2014

Optimising the training-induced changes of inhibitory control

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UNIVERSITY OF WOLLONGONG

OPTIMISING THE TRAINING-INDUCED CHANGES OF INHIBITORY CONTROL

A thesis submitted in fulfilment of the requirements

for the award of the degree

DOCTOR OF PHILOSOPHY

from the

UNIVERSITY OF WOLLONGONG

by

Nicholas P. Benikos, BPsyc (Hons)

SCHOOL OF PSYCHOLOGY

I, Nicholas P. Benikos, declare that this thesis, submitted in fulfilment of the requirements of the award of Doctor of Philosophy, in the School of Psychology, University of Wollongong, is wholly my own work unless otherwise referenced or acknowledged. The document has not been submitted for qualifications at any other academic institution.

Nicholas P. Benikos

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Acknowledgements

First and foremost, I would like to thank my two thesis supervisors – Dr. Stuart Johnstone and Dr.Steven Roodenrys for their constant support and advice. It has been a very long road to say the least, but you never gave up on me and always supported the researcher I could be. I couldn't be more grateful.

I am also very thankful to my colleagues at both the University of Wollongong and the University of Southampton. The support they provided was immense. I would also like to thank Professor Edmund Sonuga-Barke for your constant support, expertise and guidance, especially for making the final push for the last study. While you didn't need to, you gave freely of your time and effort – I will never forget that. Your heart is as big as your intellect.

To my family: Mum, Dad, Michael Steven and Andrew (not to forget the "other halves" Rose, Shanika and Lauren!). When things were hard going, you all always supported me. You even offered to read the drafts - even if you didn't know what I was talking about! Thank you.

Most importantly my wife Caroline. You have given a lot for me to follow this dream. It has not been easy to put up with all the ups and downs – I thank you with all my heart.

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Abbreviations used in text

ACC	Anterior Cingulate Cortex
ANOVA	Analysis of Variance
CNS	Central Nervous System
EEG	Electroencephalogram
EOG	Electrooculogram
ERN	Error-Related Negativity
ERP	Event-Related Potential
fMRI	Functional Magnetic Resonance Imaging
ISI	Inter-stimulus Interval
LPC	Late Positive Complex
MMN	Mismatch Negativity
NG	GNG training condition
NG-ST	Go/Nogo-Stop training condition
Pre-SMA	Pre-Supplementary Motor Area
PN	Processing Negativity
RT	Reaction Time
RTD	Reaction Time Deadline
rIFG	Right Inferior Frontal Gyrus
SCL	Skin Conductance Level
SSD	Stop-Signal Delay
SSRT	Stop-Signal Reaction Time
STN	Sub-thalmic Nucleus
WM	Working Memory

Abstract

In four studies, this thesis examined the effect of task difficulty and brief training on inhibitory processing in the Go/Nogo task, and transfer to the Stop-signal and Eriksen-flanker tasks. It also aimed to clarify how the event-related potential (ERP) of the N2 and P3, as well as the earlier N1 and P2 components, reflect training-related modulations in the underlying neural processes. This was achieved by (1) the use of three task difficulty levels (Low, Medium, High) using incremental reaction time deadlines (RTDs), (2) the effect of these three RTDs on task performance and the early (N1, P2) and inhibition-related (N2, P3) ERP components after brief training, (3) the use of another form of task difficulty – stimulus prepotency – to investigate whether training effects may be enhanced, and (4) the use of single Go/Nogo training (planned inhibition) vs. combined training of Go/Nogo (planned inhibition) and Stop-signal (action cancellation) inhibition. The main results were that the Nogo N2 effect was robustly observed to increase with greater task difficulty (i.e. RTDs), but that it reduced irrespective with time-on-task or training condition. It does not appear to reflect neural processing related to motor or pre-motor inhibition, but may instead represent the detection of conflict between responses. The Nogo P3, however, behaved in a fashion consistent with an inhibitory interpretation, being reduced with greater task difficulty (concurrent with lower levels of task performance), but showing increased amplitudes over frontal brain regions with training and improved task performance – an effect that showed near-transfer to an untrained Stop-signal task. Reduced N1, but enhanced P2 amplitudes, occurred regardless of training condition, indicating a generalised change in sensory processing with repeated task administration. The results cast doubt on the current inhibitory interpretation of the N2. Instead they suggest that, not only does the amplitude of the frontocentral Nogo P3 represent neural processing related to inhibitory control, but that it shows clear training-induced quantitative changes coinciding with performance improvements - furthering both the theoretical and applied knowledge of the key task parameters required to effectively train inhibitory control.

Publications arising from this thesis

Published Journal articles

Benikos, N., Johnstone, S. J. & Roodenrys, S. J. (2013a). Varying task difficulty in the Go/Nogo task: the effects of inhibitory control, arousal, and perceived effort on ERP components. *International Journal of Psychophysiology, 87* (3), 262-272.

Benikos, N., Johnstone, S. J. & Roodenrys, S. J. (2013b). Short-term training in the Go/Nogo Task: Behavioural and Neural Changes Depend on Task Demands. *International Journal of Psychophysiology, 87* (3), 301-310.

Submitted Journal articles

Benikos, N., Johnstone, S. J. & Roodenrys, S. J. (submitted). Training-induced improvements in inhibitory control.

Abstracts of peer-reviewed conference presentations

Benikos, N., Johnstone, S. J., Roodenrys, S. J. (2014). A comparison of two training protocols to improve inhibitory control in healthy adults. *Frontiers in Human Neuroscience.* Oral presentation at the 25th Annual meeting of the Australasian Society for Psychophysiology, Southern Cross University, Coffs Harbour, New South Wales, Australia.

Benikos, N., Johnstone, S. J., Roodenrys, S. J. (2014). Training-induced improvements in inhibitory control. *International Journal of Psychophysiology*, *94* (2), Oral presentation at the world congress of the *International Organization of Psychophysiology (IOP)* 2014, Hiroshima, Japan.

Benikos, N., Johnstone, S. J., Roodenrys, S. (2011). Brief practice in the Go/Nogo task: Behavioural and neural changes depend on task demands. *Clinical EEG and Neuroscience, 42*, p. 125. Oral presentation at the 21st Annual meeting of the Australasian Society for Psychophysiology, Swinburne University, Melbourne, Victoria, Australia.

Benikos, N., Johnstone, S. J., Roodenrys, S. (2010). Task difficulty in the Go/Nogo task: The roles of inhibition, arousal and activation. *Psychophysiology*, 47 (Supplement), p. 69. Poster presentation at the 50th Annual meeting of the Society for Psychophysiology, Portland, Oregon, United States of America.

Benikos, N. Johnstone, S. J., Roodenrys, S. (2010). Varying task difficulty in the Go/Nogo task: A preliminary analysis. *Clinical EEG and Neuroscience, 41,* p.103. Poster presentation at the 20th Annual meeting of the Australasian Society for Psychophysiology, University of Newcastle, Newcastle, New South Wales, Australia.

Overview

Inhibitory control refers to the ability to successfully suppress thoughts, behaviour and irrelevant stimuli. It has been characterised as a key factor in the aetiology of several prominent impulse control disorders including substance abuse, addiction and attention-deficit/ hyperactivity disorder (ADHD). Recently cognitive training paradigms have been advanced as offering a non-pharmacological adjunct to remediating deficits in inhibitory control. However, the development of efficient inhibitory control training regimens first requires determining whether and how inhibitory control can be improved in healthy individuals and the underlying neurophysiological mechanisms. Although the anatomo-functional organization of inhibitory control has been extensively studied, the behavioural and neural plasticity of this function remains largely unknown. Using a systematic investigation of task parameters and event-related potential (ERP) measures, this thesis aims to address the key behavioural and neural mechanisms underlying training-induced plastic changes in inhibitory control.

The first chapter of the thesis provided an introduction to the concept of inhibitory control and common interpretations of the early (N1, P2) and inhibition-related (N2, P3) ERP components associated with Go/Nogo, Stop-signal and Eriksen-flanker tasks. Chapter 2 provided a comprehensive review of the inhibitory control training literature. In particular, the final section of chapter 2 integrates the current state of literature and points towards a systematic approach of future research to advance the understanding of the key task performance measures and neural indices of inhibitory control training.

Study 1 (Chapter 3) investigated the influence of varying task difficulty, via manipulation of reaction time deadline (RTD), on measures of inhibitory control, perceived effort, and task-related arousal (indexed by Skin Conductance Level). Sixty adults

completed a visual Go/Nogo task (70% Go) after being randomly assigned to one of three task difficulty conditions: High, Medium and Low, with RTDs of 300, 500 or 1000 ms, respectively. Incremental increases in Go/Nogo errors and greater perceived effort was found with increasing difficulty. No condition differences were found for task-related arousal. Nogo N2 amplitude increased and peaked earlier with increasing task difficulty, but the frontal Nogo P3 effect was reduced in the High condition compared to the Low and Medium conditions. The amplitude of N1 and P2 showed different effects: the Nogo N1 increased with task difficulty, while the Nogo P2 decreased. It was suggested that Go/Nogo task difficulty can appropriately be manipulated using RTDs – with distinct changes seen not only in the N2 and P3, but also the N1 and P2 ERP components.

Based on the key identification that Go/Nogo task difficulty can effectively be modulated in Study 1, Study 2 (Chapter 4) aimed to extend these findings across a brief Go/Nogo training session (8 blocks; 70% Go). As described in Study 1, sixty adults were randomly assigned to one of three task difficulty conditions: High (n = 20), Medium (n = 20) and Low (n = 20), with RTDs of 300, 500 or 1000 ms, respectively. Performance, ERPs and task-related arousal were examined. Go/Nogo proficiency was optimised during the Medium than Low/High conditions. An across-session increase in task-related arousal did not differ between conditions. Training-related changes in neural processing were dependent on task demands such that the Low task difficulty condition showed an enhanced centroparietal Nogo P2, while a training-induced enhancement in the Nogo > Go P3 effect was larger in the High than Medium condition. The High condition also showed the greatest reduction in the Nogo N1.

In Study 3 (Chapter 5) another form of task difficulty – stimulus probability - was investigated to see whether training-related performance and neural changes could be enhanced. Fifty four participants were randomly allocated to one of three training conditions (8 blocks of 100 trials): Standard Prepotency (SP; 70% Go; n = 18), High

Prepotency (HP; 85% Go; n = 18) and Control (Go 30%; n = 18). After block 8, a final block containing previously untrained stimuli was used to assess if the training effects were stimulus-specific. In the absence of self-reported differences in motivation, workload and task-related arousal, all participants showed reductions in N1 and N2 amplitude, in addition to an increase of the P2. Combined, it was suggested that these changes represented a generalised increase in task proficiency with repeated task experience, and not inhibitory control per se. Performance findings indicated the greatest gain in Go/Nogo proficiency for occurred for the HP compared with the SP and Control conditions; an effect, that was reflected by a centrofrontal enhancement of the Nogo > Go P3. This effect was not stable with introduction of untrained stimuli. Unexpectedly, the SP condition showed little difference compared to the active controls in performance gains and the Nogo > P3 effect. Inspection of the methodology used in Study 3 suggested that the primary determinant of training success was the overall speed of responding rather than stimulus prepotency.

Because stimulus prepotency did not appear to augment the brief training of inhibitory control, an adaptive RTD was employed in Study 4 (Chapter 6). However, in addition to an active control condition, this study compared the effect of standard Go/Nogo training vs. combined training Go/Nogo and Stop-signal task. Fifty-four adults were randomly assigned to one of three conditions, Go/Nogo training (NG; n = 18), Go/Nogo-Stop training (NG-ST; n = 18), or a control oddball counting task (CON; n = 18), and completed a single training session (8 blocks). To investigate whether the training would extend to untrained inhibitory control tasks pre- and post-training performance was compared using a Go/Nogo task (GNG), in addition to a Stop-signal (SS) and an Eriksen-flanker task. Compared to controls, the inhibition training conditions showed similar improvements in the GNG and SS tasks. ERP analyses showed an overlapping frontocentral increase in the Nogo and SS P3 component; suggesting a top-down augmentation and near-transfer of inhibitory processes. However, this result did not extend to the Eriksen task, with no changes in performance or ERP effects seen. Across conditions, the N1 decreased, but the

P2 increased in the GNG and SS. These findings suggested that adaptively manipulating task difficulty can lead to improvements in untrained inhibition tasks but that these effects are dependent on the whether the training and Pre/Post tasks engage overlapping processing components and brain regions.

Chapter 7 provides a summary and discussion of the results of this thesis in relation to current theories of the training-related behavioural and neural changes of inhibitory control. It is suggested that reduced N1, but enhanced P2 amplitude, represent generalised changes in early neural responding with repeated task administration. Further research is suggested, particularly in relation to the use of greater training intensity and duration.
It is concluded that the N2 represents conflict processing and declines with training. By contrast, the frontal Nogo P3 effect is enhanced with training; an effect that transfers to untrained tasks concurrent with improvements in inhibitory performance.

Chapter 1 - Inhibitory Control

1.1 The concept of inhibitory control

In our daily lives some restraint is needed to effectively regulate our behaviour. Otherwise we would be swamped by irrelevant information, powerless to restrain every inappropriate or vindictive thought that crosses our mind, or endanger ourselves to oncoming traffic by being unable to wait for the traffic lights to change before crossing the road (Schmidt & Bjork, 1992). The means by which we suppress inappropriate motor actions, thoughts and emotions is referred to as inhibitory control.

The concept of inhibitory control has been invoked to describe a wealth of phenomena (Bari & Robbins, 2013; Eagle et al., 2008). Clark (1996) defines inhibition broadly as "any mechanism that reduces or dampens neuronal, mental or behavioural activity" (p.128). From this perspective, inhibitory control can be seen as operating at many interrelated levels of functioning, but in one way or another, each type involves some form of suppression. For example, at the neural level, the action of inhibitory neurons dampens the activity of other neurons and is believed to be responsible for such phenomena as prepulse inhibition, receptive fields and figure-ground alterations (Clark, 1996). At the cognitive level, behavioural evidence in selective attention tasks shows that irrelevant information is not passively ignored but actively suppressed (Posner & Cohen, 1984; Tipper, 1985; Tipper & Cranston, 1985). Reaction times and early sensory neural processing are enhanced for stimuli presented at attended locations and suppressed for to-be-ignored stimuli in negative priming tasks (Kok, 1999). Finally, at the behavioural level, the inhibition of motor responses is perhaps the most direct manifestation of inhibitory control because the latency and efficiency of this process can be objectively assessed. Although an often unnoticed feature of everyday life, motor inhibition is crucial for allowing us to effectively

regulate our responses to the external environment; from relatively minor fine-grained motor adjustments while typing on a keyboard, to more serious situations of pressing the brakes just in time to avoid a motor accident. Moreover, individual differences in motor inhibition also predict important long-term outcomes including socio-economic status and physical health (Casey et al., 2011; Moffitt et al., 2011). Unfortunately, this capacity is susceptible to impairment with disruptions linked to divergent spheres of atypical functioning; from excess consumption of food (Blumenthal & Gold, 2012) or alcohol (Wiers et al., 2007), to neurological disorders including Huntington's disease (Beste et al., 2008), and several impulse control disorders such as attention-deficit/hyperactivity disorder (Sonuga-Barke et al., 2010), substance abuse (Bechara et al., 2006) and gambling disorders (Billieux et al., 2012; Brevers et al., 2012; Goudriaan et al., 2006; Grant et al., 2010).

