data was normalized and reduced from subjects to components using principal component analysis (PCA), before subjected to the joint ICA. The number of independent components (IC's) in the analysis was estimated based on the minimum description length (MDL) algorithm running on all features, and further based on the different feature combinations, using a PCA-CCA (canonical correlational analysis) approach, as implemented in the FIT software. The ICA was run once based on the Infomax algorithm. The resulting ICA mixing matrix consists of coefficients that represent the shared loading parameters for the different modalities and the ICs. Differences between the four conditions (go25, go66, stop25 and stop66) can then be tested by using a paired sample *t*-test on the mixing coefficients. The significance level was corrected for number of comparisons (go25 vs go66, stop25 vs stop66, go25 vs stop25, go66 vs stop66) to $p = .05/4 = 0.0125$. Only z-transformed positive fMRI activity thresholded at $z > 3$ are visualized and reported.

Table 1
Behavioural data.

	Stop-signal probability condition		
	0%	25%	66%
Go-trial RT (ms)**	429.03 (54.55)	596.84 (66.83)	694.92 (121.18)
Go-trial accuracy (%)*	96.1 (4.1)	98.4 (2.1)	97.9 (2.1)
Go-trial errors of omissions (%)	1.09 (1.82)	1.05 (1.84)	1.55 (2.39)
Go-trial choice errors (%)	2.69 (3.46)	0.67 (0.93)	0.42 (0.95)
SSRT (ms)	-	244.72 (46.52)	225.25 (52.15)
SSD (ms)**	-	347.46 (85.25)	446.57 (111.30)
US-RT (ms)**	-	533.53 (63.09)	619.48 (90.67)
Stop-trial accuracy (%)**	-	49.3 (4.6)	52.7 (5.7)

Note. Table shows means of behavioural measures for each probability condition. Standard deviations are presented in the parentheses. RT = reaction time, SSRT = stop-signal reaction time, SSD = stop-signal delay, US-RT = unsuccessful stop reaction time, ms = milliseconds. Significant differences marked with ** ($p < .001$) and * ($p < .05$).

3. Results

3.1. Behavioural results

All means and SDs of the behavioural data are listed in Table 1. The go-RT varied significantly with stop-signal probability ($X(2) = 44$, $p < .001$, $W = 1$). Follow-up Bonferroni-corrected Wilcoxon signed-rank tests revealed that the go-RT was significantly higher in the 25% condition than in the 0% condition, in the 66% condition than in the 0% condition, and in the 66% condition than in the 25% condition (all $p < .001$). Similarly, the go-trial accuracy did also vary with stop-signal probability ($X(2) = 6.81$, $p = .033$, $W = 0.16$). Follow-up Bonferroni-corrected Wilcoxon signed-rank tests revealed that the go-trial accuracy was significantly lower in the 0% condition compared to the 25% condition ($p = .002$). There was no significant differences between the 25% and 66% conditions ($p = .128$) or the 0% and 66% conditions ($p = .591$).

The SSRT did not differ significantly between the 25% (*median* = 233.57, *1QR* = 218.29, *3QR* = 246.24) and the 66% (*median* = 230.20, *1QR* = 216.86, *3QR* = 258.04) condition ($p = .354$). The stop-trial accuracy in the 66% condition (*median* = 52.0, *1QR* = 51.0, *3QR* = 53.0) was significantly higher than in the 25% (*median* = 51.0, *1QR* = 50.0, *3QR* = 51.0) condition ($p < .001$). The US-RT was significantly longer in the 66% condition compared to the 25% condition ($t(21) = -6.40$, $p < .001$, $d = 1.36$), as was the SSD ($t(21) = -5.99$, $p <. 001$, $d = 1.28$). Finally, in accordance with assumptions of the horse race model, the US-RT was significantly shorter than the go-RT, in both the 25% condition ($p < .001$) and the 66% condition ($p < .001$).

3.2. Trial-averaged FM-theta activity

As expected, there was a significant effect of *trial type* ($F(2,42) = 53.40$, $p < .001$, $\eta_p^2 = 0.72$) and *probability* ($F(1,21) = 7.76$, $p = .011$, $\eta_p^2 = 0.27$) on target-locked theta activity (Fig. 2a and e). However, the interaction effect between *trial type* and *probability* was not significant ($F(2,42) = 1.38$, $p = .263$, $\eta_p^2 = 0.06$). Bonferroni-corrected post-hoc tests revealed that there was significantly higher activity in the 25% condition than in the 66% condition ($p = .002$), and that the theta activity in stop-trials was higher than in the go-trials ($p < .001$). Interestingly, the theta activity in the US-trials were higher than in both the go-trials ($p < .001$) and the stop-trials ($p <0.001$).

The cue-locked theta activity (Fig. 2b and d) also showed a significant modulation by *trial type* ($F(2,42) = 4.36$, $p = .019$, $\eta_p^2 = 0.17$) and follow-up Bonferroni-corrected post-hoc tests revealed significantly higher cue-locked activity in the US-trials compared to the go-trials ($p = .020$). There was no significant effect of probability ($F(1,21) = 0.590$, $p = .451$, $\eta_p^2 = 0.027$) nor interaction effect ($F(2, 42) = 0.81$, $p = .451$, $\eta_p^2 = 0.04$).

Table 2
Single-trial logistic regression on stop-trial outcome.

Fixed effects	Estimate (std. error)	z	p
Intercept	0.706 (0.09)	7.85	<0.001**
Cue	−0.002 (0.01)	−0.25	0.804
Stop	−0.071 (0.01)	−9.89	<0.001**

Note: Significant effects are marked with * ($p < .05$) and ** ($p < .001$).

Table 3
Single-trial regression on go-RT.

Fixed effects	Estimate (Std. Error)	df	t	p
Intercept	607.506 (14.26)	23.32	42.61	<0.001**
Cue	−0.996 (0.39)	8578.75	−2.57	0.010*
Go	−2.154 (0.37)	8579.46	−5.75	<0.001**

Note: Significant effects are marked with * ($p < .05$) and ** ($p < .001$), estimated according to the Satterthwaite approximation (Luke, 2017).

The go-trial theta activity (Fig. 2c) showed significant modulations by both *probability* ($F(2,42) = 28.88$, $p < .001$, $\eta_p^2 = 0.58$) and *time* ($F(1,21) = 20.20$, $p < .001$, $\eta_p^2 = 0.49$). The interaction effect between *time* and *probability* was not significant ($F(2,42) = 3.15$, $p = .053$, $\eta_p^2 = 0.13$). Follow-up Bonferroni-corrected post-hoc tests revealed that the activity in the 0% condition was overall significantly higher than the activity in the 25% ($p < .001$) and the 66% condition ($p < 0.001$). The difference between the 25% and the 66% condition was not significant ($p = 1.00$). Further, the go-locked activity was significantly higher than the cue-locked activity in the go-trials ($p < .001$).

3.3. Single-trial FM-theta activity

3.3.1. Single-trial mixed model logistic regression

The results of the mixed model logistic regression are shown in Table 2 and Fig. 3. Notably, there was a significant effect of stop-locked ($p < .001$), but not of cue-locked theta ($p = 0.804$). From Fig. 3, it is evident that as stop-locked theta increases, the probability of successful stopping decreases.

3.3.2. Single-trial mixed model linear regression on go-trial reaction time

The mixed model linear regression revealed a significant effect of cue-locked ($p = .010$) and go-locked ($p < .001$) theta on go-trial reaction times. All fixed effects are listed in Table 3. As can be seen by Fig. 4, there was a clear negative relationship between FM-theta activity and reaction times, such that shorter reaction times were associated with higher FM-

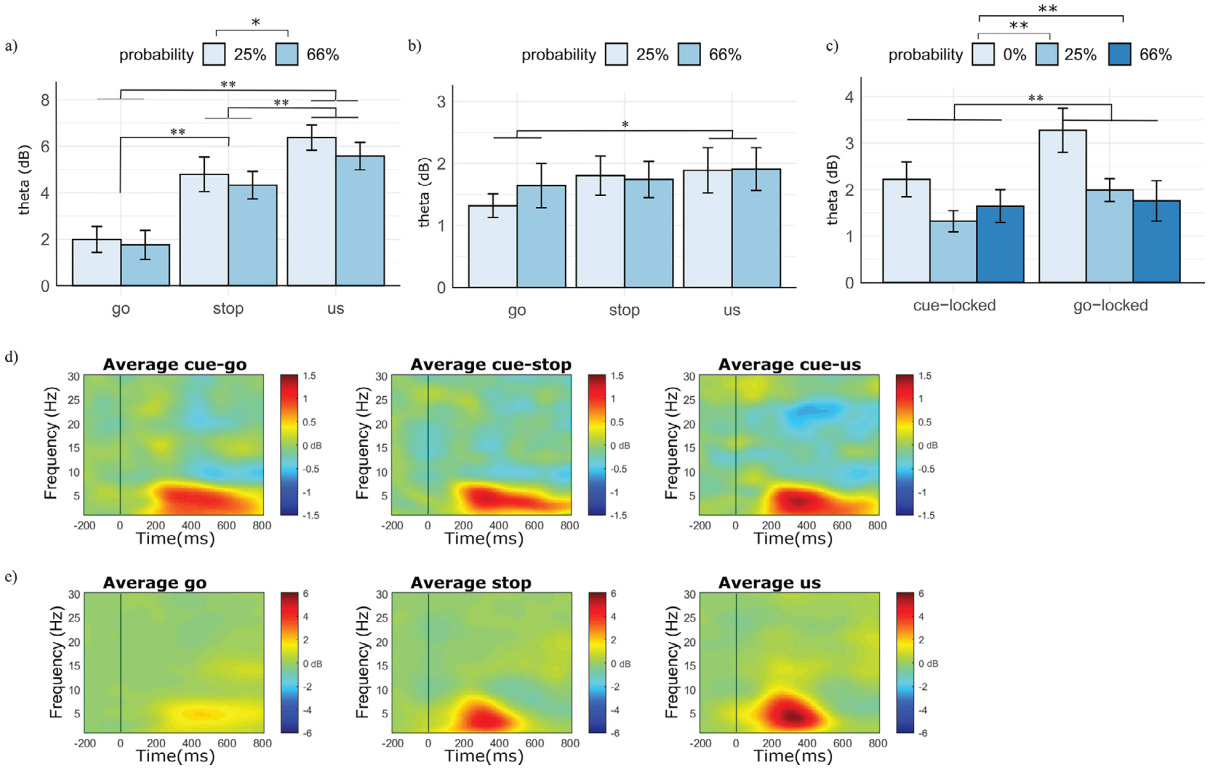

Fig. 2. Trial average FM-theta activity. a) Effect of stop-signal probability on target-locked activity b) Effect of stop-signal probability on cue-locked activity. c) Effect of stop-signal probability and time on FM-theta activity. d) Time-frequency plots of cue-locked data averaged across probability conditions (25% and 66%). e) Time-frequency plots of target-locked data averaged across probability conditions (25% and 66%). Significant effects are marked with * ($p < .05$) and ** ($p < .001$). The asterisk above the legends indicate the differences in probabilities, pooled across the trial types. Error bars represent 95% confidence intervals. Us = unsuccessful stop. Theta in decibel (dB).

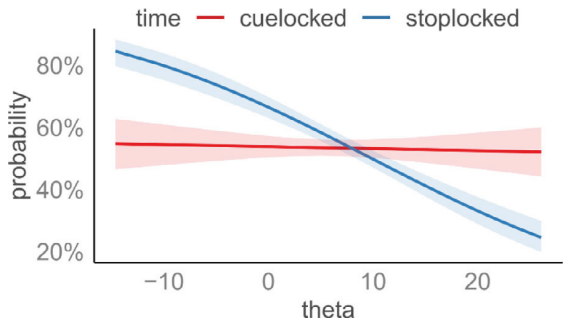

Fig. 3. Single-trial mixed model logistic regression on stop-trial outcome. Probability on the y-axis indicates the chance of successful stopping. Theta power is given in decibel (dB). Shaded areas represent 95% confidence intervals.

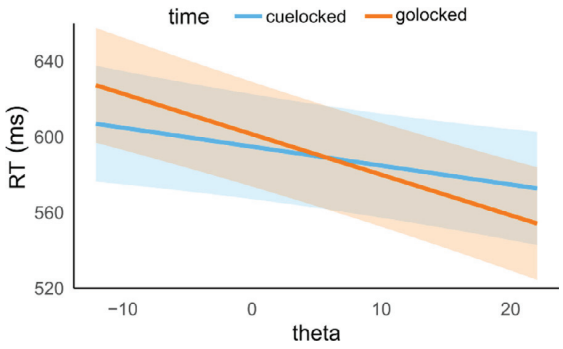

Fig. 4. Single-trial mixed model linear regression on the relationship between go-trial reaction times (RT) and FM-theta activity in go-trials. Shaded areas represent 95% confidence intervals. Theta activity is reported in decibel (dB); ms = milliseconds.

theta activity. However, this effect was larger for the go-locked than the cue-locked FM-theta activity.

3.4. Joint ICA analysis

The joint ICA analysis was performed to investigate associations between the fMRI and EEG activity in both go- and stop-trials during different degrees of proactive control. The analysis was run using five ICs. T-tests investigating differences in the mixing coefficients for the different conditions were run on four condition combinations: go25 vs go66, stop25 vs stop66, go25 vs stop25, and go66 vs stop66, with a p-value threshold at $p = .0125$. Four of the most informative components are described below. Details about the remaining component (IC1) can be found in the supplementary materials.

Independent component 3: The go component

IC3 showed go-associated FM-theta activity in both the cue-locked and target-locked features, while the stop-associated FM-theta activity was absent (Fig. 5). Cue-locked fMRI component activity was specifically prominent in the occipital gyrus, and notably also in the left medial frontal gyrus, the SFG, and the caudate. Target-locked fMRI component activity was evident in the bilateral medial frontal gyri including the SMA, the cingulate, as well as the postcentral gyrus and the occipital gyrus (Table 4). The t-tests investigating differences between conditions

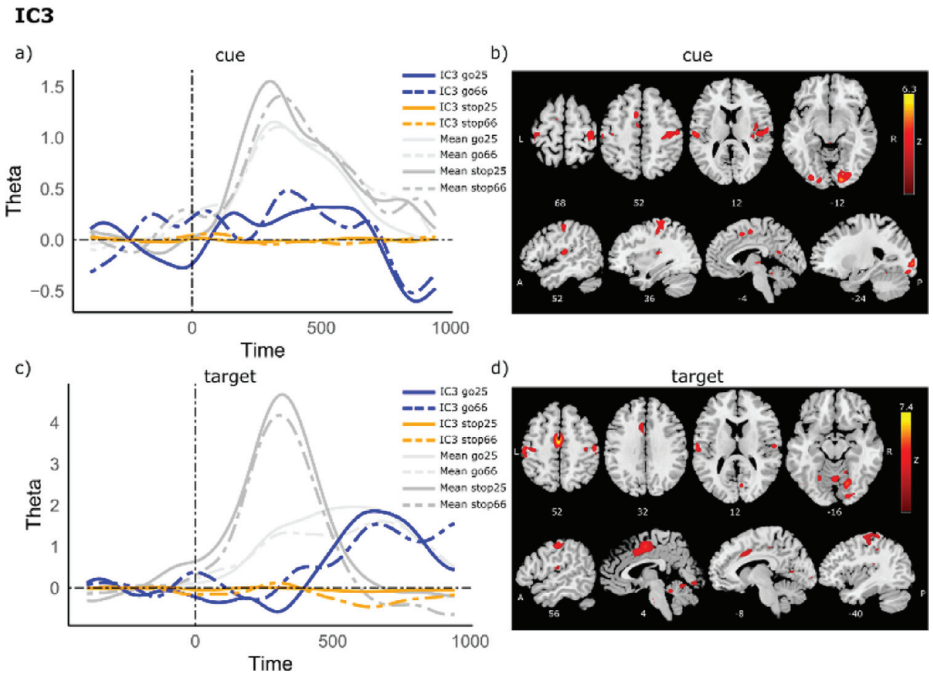

Fig. 5. Independent component 3. a) cue-locked FM-theta component activity in blue (go) and orange (stop). Average theta activity (in decibel, dB) for each condition in grey. b) cue-locked fMRI component activity. c) target-locked FM-theta component activity in blue (go) and orange (stop). Average theta activity (in decibel, dB) for each condition in grey. d) target-locked fMRI component activity. The figure shows z-transformed positive fMRI activity thresholded at $z > 3$, slice numbering in mm. L = left, R = right.

Table 4
The go component.