Nigg (2000) has put forward a taxonomy of inhibitory processing which includes four major categories of effortful inhibitory control: (a) interference control, which refers to the suppression of a stimulus and/or the associated response that interferes with the primary goal, (b) cognitive inhibition which is the suppression of irrelevant thoughts or memory contents for the maintenance and safeguarding of working memory, (c) behavioural inhibition of a prepotent motor response, and (d) oculomotor inhibition, which is the resistance of reflexive saccades.

Confirmatory factor analyses indicates that in addition task-specific processing, there exists a *domain-general* inhibitory control mechanism across all tasks indexing inhibitory control (Brocki & Bohlin, 2004; Friedman & Miyake, 2004; for a discussion see Spierer et al., 2013). Moreover, evidence indicates that the different types of effortful inhibitory control share a substantially similar neural bases: the same fronto-striatal network including the pre-supplementary motor area (pre-SMA), right inferior frontal gyrus (rIFG), and sub-thalmic nucleus (STN) have been found to underlie vocal inhibition (Xue et al., 2008), oculomotor inhibition (Chikazoe et al., 2007), and also in the suppression of

emotional thoughts and memories (Depue et al., 2007; for a review see Dillon & Pizzagalli, 2007). It has been consistently reported that exerting one type of inhibitory self-control (e.g. resisting sweets) has a negative effect on the subsequent performance of an unrelated inhibition task (e.g. Stop-signal; Muraven, 2010; Muraven & Baumeister, 2000). However, the reverse could also be true in that training-related improvements may transfer to untrained conditions or tasks supported by the same fronto-basal network (Spierer et al., 2013).

Although different forms of inhibitory control help to govern our thoughts, actions and neural activity, this thesis is primarily concerned with motor inhibition, given that the behavioural effects of these abilities are easily measureable (reaction time, errors) and that their neural mechanisms (particularly to visual stimuli) have been highly characterised in the literature.

1.2 Measures of inhibitory control

Several experimental paradigms have been designed to elicit inhibitory control. For example, the Stroop task (MacLeod, 1991), continuous performance task (Van Leeuwen et al., 1998), anti-saccade task (Roberts et al., 1994), and the delay of gratification task (Sonuga-Barke et al., 1992). However, given that these measures involve many different cognitive components in addition to inhibitory control (e.g. attention, working memory etc.), they actually index a complex aggregate of cognitive process that concern more general "executive control" constructs (for a review see Aron, 2011) and lack the specificity to distinguish isolated inhibition-related effects (Tannock, 1998). In the following section, the basic methodology and assumptions behind three types of inhibitory control tasks included in this thesis that directly assess inhibitory control are discussed. The measures considered here are the Go/Nogo, the Stop-signal and the Eriksen flanker task. Differences in their

methodologies allow different inhibitory control domains to be assessed, but generally, these tasks involve the inhibition of a response.

1.2.1 The Go/Nogo task

The Go/Nogo task is among the most commonly employed paradigms used to investigate prepotent response inhibition. In this task, participants are required to respond to a Go stimulus (typically by a button press, but sometimes by counting, lever movements, etc.), while withholding a response to the Nogo stimulus. Typically, the Go stimulus is presented more frequently than the Nogo stimulus, which encourages a bias towards responding, rather than withholding the Go response. The underlying assumption is that inhibitory control is required to successfully inhibit the rare Nogo stimulus. The major dependent variable is the proportion of errors on Nogo trials (i.e. responses to Nogo stimuli). Go/Nogo task difficulty can be enhanced by requiring faster responses to Go stimuli (Jodo & Kayama, 1992). The relationship between fast Go responding and an increased requirement for inhibition on Nogo trials is well-established (Falkenstein et al., 2000; Falkenstein et al., 1999; Lindqvist & Thorell, 2009; Manuel et al., 2010; Smith et al., 2006). When responses grow progressively faster on average, the relative strength of inhibition must increase in order to overcome the fast Go response (Smith et al., 2006). A further method to enhance Go/Nogo task difficulty is to make the Go response prepotent by increasing the frequency of the Go response, which leads to an increase in the probability of Nogo errors (Bruin & Wiers, 2002; Enriquez-Geppert et al., 2010; Nieuwenhuis et al., 2003). By contrast, oddball-type tasks, where participants are required to respond to the Go (i.e., Target) stimulus on the minority of trials, and withhold that response to the remaining Nogo (or ‘Standard’) stimuli, are particularly well suited for indexing attentional capacity (Barry et al., 2003), given that it can be questioned whether participants actively inhibit a response on frequent Nogo trials

(Smith et al., 2004), and that the oddball task does not show strong involvement of frontal inhibitory networks (e.g. Di Russo et al., 2000).

1.2.2 The Stop-signal task

The Stop-signal task (SST) is an index of inhibitory control where responses that have already been initiated must be countermanded or stopped (Logan & Burkell, 1986; Logan & Cowan, 1984). In a typical Stop-signal task, participants are instructed to respond as quickly as possible to all stimuli as part of the primary reaction time task. On a proportion of trials, a "stop-signal" is presented after the presentation of the primary task stimulus, which requires participants to withhold their response. An advantage of the Stop-signal task over other inhibition tasks is that it can accurately index task performance in terms of the "horse race" model where Go response activation elicited by the primary task, and stop inhibition process evoked by the stop-signal, "race" independently of each other. Whether the Go response will be stopped depends on the relative finishing time of each process. If the Go response finishes before the Stop process, a response will be executed. If the Stop process finishes first, then the response will be inhibited. Manipulation of the stop-signal delay (SSD; the time between the Go stimulus and stop-signal) will produce different probabilities of successfully stopping the Go response, and allows the calculation of the main dependent variable of the stop-signal task - stop-signal reaction time (SSRT), which refers to the latency of the stop process.

1.2.3 The Eriksen-flanker task

The Eriksen-flanker task (Eriksen & Eriksen, 1974) is a choice reaction time paradigm designed to index interference control. The task requires participants to make a fast response to a centrally presented target stimulus that is flanked by several distractor

stimuli (or flankers). The target stimulus may be flanked by congruent distracters (e.g. < < < < <), while on incongruent trials, the flankers represent a competing response tendency (e.g. < < > < <). A dominant explanation put forward by Gratton and colleagues (1992; 1988), is that the presentation of flankers results in automatic activation of the response channel associated with the flanker stimuli leading to fast correct responses on congruent trials. By contrast, on incongruent trials, the distracting flankers are believed to elicit the automatic activation of an incorrect response, requiring interference control processes to override the incorrect response tendency, resulting in slower and more error-prone task performance. The major dependent variables in the Erisken-flanker task is the difference for reaction times and errors for incongruent *minus* the congruent trials (termed the "interference effect"). Reductions in the interference effect represent an improvement in interference control.

1.3 Electrophysiological indices of inhibitory control

The aims of this section are to provide a general introduction to event-related potentials (ERPs), outline the issues related to the identification and interpretation of ERP components, and to review the literature on the functional significance of ERPs in the inhibitory control tasks considered in this thesis (Go/Nogo, Stop-signal and Eriksen-flanker).

1.3.1 General introduction to event-related potentials (ERPs)

The central nervous system processes information by means of electrical signals, which can be non-invasively studied in humans by recording ERPs (Hillyard & Kutas, 1983; Picton et al., 2000). ERPs are transient voltage fluctuations that reflect the brain's average electrical response to sensory, cognitive or motor events (Rugg & Coles, 1995). It is believed that this activity represents the synchronous firing of larger neuronal populations

that are geometrically orientated to produce the field measured at the scalp (Rugg & Coles, 1995).

ERPs are derived from the on-going electroencephalogram (EEG), a measure of continuous brain electrical activity over time, by averaging segments of EEG (termed epochs) that are time-locked to a stimulus or cognitive event. An ERP is composed of several positive- and negative-going peaks that vary in magnitude (i.e. amplitude) and are typically characterised by their polarity, peak latency, topographic distribution, and eliciting conditions (e.g. Nogo N2, mismatch negativity). For example, a negative-going peak occurring approximately 100 ms post-stimulus may be referred to as the N1 (or N100) component. Furthermore, if the N1 shows maximal amplitude in the central region, this component may be described as the "central N1".

Differences in component amplitude, latency or topographic distribution allow inferences to be made about the degree of engagement, and the temporal sequencing of the sensory and cognitive processes required for task performance. *Quantitative* changes in ERP component amplitude represent an increase or decrease in the engagement of the underlying neural process, while variations in peak latency provide an indication of its timing. Changes in the topographic scalp distribution of an ERP component reflect differences in the neural generators of that component, and are indicative of a *qualitative* change in the underlying cognitive process (Johnson, 1993; Picton et al., 2000; Spencer et al., 2001). ERP components historically have been classified into either early or 'exogenous' components, that are determined by the physical characteristics of a stimulus, or 'endogenous' components, which reflect the cognitive response to stimuli (Picton et al., 2000). However, research has indicated that early components also vary with cognitive processing demands (Rugg & Coles, 1995), and appear to share characteristics of both exo- and-endogenous processes dependent on the properties of the stimulus (e.g. N1, N2; Shibasaki & Miyazaki, 1992). As a result, the exogenous-endogenous dichotomy is generally seen as an

oversimplification and the ERP literature has shifted towards identifying specific cognitive processes reflected by each component (Hillyard & Kutas, 1983; Key et al., 2005; Luck, 2014; Luck & Hillyard, 1994a; Picton et al., 2000).

1.4 ERP Components

1.4.1 N1

The N1 is a negative component and typically peaks at approximately 100 to 150 ms post-stimulus onset, which shows a modality-specific distribution; displaying a frontocentral maxima to auditory stimuli, but an occipital maxima to visual stimuli. The N1 component is believed to represent the initial extraction of information from a stimulus (Näätänen & Picton, 1987), and is enhanced to stimuli that have been directly attended to compared to when attention is distributed (Luck & Yard, 1995). The literature has robustly reported that the auditory N1 component is composed of multiple neural generators, with separate but overlapping components underlying this early negativity (Näätänen & Picton, 1987a). These components consist of the processing negativity (PN), a sensory-specific negativity that is enhanced to attended relative to unattended stimuli, and an "attentional supervisor", which is a longer latency second component of the processing negativity (Näätänen & Picton, 1987a). Similar to the auditory N1, the visual N1 is composed of two distinct sub-components. The first being largest over the central region at 100 ms, and the second largest over the posterior region and present at about165 ms (Luck et al., 2000). Consistent with the interpretation that the N1 likely reflects early attentional processes rather than purely visuo-sensory processing, evidence suggests that the source of the N1 does not only originate in the primary visual cortex, but has neural generators in the occipito-temporal and frontal cortex (Clark et al., 1994).

There have been few reports documenting the role of the N1 in the Go/Nogo task. While one early study reported a larger P1-N1 peak-to-peak amplitude to Nogo than Go stimuli (Nativ et al., 1992), most have found no effect of stimulus type on this component (Bokura et al., 2001; Mäntysalo, 1987). Similarly, the N1 has rarely been studied in the Eriksen-flanker task, but some have suggested that this component may be sensitive to the presence of flankers in children (Neutral > Congruent; Johnstone et al., 2009a) and adults (Incongruent > Congruent; Mahé et al., 2014); indicating an early modulation of attentional processing based on the congruency of flankers (Näätänen & Picton, 1987a). By contrast, it has been argued, that given the latency of inhibitory response in the Stop-signal task of typically 200-250 ms, it may be expected that the decision to countermand a response would occur early in the processing chain (Dimoska & Johnstone, 2007). Larger N1 for successful compared to failed Stop trials has led some researchers to suggest that the enhanced N1 amplitude may reflect a reduced attentional switch that is determinative for the quality of subsequent success of inhibitory control processing (Bekker et al., 2005a; Berkman et al., 2014; Boehler et al., 2009; Dimoska & Johnstone, 2007; Dimoska & Johnstone, 2008; Shen et al., 2014).

1.4.2 P2

The P2 is a positive component that peaks at approximately 150 to 200 ms post-stimulus. It typically shows a central (e.g. Dimoska et al., 2006) or centroparietal maxima (e.g. Freunberger et al., 2007) and does not appear to differ with modality (for reviews see Crowley & Colrain, 2004; Key et al., 2005).The functional significance of the P2 has yet to be resolved in the literature. While some researchers have generally linked the P2 to higher-order perceptual and attentional process (Crowley & Colrain, 2004), these processes may relate to the effective identification and classification of stimuli (Lindholm & Koriath, 1985). The P2 is enhanced when participants efficiently find targets in feature detection paradigms

(Luck & Hillyard, 1994a) and when actions are initiated (Kühn et al., 2009). By contrast, in discrimination paradigms, the P2 is thought to be involved in protection against interference from irrelevant stimuli (Garcia-Larrea et al., 1992), giving the imperative stimulus a clear path for further processing (Oades, 1998); with smaller amplitudes being associated with more effective inhibitory processes in children (Johnstone et al., 1996; Oades, 1998). However, the interpretation of the P2 may depend on scalp topography. Larger parietal P2 amplitudes have been linked to perceptual performance given that they parallel performance improvements during perceptual learning (Ding et al., 2003; Qu et al., 2010; Song et al., 2002; Song et al., 2005). Whereas, frontally maximal P2 amplitudes are enhanced by task relevance in the visual oddball task (Potts, 2004; Potts et al., 1996), and suggested to reflect the suppression of task-irrelevant information, in order to enhance processing. In addition, source analysis did not reveal different P2 sources for each response type (key press compared with count), which implies a stimulus evaluation rather than a response-related function (Potts, 2004).

Within the Go/Nogo task, Mäntysalo et al. (1987) and Falkenstein et al. (1995) reported no effect of stimulus type, while Bruin and Wijers (2002) found that the Nogo P2 increased with decreasing stimulus probability; in line with previous research arguing that that earlier components such as the P2 may play an important role in effective Go/Nogo task performance (Roche et al., 2005b; Thomas et al., 2009). Little is known about the role of the P2 in the Stop-signal task and Eriksen flanker tasks. The Stop P2 is typically superimposed on the Stop N2 making it difficult to experimentally distinguish (Dimoska & Johnstone, 2007). Inspection of grand mean ERP waveforms shows little evidence of the stop P2 at central or parietal sites (e.g. see Figure 1; Bekker et al., 2005a; see Figure 6; De Jong et al., 1990). In contrast, there is some evidence that P2 varies with trial type in the Eriksen- flanker task facilitating automatic stimulus discrimination when response conflict is

low, with the P2 being increased to congruent flankers in typically developing children (Johnstone et al., 2009a).

1.4.3 N2

The N2 component is a frontal negativity that occurs approximately 200-400 ms post-stimulus. Several different ERP components have been differentiated within the N2 time-range such that the N2 is considered to be a "family" of components that differ based on the characteristics of the eliciting task (Folstein & Van Petten, 2008; Näätänen & Picton, 1986). In an initial classification by Näätänen and Picton (1986), the N2 was described as including three sub-components: the "basic N2", which is evoked to repetitive stimuli requiring no action, the "N2b" which is elicited to deviant (i.e. oddball) stimuli, and the "N2c", which occurs when stimuli are required to be categorised. The N2a is now more commonly referred to as the mismatch negativity (MMN) which is observed for auditory mismatches, even when they are irrelevant to task performance (Näätänen et al., 1982). By contrast, further research has shown that the N2b and N2c are evoked only to task-relevant stimuli and that they also show differential modality-dependent topographies, such that the N2b is recorded over central regions for auditory stimuli, and the N2c observed over posterior regions for visual stimuli (Simson et al., 1977). Moreover, it has more recently been shown that an anterior N2 (N2b) effect can also be robustly elicited in conditions requiring cognitive control (e.g. Go/Nogo, Stop-signal and Eriksen-flanker tasks as described below). Thus the terms N2b and N2c have largely been replaced by the terms anterior N2 and posterior N2 (Folstein & Van Petten, 2008; Luck, 2014).