IC3: cue-locked activity Region	volume (cc) L/R	Max z L/R	MNI (x, y, z) L/R
Caudate	0.16/0.14	6.3/3.9	(−6, 8, 5)/(9, 8, 8)
Middle Occipital Gyrus	0.24/1.13	4.0/6.1	(−21, −100, −1)/(30, −91, −1)
Cuneus	0.54/0.86	4.8/5.8	(−15, −100, −1)/(12, −97, −1)
Lingual Gyrus	0.16/1.19	3.4/5.6	(−18, −97, −13)/(18, −94, −13)
Inferior Occipital Gyrus	0.54/0.30	5.4/5.2	(−27, −91, −16)/(27, −88, −16)
Third Ventricle	0.14	5.2	(0, −19, −4)
Transverse Temporal Gyrus	0.19/0.30	4.4/3.6	(−60, −19, 11)/(51, −19, 11)
Cerebellar Lingual	0.11/0.11	4.0/4.4	(0, −43, −19)/(3, −46, −22)
Extra-Nuclear	0.14	3.8	(−3, −22, −1)
Sub-Gyral	0.11/0.14	4.1/4.4	(−24, −94, −4)/(27, −94, −4)
Culmen	0.22	4.3	(15, −34, −19)
Postcentral Gyrus	0.38/0.97	4.1/4.3	(−60, −19, 14)/(42, −34, 65)
Medial Frontal Gyrus	0.22	3.9	(−6, 8, 50)
Precentral Gyrus	1.03	3.8	(45, −16, 59)
Superior Frontal Gyrus	0.11	3.5	(−3, 8, 53)
Insula	0.14	3.3	(51, −19, 14)
IC3: target-locked activity Region	volume (cc) L/R	Max z L/R	MNI (x, y, z) L/R
Fourth Ventricle	0.11	7.4	(0, −43, −25)
*Postcentral Gyrus	0.11	4.2	(57, −19, 53)
Medial Frontal Gyrus	0.70/0.40	6.4/5.2	(0, −7, 53)/(3, −4, 53)
Cingulate Gyrus	1.57/1.03	6.0/5.3	(0, −7, 50)/(3, −4, 50)
Postcentral Gyrus	1.94/0.86	5.8/4.6	(−57, −25, 50)/(57, −16, 50)
Culmen	0.11	5.7	(3, −46, −25)
Precentral Gyrus	0.84	4.8	(−33, −25, 71)
Lingual Gyrus	0.27	4.5	(18, −73, −16)
Fusiform Gyrus	0.22	4.2	(21, −70, −16)
Paracentral Lobule	0.14	4.1	(0, −13, 50)
Inferior Occipital Gyrus	0.14	3.9	(18, −91, −16)
Transverse Temporal Gyrus	0.22	3.7	(−63, −16, 11)
Insula	0.14	3.4	(−51, −22, 17)

Note: Table shows z-transformed fMRI activity clusters for IC3, thresholded at $z > 3$, cluster size > 0.1 cc. Region labelling via the FIT software (*AAL labelling).

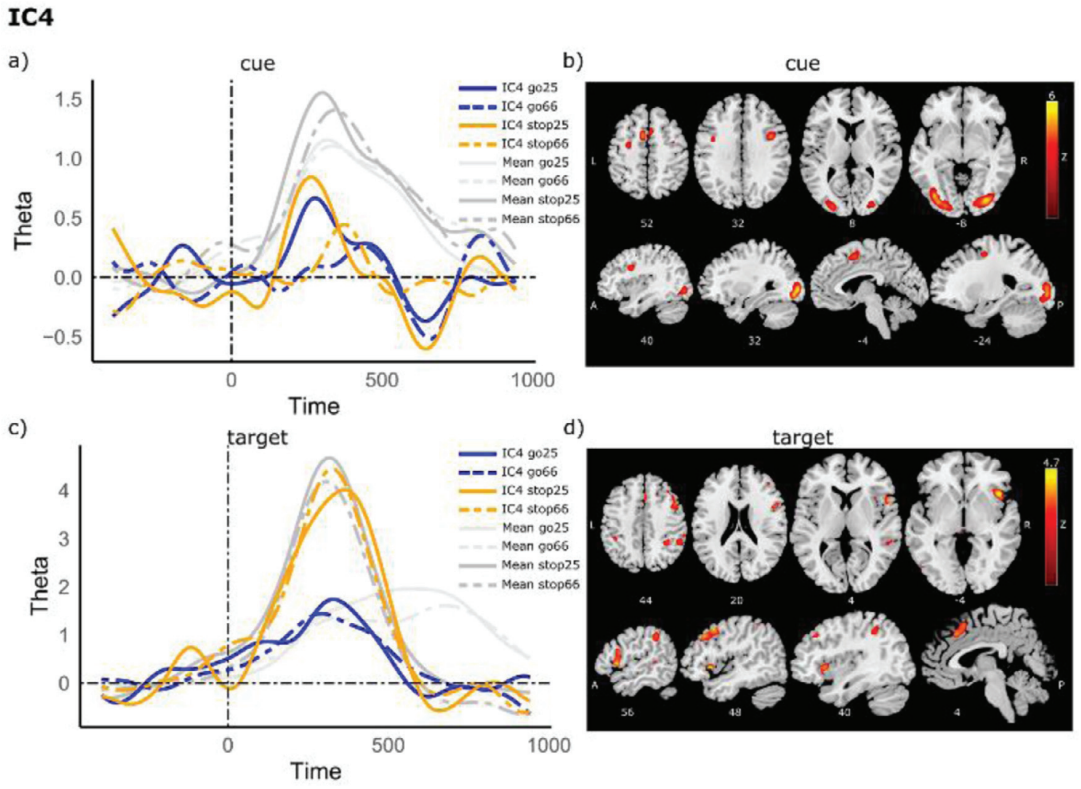

Fig. 6. Independent component 4. a) cue-locked FM-theta component activity in blue (go) and orange (stop). Average theta activity (in decibel, dB) for each condition in grey. b) cue-locked fMRI component activity. c) target-locked FM-theta component activity in blue (go) and orange (stop). Average theta activity (in decibel, dB) for each condition in grey. d) target-locked fMRI component activity. The figure shows z-transformed positive fMRI activity thresholded at $z > 3$, slice numbering in mm. L = left, R = right.

revealed that this component differed significantly between the go25 and stop25 condition ($p < .001$), the go66 and stop66 condition ($p < .001$), and between the go25 and go66 condition ($p = .004$). There was no difference between the stop25 and stop66 condition ($p = .152$).

Independent component 4: The stop component

IC4 captured both go- and stop-associated cue-locked FM-theta activity, while target-locked FM-theta activity was dominated by the stop-associated activity (Fig. 6). Interestingly, both cue- and target-locked fMRI activity was evident in the rIFG. Specifically, cue-locked fMRI component activity was evident in the occipital gyrus, bilateral MFG, right IFG, as well as the superior and medial frontal gyrus. Target-locked fMRI component activity was evident in a clear right-lateralized network consisting of the right IFG, SFG, MFG, IPC and the cingulate gyrus (Table 5). There was a significant difference between go and stop activity in the 66% condition in this component ($p = .0123$), although not in the 25% condition ($p = .023$). There was no difference in component activity between the stop25 and stop66 conditions ($p = .382$), nor between the go25 and go66 conditions ($p = .023$).

Independent component 2 and 5: The proactive components

As can be seen from Fig. 7, both IC2 and IC5 displayed clear cue-locked FM-theta component activity, while no apparent target-locked FM-theta component activity were evident. The FM-theta activity pattern differed slightly between the two components, with IC2 showing more sustained cue-locked activity, and IC5 a somewhat noisier activity pattern witht a smaller, early peak. Both components, however, showed clear fMRI activity in the occipital cortex and nearby gyri, such as the cuneus and the lingual gyri (Table 6). While IC2 in addition showed cue-locked fMRI component activity in the rIFG, a small activity cluster in the rMFG was evident in IC5. The t-tests investigating differences between the conditions revealed that IC5 component activity differed significantly between the go25 and go66 condition ($p < .001$). The difference between the other conditions was not significant (stop25 vs stop66: $p = .208$, go25 vs stop25: $p = .014$, go66 vs stop66: $p = .138$). The t-tests did not reveal any significant differences between any of the conditions for IC2 (go25 vs go66: $p = .319$, stop25 vs stop66: $p = .885$, go25 vs stop25: $p = .583$, go66 vs stop66: $p = .999$).

4. Discussion

The present study investigated the temporal dynamics of the neural correlates of proactive and reactive control of inhibition, using simultaneously recorded EEG and fMRI data and a cued stop-signal task. Behavioural results clearly indicated that participants adjusted their behaviour proactively, as seen in modulations of go-trial reaction times, as well as go and stopping accuracies (see also Messel et al., 2019). Several different approaches were used to elaborate on the relationship between going and stopping in reactive and proactive control modes. First, as expected, the analyses of trial averages indicated that target-locked theta activity was stronger in stop- than in go-trials, and overall higher in the 25% condition than in the 66% condition. Interestingly, cue-locked theta activity did not show such probability modulations. Second, single-trial analyses revealed that both cue- and target-locked theta activity were associated with behavioural outcomes. Specifically, higher cue-locked FM-theta was associated with faster reactions in go trials, while higher target-locked FM-theta was associated with faster reactions in go trials and unsuccessful stopping in stop trials. These results collectively indicate a double role for the FM-theta, where higher theta is associated with faster responding, but simultaneously is generally higher in stop trials. This dissociation was supported by the third analysis. Here, the joint ICA on the fMRI and EEG data, revealed several

Table 5
The stop component.

IC4: cue-locked activity Region	volume (cc) L/R	Max z L/R	MNI (x, y, z) L/R
Middle Occipital Gyrus	2.97/2.75	5.3/6.0	(−33, −88, −4)/(27, −91, −1)
Inferior Occipital Gyrus	1.19/0.92	5.4/5.8	(−36, −79, −10)/(33, −85, −10)
Sub-Gyral	0.92/0.86	5.2/5.8	(−33, −88, −7)/(27, −91, −4)
Superior Frontal Gyrus	0.51/0.14	4.9/3.2	(−6, 8, 53)/(6, 11, 56)
Medial Frontal Gyrus	0.46	4.7	(−6, 5, 53)
Cuneus	0.65/0.16	4.7/4.0	(−24, −97, −4)/(24, −97, −4)
Inferior Frontal Gyrus	0.65	4.7	(42, 8, 32)
Lingual Gyrus	0.76/0.70	4.7/4.7	(−21, −94, −7)/(27, −85, −10)
Third Ventricle	0.11	4.1	(0, −25, −4)
Middle Frontal Gyrus	0.40/0.11	4.1/3.9	(−27, −7, 53)/(42, 11, 32)

IC 4: target-locked activity Region	volume (cc) L/R	Max z L/R	MNI (x, y, z) L/R
Inferior Frontal Gyrus	1.16	4.7	(45, 20, −4)
*Rolandic Gyrus	0.27	4.6	(57, 14, 2)
Middle Frontal Gyrus	1.4	4.2	(48, 14, 50)
Medial Frontal Gyrus	0.22	3.9	(3, 26, 41)
Insula	0.11	3.8	(42, 17, −1)
Superior Frontal Gyrus	0.11	3.6	(3, 17, 53)
Cingulate Gyrus	0.16	3.6	(3, 23, 44)
Superior Temporal Gyrus	0.11	3.5	(48, 14, −4)
Inferior Parietal Lobule	0.24	3.3	(36, −46, 44)
Superior Parietal Lobule	0.16	3.3	(33, −61, 53)
Precentral Gyrus	0.14	3.1	(54, 14, 8)

Note: Table shows z-transformed fMRI activity clusters for IC4, thresholded at $z > 3$, cluster size > 0.1 cc. Region labelling via the FIT software (*AAL labelling).

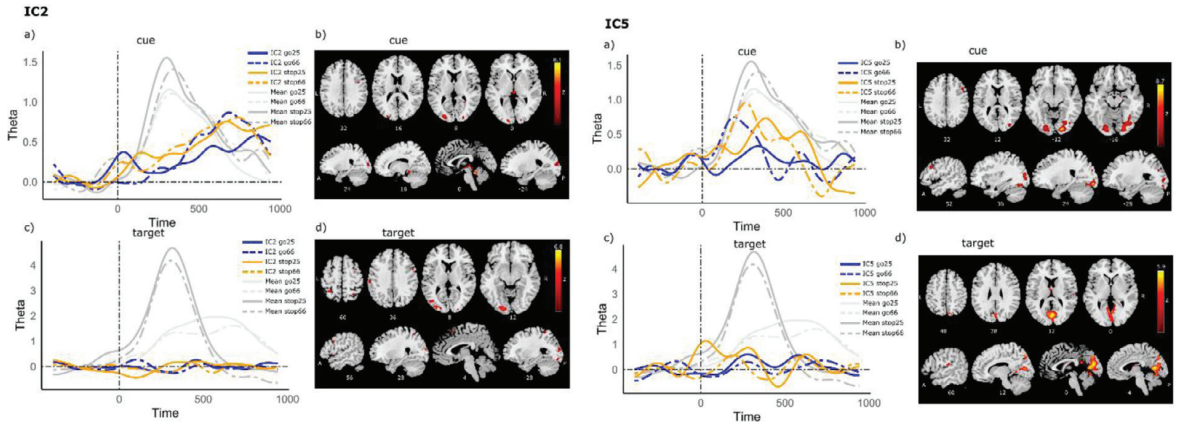

Fig. 7. Independent component 2 (left) and independent component 5 (right). a) cue-locked FM-theta component activity in blue (go) and orange (stop). Average theta activity (in decibel, dB) for each condition in grey. b) cue-locked fMRI component activity. c) target-locked FM-theta component activity in blue (go) and orange (stop). Average theta activity (in decibel, dB) for each condition in grey. d) target-locked fMRI component activity. The figure shows z-transformed positive fMRI activity thresholded at $z > 3$, slice numbering in mm. *L* = left, *R* = right.

independent FM-theta components, either related to stopping, going, or cue-associated proactive control. In sum, FM-theta activity does not seem to reflect a unitary mechanism, but rather appears to be associated with different mechanisms that support both fast responding and successful inhibition.

At the neural level, it was expected that the trial-averaged, target-locked theta activity would be higher in the stop-trials than in the go-trials, and indeed this was the case. Further, in line with previous research, target-locked theta activity was sensitive to proactive control modulations (Dippel et al., 2016; Dippel et al., 2017; Enriquez-Geppert et al., 2010; Nieuwenhuis et al., 2003; Ramautar et al., 2004), with stronger theta activity in the 25% than in the 66% condition. Interestingly, US-trials had higher target-locked theta activity than both go- and stop-trials, and higher cue-locked theta activity than go-trials. As US-trials may be a result of a fast and error-prone response strategy, it may be that the increased theta activity in these trials reflects mechanisms associated with fast responding. This is supported by the fact that go-trial theta activity was highest in the 0% condition, the condition with the behaviourally fastest responses and lowest accuracy.

Although it was hypothesized that lower target-locked theta activity in the 66% condition than in the 25% condition may be a result of more efficient proactive preparation in the former, this was not evident in the cue-locked theta activity, that did not show any probability modulations. It may be, however, that such an interplay between mechanisms of proactive and reactive control of inhibition are subject to single-trial variations that are not evident by the more traditional analysis of trial averages. Previous research has indicated that there may be an interaction between proactive and reactive inhibitory control processes (Jahfari et al., 2010), such that increased proactive activity may result in less need of reactive inhibition. This is in line with assumptions of the DMC framework, where proactive and reactive modes of control are conceptualized as opposite poles of a continuum (Braver, 2012;

Table 6
The proactive components.

IC2: cue-locked activity Region	volume (cc) L/R	Max z L/R	MNI (x, y, z) L/R
Fourth Ventricle	0.11	8.1	(0, −46, −25)
Culmen	0.14/0.51	5.6/7.3	(−3, −46, −25)/(12, −37, −16)
Cerebellar Lingual	0.11	5.3	(0, −43, −19)
Cuneus	0.43/0.14	5.1/3.5	(−12, −100, −1)/(18, −97, −1)
Third Ventricle	0.16	5.1	(0, −19, −4)
Extra-Nuclear	0.11	4.5	(3, −13, −4)
Middle Occipital Gyrus	0.76/0.35	4.4/4.0	(−27, −94, 11)/(21, −97, 2)
Inferior Frontal Gyrus	0.11	3.7	(42, 2, 29)
IC2: target-locked activity **Region**	**volume (cc) L/R**	**Max z L/R**	**MNI (x, y, z) L/R**
Middle Occipital Gyrus	0.97/0.27	6.8/4.2	(−36, −91, 5)/(24, −94, 14)
Lingual Gyrus	0.57	4.3	(−18, −94, −13)
Middle Temporal Gyrus	0.32	3.9	(−42, −76, 8)
Inferior Frontal Gyrus	0.14	3.9	(57, 11, 35)
Declive	0.27	3.7	(−42, −70, −22)
Fusiform Gyrus	0.16	3.6	(−18, −91, −19)
Inferior Occipital Gyrus	0.32	3.6	(−18, −91, −16)
Cuneus	0.14/0.11	3.4/3.5	(−9, −97, 2)/(12, −103, −1)
Postcentral Gyrus	0.14	3.3	(−57, −25, 38)
IC5: cue-locked activity **Region**	**volume (cc) L/R**	**Max z L/R**	**MNI (x, y, z) L/R**
Lingual Gyrus	0.78/1.75	4.9/8.7	(−18, −91, −13)/(24, −91, −13)
Middle Occipital Gyrus	0.43/1.38	4.1/6.8	(−21, −88, −13)/(24, −88, −13)
Inferior Occipital Gyrus	0.24/0.43	4.3/5.4	(−18, −94, −16)/(27, −88, −13)
Cuneus	0.73	5.3	(9, −94, 2)
Middle Frontal Gyrus	0.38	4.6	(54, 23, 35)
Fusiform Gyrus	0.32	3.9	(33, −73, −19)
Sub-Gyral	0.14/0.14	3.5/3.7	(−30, −79, 23)/(24, −94, −7)
IC5: target-locked activity **Region**	**volume (cc) L/R**	**Max z L/R**	**MNI (x, y, z) L/R**
Precuneus	0.59/1.11	4.5/5.9	(0, −76, 35)/(9, −79, 47)
Cuneus	2.62/4.32	4.9/5.2	(−3, −67, 5)/(3, −76, 11)
Posterior Cingulate	0.73/1.43	5.2/4.5	(−3, −67, 8)/(6, −61, 8)
*Vermis	0.32	4.3	(−3, −67, 2)
Lingual Gyrus	0.94/0.38	4.3/3.9	(−3, −70, 2)/(3, −70, −4)
Culmen	0.27	4	(−6, −67, −7)
Culmen of Vermis	0.14	3.9	(−3, −64, −1)
Extra-Nuclear	0.11	3.4	(−3, −7, 14)
Declive	0.19	3.4	(−27, −70, −19)
Postcentral Gyrus	0.16	3.4	(63, −22, 14)

Note: Table shows z-transformed fMRI activity clusters for IC2 and IC5, thresholded at $z > 3$, cluster size > 0.1 cc. Region labelling via the FIT software (*AAL labelling).