In the Go/Nogo task, the N2 component is increased to Nogo compared to Go stimuli at frontal or frontocentral sites referred as the "Nogo N2 effect" (Bekker et al., 2004; Beste et al., 2008; Beste et al., 2010; Bokura et al., 2001; Bruin & Wiers, 2002; Bruin et al.,

2001; Falkenstein et al., 1999, 2002; Falkenstein et al., 1995; Fallgatter & Strik, 1999; Huster et al., 2013; Jodo & Kayama, 1992; Kok, 1986; Nieuwenhuis et al., 2003; Schapkin et al., 2007). The Nogo N2 effect varies in response to different experimental manipulations designed to increase inhibitory load. For example, greater amplitudes have been reported with increasing stimulus prepotency by presenting frequent Go and rare Nogo stimuli (Bruin & Wiers, 2002; Nieuwenhuis et al., 2003). Larger Nogo N2 effects are reported during cued Go/Nogo tasks whenever the Nogo stimulus is presented instead of the expected Go stimulus (Smith et al., 2007), and also when Go responses are speeded via the use of reaction time deadlines (Jodo & Kayama, 1992).

The Nogo N2 effect was initially believed to be modality-specific and isolated to visual Go/Nogo tasks, given that it was not reliably produced in the auditory modality (Falkenstein et al., 1999, 2002; Falkenstein et al., 1995). However, Nieuwenhius, Cohen and Yeung (2004) argued these results were most likely due to perceptual overlap. For example, when using the letters “M” or “W” as Go/Nogo stimuli, these letters may be more perceptually difficult to discriminate in the visual modality compared to when the letters are spoken; leading to greater levels of response activation and resulting in a larger Nogo N2 effect in visual paradigms. By varying perceptual overlap in visual and auditory Go/Nogo tasks, resulting in stimuli looking similar and sounding different (i.e., “T” and “F”) or sounding similar but looking different (i.e., “S” and “F”), Nieuwenhuis et al. (2004) found that when the discrimination of auditory stimuli was at least as difficult as that of visual stimuli, the typical Nogo N2 was observed in both modalities. This result has since been directly replicated (Smith & Douglas, 2011). In addition, several further studies using auditory (Johnstone et al., 2005; Smith et al., 2006; Smith et al., 2007; Smith et al., 2008) and somato-sensory stimuli (Huster et al., 2010; Huster et al., 2011a; Huster et al., 2011c; Nakata et al., 2004; Nakata et al., 2005) have demonstrated that the Nogo N2 effect can be reliably elicited, suggesting that it likely reflects a supramodal processing stage (Huster et al., 2013). With respect to Nogo N2 latency, there have been variable results. Some have

reported no effects of stimulus type (Pfefferbaum et al., 1985), while others report that Nogo N2 latency is longer (Jodo & Kayama, 1992; Thomas et al., 2009) or shorter (Mäntysalo, 1987) compared to Go N2 latency.

In the Stop-signal task, the frontcentral Stop N2 is typically larger to failed compared to successful stop trials and peaks approximately 210 to 220 ms after the presentation of the stop-signal (Bekker et al., 2005a; Bekker et al., 2005f; Dimoska & Johnstone, 2007; Dimoska & Johnstone, 2008; Dimoska et al., 2006; Dimoska et al., 2003; Johnstone et al., 2007; Kok et al., 2004; Logemann et al., 2013; Upton et al., 2010; van Boxtel et al., 2001). With respect to latency, the N2 has been reported to peak later for failed compared to successful stop trials (Dimoska et al., 2003; Ramautar et al., 2004). The amplitude of the Stop N2 may be related to the increased control of response processes (Folstein & Van Petten, 2008) given that it is associated with the probability of inhibition (Pliszka et al., 2000) and that larger Stop N2 amplitudes are seen when stop signals are rare (Ramautar et al., 2004). However, it has also been related to error monitoring (Dimoska et al., 2006), response conflict (Van Veen & Carter, 2002a) and task switching (Upton et al., 2010).

In the Eriksen-flanker task, the N2 peaks at around 200 to 450 ms post-stimulus onset (Johnstone & Galletta, 2013; Johnstone et al., 2009) and consistently shows enhanced frontal or frontocental amplitudes to incongruent compared to congruent stimuli (Gehring et al., 1992; Heil et al., 2000; Kopp et al., 1996; van Veen & Carter, 2002b Wang et al., 2013). There is some evidence that the flanker N2 is composed of two separate but functionally distinct N2 components: the first maximal to neutral flankers and believed to reflect detection of perceptual deviation (Gehring et al., 1992; Kopp et al., 1996), while the second may represent processes related to an increased requirement for cognitive control on incongruent trials (Folstein & Van Petten, 2008; Huster et al., 2013; Kopp et al., 1996). Johnstone and colleagues (2009) reported greater N2b amplitudes when stimuli were

degraded compared to standard flanker stimuli in children; an effect recently replicated in adults (Kóbor et al., 2014).

1.4.4 P3

The P3 is a positive component occurring approximately 300 to 600 ms post-stimulus. Similar to the N2, several ERP sub-components can be distinguished in the time range of the P3 (for a recent review see Polich, 2012), such that the P3 is currently identified as the "late positive complex" or LPC (Spencer et al., 2001), with at least three sub-components identified (Rushby et al., 2005).

First, the "classic P3" displays a centroparietal maxima with enhanced amplitudes (Johnson & Donchin, 1980; Mecklinger & Ullsperger, 1993; Polich, 1987; Squires et al., 1975) and increased P3 latency to attended stimuli that require stimulus categorisation (Duncan-Johnson, 1981; Kutas et al., 1977; Magliero et al., 1984; McCarthy & Donchin, 1981). This component shows a positive association with response time at parietal sites (Polich, 2007) and an inverse relationship with stimulus probability (Courchesne et al., 1977; Duncan‐Johnson & Donchin, 1977; Squires et al., 1975). However, the length of the inter-stimulus interval has also been shown to affect P3 amplitude independently of stimulus probability with shorter intervals resulting in larger P3 amplitudes (Polich, 1987). Several interpretations have been put forward to explain the functional significance of the classic P3, with the most influential being the 'context updating' hypothesis of Donchin and colleagues (1981; 1988) who suggest that the P3 reflects a mechanism that updates a model of the environment that is held in contextual memory. However, debate is ongoing as to whether the P3 instead indexes the closure of expectancies (Verleger, 1988), resource allocation/processing capacity (Kok, 2001) or a complex 'triarchic' combination of resource allocation, probability and uncertainty (Johnson, 1993).

Second, the “novelty” P3 is a frontocentral component evoked to rare non-target stimuli inserted unexpectedly as a third stimulus type (e.g. environmental sounds) during an otherwise standard oddball task (Courchesne et al., 1975; Squires et al., 1975). Despite showing a similar magnitude and latency to that of the classic P3 (Courchesne et al., 1975), this component readily habituates to repeated stimuli suggesting that it may be a cortical reflection of the orienting response (Rushby et al., 2005).

Third, the “P3a” is observed in response to rare stimuli (target or non-target) that are presented amongst frequent standards and infrequent target stimuli in the oddball task (Courchesne et al., 1975; Squires et al., 1975) . Typically, the P3a displays a frontocentral maxima and a relatively shorter peak latency compared to the novelty P3 (Debener et al., 2005; Friedman et al., 2001; Simons et al., 2001). Despite differences in the latency and topographic distribution of the novelty P3 and P3a, it has been argued that the P3a may instead be due to contributions from the classic P3 and novelty P3, and may not reflect separate components (Spencer et al., 2001). It has also been argued that the novelty P3 should be subsumed with P3a to describe a single component (collectively termed the P3a) whose topography varies as a function of attentional and task demands (Polich, 2007).

In the Go/Nogo task, the P3 is a positive-going component that has a more anterior topography to Nogo than Go stimuli (referred to as the “Nogo P3 anteriorisation effect”), and peaks approximately 300 to 500 ms post-stimulus (Albert et al., 2010; Albert et al., 2013; Bokura et al., 2001; Bruin & Wiers, 2002; Donkers & van Boxtel, 2004; Jodo & Inoue, 1990; Johnstone et al., 2007; Johnstone et al., 2005; Randall & Smith, 2011; Smith et al., 2013a; Smith & Douglas, 2011; Smith et al., 2004, 2006; Smith et al., 2007; Smith et al., 2008; Smith et al., 2010; Thomas et al., 2009). The Nogo P3 anteriorisation effect has been proposed to be a reproducible temporally stable electrophysiological index of Go/Nogo task performance (Fallgatter & Strik, 1999), with larger amplitudes reflecting better inhibitory

control function (Fallgatter & Strik, 1999); while the opposite is also true, with reduced frontocentral P3 amplitudes seen in situations of reduced inhibition capacity, such as with fatigue (Kato et al., 2009), sleep deprivation (Qi et al., 2010) and in psychopathological disorders characterised by inhibition deficits, such as ADHD (Fallgatter et al., 2005). The frontocentral Nogo P3 effect also appears to be *domain-general* and reliably evoked in auditory (Etchell et al., 2012; Johnstone et al., 2005; Smith & Douglas, 2011; Smith et al., 2006; Smith et al., 2007; Smith et al., 2008), visual (e.g. Albert et al., 2010; Albert et al., 2013; Bokura et al., 2001; Bruin & Wiers, 2002; Donkers & van Boxtel, 2004; Johnstone et al., 2007; Randall & Smith, 2011; Thomas et al., 2009) and audio-visual Go/Nogo paradigms (Falkenstein et al., 2002; Tekok-Kilic et al., 2001). There is evidence that P3 latencies in Go/Nogo tasks are modulated by stimulus type. Peak P3 latency is reliably longer for Nogo than Go stimuli (Filipović et al., 2000; although see for exception Nativ et al., 1992; Pfefferbaum & Ford, 1988; Pfefferbaum et al., 1985; Thomas et al., 2009), which is believed to reflect the increased processing demands required in response to Nogo stimuli (Fallgatter & Strik, 1999; Salisbury et al., 2004; Thomas et al., 2009).

In the Stop-signal task, the P3 component shows a central maximum that peaks approximately 300 to 500 ms post-stimulus and is larger to successful than failed stop-signal trials (Dimoska & Johnstone, 2007; Dimoska & Johnstone, 2008; Dimoska et al., 2006; Dimoska et al., 2003; Johnstone et al., 2007). The Stop P3 has also been reported to peak later for failed than successful inhibition trials (Bekker et al., 2005a; Kok et al., 2004; Ramautar et al., 2004). An effect, in line with the race model, where the late engagement of inhibitory process results in a failed stop (Logan & Cowan, 1984). The interpretation of the Stop P3 is subject to debate with some suggesting that it reflects the inhibition process (Dimoska et al., 2006; Kok et al., 2004; Ramautar et al., 2004), whereas others argue that the peak occurs too late , and that it may reflect the termination of the inhibition process, itself represented by the Stop N2 (Naito & Matsumura, 1996). This issue will be returned to in the next section.

In the Eriksen-flanker task, the P3 component is a centroparietal positivity that occurs 300 to 600 ms post-stimulus. Flanker type does not appear to consistently affect P3 amplitude: Kopp et al. (1996) reported larger central and parietal P3 amplitudes to incongruent relative to congruent flankers, an effect consistent with that described by Hajack et al. (2005). However, both Gehring et al. (1992) and Kóbor et al. (2014) found no difference in amplitude between flanker types, while Kopp et al. (1996) found no effect of flankers that were the same as the target stimulus (e.g. triangles) compared to those that were not (e.g. squares), compatible with the notion that P3 latency is an index of stimulus evaluation time for incongruent flankers (Polich, 2007).

1.5 Functional significance of the inhibition-related N2 and P3 components

The following section provides a review of the current functional interpretations of the N2 and P3 components in the context of inhibitory control.

1.5.1 The N2 component in inhibitory control tasks

In inhibitory tasks such as the Go/Nogo, Stop-signal and Eriksen-flanker, the N2 is frontocentrally maximal and is enhanced with task demands (!!! INVALID CITATION !!!). Increasing the time pressure via reaction time deadlines results in larger N2 amplitudes (Band et al., 2003; Jodo & Kayama, 1992). Furthermore, enhanced N2 amplitude has been reported to be associated with the effectiveness of inhibitory performance, with a larger N2 component coinciding with reduced commission error rates in Go/Nogo (Falkenstein et al., 1999) and Stop-signal tasks (Schmajuk et al., 2006), in addition to shorter SSRTs (van Boxtel et al., 2001). These results led early researchers to assume that the N2 was a marker

of more effective inhibitory control, such that it reflects a “red flag” signalling the need for subsequent inhibition (Kok, 1986) or that it may represent a pre-motor modality-specific inhibition process (Falkenstein et al., 1999, 2002). However, interpretation of the N2 purely in terms of inhibitory control has been challenged by further evidence showing enhanced amplitudes when no inhibition of a response was required. Nieuwenhuis et al. (2003) varied Go stimulus probability and showed that the N2 was increased for rare relative to frequent trials, irrespective of whether Go or Nogo response was required; an effect, corroborated by further research (Donkers & van Boxtel, 2004; Randall & Smith, 2011; Smith et al., 2010). In two-choice Go/Nogo paradigm the N2 is larger for invalidly cued than non-cued targets (Band et al., 2003). The inhibitory interpretation also predicts larger N2 amplitudes with more effective inhibitory performance (Falkenstein et al., 1999). However, further research has shown that the N2 is larger for failed than successful inhibition trials in Stop-signal tasks (Dimoska et al., 2006; Kok et al., 2004)

An influential review from Folstein and colleagues (2008) has indicated that the frontal N2 is not unique to inhibitory control paradigms, with similar N2 components being reported in response to errors where inhibitory control is not required, including the error-related negativity (ERN; Yeung et al., 2004) and feedback-related negativity (Hajcak et al., 2006). Forming a new classification of this waveform, Folstein et al. (2008) suggested that the N2 should be differentiated into three sub-components: (1) an anterior N2 linked to the detection of sensory mismatch (i.e. novelty) that is independent of cognitive control; (2) a further anterior N2 that is enhanced when cognitive control is required; and (3) an N2 component that shows a posterior maximum linked to variations in visual attentional processing.

With respect to sensory mismatch, Huster and colleagues (2013) have suggested that for this phenomena to occur in inhibitory control tasks the presentation of stimuli should not only be infrequent, but also novel. From this perspective, the N2 is elicited not only by the

need for inhibitory control, but by mismatch between the mental template of an expected compared to the actual event (e.g. rarely presented Nogo or Stop stimuli). However, Smith and Douglas (2011) reported that dissimilar tones evoke attenuated N2 amplitude compared to similar tones. If the N2 was driven solely by sensory mismatch, the N2 should have been enhanced to the dissimilar stimuli (Huster et al., 2013). In addition, the sensory mismatch hypothesis cannot explain why the N2 is also sensitive to response-related manipulations, where enhanced amplitudes are seen to overt rather than covert responses (Bruin & Wiers, 2002).

In the inhibitory control literature, the interpretation of the N2 as reflecting response conflict has gained ground in recent years to become the dominant theory (Smith et al., 2013). The response conflict hypothesis predicts that the N2 is increased to inhibition-evoking stimuli, not because of sensory mismatch or inhibitory control, but because of the detection of conflict between competing activated responses (Van Veen & Carter, 2002a; van Veen & Carter, 2002b). In the Go/Nogo task, conflict is generated to Nogo trials because they require a different response than expected. Similarly, this interpretation can also be applied to the presentation of stop-signals and incongruent stimuli, in Stop-signal and Eriksen-flanker tasks, respectively; given that that increased N2 amplitudes have been reported to failed stop-signal inhibition and incongruent flanker trials.