Chiew and Braver, 2017). Stop-trial outcome may be an indicator of how efficient the mechanisms resulting in inhibition are in that particular trial. Thus, one can predict whether a stop-trial results in successful or unsuccessful inhibition by the preceding cue-locked and target-locked FM-theta activity. The single-trial logistic regression analysis revealed that stop-locked FM-theta activity predicted stop-trial success, such that higher FM-theta activity was associated with lower probability of successful stopping. This is in line with the findings of higher N2 amplitudes and FM-theta activity during unsuccessful compared to successful stop-trials (González-Villar et al., 2016; Knyazev et al., 2008), and supports the notion that successful inhibition is not due to higher stop-locked FM-theta activity specifically. This finding is also in line with the role of stop-locked FM-theta as important in conflict-monitoring and error detection (Cavanagh et al., 2012; Cavanagh and Frank, 2014). It may be that higher stop-locked FM-theta results from stop-signals that were more surprising, and that thus are associated with less efficient signal-detection and the instantiation of reactive response inhibition mechanisms. Thus, more surprising stop-signals have a higher probability to end in a failure to inhibit the initiated response. As target-locked theta activity was also associated with fast responses at the single-trial level in go-trials, another explanation can be based on how inhibition is conceptualised in the horse race model (Band et al., 2003; Logan and Cowan, 1984). Here, the outcome of a stop-trial is determined by a race between a go- and a stop-runner, and an unsuccessful stop-trial is the result of a go-runner that is faster than the stop-runner. In addition, the unsuccessful stop-trials even have faster reaction times than go-trials. Thus, perhaps the stronger target-locked theta effect in unsuccessful stop-trials reflect an additive effect associated with fast go responses as well as reactive activity in response to a stop signal. Future research needs to investigate this further.

Although cue-locked FM-theta did not predict stop-trial outcome, cue-locked FM-theta activity in the go-trials was a significant predictor of faster reaction times. The relationship between cue-locked theta and reaction times has been shown using other cognitive control tasks (Cohen and Cavanagh, 2011; Cohen and Donner, 2013; Cooper et al., 2017; Cooper et al., 2019). The present study is one of the first to show, however, that both cue-locked and target-locked FM-theta activity were associated with go-trial reaction times in a stop-signal task on a single-trial level. It may be that cue-locked FM-theta activity is reflecting a heightened preparation of the motor control network in general, which leads to fast responses in go-trials. Although no association between cue-locked theta and behaviour was found in stop-trials at the single-trial

level (as cue-locked theta did not predict stop-trial outcome), the analyses of trial averages did reveal heightened cue-locked theta activity in unsuccessful stop-trials compared to the go-trials, and in go-trials in the 0% condition, compared to the 25% condition. These are conditions that exhibit a prepotent tendency for fast responding. In sum, the relationship between cue-locked theta and fast responses in go-trials, as well as heightened theta activity in conditions with a strong prepotent tendency for fast responding, suggests a role of theta in heightened preparation of the motor control system.

The most novel findings of the present study were those from the combined EEG and fMRI analysis. It was hypothesized that if proactive and reactive control mechanisms rely on the same neural underpinnings that manifest in FM-theta activity on the scalp, then one should be able to trace FM-theta activity during proactive and reactive conditions back to the same brain regions. We found partial support for this hypothesis, as we did find a component (IC4) in the joint ICA analysis, which was related to both stopping and cue-related processing. This component showed a clear stop-associated FM-theta peak around 200–250 ms after stop-signal onset, as well as an early theta peak around 200 ms after cue onset. The theta activity was associated with activity in a right-lateralized network, including the IFG, MFG, insula, IPC, cingulate, and the SFG/SMA. Interestingly, rIFG activity was evident both in the cue-locked and target-locked features. The right IFG has been suggested as an important region for successful response inhibition, and has been associated with both reactive and proactive control of inhibition (Aron, 2011; Chikazoe et al., 2009; Messel et al., 2019; Wessel et al., 2013). However, the single trial data did not reveal any associations between cue-locked FM-theta activity and stop-trial outcome, indicating that FM-theta activity might not be directly related to inhibition per se. Indeed, it has been suggested that both FM-theta and rIFG activity might reflect more general mechanisms of control (Cooper et al., 2017) or attention (Hampshire et al., 2010), as well as being related to the novelty of a stimulus (Cavanagh et al., 2012; Cavanagh and Frank, 2014).

IC3, on the other hand, seemed to capture most of the go-related theta activity, which was associated with component activity in the occipital gyrus, and notably the caudate, the left medial frontal gyrus and the SFG for the cue-locked features on the one hand, as well as target-locked activity in the bilateral postcentral gyrus, the cingulate gyrus and the medial frontal gyrus (including the SMA region) on the other hand. The significant difference between the go25 and go66 condition, together with the unimodal EEG results, indicates that such a difference reflects a heightened preparation of the motor control network, leading to decreased reaction times in go-trials. Indeed, the SMA and pre-SMA are important regions of the motor control network (Cunnington et al., 2005; Lee et al., 1999; Obeso et al., 2013).

Although IC4 seemed to capture both cue-associated and stop-associated theta activity, cue-associated activity was also evident in two other components, IC2 and IC5. Specifically, IC2 seemed to capture more sustained cue-locked theta activity, with a later peak between 500 and 800 ms post cue, while target-locked theta activity was absent. This component showed cue-locked fMRI activity in the bilateral occipital gyrus, but also in the rIFG. IC5, on the other hand, showed a noisier FM-theta activity pattern in the cue-locked feature, with a somewhat earlier peak. Cue-locked fMRI component activity was again evident in the occipital cortex, as well as in the rMFG. The MFG specifically has been associated with working memory processes needed for active maintenance of cue information (Collette et al., 1999; Hampson et al., 2006). Together with the significant difference between go25 and go66 in this component, this indicates that IC5 may reflect some proactive adjustments that increase with increasing stop-signal probability, such as working memory processes reliant on the MFG. However, IC4 also showed cue-locked fMRI activity in the rMFG as well as the SMA, together with a distinct early cue-locked theta peak. Thus, it seems clear that there is no one-to-one relationship between the regions of the stopping network and sub-components of response inhibition. Rather, it seems more likely that proactive and reactive control is dependant on wide-spread activity in the stopping network that reflects the complex processes necessary to facilitate efficient inhibition. Nevertheless, the idea of FM-theta as a multidimensional feature is in line with recent research (Zuure et al., 2020), and here we suggest that FM-theta activity reflects several processes related to both motor initiation, inhibition and proactive control.

It needs to be noted that if FM-theta activity is related to the novelty of a stimulus (Cavanagh et al., 2012; Cavanagh and Frank, 2014), this would indicate that cue-locked FM-theta activity may be a result of the infrequency or validity of the cue, rather than proactive control mechanisms per se (Kaiser and Schütz-Bosbach, 2019; Mäki-Marttunen et al., 2019; van Driel et al., 2015). In the present study, the number of cues signalling the different stop-signal probabilities vary, with 50 0% cues, 400 25% cues and 150 66% cues. While this mapping was necessary to enable the experimental modulation of stop-signal probabilities without making the task unnecessary long, it does yield the possibility that the cue-locked FM-theta activity also depends on the frequency of the cue itself, and not the stop-signal probability it represents. If this is the case, the 0% cue should be the most novel one, followed by the 66% cue. Indeed, the 0% condition did elicit the strongest FM-theta response compared to the other go-trial conditions. However, this effect was across both cue-locked and go-locked activity, not specific to the cue-locked activity itself. Further, there was also a novelty difference between 25% and 66% conditions without any differences in the theta activity, such that this explanation seems unlikely.

Not least, one has to acknowledge that the probability of successfully inhibiting a response is obviously dependant on additional mechanisms that are not captured by FM-theta activity, such as sensory-, attentional- or motor control mechanisms (Kaiser and Schütz-Bosbach, 2019; Salinas and Stanford, 2013; Verbruggen et al., 2014). For example, proactive activity in the form of mu desynchronization (Raud et al., 2020), central beta activity related to motor processing, and occipital alpha related to visual detection, are all modulated by proactive control (Kaiser and Schütz-Bosbach, 2019). It seems likely that complex processes such as proactive and reactive control of inhibition are reflected in a magnitude of frequency bands and other neural measures, beyond what is discussed in the present paper.

5. Concluding remarks

The present study looked at the interplay between proactive and reactive mechanisms using a multimodal EEG-fMRI perspective. The results clearly show that varying stop-signal frequency leads to proactive response strategy adaptations in form of increased go-trial reaction times and modulations of go- and stop-trial accuracies. Further, FM-theta activity can be dissociated into several mechanisms associated with proactive control, response initiation and response inhibition processes. Specifically, we propose that FM-theta activity is not a reflection of a unitary cognitive control mechanism, but rather reflects both heightened preparation of the motor control network in general, which leads to fast responses in the go-trials, as well as stopping-related processes evident in both cue- and stop-locked FM-theta activity, associated with a right lateralized cortical network.

Declaration of Competing Interest

None.

Credit author statement

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Supplementary materials

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References

Adelhöfer, N., Beste, C., 2020. Pre-trial theta band activity in the ventromedial prefrontal cortex correlates with inhibition-related theta band activity in the right inferior frontal cortex. Neuroimage 219, 117052. doi:10.1016/j.neuroimage.2020.117052.

Aron, A.R., 2011. From Reactive to Proactive and Selective Control: developing a Richer Model for Stopping Inappropriate Responses. Biol. Psychiatry 69 (12), e55–e68. doi:10.1016/j.biopsych.2010.07.024.

Aron, A.R., Robbins, T.W., Poldrack, R.A., 2014. Inhibition and the right inferior frontal cortex: one decade on. Trends Cogn. Sci. (Regul. Ed.) 18 (4), 177–185. doi:10.1016/j.tics.2013.12.003.

Band, G.P.H., van der Molen, M.W., Logan, G.D., 2003. Horse-race model simulations of the stop-signal procedure. Acta Psychol. (Amst) 112 (2), 105–142. doi:10.1016/S0001-6918(02)00079-3.

Bengson, J.J., Mangun, G.R., Mazaheri, A., 2012. The neural markers of an imminent failure of response inhibition. Neuroimage 59 (2), 1534–1539. doi:10.1016/j.neuroimage.2011.08.034.

Boulinguez, P., Ballanger, B., Granjon, L., Benraiss, A., 2009. The paradoxical effect of warning on reaction time: demonstrating proactive response inhibition with event-related potentials. Clin. Neurophysiol. 120 (4), 730–737. doi:10.1016/j.clinph.2009.02.167.

Braver, T.S., 2012. The variable nature of cognitive control: a dual mechanisms framework. Trends Cogn. Sci. (Regul. Ed.) 16 (2), 106–113. doi:10.1016/j.tics.2011.12.010.

Calhoun, V.D., Adali, T., Pearlson, G.D., Kiehl, K.A., 2006. Neuronal chronometry of target detection: fusion of hemodynamic and event-related potential data. Neuroimage 30 (2), 544–553. doi:10.1016/j.neuroimage.2005.08.060.

Cavanagh, J.F., Frank, M.J., 2014. Frontal theta as a mechanism for cognitive control. Trends Cogn. Sci. (Regul. Ed.) 18 (8), 414–421. doi:10.1016/j.tics.2014.04.012.

Cavanagh, J.F., Shackman, A.J., 2015. Frontal midline theta reflects anxiety and cognitive control: meta-analytic evidence. J. Physiol.-Paris 109 (1), 3–15. doi:10.1016/j.jphysparis.2014.04.003.

Cavanagh, J.F., Zambrano-Vazquez, L., Allen, J.J.B., 2012. Theta lingua franca: a common mid-frontal substrate for action monitoring processes: omnipresent theta. Psychophysiology 49 (2), 220–238. doi:10.1111/j.1469-8986.2011.01293.x.

Chang, A., Ide, J.S., Li, H.-.H., Chen, C.-.C., Li, C.-S.R., 2017. Proactive Control: neural Oscillatory Correlates of Conflict Anticipation and Response Slowing. eNeuro 4 (3). doi:10.1523/ENEURO.0061-17.2017.

Chiew, K.S., Braver, T.S., 2017. Context processing and cognitive control: from gating models to dual mechanisms. In: The Wiley handbook of Cognitive Control. Wiley Blackwell, pp. 143–166. doi:10.1002/9781118920497.ch9.

Chikazoe, J., Jimura, K., Hirose, S., Yamashita, K.-i., Miyashita, Y., Konishi, S., 2009. Preparation to Inhibit a Response Complements Response Inhibition during Performance of a Stop-Signal Task. J. Neurosci. 29 (50), 15870–15877. doi:10.1523/JNEUROSCI.3645-09.2009.

Cieslik, E.C., Mueller, V.I., Eickhoff, C.R., Langner, R., Eickhoff, S.B., 2015. Three key regions for supervisory attentional control: evidence from neuroimaging meta-analyses. Neurosci. Biobehav. Rev. 48, 22–34. doi:10.1016/j.neubiorev.2014.11.003.

Cohen, M.X., Cavanagh, J.F., 2011. Single-trial regression elucidates the role of prefrontal theta oscillations in response conflict. Front. Psychol. 2. doi:10.3389/fpsyg.2011.00030.

Cohen, M.X., Donner, T.H., 2013. Midfrontal conflict-related theta-band power reflects neural oscillations that predict behavior. J. Neurophysiol. 110 (12), 2752–2763. doi:10.1152/jn.00479.2013.

Collette, F., Salmon, E., Van der Linden, M., Chicherio, C., Belleville, S., Degueldre, C., Delfiore, G., Franck, G., 1999. Regional brain activity during tasks devoted to the central executive of working memory. Cognit. Brain Res. 7 (3), 411–417. doi:10.1016/S0926-6410(98)00045-7.

Congdon, E., Mumford, J.A., Cohen, J.R., Galvan, A., Canli, T., Poldrack, R.A., 2012. Measurement and reliability of response inhibition. Front. Psychol. 3. doi:10.3389/fpsyg.2012.00037.

Cooper, P.S., Karayanidis, F., McKewen, M., McLellan-Hall, S., Wong, A.S.W., Skippen, P., Cavanagh, J.F., 2019. Frontal theta predicts specific cognitive control-induced behavioural changes beyond general reaction time slowing. Neuroimage 189, 130–140. doi:10.1016/j.neuroimage.2019.01.022.

Cooper, P.S., Wong, A.S.W., McKewen, M., Michie, P.T., Karayanidis, F., 2017. Frontoparietal theta oscillations during proactive control are associated with goal-updating and reduced behavioral variability. Biol. Psychol. 129, 253–264. doi:10.1016/j.biopsycho.2017.09.008.

Criaud, M., Longcamp, M., Anton, J.-.L., Nazarian, B., Roth, M., Sescousse, G., Strafella, A.P., Ballanger, B., Boulinguez, P., 2017. Testing the physiological plausibility of conflicting psychological models of response inhibition: a forward inference fMRI study. Behav. Brain Res. 333, 192–202. doi:10.1016/j.bbr.2017.06.030.

Cunnington, R., Windischberger, C., Moser, E., 2005. Premovement activity of the pre-supplementary motor area and the readiness for action: studies of time-resolved event-related functional MRI. Hum. Mov. Sci. 24 (5–6), 644–656. doi:10.1016/j.humov.2005.10.001.

Delorme, A., Makeig, S., 2004. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. J. Neurosci. Methods 14.

Dippel, G., Chmielewski, W., Mückschel, M., Beste, C., 2016. Response mode-dependent differences in neurofunctional networks during response inhibition: an EEG-beamforming study. Brain Struct. Function 221 (8), 4091–4101. doi:10.1007/s00429-015-1148-y.

Dippel, G., Mückschel, M., Ziemssen, T., Beste, C., 2017. Demands on response inhibition processes determine modulations of theta band activity in superior frontal areas and correlations with pupillometry – implications for the norepinephrine system during inhibitory control. Neuroimage 157, 575–585. doi:10.1016/j.neuroimage.2017.06.037.

Enriquez-Geppert, S., Konrad, C., Pantev, C., Huster, R.J., 2010. Conflict and inhibition differentially affect the N200/P300 complex in a combined go/nogo and stop-signal task. Neuroimage 51 (2), 877–887. doi:10.1016/j.neuroimage.2010.02.043.

Fillmore, M.T., Rush, C.R., 2002. Impaired inhibitory control of behavior in chronic cocaine users. Drug Alcohol Depend. 66 (3), 265–273. doi:10.1016/S0376-8716(01)00206-X.

González-Villar, A.J., Bonilla, F.M., Carrillo-de-la-Peña, M.T., 2016. When the brain simulates stopping: neural activity recorded during real and imagined stop-signal tasks. Cognit. Affect. Behav. Neurosci. 16 (5), 825–835. doi:10.3758/s13415-016-0434-3.

Grandchamp, R., Delorme, A., 2011. Single-trial normalization for event-related spectral decomposition reduces sensitivity to noisy trials. Front. Psychol. 2. doi:10.3389/fpsyg.2011.00236.

Hampshire, A., Chamberlain, S.R., Monti, M.M., Duncan, J., Owen, A.M., 2010. The role of the right inferior frontal gyrus: inhibition and attentional control. Neuroimage 50 (3), 1313–1319. doi:10.1016/j.neuroimage.2009.12.109.