In summary, this review suggests that the N2 component for tasks indexing inhibitory control likely represents response conflict, but may also be modulated by novel stimuli or sensory mismatch.

1.5.2 The P3 component in inhibitory control tasks

The predominant interpretation of the P3 to inhibition-evoking stimuli is that it reflects the activity of an underlying inhibitory control network. As outlined in section 1.4.4, the Nogo P3 has consistently been shown to be enhanced to Nogo compared to Go trials, with this effect increasing with greater inhibitory demands such as when participants are required to increase response speed to Go stimuli (faster response increase the need for inhibitory control; Smith et al., 2006), with greater Go stimulus probability (Bruin & Wiers, 2002; Thomas et al., 2009), when the Go stimulus probability has been invalidly cued (Bruin et al., 2001; Randall & Smith, 2011; Smith et al., 2007), or when inhibition is unexpected (Smith et al., 2010). Although some researchers have argued that the larger P3 amplitudes for Nogo than Go trials is due to the resolution of the motor-related contingent negative variation (CNV), enhanced Nogo P3 amplitudes have been found to both overt and covert Nogo responses; suggesting that motor activity does not account for this effect. Recent reports corroborate these findings (Oddy et al., 2005; Smith et al., 2013; Smith et al., 2008). Moreover, the P3 is enhanced to inhibition-evoking stimuli in the Stop-signal task with larger P3 amplitudes found for successful compared to failed stop-signal inhibitions (Dimoska & Johnstone, 2008; Dimoska et al., 2006; Kok et al., 2004; Ramautar et al., 2004). Imaging evidence suggests tasks indexing prepotent response inhibition (GNG), action cancellation (SST) and interference (Eriksen-flanker) share a common underlying inhibition network including the right inferior frontal gyrus (rIFG) and the pre-supplementary area (for a review see Huster et al., 2013; Swick et al., 2008, 2011).

However, it has been argued that inhibition-related P3 component occurs too late to accurately correspond to the actual motor inhibition process (Beste et al., 2008; Beste et al., 2010; Bruin et al., 2001; Falkenstein et al., 1999; Huster et al., 2013; Naito & Matsumura, 1996; Roche et al., 2005b). For example, at the behavioural level in Stop-signal tasks, SSRT is estimated to have a latency of 200 to 250 ms (Logan & Burkell, 1986; Logan & Cowan,

1984), but the Stop P3 does not reach its peak amplitude until after 300 ms (Dimoska & Johnstone, 2007; Dimoska & Johnstone, 2008; Dimoska et al., 2006). The latency of the Nogo P3 has also been reported to be longer to overt reactions (Beste et al., 2008; Beste et al., 2010; Smith et al., 2006). Thus the P3 may actually represent an after-effect of inhibition, such as the monitoring of the inhibition outcome, rather than the inhibition process itself (Beste et al., 2008; Beste et al., 2010; Roche et al., 2005b; Schmajuk et al., 2006) . Outcome monitoring has been associated with the anterior cingulate cortex (ACC), which has been commonly implicated in the generation in both the Nogo P3 (Beste et al., 2008; Enriquez-Geppert et al., 2010; Huster et al., 2010; Huster et al., 2011a; Huster et al., 2011c) and Stop P3 (Kok et al., 2004; Ramautar et al., 2004).

In summary, this review suggests that the inhibition-related P3 components reflect the activation of an underlying inhibitory control mechanism, but may also receive contributions from attentional or outcome monitoring processes, potentially dependent on task demands.

1.6 Chapter summary

In this chapter, the concept of inhibitory control and its electrophysiological correlates have been discussed. Inhibitory control can be considered a crucial amalgam of abilities that serve to help us optimise our behaviour. In light of its importance in our everyday lives and the role it plays in the development of clinical disorders, the possibility of developing effective inhibition training paradigms as an adjunct to existing rehabilitation methods offers a promising avenue for the development of targeted remediation programs. Moreover, given that atypical brain activity often accompanies inhibition deficits, it is

important to uncover the underlying mechanisms behind training-induced performance improvements; this is the topic of the next chapter.

Chapter 2 - Training-induced changes in inhibitory control

2.1 The concept of neural plasticity

Neural plasticity refers to the brain's potential to anatomically change and reorganise in response to environmental challenges or demands (Lövdén et al., 2010). Apart from certain events, such as maturation, traumatic brain injuries, or deprivation, neural plasticity can be induced by the demands placed on it due to practice, training or learning (Enriquez-Geppert et al., 2013; Kelly & Garavan, 2005; Lövdén et al., 2010). These changes can either manifest in the modification of knowledge (e.g. improved strategies or skills) and/or available capacity of the underlying neural mechanisms (Enriquez-Geppert et al., 2013) resulting in improvements in behavioural performance (Kelly & Garavan, 2005; Markomichali et al., 2009).

Research within the last two decades has revealed that the neural processes which underlie our higher-order cognitive functions can change substantially as a result of practice and experience (Buonomano & Merzenich, 1998b; Kolb & Whishaw, 1998), overthrowing the long-held belief that the human brain is "hard-wired" and resistant to change (Tremblay, 2007). Plastic brain changes can occur at a variety of levels, from the synaptic to molecular, or the cortical level and large scale neural networks (for extensive reviews see Kelly et al., 2006b; Kelly & Garavan, 2005). Consequently, it has been suggested that further research into the training-induced changes in neural processing may not only extend theories of learning and skill acquisition, but also aid in the understanding of the mechanisms behind the repair and recovery of damaged or atypical brain processing (Cramer et al., 2011; Kelly

et al., 2006; Kelly & Garavan, 2005; Klingberg, 2010). However, despite a recent upsurge of investigations examining the training of other executive functions (e.g. working memory, attention, task switching; for reviews see Cramer et al., 2011; Green & Bavelier, 2008; Kelley & Yantis, 2009; Klingberg, 2010; Kujal & Näätänen, 2010), whether inhibitory control can be effectively trained and the neural underpinnings of training effects remains unresolved.

2.2 Training-induced neural changes

Several influential theories on the effect of training suggest that the shift from effortful to automatic expert performance entails changes in the processes that were already involved in the task. For example, Newell & Rosenbloom (1981) have postulated that practice results in *quantitative* changes, such that the same processes mediates both novel and skilled task performance by increased efficiency. At the neural level, decreases in activations or the topographic extent of activity have been suggested to indicate increased neural efficiency, corresponding to a sharpened neural network (for reviews see Enriquez-Geppert et al., 2013; Haier et al., 1992; Kelly et al., 2006a; Kelly & Garavan, 2005). However, the manifestation of quantitative changes has also been shown to result in increased activation and spatial extent, potentially reflecting the additional recruitment of cortical units for task performance (Klingberg et al., 2002; Olesen et al., 2004; Schapkin et al., 2007).

Other theories have, in contrast, suggested that performance on new tasks relies heavily on capacity-limited control processes; whereas, well-practiced tasks depend on automatic processes, which are not capacity limited. Specifically, as a result of training, there is a *qualitative* shift in processing such that slow, effortful, controlled processing is replaced by more automatic skills, which require less attentional resources, are more precise,

and interfere less with other tasks (Logan, 1988; Schneider & Shiffrin, 1977). At the neural level, two subtypes can be differentiated: redistribution and reorganisation of neural activations. Redistribution is said to reflect changes in the relative contribution of specific neural regions, but that the overall pattern remains the same. By contrast, a reorganisation is thought to be reflected by a different pattern of neural responding with training, such that for example, frontal activations are particularly apparent in the beginning stages of practice, but shift to more automatic parietal activations with growing expertise (Hill & Schneider, 2006)

These different perspectives have received support from the imaging and ERP literatures. Several imaging studies have found distinct brain regions involved in the performance of novel versus well-practiced tasks (Garavan et al., 2000; Landau et al., 2004; Milham et al., 2003). For example, Jansma, Ramsey, Slagter and Kahn (2001) demonstrated that practice in a verbal Sternberg task led to reduced activity in working memory-related regions (dorsolateral prefrontal cortex, right superior frontal cortex and right frontopolar area) and in the supplementary motor cortex. The amplitude of the N2 in a visual matching task has been reported to be enhanced with practice and associated with a reduction in RT (Cieslielski & French, 1989). However, others' have demonstrated a shift in activation and a restructuring of the underlying processes (Jueptner & Weiller, 1998; Peterson et al., 1998; Raichle et al., 1994). Different activation patterns within the primary motor cortex as a result of increasing practice have been reported in a complex finger movement task (Karni et al., 1995).

2.3 Inhibitory control training

The training of inhibitory control has been conducted in a number of different contexts leading to disparate results depending on the nature of the paradigm and effects considered. For this reason, this review has been divided into studies involving purely

behavioural measures and those investigating the training-induced changes in neural activity. Behavioural studies include those that either directly trained inhibitory performance or those that looked at more indirect effects, such as whether inhibition training to food, alcohol or gambling-related stimuli reduced subsequent behaviour. In the literature, *practice* has be differentiated from *training*, with practice denoting paradigms involving repeated exposure to a task, and training referring to paradigms involving the manipulation of task difficulty and/or performance feedback with the aim of improving task performance (Green & Bavelier, 2008; Jolles & Crone, 2012; Klingberg, 2010; Klingberg et al., 2002).

2.3.1 Direct training effects on inhibitory performance

Details of the following studies in this section are provided in Table 2.1.

In one of the first investigations of practice-related changes in the Stop-signal task, Logan and Burkell (Experiment 2; 1986) split participants into one of three groups that practiced on either a dual-task, Stop-signal or Stop-change paradigm. In all three tasks, the first stimulus was single letter and the second was a tone. In the dual-task paradigm, participants made a separate overt response to the tone while concurrently responding to the letter. In the stopping paradigm, participants tried to inhibit their response to the letter when they heard the tone. In the change paradigm, when the tone was presented, participants were instructed to inhibit their responses to the letter and make a separate overt response to the tone. All three groups performed a total of 4,320 letter-only and letter-plus-tone trials over a period of 6 days. Despite extensive practice, there was no significant change in performance (e.g. RT, errors, SSRT) in all three tasks; suggesting that Stop-signal performance is relatively stable over practice.

Dowsett and Livesey (2000) examined the training of inhibitory control in preschool children (aged 3 to 5). Based on their performance on a Go/Nogo discrimination task, 3-, 4- and 5-year children classified as “non-inhibitors” (i.e. those that were unable to inhibit their responses on 80% of Nogo trials) were subsequently allocated into either a no-intervention control group, a group that practiced on the Go/Nogo task, or another that performed “executive function training” (EFT) on the dimensional card sorting and change tasks. The training consisted of three sessions of 20 minutes and post-training performance gains were assessed using the original Go/Nogo task. The children in the EFT group demonstrated significantly greater performance improvements in the Go/Nogo task, compared to both the no-intervention control and Go/Nogo training group. It was suggested by the authors that the practice-related improvements were due to increased demands placed on the children in the EFT group.

Using a young (mean age 21 years) and older adult sample (mean age 70 years), Tomporowksi (2003) assessed age-related performance and subjective rating of workload during brief practice (single session, 6 blocks of 30 trials) of three tasks: Stop-signal, paced auditory attention (PATT) and attentional switching (AS) paradigms. The PATT showed no practice-related modulations, but both the young and older adults reported similar reductions in subjective workload for the PATT and Stop-signal task. However, practice did not improve performance in either task (e.g. errors, SSRT), implying that while repeated task performance grows subjectively easier with time-on-task, inhibitory control (as measured by SSRT) does not improve.

Over the course of five experiments using Go/Nogo and Stop-signal tasks, Verbruggen and Logan (2008) investigated whether automatic response inhibition may develop with practice when stimuli are consistently associated with each other. All five experiments consisted of a “training phase” with consistent stimulus-response mapping, and a “test phase” in which the stimulus-response mappings were reversed. The authors found

Table 2-1. Inhibition training studies using direct training measures of task performance. For this and subsequent tables, studies are grouped according to the year of publication, task type, training task parameters (trials, duration, difficulty), training results and whether transfer to untrained tasks occurred.

Study	Task	Sample	Comparison/ Control Groups	Recording Method	Trials	Training Duration	Task Difficulty	Individual differences, motivation, arousal workload, personality	Training Results	Transfer
Logan and Burkell (1986)	SST Dual-task Change-task	6 adults in each group	-	Perf	4320	6 days	SSD	-	No change in performance	-
Dowsett & Livesey (2000)	GNG Wisconsin Change-task	47 children (3 to 5 yrs)	Control No-intervention group	Perf	60	3 days	-	-	Nogo errors ↓	Performance ↑ on untrained Go/Nogo task
Tomporowksi (2003)	SST	13 young adults (20 to 23 yrs) 18 older adults (59 to 78 yrs)	-	Perf	180	Single session	SSD	Workload ↓	No change in performance	-
Verbruggen et. al. (2008)	GNG SST	~ 20 adults per study (age not reported)	-	Perf	800 to 1600	Single session	-	-	Go RT ↓ Nogo errors ↓	-
Thorell et al. (2009)	Go/Nogo SST Eriksen	64 children WM Inhibition Active control Passive control (Mean 5 yrs)	Active control Passive Control	Perf	15 minutes per day	5 weeks	RTD	-	Nogo errors ↓ Stop errors ↓ Incongruent errors ↓	No transfer to inhibition or WM tasks
Enge et al. (2014)	Go/Nogo SST Stroop	122 adults Adaptive training Non-adaptive control Passive control (Mean 21 yrs)	Non-adaptive control Passive control	Perf	Letter GNG 400 trials per day SST 400 trials per day	3 weeks Pre/post/ follow-up	Stimulus druation Nogo % SSD	Mood no differences	Adaptive Go RT ↓ > passive control at post & follow-up Adaptive SST RT ↓ > passive control at post & follow-up	No transfer to Stroop or fluid IQ

Note: GNG, Go/Nogo task; SST, Stop-signal task; Eriksen, Eriksen-flanker task; Perf, task performance; RT, reaction time; ↑, increase; ↓, decrease.

that responding in the test phase was slowed when stimuli had been consistently associated with stopping in the training phase. It was argued that with training, automatic processes progressively replace top- down inhibitory control due to consistent stimulus-stop mappings in the Go/Nogo task. By contrast, automatic inhibition is unlikely to occur in the Stop-signal task given that stimulus-stop mappings are inconsistent. Collectively, these results suggested that (1) inhibitory control can be trained in the Go/Nogo task, and (2) that the Go/Nogo and Stop- signal tasks may not be equivalent measures of inhibitory control because they elicit different forms of inhibition.

Thorell, Lindqvist, Bergman Nutley, Bohlin and Klingberg (2009) tested the effect of computerised training on either a visuo-spatial working memory task (WM) or three different inhibition paradigms (Go/Nogo, Stop-signal, Eriksen-flanker) for 5 weeks (20 minutes per day) in pre-schoolers (aged between 4 and 5 years). Training-related changes in performance were compared to both an active control group that played commercially available computer games, and a passive control group that only participated in the pre- and post-testing. The working memory training group showed significant training gains on the training tasks, as well as transfer effects on a Continuous Performance Task (CPT). Although, significant training gains were seen for all three inhibition tasks, no transfer effects were seen post-training compared to controls. Neither the WM or the inhibition training groups showed transfer effects on non-trained inhibition tasks. Although WM appears to show positive training and transfer effects, the authors suggested that the underlying inhibition-related neural processes may be resistant to training.