Hampshire, A., Sharp, D.J., 2015. Contrasting network and modular perspectives on inhibitory control. Trends Cogn. Sci. (Regul. Ed.) 19 (8), 445–452. doi:10.1016/j.tics.2015.06.006.

Hampson, M., Driesen, N.R., Skudlarski, P., Gore, J.C., Constable, R.T., 2006. Brain connectivity related to working memory performance. J. Neurosci. 26 (51), 13338–13343. doi:10.1523/JNEUROSCI.3408-06.2006.

Hong, X., Sun, J., Wang, J., Li, C., Tong, S., 2020. Attention-related modulation of frontal midline theta oscillations in cingulate cortex during a spatial cueing Go/NoGo task. Int. J. Psychophysiol. 148, 1–12. doi:10.1016/j.ijpsycho.2019.11.011.

Hughes, M.E., Fulham, W.R., Johnston, P.J., Michie, P.T., 2012. Stop-signal response inhibition in schizophrenia: behavioural, event-related potential and functional neuroimaging data. Biol. Psychol. 89 (1), 220–231. doi:10.1016/j.biopsycho.2011.10.013.

Huster, R.J., Enriquez-Geppert, S., Lavallee, C.F., Falkenstein, M., Herrmann, C.S., 2013. Electroencephalography of response inhibition tasks: functional networks and cognitive contributions. Int. J. Psychophysiol. 87 (3), 217–233. doi:10.1016/j.ijpsycho.2012.08.001.

Jahfari, S., Verbruggen, F., Frank, M.J., Waldorp, L.J., Colzato, L., Ridderinkhof, K.R., Forstmann, B.U., 2012. How preparation changes the need for top-down control of the basal ganglia when inhibiting premature actions. J. Neurosci. 32 (32), 10870–10878. doi:10.1523/JNEUROSCI.0902-12.2012.

Jahfari, Sara, Stinear, C.M., Claffey, M., Verbruggen, F., Aron, A.R., 2010. Responding with Restraint: what Are the Neurocognitive Mechanisms? J. Cogn. Neurosci. 22 (7), 1479–1492. doi:10.1162/jocn.2009.21307.

Kaiser, J., Schütz-Bosbach, S., 2019. Proactive control without midfrontal control signals? The role of midfrontal oscillations in preparatory conflict adjustments. Biol. Psychol. 148, 107747. doi:10.1016/j.biopsycho.2019.107747.

Kaiser, J., Simon, N.A., Sauseng, P., Schütz-Bosbach, S., 2019. Midfrontal neural dynamics distinguish between general control and inhibition-specific processes in the stopping of motor actions. Sci. Rep. 9 (1), 13054. doi:10.1038/s41598-019-49476-4.

Knyazev, G.G., Levin, E.A., Savostyanov, A.N., 2008. A failure to stop and attention fluctuations: an evoked oscillations study of the stop-signal paradigm. Clin. Neurophysiol. 119 (3), 556–567. doi:10.1016/j.clinph.2007.11.041.

Ko, L.-.W., Shih, Y.-.C., Chikara, R.K., Chuang, Y.-.T., Chang, E.C., 2016. Neural Mechanisms of Inhibitory Response in a Battlefield Scenario: a Simultaneous fMRI-EEG Study. Front. Hum. Neurosci. 10. doi:10.3389/fnhum.2016.00185.

Kuznetsova, A., Brockhoff, P.B., Christensen, R.H.B., 2017. lmerTest package: tests in linear mixed effects models. J. Stat. Softw. 82 (1), 1–26. doi:10.18637/jss.v082.i13.

Lavallee, C.F., Herrmann, C.S., Weerda, R., Huster, R.J., 2014. Stimulus-response mappings shape inhibition processes: a combined EEG-fMRI study of contextual stopping. PLoS One 9 (4), e96159. doi:10.1371/journal.pone.0096159.

Lee, K.-.M., Chang, K.-.H., Roh, J.-.K., 1999. Subregions within the supplementary motor area activated at different stages of movement preparation and execution. Neuroimage 9 (1), 117–123. doi:10.1006/nimg.1998.0393.

Leunissen, I., Coxon, J.P., Swinnen, S.P., 2016. A proactive task set influences how response inhibition is implemented in the basal ganglia: basal Ganglia in Proactive and Reactive Inhibition. Hum. Brain Mapp. 37 (12), 4706–4717. doi:10.1002/hbm.23338.

Levy, B.J., Wagner, A.D., 2011. Cognitive control and right ventrolateral prefrontal cortex: reflexive reorienting, motor inhibition, and action updating: cognitive control and right ventrolateral PFC. Ann. N. Y. Acad. Sci. 1224 (1), 40–62. doi:10.1111/j.1749-6632.2011.05958.x.

Logan, G.D., Cowan, W.B., 1984. On the ability to inhibit thought and action: a theory of an act of control. Psychol. Rev. 91 (3), 295–327. doi:10.1037/0033-295X.91.3.295.

Loof, E.D., Vassena, E., Janssens, C., Taeye, L.D., Meurs, A., Roost, D.V., Boon, P., Raedt, R., Verguts, T., 2019. Preparing for hard times: scalp and intracranial physiological signatures of proactive cognitive control. Psychophysiology 56 (10), e13417. doi:10.1111/psyp.13417.

Luke, S.G., 2017. Evaluating significance in linear mixed-effects models in R. Behav. Res. Methods 49 (4), 1494–1502. doi:10.3758/s13428-016-0809-y.

Mäki-Marttunen, V., Hagen, T., Espeseth, T., 2019. Proactive and reactive modes of cognitive control can operate independently and simultaneously. Acta Psychol. (Amst) 199, 102891. doi:10.1016/j.actpsy.2019.102891.

Messel, M.S., Raud, L., Hoff, P.K., Skaftnes, C.S., Huster, R.J., 2019. Strategy switches in proactive inhibitory control and their association with task-general and stopping-specific networks. Neuropsychologia 135, 107220. doi:10.1016/j.neuropsychologia.2019.107220.

Monterosso, J.R., Aron, A.R., Cordova, X., Xu, J., London, E.D., 2005. Deficits in response inhibition associated with chronic methamphetamine abuse. Drug Alcohol Depend. 79 (2), 273–277. doi:10.1016/j.drugalcdep.2005.02.002.

Nieuwenhuis, S., Yeung, N., van den Wildenberg, W., Ridderinkhof, K.R., 2003. Electrophysiological correlates of anterior cingulate function in a go/no-go task: effects of response conflict and trial type frequency. Cognit. Affect. Behav. Neurosci. 3 (1), 17–26. doi:10.3758/CABN.3.1.17.

Nigbur, R., Ivanova, G., Stürmer, B., 2011. Theta power as a marker for cognitive interference. Clin. Neurophysiol. 122 (11), 2185–2194. doi:10.1016/j.clinph.2011.03.030.

Obeso, I., Robles, N., Marrón, E.M., Redolar-Ripoll, D., 2013. Dissociating the role of the pre-SMA in response inhibition and switching: a combined online and offline TMS approach. Front. Hum. Neurosci. 7. doi:10.3389/fnhum.2013.00150.

Pinner, J.F.L., Cavanagh, J.F., 2017. Frontal theta accounts for individual differences in the cost of conflict on decision making. Brain Res. 1672, 73–80. doi:10.1016/j.brainres.2017.07.026.

Ramautar, J.R., Kok, A., Ridderinkhof, K.R., 2004. Effects of stop-signal probability in the stop-signal paradigm: the N2/P3 complex further validated. Brain Cogn. 56 (2), 234–252. doi:10.1016/j.bandc.2004.07.002.

Raud, L., Huster, R.J., Ivry, R.B., Labruna, L., Messel, M.S., Greenhouse, I., 2020. A single mechanism for global and selective response inhibition under the influence of motor preparation. J. Neurosci. doi:10.1523/JNEUROSCI.0607-20.2020.

Salinas, E., Stanford, T.R., 2013. The countermanding task revisited: fast stimulus detection is a key determinant of psychophysical performance. J. Neurosci. 33 (13), 5668–5685. doi:10.1523/JNEUROSCI.3977-12.2013.

Sauseng, P., Tschentscher, N., Biel, A.L., 2019. Be Prepared: tune to FM-Theta for Cognitive Control. Trends Neurosci. 42 (5), 307–309. doi:10.1016/j.tins.2019.02.006.