In a recent large-scale inhibition training study, Enge, Kliegel and Strobel (2014) recruited 122 young adults using a randomised double-blind pre/post/follow-up training design. Participants were dived into one of three conditions: either an adaptive training or non-adaptive training condition that trained participants on Go/Nogo and Stop-signal tasks for 3 weeks (9 total sessions; 400 trials per session for each task); or a passive control

condition that only performed the pre/post/follow-up measures. Training task difficulty was manipulated in the adaptive training condition by a reduction in stimulus duration and increases in Nogo proportion in the Go/Nogo task. An adaptive staircase method was used in the Stop-signal task. Training-related improvements and near-to-transfer were assessed using an untrained Stroop task, and far-transfer to fluid intelligence was indexed by the Ravens Progressive Matrices (RPM). Findings indicated that training resulted in faster reaction times in the Go/Nogo and Stop-signal tasks for the adaptive than passive condition; an effect, which remained stable at follow-up four months post-training (with no transfer to the RPM). Despite these results, further analyses found no performance differences when comparing the adaptive and non-adaptive conditions - either during training or at post-training/follow-up – leading the authors' to question whether 'true' transfer effects are possible after inhibitory control training. However, performance was excellent at baseline for the Stroop task, suggesting ceiling effects for this task – questioning whether this measure could adequately index pre vs. post changes. In addition, inadequate monitoring of participants response style, where they trade speed for accuracy in the Stop-signal tasks, can distort the estimation of stopping latencies (i.e. SSRT). Given that all participants showed significantly reduced Go RT in the Stop-signal task post-training, it can be questioned whether training-related gains were adequately measured - highlighting the importance of setting adequate task difficulty levels and task controls for the pre/post/follow-measures to effectively measure training effects.

2.3.2 Indirect behavioural inhibition training paradigms

Details of the following studies in this section are provided in Table 2.2.

Table 2-2. Inhibition training studies using indirect measures of training effects: subsequent food intake, alcohol consumption and gambling behaviours.

Study	Task	Sample	Comparison/ Control Groups	Recording Method	Total Trials	Training Duration	Task Difficulty	Individual differences, motivation, arousal workload, personality	Training Results	Transfer
Houben and Jansen (2011)	GNG	69 adults (rated as chocolate lovers) (Mean 20 yrs)	Chocolate-go Control	Perf	320	Single session	-	-	-	Chocolate consumption ↓
Houben (2011)	SST	29 adults (Mean 21 yrs)	Inhibition Impulsivity Control	Perf	288	Single session	-	-	-	Food consumption ↓
Houben et al. (2011)	GNG	52 adults (rated as heavy drinkers) (Mean 22 yrs)	Beer-nogo Beer-go	Perf	80	Single session	-	-	-	Alcohol consumption ↓ (Stable at 1 week follow-up) Negative attitudes to alcohol ↑
Jones & Field (2012)	SST	90 adults (Mean 21 yrs)	Alcohol-stop Alcohol-go Control	Perf	240	Single session	-	Impulsivity	Alcohol cues: RT ↑ errors ↓	Alcohol consumption ↓ (Not stable 1 week later)
Houben et al. (2012)	SST	57 adults (rated as heavy drinkers) (Mean 20 yrs)	Beer-nogo Beer-go	Perf	320	Single session	-	-	-	Alcohol consumption ↓ (Stable at 1 week follow-up) Implicit attitudes ↓
Verbruggen et al. (2012)	SST	179 adults (Mean 23 yrs)	No-stop Stop	Perf	720	Single session	-	-	Gambling risk ↓	Gambling behaviours ↓
Guerrieri et al. (2012)	SST	61 adults (Mean 21 yrs)	Inhibition Impulsivity Reading (control)	Perf	600	Single session	-	-	-	Impulsivity ↑ food intake
Bowley et al. (2013)	GNG	29 adults (Mean 21 yrs)	Beer-nogo Beer-go Active control	Perf	80	Single session	-	-	-	Alcohol consumption ↓ (not stable at 1 week follow-up)
Verbruggen et al. (2013)	SST	107 adults (Mean 21 yrs)	No-stop Stop	Perf	Experment 1: 840 Experiment 2: 2 x 720	Two sessions 24 hours apart	-	-	Gambling risk ↓	No change in gambling behaviours 24 h later

Note: GNG, Go/Nogo task; SST, Stop-signal task; Perf, task performance;; RT, reaction time; ↑, increase; ↓, decrease.

2.3.2.1 Food consumption

Houben and Jansen (2011) investigated whether brief training using a Go/Nogo task embedded with chocolate-related stimuli would alter subsequent chocolate consumption in trait chocolate lovers (assessed by the Attitudes to Chocolate Questionnaire, ACQ; Benton et al., 1998). Participants were randomly allocated into one of three conditions: (1) chocolate-nogo, where participants inhibited responses to chocolate stimuli, (2) chocolate-go, which required Go responses to chocolate stimuli, and (3) participants who responded to chocolate stimuli during half of the trials (control condition). The brief training consisted of 2 blocks of 160 trials. While subsequent chocolate consumption did not differ between the chocolate-go or control conditions, the chocolate-nogo condition showed significantly reduced consumption; suggesting that training-induced enhancements in inhibitory control.

In another study, Houben (2011) randomly allocated participants into one of three conditions: (1) an "inhibition" condition where high- calorie food items were systematically paired with the stop signal, (2) an "impulsivity" condition, where high-calorie food items were never paired with a stop signal, or (3) a control condition, where high-calorie food items were paired with the stop-signal on half the trials. Baseline inhibitory performance was assessed by a standard Stop-signal task with the study consisting of a single session of 4 blocks of 64 trials (25% stop-signals). The results revealed that baseline stop-signal performance mediated the results: "inhibition" training decreased subsequent food consumption, but only in participants with lower baseline inhibitory control. Conversely, the impulsivity manipulation increased food intake in participants with high levels of inhibitory control. The authors' suggested that
inhibition training can improve control over eating behaviour, but that it depends on the initial level of inhibition ability.

Building on the work of Houben (2011), Guerrieri, Nederkoorn and Jansen (2012) questioned whether the training of inhibitory control against overeating behaviours would be similarly as effective as training the opposite ability; impulsive eating. The training consisted of a single training session using a SST (six blocks of 100 trials each). Sixty one female participants were randomly allocated to either an inhibition condition, where stop trials were gradually increased (25% to 50% from block 1 to 6), an impulsivity condition where Go trials were incrementally increased across the session (75% to 100% by block 1 to 6), and control condition which were asked to perform a reading task for the same amount of time as the other two conditions. Results indicated that the impulsivity condition showed a higher post-training increase at a subsequent taste test. By contrast, there were no differences seen between the inhibition and control conditions; against previous positive findings (Houben, 2011) and questioning whether inhibitory control training can help reduce overeating behaviours.

2.3.2.2 Alcohol consumption

In the first investigations exploring the effect if inhibitory control training and alcohol intake, Houben, Nederkoom, Wiers and Jansen (2011) briefly trained heavy alcohol drinking participants on a Go/Nogo task (one block 80 trials). In one group (alcohol-go), Go stimuli were consistently paired with alcohol-related stimuli, whereas in the second group (alcohol-nogo), the Nogo stimuli were paired with alcohol-related stimuli. The results revealed that participants in the alcohol-nogo group had increased negative attitudes toward alcohol and significantly reduced weekly alcohol consumption, immediately post-training and also in the subsequent week (measured by self-report). These results demonstrated that the positive effect of relatively brief training can extend for at least a week after training. However, given that no post-training measure of inhibitory control was conducted, it is

unclear whether these results were mediated by improved inhibition mechanisms or implicit attitudes to drinking.

Building on previous work from this group, Houben, Havermans, Nederkoom and Jansen (2012) investigated the effect of short-term Go/Nogo training involving self-reported heavy drinkers. Participants were randomly assigned to either a beer/nogo condition, where alcohol-related stimuli were consistently paired with Nogo stimuli, or a beer/go condition where participants Go stimuli was paired with alcohol-related stimuli. Implicit attitudes towards beer, weekly alcohol intake, approach-avoidance actions towards beer and performance on a stop-signal task were measured pre- and post-training. The findings showed a significant reduction in the implicit attitudes and weekly alcohol intake in the beer/Nogo, but not the beer/go condition post-training. However, no significant change in stop-signal performance or action tendencies was found; in turn, suggesting that this form of training does alter higher-order inhibitory control. Rather the reduction in drinking was mediated by changes in implicit attitudes toward alcohol-related stimuli.

Jones and Field (2013) used a similar training procedure to Houben and colleagues (2011) but instead employed a Stop-signal task to try to identify whether this type of task would help to improve inhibitory control (rather than by changing affective associations). Participants were required to categorise alcohol-related and neutral pictures as quickly as possible but to inhibit their responses when they heard a stop-signal tone. In one group of participants, the majority of tones occurred during presentation of alcohol pictures (inhibition group), whereas for the other group, the tone was paired with neutral pictures (neutral group). The findings showed that the inhibition group displayed a progressive decrease in inhibition errors and slowing of reaction times to alcohol cues. Importantly, immediately after the training this group consumed less beer than controls, which suggests that this inhibition training in which participants learn to inhibit their responding to alcohol-related pictures had beneficial effects on drinking behaviour. However, unlike in the studies

reported by Houben et al. (2011), the positive effects of training were not seen at the follow-up one week later.

Bowley, Faricy, Hegarty, Johnstone, Smith, Kelly and Rushby (2013) used a modified Go/Nogo task similar to that used by (Houben, 2011; Houben et al., 2012) to investigate the effect of cue-specific inhibition training on ad-libitum alcohol consumption and other measures. In addition to the beer-go and beer-nogo conditions, Bowley and colleagues aimed to extend previous findings by adding an active control group that received a brief alcohol intervention (BAI) and included frontal EEG asymmetry as an objective measure of approach motivation. The results indicated that participants in the beer-nogo condition consumed significantly less alcohol than the beer-go condition and that the reduction was comparable to that seen in an active control group; suggesting that short-term inhibition training has similar effects to an established method of alcohol reduction in the BAI. However, this study also did not demonstrate beneficial effects of the training at 1-week follow-up. In addition, no significant changes in EEG asymmetry or implicit alcohol-related cognitions were found.

2.3.2.3 Gambling behaviour

Recently, Verbruggen, Adams and Chambers (2012) demonstrated that the training of proactive inhibitory control may help to diminish subsequent risky gambling behaviours. The authors' employed a modified Stop-signal training paradigm where participants were presented with six free-choice gambling options on each trial. Each option was associated with a certain amount to win, but the higher the amount wagered, the less probable the chance of winning (i.e. "no-stop" condition). On some blocks, in addition to gambling choice, participants were required to stop the planned gambling choice when a stop-signal occurred (i.e. "stop" condition). Results indicated that participants reduced risky gambling

choices in the stop compared to no-stop condition. It was hypothesised that the stop condition induced a general state of cautiousness that enhanced participants' inhibitory control; thereby reducing the chance of making risky decisions. Initially these promising results suggested that the far-transfer of inhibitory control to other domain was possible, which could open up new useful treatment avenues for addictive psychopathologies.

Unfortunately, a follow-up to this study by the same group (Verbruggen et al., 2013), found that the reductions in gambling choices were negligible 24 hours later; suggesting instead that the original results were simply a carryover effect whereby participants simply adopted short-term proactive control strategy, rather than a true improvement in an underlying inhibitory control network.

2.4 Combined behavioural and neural studies

Details of the following studies in this section are provided in Table 2.3.

Jodo and Inoue (1990) used an equiprobable Go/Nogo location task and reported that at baseline, the P3 peaked later for Nogo than Go trials, and P3 amplitude showed a parietal maximum for Go and a central maximum for Nogo stimuli, with a significant Nogo > Go effect at Cz. However, after six sessions of training, these effects were shown to change, such that the Nogo P3 peaked earlier than the Go P3, and the Nogo effect at Cz was no longer significant. Further analyses revealed that the Nogo P3 latency became shorter with practice while the Go P3 latency was unchanged. Accordingly, it seems that the training reduced the processing time required to inhibit the Nogo stimulus, as seen by the reduction in the latency of the Nogo P3.

Table 2-3. Inhibition training studies using task performance and neural indices.

Study	Task	Sample	Comparison/ Control Groups	Recording Method	Total Trials	Training Duration	Task Difficulty	Individual differences, motivation, arousal workload, personality	Training Results	Transfer
Jodo & Inoue, 1990	GNG	10 adults (Mean 22 yrs)	-	Perf ERP	1200	6 days	-	-	Go RT ↓ Nogo P3 latency ↓	-
Kelly et. al. (2006)	Sternberg + GNG	18 adults (Mean 28 yrs)	-	Perf ERP	800	Single session	Memory set of 5 letters (highest possible)	-	No change in performance dorso-lateral ↑	-
Schapkin et al. (2007)	GNG	8 adults (Mean 23 yrs)	-	Perf ERP	200 per day	15 days	Static; RTD 500 ms	-	Nogo errors↓ Nogo N2 ↑ (only after 3 days)	-
Manuel et al. (2010)	GNG	11 adults (Mean 29 yrs)	-	Perf ERP	528	Single session	Adaptive RTD	-	Go RT ↓ Nogo errors ↑ Left parietal ↓ (80 ms post-Nogo)	Tempero-parietal ↓ (80 ms post-Go)
Ditye et al. (2012)	SST	22 adults (Mean 24 yrs)	SST + tCDS Training Sham controls	Perf tDCS	1092 per day	5 days	Adaptive SSD	Impulsivity	SSRT ↓ in tCDS (not on 5th day)	-
Manuel et al. (2013)	SST	13 adults	-	Perf ERP	1020	Single session	Adaptive SSD	-	SSRT ↓ rIFG ↓ to Go pre-SMA ↓ basal ganglia ↓	-
Millner et al. (2013)	ERIKSEN Simon GNG Stroop	20 adults	-	Perf ERP		5 days	-	-	Simon RT ↓ GNG no change Sensitivity (D') ↑ Stroop, no change	ERIKSEN RT ↓ Incongruent N2 ↓
Berkamn et al. (2014)	SST	60 adults (Mean age 21 yrs)	Active training Sham controls	Perf fMRI	128 per day	10 days	Adaptive SSD	-	SSRT ↓ rIFG ↓ to stop-signal rIFG ↑to cues	-

Note: GNG, Go/Nogo task; SST, Stop-signal task ;Eriksen-flanker task, ERIKSEN; Perf, task performance; WM, working memory; IC, inhibitory control; min, minutes; RT, reaction time; ADHD, attention-deficit/hyperactivity disorder; RTD, reaction time deadline; ISI, inter-stimulus-interval; SSRT, stop-signal reaction time; SSD, stop-signal delay; SCL, skin conductance level. rIFG, right inferior frontal gyrus; pre-SMA, pre-supplementary motor area; ↑, increase; ↓, decrease.

Using fMRI, Kelly, Hester, Foxe, Shapner, & Garavan (2006b) investigated the effect of repeated presentation of a hybrid Sternberg/Go/No-Go and reported that prepotent response inhibition can be trained using relatively brief practice (a single session of 8 bocks,120 trials, 88% Go probability). The results indicated that, in the absence of practice-related changes in behavioural performance, brief practice resulted in increased activity in a number of regions previously associated with inhibitory processing (dorsolateral/inferior prefrontal and inferior parietal cortex). Notably, when participants were split into "good" and "poor" performers (based on the training-related reduction in inhibition errors); greater practice-related increases over inhibitory control regions were seen in the "good" compared to "poor" group. The authors suggested that practice-induced changes in prepotent response inhibition can be reflected by increases in brain activation.

Schapkin, Falkenstein, Marks and Griefahn (2007) considered the effect of practice on an equiprobable visual Go/Nogo task which contained either compatible or incompatible stimuli. Stimuli were the German words for denoting actions "druck" (press) and "stopp" (stop). To enhance stimulus-related conflict, participants had to perform a Go response after the word "STOPP" (uppercase) or "druck" (lowercase) and refrain from responding after "stopp" (lowercase) or "DRUCK" (uppercase). Task difficulty was set using a reaction time deadline of 500 ms for the duration of the training. For three consecutive weeks (except weekends; 15 days total) participants practiced the task using 200 stimuli each day. After three days, Nogo errors significantly decreased along with an enhanced frontal Nogo N2 effect; interpreted by the authors in terms of a training-induced increase in the activation of the underlying inhibitory control mechanism. Interestingly, these changes were not stable across the study, with no significant change in performance or the N2 effect being reported at the conclusion of the training. In addition, no training effects were found for the Nogo P3. However, this study suffered from a small sample size of only 8 participants, limiting confidence in its findings.

Manuel, Grivel, Bernasconi, Murray and Spierer (2010) investigated the training-related changes in performance and ERPs after 40 min auditory spatial Go/NoGo training, in addition to post-training responses during a passive listening of the same auditory stimuli used during the training. Using source analysis (local autoregressive average (LAURA) regularization; de Peralta Menendez et al., 2001; 128 channels), the results indicated that early neural responding to Nogo, but not Go stimuli, showed reduced activity over left parietal cortices at 80 ms post-stimulus during the active training condition. This decrease in brain activity correlated positively with the behavioral improvement in Go/Nogo proficiency (i.e. reduced Go RT). In a passive listening condition, the training modulated ERPs in response to Go stimuli 50ms, due to decreased right anterior temporo-parietal activity. These results led the authors to suggest that repeated stimulus-response associations between Nogo stimuli and response withholding resulted in automatic inhibition and decreased engagement of top-down inhibitory control with practice. However, given that authors did not include the Nogo N2 or P3 in their analysis, it can be questioned whether this was the case.

Ditye, Jacobson, Walsh and Lavidor (2012) explored the effect of transcranial direct current stimulation (tCDS) of the right inferior frontal gryus (rIFG) combined with 5 days of training on a Stop-signal task (25% stop-signals) compared to a sham control group. It was hypothesised that stimulation of the rIFG would enhance training effects given its role in inhibiting responses. For the first four days, the tCDS group showed significant reductions in SSRT compared to controls. However, by the fifth day no difference between the groups was found. It appears that while tCDS may enhance inhibitory control in the short-term but these effects are not long-lasting.

Following on from the previous Go/Nogo training study, Manuel, Bernasconi and Spierer (2013) employed a Stop-signal task to test whether a different form of inhibitory control (i.e. the inhibition of an ongoing response) would show training-related improvements. ERPs to Go stimuli were measured for the duration of a one hour training

session (1024 trials; 25% stop-signals). Task difficulty was manipulated using the adaptive SSD staircase method. Coinciding with a reduction in SSRT, regions previously associated with top-down inhibitory control including the right-IFG, pre-SMA and basal ganglia showed reduced EEG source activations to Go stimuli by the conclusion of the training session. The authors theorised that this effect reflected a top-down plastic change of the inhibitory control network. However, given that the source activations were quantified to Go stimuli (and not Stop), it can be questioned whether this reduction reflected a change in the proactive Go control strategies and not to inhibitory control. Moreover, this study did not include a control group so was unable to rule-out other reasons for reduced neural activity with time-on-task (e.g. fatigue, boredom).

Millner, Jaroszewski, Chamarthi and Pizzagalli (2012) trained participants for three days on the Simon (5 blocks of 74 trials per day) and an emotional Go/Nogo task (8 blocks of 90 trails per day). Pre- and post-training changes were assessed on two separate session using a battery of tasks assumed to index comparable interference control mechanisms including the Eriksen-flanker, emotional Stroop and a two-choice RT task. Participants showed a training-related increase in accuracy and reduced RT for the Simon task and improved sensitivity (i.e. D') for the emotional Go/Nogo task. Notably, these improvements appeared to transfer to an untrained Eriksen-flanker task; relative to pre-training, participants displayed reduced RT and N2 amplitudes to incongruent stimuli – highlighting a training-related improvement in interference control. Pearson's correlation between the change in RT and N2 amplitude showed that participants displaying the largest improvement in performance displayed the greatest reductions in N2 amplitude. No pre vs. post-training change were found for the emotional Go/Nogo, with a small improvement seen in the two-choice RT task, suggesting that transfer effects for this ability is limited. In addition, given that this study employed no control condition, and that reduced N2 amplitudes have been seen as a result simple stimulus repetition (e.g. Boksem et al., 2006), it is unclear whether the results represent a true transfer effect.

In a recent study using fMRI to investigate the effect of training in the stop-signal task, Berkman, Kahn and Merchnat (2014) randomly assigned participants to a Stop-signal training or an active sham-training control condition for 10 sessions across 3 weeks. Each trial began with a cue followed by a Go stimulus, with 25% of trials followed by a stop-signal only for participants in the training condition. Task difficulty was manipulated by an adaptive staircase stop-signal delay (SSD) method. SSRT improved to a greater degree in the training than control condition, indicating a larger training-related improvement of inhibitory control. Interestingly, participants in the training condition showed activation decreases in the rIFG to stop signals, but enhanced activation in this region to cues. Berkman et al. suggested that this result partially explains why previous inhibition training studies have generally failed to show transfer effects: to the extent that training creates an association between the activation of the inhibition network and task-related cues, training will not generalise to novel tasks that do not include the same cues as the training tasks.

2.5 Methodological considerations, integration of previous findings and thesis aims

From a review of the inhibition training literature, a major challenge for future work is to pinpoint which aspects are responsible for the enhancing inhibitory performance and processing. A major problem when determining the effectiveness of previous inhibition training paradigms is that the tasks, parameters, study design and methodological precision very widely from study-to-study, leaving an unclear picture of the performance and neural changes that should be expected as a result of training inhibitory control. I will consider these in turn and outline how they will be addressed in the current work.

2.6 Methodological considerations

2.6.1 The nature or "purity" of the training task

Existing training regimes have employed both single task (e.g. Go/Nogo; Jodo & Inoue, 1990) or multiple task paradigms that index broader inhibition domains (e.g. combined Go/Nogo, Stop-signal, Eriksen training; Thorell et al., 2009). In addition, the application of these paradigms has varied extensively in terms of aims, context and measures; from those indexing pure performance (e.g. Verbruggen & Logan, 2008), excessive food (e.g. Houben, 2011) and alcohol consumption (e.g. Houben, 2011), to risky gambling behaviours (Verbruggen et al., 2012). Due in large part to these variations, a review of the literature shows disparate results (see table 2.1, 2.2, 2.3). It is not clear whether any performance gains seen in inhibitory control, or the subsequent reduction of different behaviours (e.g. alcohol or food consumption, risky gambling behaviours), actually result from an improvement in an underlying inhibition mechanism; questioning whether inhibition can in fact be trained *at all*. Also, another question which is not clear is whether the particular type of inhibition task [e.g .planned inhibition (Go/Nogo) vs. inhibition cancellation (Stop-signal)] results in training-related gains and, if so, how they may be expressed? Performance (e.g. Verbruggen & Logan, 2008) and ERP measures (e.g. Johnstone et al., 2009a) show distinct differences in the manifestation of inhibitory control in general. Further, training effects may instead be simply due to altering automatic affective associations rather than inhibitory control (Bowley et al., 2013; Houben et al., 2012; Jones et al., 2013; Jones et al., 2011; Jones & Field, 2013; Verbruggen et al., 2013). Although determining the efficacy of a training paradigm is an important clinical goal, it is equally important that training studies provide key insights into the processes of cognitive plasticity and their underlying mechanisms to facilitate the optimal design parameters. The literature has lacked an objective and systematic investigation (indeed, true for the cognitive training

literature as a whole) as to the key variables required for training gains. Therefore, a major goal of future inhibition research should be to systematically isolate the key training variables to further the theoretical understanding of, whether, how, and to the extent, inhibitory control can be trained. A systematic validation of different combinations of training designs will be conducted in this thesis to further the literature (Study1, 2, 3 and 4). Importantly, within-study comparisons of different training paradigms as these relate to intensity (Study 2, 3) and task type (Study 4) will be key issues addressed in this thesis.

2.6.2 The adjustment of task difficulty

The idea behind task difficulty procedures is to keep the task challenging throughout the training phase, thereby maximizing performance gains. This rationale is driven by the assumption that plasticity is induced by a mismatch between the functional resources of a cognitive process and environmental demands (Lövdén et al., 2010). Supporting evidence stems from an increasingly strong literature showing enhanced executive function training gains on difficult compared to those conditions where task difficulty is set at low levels of capacity (Garcia et al., 2013; Klingberg, 2010; Klingberg et al., 2005; Klingberg et al., 2002; McNab et al., 2009; Olesen et al., 2004; Thorell et al., 2009; Wang et al., 2010). As to how inhibition task difficulty can be manipulated and whether this may enhance training gains in performance and neural activity remains unclear. Different variations of task difficulty will be addressed in all 4 studies of this thesis, resulting in increasingly clear conclusions as to the most efficient means in manipulating task demand to induce training gains.

2.6.3 The use of a control condition

To clarify the nature of performance and neural changes when training inhibitory control, it is important for the trained participants to be compared to a control group (Enge et al., 2014; Jolles & Crone, 2012; Klingberg, 2010; Shipstead et al., 2012). Although waitlist controls rule-out mere retest effects, an active control group additionally excludes more general intervention effects (i.e. the experience of testing) and expectancy effects (e.g. Oken et al., 2008). This appears to be a particular problem in the ERP inhibition training literature. The two studies which have shown reduced EEG source activations as a result of training in Go/Nogo (Manuel et al., 2010) and Stop-signal tasks trained participants used single-session training paradigms and the same stimuli throughout the testing without a control group (Manuel et al., 2013). However, ERPs responses habituate with simple repetition of stimuli in the absence of any performance changes (Ravden & Polich, 1998). Fatigue also results in reduced inhibition-related ERP amplitudes with time-on-task (Kato et al., 2009). The imaging literature also indicates reduced activations in inhibition-related regions with fatigue (Persson et al., 2013). Without a control group to compare to, reduced ERP amplitudes or source activations cannot be unambiguously interpreted; questioning whether these effects represent training-related modifications in inhibitory control at all. Throughout study 2, 3 and 4, this thesis included an active control group to help rule-out factors unrelated to changes in performance and neural activity.

2.6.4 Feedback

As previously discussed, *practice* has been differentiated from *training.* The term *practice* indicates protocols or paradigms that involve repeated exposure to a task, while training refers to paradigms providing performance feedback with the aim of improving task performance. Feedback is a key ingredient for positive training-induced effects (Green &

Bavelier, 2008; Jolles & Crone, 2012; Klingberg, 2010; Klingberg et al., 2002), but has yet to been included in the context of inhibition training (Houben, 2011; Houben et al., 2012; Houben et al., 2011; Jodo & Inoue, 1990; Jones et al., 2013).

2.6.5. Motivation, arousal, workload, fatigue and individual differences

The issue of training-related variations in task-related arousal, motivation and workload has been largely unexplored in the field of inhibitory control training. For the consideration of an effective control condition, these features need to be kept constant between conditions (Jolles & Crone, 2012; von Bastian & Oberauer, 2013). In the context of no performance changes in stop-signal training, perceived workload and motivation increases (Tomporowski, 2003). In addition, Dawson et al. (1990) have suggested that elevations in skin conductance level (SCL) reflects the effortful mobilisation of mental resources directed towards a task (for similar conclusions see Larue et al., 2011; Naccache et al., 2005; Thomas et al., 2009). If this is the case, the objective measurement of SCL would help to isolate whether training and control conditions are comparable. In addition individual differences in impulsivity may potentially interact with training-related gains in inhibitory performance (Horn et al., 2003).

2.7 Neural correlates of task difficultly and inhibitory control training

2.7.1 1inhibition-related N2 and P3?

In the inhibitory control tasks reviewed above, robust differences in the N2 and P3 components have been shown to be dependent on whether a response is to be executed or inhibited. The N2 is enhanced to inhibition-evoking stimuli for the Go/Nogo (Nogo > Go), Stop-signal (Successful > failed inhibition), and Eriksen flanker tasks (Incongruent > Congruent). Although initially interpreted as reflecting an underlying inhibition mechanism, the N2 is typically larger when inhibition fails than when it is successful in the Stop-signal task, which is evidence against a simple inhibitory interpretation of the N2. By contrast, the N2 as reflecting response conflict has gained ground in recent years to become the leading theory. The P3 is frontocentrally larger in Go/Nogo and Stop-signal tasks, with larger amplitudes seen over centroparietal regions seen in Eriksen task. As with the N2, debate is ongoing as to its functional significance, but it has increasingly been seen as representing the inhibitory mechanism itself.

The Nogo N2 has been consistently reported to be enhanced with task difficulty, such as in response to reduced reaction time deadlines and increased stimulus probability - making it difficult to inhibit responses on Nogo, Stop or Incongruent trials (e.g. Broyd, 2008; Bruin & Wiers, 2002; Jodo & Kayama, 1992). But given that this component likely reflects response conflict - and not inhibitory control – it is difficult to interpret increased N2 amplitudes in terms of training-induced improvement in inhibitory control with increasing task difficulty. A more useful component therefore to investigate the training-induced improvements that might be the frontocentral Nogo P3; given that it has increasingly been linked to inhibitory control in recent years (e.g. Randall & Smith, 2011; Smith et al., 2013a; Smith & Douglas, 2011; Smith et al., 2013; Smith et al., 2008; Smith et al., 2010). But

whether task difficulty modulates this component has either not been considered by previous research (Band et al., 2003; Jodo & Kayama, 1992); or the few investigations which have manipulated task difficulty have used a 50/50 Go/Nogo split (Jodo & Kayama, 1992; Smith et al., 2006); which may not reliably induce prepotent response inhibition (e.g. Braver et al., 2001; Tekok-Kilic et al., 2001). Baseline research is required to test whether and to what degree the Nogo N2 and P3 can be modulated by task difficulty (Study 1).

It is also clear that the literature does not paint a straightforward picture of how these components should change as a result of training inhibitory control. Previous research has either reported reduced Nogo P3 latency (Jodo & Inoue, 1990), increased Nogo N2 amplitudes (Schapkin et al., 2007) or did not included the N2/P3 in the analysis (Manuel et al., 2010); leading to an unclear picture of training-related effects. A systematic approach is needed comparing different levels of task intensity to reveal what electrophysiological changes result from inhibition training; providing proof of principle that this ability can be trained and how the relevant underlying processes change.

2.7.2 Early components – N1 and P2?

A yet to be considered issue is whether the early sensory components (Picton et al., 2000), such as the N1 and P2, modulate in response to task difficulty or as a result of training inhibitory control. The perceptual training literature has shown variable results: the N1 has been reported to be enhanced (e.g. Mishra et al.; Zhang et al., 2013) or reduced with training (Song et al., 2005; Song et al., 2007; Wang et al., 2010). The P2 decreases with task difficulty (Wang et al., 2010), but generally increases with training (Tremblay, 2007; Tremblay et al., 2014). However, whether this component is a marker of perceptual learning is under debate (Tremblay et al., 2014). How these components change with task difficulty

and training will be considered throughout this thesis; adding important results to the literature of their role, in general, and the resultant effects of training.