Ullsperger, M., Danielmeier, C., Jocham, G., 2014. Neurophysiology of performance monitoring and adaptive behavior. Physiol. Rev. 94 (1), 35–79. doi:10.1152/physrev.00041.2012.

van Belle, J., Vink, M., Durston, S., Zandbelt, B.B., 2014. Common and unique neural networks for proactive and reactive response inhibition revealed by independent component analysis of functional MRI data. Neuroimage 103, 65–74. doi:10.1016/j.neuroimage.2014.09.014.

van den Wildenberg, W.P.M., van Boxtel, G.J.M., van der Molen, M.W., Bosch, D.A., Speelman, J.D., Brunia, C.H.M, 2006. Stimulation of the subthalamic region facilitates the selection and inhibition of motor responses in Parkinson's Disease. J. Cogn. Neurosci. 18 (4), 626–636. doi:10.1162/jocn.2006.18.4.626.

van Driel, J., Sligte, I.G., Linders, J., Elport, D., Cohen, M.X., 2015. Frequency band-specific electrical brain stimulation modulates cognitive control processes. PLoS One 10 (9), e0138984. doi:10.1371/journal.pone.0138984.

Verbruggen, F., Aron, A.R., Band, G.P., Beste, C., Bissett, P.G., Brockett, A.T., Brown, J.W., Chamberlain, S.R., Chambers, C.D., Colonius, H., Colzato, L.S., Corneil, B.D., Coxon, J.P., Dupuis, A., Eagle, D.M., Garavan, H., Greenhouse, I., Heathcote, A., Huster, R.J., …, Boehler, C.N., 2019. A consensus guide to capturing the ability to inhibit actions and impulsive behaviors in the stop-signal task. Elife 8, e46323. doi:10.7554/eLife.46323.

Verbruggen, F., Best, M., Bowditch, W.A., Stevens, T., McLaren, I.P.L., 2014. The inhibitory control reflex. Neuropsychologia 65, 263–278. doi:10.1016/j.neuropsychologia.2014.08.014.

Verbruggen, F., Logan, G.D., 2008. Response inhibition in the stop-signal paradigm. Trends Cogn. Sci. (Regul. Ed.) 12 (11), 418–424. doi:10.1016/j.tics.2008.07.005.

Verbruggen, F., Logan, G.D., 2009a. Proactive adjustments of response strategies in the stop-signal paradigm. J. Exp. Psychol. Hum. Percept. Perform. 35 (3), 835–854. doi:10.1037/a0012726.

Verbruggen, F., Logan, G.D., 2009b. Models of response inhibition in the stop-signal and stop-change paradigms. Neurosci. Biobehav. Rev. 33 (5), 647–661. doi:10.1016/j.neubiorev.2008.08.014.

Wessel, J.R., Conner, C.R., Aron, A.R., Tandon, N., 2013. Chronometric electrical stimulation of right inferior frontal cortex increases motor braking. J. Neurosci. 33 (50), 19611–19619. doi:10.1523/JNEUROSCI.3468-13.2013.

Wodka, E.L., Mark Mahone, E., Blankner, J.G., Gidley Larson, J.C., Fotedar, S., Denckla, M.B., Mostofsky, S.H., 2007. Evidence that response inhibition is a primary deficit in ADHD. J. Clin. Exp. Neuropsychol. 29 (4), 345–356. doi:10.1080/13803390600678046.

Yamanaka, K., Yamamoto, Y., 2010. Single-trial EEG power and phase dynamics associated with voluntary response inhibition. J. Cogn. Neurosci. 22 (4), 714–727. doi:10.1162/jocn.2009.21258.

Zandbelt, B.B., Bloemendaal, M., Hoogendam, J.M., Kahn, R.S., Vink, M., 2013. Transcranial Magnetic Stimulation and Functional MRI Reveal Cortical and Subcortical Interactions during Stop-signal Response Inhibition. J. Cogn. Neurosci. 25 (2), 157–174. doi:10.1162/jocn_a_00309.

Zandbelt, B.B., Vink, M., 2010. On the Role of the Striatum in Response Inhibition. PLoS One 5 (11), e13848. doi:10.1371/journal.pone.0013848.

Zuure, M.B., Hinkley, L.B., Tiesinga, P.H.E., Nagarajan, S.S., Cohen, M.X., 2020. Multiple midfrontal thetas revealed by source separation of simultaneous MEG and EEG. J. Neurosci. 40 (40), 7702–7713. doi:10.1523/JNEUROSCI.0321-20.2020.

Frontal-midline theta reflects different mechanisms associated with proactive and reactive control of inhibition: Supplementary materials

Joint ICA analysis. The joint ICA analysis resulted in four independent components. The component activity for IC2 is displayed in Figure S.1, and MNI coordinates in Table S.1. There was no difference in component activity between any of the conditions (all $p > .0125$)

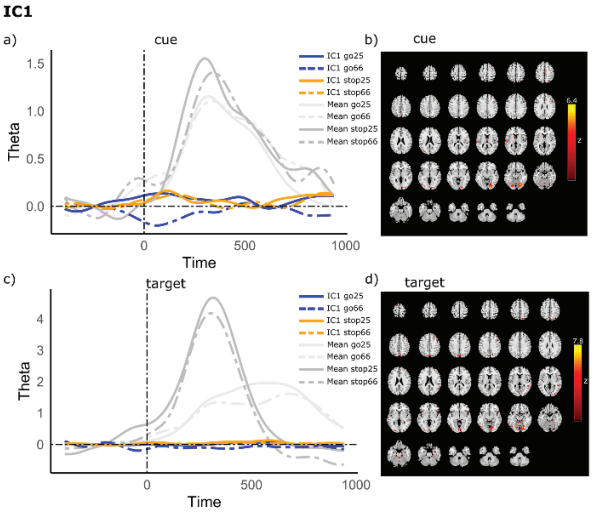

Figure S.1: Independent component 1. a) cue-locked FM-theta component activity in blue (go) and orange (stop). Average theta activity (in decibel, dB) for each condition in grey. b) cue-locked fMRI component activity. c) target-locked FM-theta component activity in blue (go) and orange (stop). Average theta activity (in decibel, dB) for each condition in grey. d) target-locked fMRI component activity. The figure shows z-transformed positive fMRI activity thresholded at z > 3, slice numbering in mm. L = left, R = right.

Table S.1: Independent component 1

IC1: cue-locked activity

Region	**volume (cc) L/R**	**Max z L/R**	**MNI (x, y, z) L/R**
Lingual Gyrus	0.49/2.59	4.0/6.4	(-21, -82, -16)/(21, -94, -13)
Middle Occipital Gyrus	0.24/0.97	3.6/5.2	(-30, -82, 17)/(24, -88, -13)
Fusiform Gyrus	0.24/0.81	4.5/5.1	(-21, -82, -19)/(30, -70, -16)
Caudate	0.43/0.22	4.8/4.8	(-9, 5, 8)/(9, 5, 5)

Declive	0.19	4.7	(30, -70, -19)
Inferior Occipital Gyrus	0.19	4.5	(24, -91, -16)
Transverse Temporal Gyrus	0.27	4.3	(-54, -22, 11)
Superior Parietal Lobule	0.27	4.3	(27, -70, 56)
Precuneus	0.27/0.14	3.8/4.3	(-6, -79, 50)/(12, -79, 50)
Sub-Gyral	0.16	3.5	(-30, -82, 20)
Extra-Nuclear	0.16	4.2	(-6, -1, 8)
Middle Frontal Gyrus	0.54	4.2	(54, 17, 32)
Superior Temporal Gyrus	0.51	4.1	(-60, -16, 8)
Cuneus	0.19	4	(12, -94, -1)
Medial Frontal Gyrus	0.19	3.5	(-3, -19, 53)
Paracentral Lobule	0.16	3.7	(3, -28, 53)
Inferior Temporal Gyrus	0.11	3.5	(-48, -76, -7)
IC1: target-locked activity			
Region	**volume (cc) L/R**	**Max z L/R**	**MNI (x, y, z) L/R**
Fourth Ventricle	0.14	7.8	(0, -43, -25)
Precuneus	0.70/1.24	5.9/6.4	(-6, -82, 44)/(9, -79, 47)
Lingual Gyrus	0.59/1.65	4.9/5.7	(0, -88, -13)/(18, -76, -16)
Culmen	0.43/0.62	4.6/5.6	(-3, -46, -25)/(3, -46, -25)
Superior Temporal Gyrus	0.43	4.8	(30, 11, -28)
Parahippocampal Gyrus	0.24	4.7	(9, -40, 2)
Superior Parietal Lobule	0.19	4.7	(30, -73, 53)
Middle Occipital Gyrus	0.57/0.62	4.3/4.2	(-48, -76, -10)/(30, -94, 2)
Middle Frontal Gyrus	0.76	4.2	(48, 23, 44)
Fusiform Gyrus	0.46	4.2	(24, -70, -16)
Inferior Temporal Gyrus	0.11	3.9	(-51, -76, -7)/
Inferior Frontal Gyrus	0.27/0.59	3.9/3.9	(-45, 20, -7)/(36, 11, -16)
Cuneus	0.14	3.7	(6, -91, 23)
Inferior Parietal Lobule	0.19	3.6	(54, -46, 53)
Middle Temporal Gyrus	0.22	3.4	(51, -43, 5)

Note: Table shows z-transformed fMRI activity clusters for IC1, thresholded at z > 3, cluster size > 0.1 cc.

Region labelling via the FIT software.