2.7.3 Training-related changes in amplitude and/or topographic distribution of ERP components?

Although the current literature suggests that inhibitory control is potentially subject to plastic changes, the underlying neural mechanisms remain largely unresolved. To-date there is no evidence of functional restructuring or redistribution of neural responding in the context of inhibition training, As discussed in section 2.2, training-related enhancements in inhibitory control could lead to the strengthening of the underlying mechanism, resulting in an a quantitative increase in neural responding; potentially via more coherent activation of the related brain units (Kelly & Garavan, 2005; Kelly et al., 2006; Schapkin et al., 2007; Tremblay et al., 2014). This is consistent with report of enhanced Nogo N2 amplitude after training (in combined WM and inhibition training Johnstone et al., 2010; Schapkin et al., 2007) and by further findings showing that the Nogo N2 was larger for good compared to poor inhibitors (Falkenstein et al., 1999). While the Nogo P3 has increasingly been seen as reflecting the inhibition process in recent years (e.g. Bruin & Wiers, 2002), little is known about how it varies with increasing task difficulty (as a predictor of increased inhibitory demand) or whether it is subject to training-related changes and changes in its topographic distribution.. By contrast, performance improvements in inhibitory control have been accompanied by a decrease in activation strength (Manuel et al., 2013; Manuel et al., 2010) and reduced latency of responding to inhibition-evoking stimuli. Such a pattern may follow from improved synaptic and/or neural efficiency (Haier et al., 1992), resulting in a decrease of the number of neurons required for task performance (Kelly & Garavan, 2005; Kelly et al., 2006; Poldrack, 2000; Song et al., 2002). Baseline research is required to test whether (and if so, to what degree) the Nogo P3 can be modulated by task difficulty, and whether

variations in training gains may be reflected by this component as an objective marker of training-induced improvement in inhibitory control.

The four studies of this thesis were designed to examine these possibilities. Given the potentially important role of task difficulty in eliciting training gains in performance and neural activity, the first study involves a between-subject comparison of the effect of one measure of task difficulty – reaction time deadline. The aim of this study was to provide important baseline task performance and ERP indications for the effect of task difficulty to inform further investigations in the effective design of inhibition training paradigms.

Chapter 3 - Study 1: Varying task difficulty in the Go/Nogo task: the effects of inhibitory control, arousal, and perceived effort on ERP components

Published as:

Benikos, N., Johnstone, S. J. & Roodenrys, S. J. (2013a). Varying task difficulty in the Go/Nogo task: the effects of inhibitory control, arousal, and perceived effort on ERP components. *International Journal of Psychophysiology, 87* (3), 262-272.

Abstract

Similar to other executive functions, inhibitory control is thought to be a dynamic process that can be influenced by variations in task difficulty. However, little is known about how different task parameters alter inhibitory performance and processing as a task becomes more difficult. The aim of this study was to investigate the influence of varying task difficulty, via manipulation of reaction time deadline (RTD), on measures of inhibitory control, perceived effort, and task-related arousal (indexed by Skin Conductance Level). Sixty adults completed a visual Go/Nogo task (70% Go) after being randomly assigned to one of three task difficulty conditions: High, Medium and Low, with RTDs of 300, 500 or 1000 ms, respectively. Results revealed incremental increases in Go/Nogo errors and greater perceived effort with increasing difficulty. No condition differences were found for arousal, but the amplitude of the Nogo N2 increased and peaked earlier with increasing task difficulty. In contrast, the Nogo P3 effect was reduced in the High condition compared to the Low and Medium conditions. Finally, the amplitude of N1 and P2 showed differential effects, with Nogo N1 increasing with task difficulty, while the Nogo P2 decreased. This study provides valuable baseline behavioural and ERP data for appropriately manipulating difficulty (via RTD) in Go/Nogo tasks – highlighting the potentially key role of not only the N2 and P3, but also the N1 and P2 components for task performance.

3.1 Introduction

Inhibitory control refers to the ability to successfully suppress thoughts, behaviour and irrelevant stimuli (Aron et al., 2004). Crucial for the proper functioning of many other cognitive capacities (Clark, 1996), inhibitory control is an important, but often unnoticed, feature of everyday life: Its effective execution potentially means the difference between safely crossing a busy road or endangering oneself to oncoming traffic.

Among the most commonly employed paradigms used to investigate inhibitory processing is the Go/Nogo task, which requires participants to respond to a frequently presented Go stimulus, while withholding a response to a rare Nogo stimulus. Event-related potentials (ERPs) to Go/Nogo tasks typically contain two inhibition-related components: an augmented N2 for Nogo relative to Go stimuli, primarily at frontal sites (e.g. Falkenstein et al., 1999; Fallgatter & Strik, 1991; Oddy et al., 2005), and a more anterior focus for the Nogo P3, where P3 is larger for Nogo than Go stimuli at frontal and central leads (Smith et al., 2006; Smith et al., 2007; Smith et al., 2008). The Nogo N2 has been suggested to reflect the pre-motor 'need' for inhibition (Kok, 1986), but more recent research has instead linked the N2 to response conflict (Donkers & van Boxtel, 2004; Nieuwenhuis et al., 2003). By contrast, the Nogo P3 has primarily been related to motor inhibition in recent years (Smith, Johnstone & Barry, 2006, 2007, 2008; Smith et al., 2010). But further work has also suggested that it may not be linked to inhibition itself, but more to the evaluation of the inhibitory process (Band & van Boxtel, 1999; Bruin et al., 2001). Notably, both components appear to be modulated by different neurobiological pathways (Beste et al., 2008; Beste et al., 2010) supporting the idea that they reflect different inhibition-related sub-processes.

Like other executive functions, inhibitory control is assumed to be a dynamic process that should be influenced by variations in task difficulty. However, relatively little is known about how different experimental parameters affect the behavioural and neural

underpinnings of this ability (Beste et al., 2010; Lindqvist & Thorell, 2009; Thorell et al., 2009). There are a number of key reasons why it is important to study the influence of task difficulty on inhibitory control. Firstly, from a clinical perspective, the nature of inhibition deficits can only be ascertained if the paradigms employed are sufficiently difficult to differentiate performance between clinical participants and healthy controls (Beste et al., 2010; Lindqvist & Thorell, 2009). Further, variations in task difficulty, in and of themselves, have been linked to differences in neural activation, leading to inconsistencies in the Go/Nogo literature (for a meta-analysis see Simmonds et al., 2008). Baseline ERP data are required to clarify these effects. Finally, the possibility of developing targeted inhibition training paradigms as an adjunct to existing rehabilitation programs may offer a potentially useful aid for individuals suffering from deficits in inhibitory control (for e.g. Attention-deficit/Hyperactivity disorder, ADHD; Johnstone et al., 2010; Thorell et al., 2009). Training outcomes in these studies may be enhanced if the approach taken is based on fundamental research into the optimal way to manipulate inhibition difficulty. Thus, studying how task difficulty influences inhibitory control is important from both a 'pure science' and applied perspective, and is the major aim of this study.

Previous research examining the influence of task difficulty on inhibition-related ERP components has been varied with respect to methodologies and findings. Jodo and Kayama (1992) manipulated task difficulty with reaction time deadline, asking one group of participants to respond within 300 ms of the Go signal, and another to respond within 500 ms. They reported an enhancement of the Nogo N2 only in the fast responders. Although this effect was interpreted as being due to increased inhibition difficulty, this was unable to be confirmed since no behavioural results for inhibitory performance were reported. In a subsequent investigation, Band, Ridderinkhof and van der Molen (2003) divided participants into one of two instructional conditions: a speed condition, where participants were required to respond as fast as possible, and a balance condition, where speed as well as accuracy was emphasised. The speed of response was found to modulate both inhibitory performance and

ERPs, with increased Nogo errors and Nogo N2 for the speed condition. In contrast to these reports, Smith et al. (2006), who separated participants into 'fast' and 'slow' responders via median split post-hoc, reported no differences for the N2.

Furthermore, despite clear effects being reported for the N2, the Go/Nogo literature examining the influence of task difficulty on the P3 is limited**.** Previous investigations have either not considered the P3 (Band et al., 2003; Jodo & Kayama, 1992), or have used a 50/50 Go/Nogo split (Jodo & Kayama, 1992; Smith et al., 2006) which may not reliably induce prepotent response inhibition, depending on the paradigm (e.g. Braver et al., 2001; Tekok-Kilic et al., 2001). Moreover, these studies have generally only employed two difficulty levels (i.e. low vs. high). Given that both theoretical viewpoints (e.g. Cognitive-energetic model; Sanders, 1983) and experimental findings (Wodka et al., 2009) have suggested performance improvements only during moderate rather than easy/hard difficulty levels, the use of the three task difficulty conditions in the present study allows examination of a range of effects, rather than simply assuming linear changes. Thus, one aim of this study was to extend previous research by clarifying the effect of task difficulty (as manipulated by reaction time deadline: RTD) on not only the N2, but also the P3, using a 70/30 Go/Nogo split and three difficulty conditions (Low, Medium and High).

Although the main focus of this study was the influence of task difficulty on inhibitory processing, the measurement of skin conductance level (SCL) - a well-established measure of central nervous system (CNS) arousal (Barry & Sokolov, 1993) - allows examination of the effect of arousal level on inhibitory performance and processing. A review of the literature suggests that arousal may amplify or improve task performance (for a discussion see VaezMousavi et al., 2007), which may be characterised by an inverted-U relationship, where moderate levels of physiological arousal result in optimal performance, with a deterioration in performance seen during low-or high-arousal levels (Yerkes & Dodson, 1908). Additionally, as initially proposed by Yerkes and Dodson (1908), optimal

arousal levels may depend on the difficulty of a given task. In line with the findings of Yerkes and Dodson (1908) are results showing that inhibition performance was optimised only at moderate inter-stimulus intervals (ISIs;Wodka et al., 2009). Further work by Barry et al. (2007) has reported that increased arousal, via caffeine ingestion, resulted in not only increased SCL, but also concurrent improvements in Go/Nogo performance. However, findings from research using similar tasks have been mixed, showing no relationship between arousal and performance (Barry et al., 2005; VaezMousavi et al., 2009; VaezMousavi et al., 2007). The paucity of errors in the previous studies may help to explain these results, and as such, the manipulation of task difficulty would ensure greater errors and help to more thoroughly explore the arousal/performance link.

3.1.1 The Present Study

In sum, this study sought to extend previous research by examining the behavioural and neural effects of varying task difficulty, via RTD, on inhibitory processing. To this end, we used a modified version of the Go/Nogo task that required the inhibition of a prepotent response during three task difficulty conditions: Low (1000 ms), Medium (500 ms) and High (300 ms). As mentioned above, the Nogo N2 and Nogo P3 have been associated with different aspects of response inhibition so the ERP analyses focused on these components. While no specific predictions were made for the early ERP components, given the potential modulatory effects of task difficulty on early stimulus processing (e.g. Miller et al., 2011), any differences found would be explored. Moreover, participants provided perceived effort ratings and we recorded skin conductance to assess the contribution of arousal on performance and processing.

3.2 Method

3.2.1 Participants

A total of 69 adults enrolled in the present study to fulfil an undergraduate course requirement, with three being excluded according to the selection criteria. To be included in the study, participants were required to refrain from caffeine for 2 hours prior to testing and have not taken any psychotropic substances (prescription or illegal) for 24 hours prior to testing, or no more than once a month in the previous six months. Participants were also screened for neurological disorders and all reported normal or corrected-to-normal vision.

The remaining 66 participants were randomly assigned to one of three conditions: Low, Medium or High task difficulty. Of these, data from 6 participants were rejected either due to excessive eye artefact (3 participants), technical problems (2 participants) or for failure to perform the task properly (1 participant). Therefore, 20 participants each were included in the final analyses for the Low (Low: 17 females, 3 males, mean age 21.23, SD 4.12), Medium (14 females, 6 males, mean age 21.5, SD 5.89) and High condition (14 females, 6 males, mean age 21.4, SD 3.32). All but 5 of the 60 participants were right-handed. The research protocol was approved by the joint University of Wollongong and Illawarra Area Heath Service Human Research Ethics Committee.

3.2.2 Task

Stimuli were generated using Presentation (Version 11.0; Neurobehavioral Systems, Albany, CA, USA). Each trial began with a central fixation cross (+) presented for a variable interval of 500-1000 ms (M = 750 ms), followed by the Go/Nogo stimulus presented in the centre of the screen for 200 ms. A blank screen then replaced the stimulus for a variable

blank period of 1250 – 1750 ms (M = 1250 ms). Within this period, participants in the High, Medium and Low task difficulty conditions were required to respond via a button press to Go stimuli within 300, 500 or 1000 ms, respectively (see Figure 3.1), or to refrain from responding to Nogo stimuli. Performance feedback was provided via the following fixation cross, which remained white for correct response, but changed to a red colour for incorrect responses. Incorrect responses (i.e. presses to Nogo stimuli during the variable blank period, omissions and responses outside the RTD) were recorded in order to calculate error rates. Only presses to the Go stimulus within the predefined response window were regarded as correct.

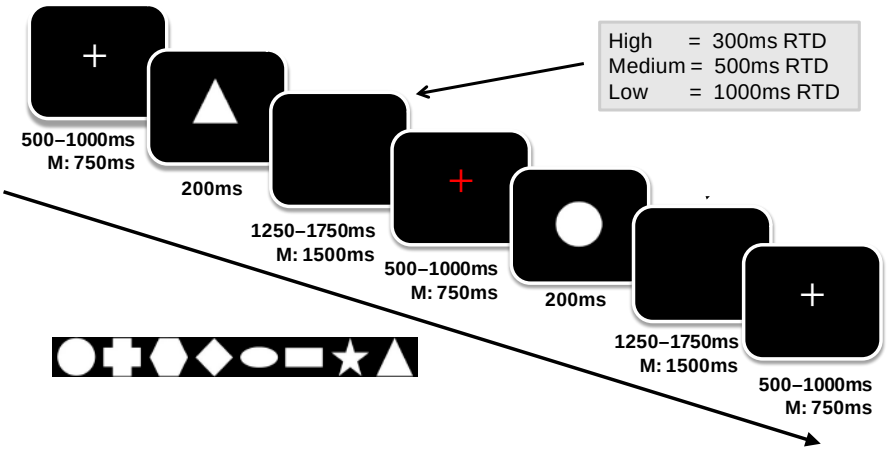


Figure 3-1. Schematic presentation of each task difficulty condition to Go (triangle) and Nogo (circle) stimuli.

After an initial practice block of 30 trials (50% Nogo), all participants completed eight experimental blocks (30% Nogo) of 100 trials each. Only data from the first two blocks is reported here. Target Go/Nogo stimuli for each block was selected from a pool of eight shapes (i.e. triangle, cross, hexagon, diamond, ellipse, rectangle, star and circle; see Figure 1) and were presented on a 15” computer monitor, with participants seated one metre from the screen. The stimuli measured approximately 3 x 3 cm on the screen. Presentation of

shape stimuli were counterbalanced using a Latin square design (Bradley, 1958), with Go/Nogo response assignment counterbalanced across participants. Total task time was approximately 43 minutes.

3.2.3 Procedure

Participants were given an outline of the testing procedure and familiarised with the laboratory equipment before informed consent was given. The experimenter emphasised that participants could withdraw at any time without penalty. They were then asked to complete a short screening questionnaire to assess vision problems, medication/psychotropic substance use, and neurological disorders. Participants were then fitted with EEG and skin conductance recording equipment, and seated in a dimly-lit sound-attenuated and electrically-shielded testing booth. An incandescent light in the booth was dimmed for the duration of the experiment. An initial 3 min baseline recording was conducted while participants were asked to sit quietly with eyes closed. Participants were then presented with a modified Go/Nogo task and were instructed that they would see either of two shapes, one representing the Go stimulus, and the other representing the Nogo stimulus. They were asked to press the button before the pre-determined RTD with the thumb of their right hand to Go stimuli, and to refrain from responding to Nogo stimuli. Performance feedback was provided by the following fixation cross, which changed from a white to red colour on incorrect trials (i.e. Go responses exceeding the RTD and presses to Nogo stimuli) and remained white on correct trials. Participants were asked to “do their best” to avoid the incorrect feedback, and were encouraged to keep as still as possible and to minimise eye movements during the testing blocks. Go/Nogo shape assignment was shown on the screen and verbally confirmed by the participant prior to each block. After a short practice block, all participants completed the experimental blocks. At the end of each block, mean Go RT, the percentage of Go and Nogo errors were displayed for participants to review. They were

then asked to rate their perceived level of effort with the question “How much effort did you use to complete that block?” and responded by a 5-point Likert scale ranging from: 1 = Very little, 2 = Moderate effort, and 5 = Everything I had. Prior to the first rating a basic example was shown to the participant to ensure understanding. Participants were given a short break at the end of each block and asked to continue on.

3.2.4 Electrophysiological recording

The continuous scalp electroencephalogram (EEG was recorded from 19 sites (Fp1, Fp2, F3, F4, F7, F8, Fz, C3, C4, Cz, P3, P4, Pz, T3, T4, T5, T6, O1, O2) using an electrode cap containing tin electrodes fitted according to the international 10-20 system (Jasper, 1958). A ground electrode located between Fpz and Fz, and all electrodes were referenced to linked ears. EOG was measured vertically with two tin cup electrodes, 1 cm above and below the left eye. Impedance was kept below 3 kΩ for EOG and reference electrodes, and below 5 kΩ for cap electrodes. EEG and EOG signals were amplified 19 times and sampled at 500 Hz, with bandpass down 3 db at 0.1 and 100 Hz via a NuAmps system (Compumedics Limited, Melbourne, Australia). Prior to processing, the EEG data were digitally filtered using a low-pass filter 3 db down at 30 Hz.

3.2.5 Skin Conductance recording

Electrodermal activity was recorded using two Ag/AgCl electrodes placed on the distal phalanges of the third and fourth digits of the left hand. Recording electrodes were filled with electrode paste (0.05 M NaCl in an inert viscous ointment base) and secured using velcro straps and tape. A constant voltage device (UFI Bioderm model 2701) set at 0.5 V was used. This system separately recorded tonic DC-coupled SCL and AC-coupled skin

conductance fluctuations (Skin Conductance Response; SCR), measured in microsiemens (μS). Only SCL is reported here.

3.2.6 Data Quantification

The ERP epoch was defined as 100 ms pre-stimulus to 900 ms post-stimulus onset. Epochs were excluded if they contained activity greater than ± 100 μV at any non-frontal site. EOG artefact reduction was carried out based on vertical EOG (Semlitsch et al., 1986). ERPs were averaged across epochs for correct responses only. This resulted in a minimum of 32 artefact-and-error-free Nogo trials being included in each average. Go epochs were averaged separately, chosen randomly from the available correct Go epochs to equal the number of Nogo epochs. Grand average ERP waveforms for Go and Nogo stimuli were displayed in order to define the components latency range. Latency was fixed across sites to the peak latency of the site of maximum amplitude (Picton et al., 2000; Spencer et al., 2001). ERP component peaks were quantified using automatic peak-picking software which identified the largest positive or negative deflections within the predefined latency range, relative to the 100 ms pre-stimulus baseline period. Peak latency ranges and sites were as follows: N1 (100 -160 ms Fz), P2 (180-240 ms Pz), N2 (200-280 ms Fz), P3 (280-520 ms Pz). Skin conductance level was taken as the average value (in μS) for each 30 sec period over the 3.5 min duration of each block of the Go/Nogo task.

3.2.7 Statistical analyses

The error rate (Go omission errors, RTD and Nogo errors) were calculated as the number of responses divided by the total number of presentations. Univariate analysis of variance (ANOVA) was used to analyse task performance perceived effort and skin

conductance level data with Condition (Low vs. Medium vs. High) as the between-subjects factor. Planned polynomial (Linear, Quadratic) contrasts were used to analyse differences within Condition.

Primary analyses of the ERP data were restricted to the sites F3, Fz, F4, C3, Cz, C4, P3, Pz and P4. Go and Nogo data were subject to a Condition [Low (L) vs. Medium (M) vs. High (H)] x Lateral (Left vs. Midline vs. Right) x Sagittal (Frontal vs. Central vs. Parietal) x Stimulus (Go vs. Nogo) ANOVA, with repeated measures on the within-subjects factors. Differences within Condition were assessed using polynomial contrasts (Linear, Quadratic). Analyses for component latency omitted the site contrasts. Planned orthogonal contrasts, which allow insight into the topographic distribution of each component, were performed on the within-subjects factors. The Lateral factor compared activity in the left hemisphere (mean of F3, C3 and P3) with the right (mean of F4, C4 and P4), and the mean of these with activity in the midline region (mean of Fz, Cz and Pz). Contrasts within the Sagittal factor compared frontal activity (mean of F3, Fz and F4) with parietal (mean of P3, Pz and P4), and the mean of these with activity in the central region (mean of C3, Cz and C4). As these contrasts were planned with no more of them than the degrees of freedom for each effect, no Bonferroni type adjustment to α were necessary (Tabachnick & Fidell, 1996). Also, single degrees of freedom contrasts are not affected by violations of symmetry assumptions common in repeated measures analyses, and thus do not require Greenhouse–Geisser-type corrections. As these analyses are carried out over a substantial number of variables, each may be considered to constitute a separate experiment. It should be noted that this increases the frequency of type 1 errors, however, as this is an increase in frequency, rather than probability, it cannot be ‘controlled’ by adjustment of a levels (Howell, 2009). All ERP statistics have (1,58) degrees of freedom unless otherwise indicated. Outliers in the data were corrected for by replacing with the series mean. Data were normalised using the vector scaling method (McCarthy & Wood, 1985), and only interactions with topography that remained significant in the normalised data are reported here.

3.3 Results

3.3.1 Manipulation check and perceived effort

As can be seen in Figure 3.2, participants perceived effort was greater in the High than Medium and Low conditions (Linear: $F = 6.64$, $p = .013$, $\eta 2 = .104$), suggesting that the difficulty manipulation was successful, with greater perceived effort seen with each increase in task difficulty.

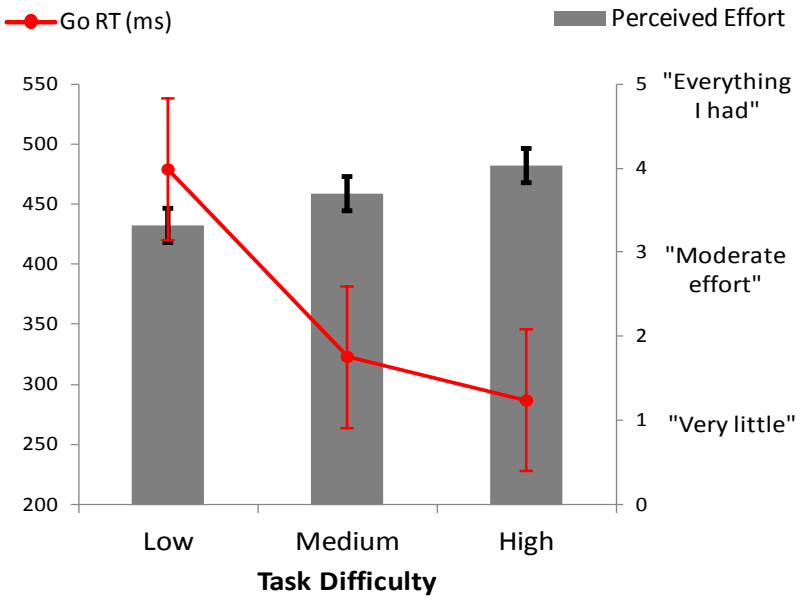


Figure 3-2. Reaction time and perceived effort ratings for each task difficulty condition. Error bars represent standard error of the mean.

3.3.2 Task performance

Means and standard deviations of RT and errors are summarised in Table 1. Consistent with our experimental manipulation, RT to Go stimuli decreased with each RTD reduction (L > M > H; Linear: $F = 403.55$, $p < .001$, $\eta 2 = .787$), with the steepest drop from the Low to Medium conditions (Quad: $F = 52.02$, $p < .001$, $\eta 2 = .101$).

Both Go RTD and omission errors (Go Om) showed linear (Go RTD: $F = 222.93$, $p < .001$, $\eta 2 = .673$; Go Om: $F = 38.80$, $p < .001$, $\eta 2 = .382$), and quadratic trends (Go RTD: $F = 51.31$, $p < .001$, $\eta 2 = .155$; Go Om: $F = 4.17$, $p = .046$, $\eta 2 = .043$), highlighting a steep increase in Go errors with increasing task difficulty, particularly apparent for the High condition. Inhibition performance showed a similar pattern, with incremental increases in Nogo errors with increasing task difficulty (i.e. H > M > L), with the greatest percentage of errors seen in the High condition (Linear: $F = 45.62$, $p < .001$, $\eta 2 = .423$; Quad: $F = 5.15$, $p = .027$, $\eta 2 = .048$).

Table 3-1. Summary statistics for task performance measures for each task difficulty condition.

	Task Difficulty		
	Low	**Medium**	**High**
RT (ms)			
Go RT	479.0	323.0	286.6
SDRT	87.4	67.4	57.7
Error rate (%)			
Go RTD	0.0	2.7	30.9
Go Omission	0.7	1.6	5.0
Nogo Errors	7.4	11.1	25.0

3.3.3 Skin conductance level

While SCL appeared to show a quadratic trend among task difficulty conditions (i.e. H/L > M), no significant differences were found between the High (12.49 µS), Medium (10.80 µS) or Low conditions (12.17 µS; Quad: $F = 1.90$, $p = .174$).

3.3.4 Event related potentials

Figure 3.3 presents grand mean ERPs to Go and Nogo stimuli across groups (top left panel) and for each condition separately (remaining three panels), with scalp distribution maps for each component in Figure 4. The waveforms are characterised by an N1-P2 complex, most apparent at frontal and central sites. An N2 component is apparent at about 270 ms primarily in the frontocentral region. Evident at approximately 300-400 ms post-stimulus, the P3 is a large positivity which peaks parietally for the Go condition and central-frontally for the Nogo condition.

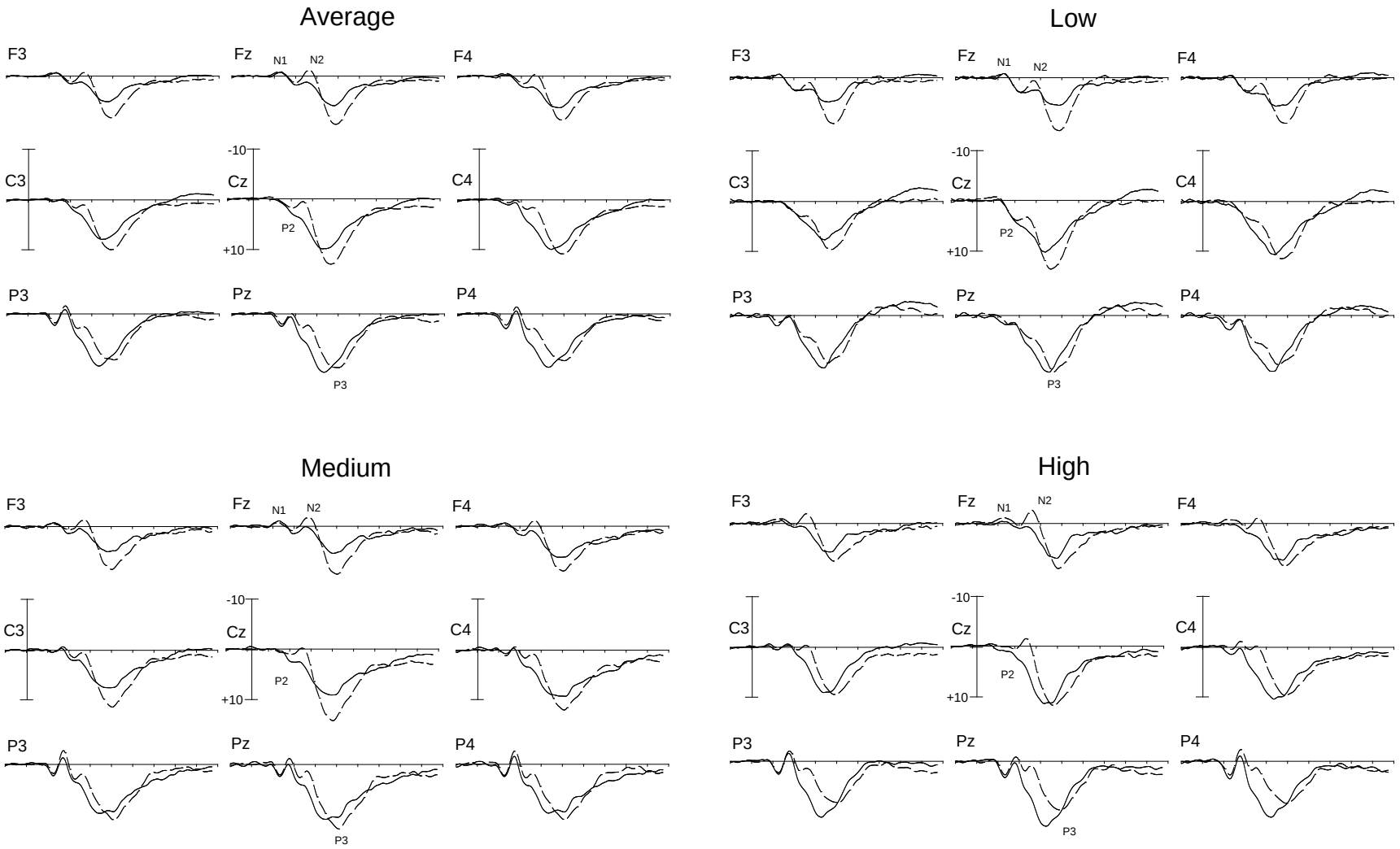


Figure 3-3. Grand mean ERPs to Go (solid line) and Nogo (dashed line) across condition (top left panel) and for each task difficulty condition separately (remaining three panels) at nine scalp locations.

3.3.4.1 N1

N1 peaked at 143.7 ms, with no condition differences for latency (Low = 139 ms, Medium = 144 ms, High = 147 ms).

The general topography of the N1 (i.e. across stimulus and condition) showed a frontocentral maximum, with a left-midline focus (see Table 3.2 for effect summaries and means). Between task difficulty conditions and across stimulus, the central > frontoparietal difference was reduced with increasing task difficulty (i.e. L > M > H), highlighting a larger N1 amplitude in posterior regions for the Medium/High, relative to the Low condition. On the Lateral dimension, the Low condition showed a large midline > hemispheres effect, in contrast to the Medium and High conditions, which displayed little hemispheric variation.

Notably, there was a significant difference for the N1 to Go vs. Nogo stimuli among the conditions. The Low condition showed a clear Go > Nogo N1, while this effect was reduced to be almost equipotential for the Medium condition, and reversed for the High condition (i.e. Nogo > Go N1; see Figure 3.4 for head maps and Figure 3.5, top left panel, for Go vs. Nogo comparisons).

3.3.4.2 P2

P2 peaked at 226.1 ms, with no condition differences in latency (Low = 231 ms, Medium = 224 ms, High = 222 ms), showed a parietal maxima, with a right > left effect also reaching significance (see Table 2 for effect summaries and means).

Table 3-2. Significant results for the early ERP components, the N1 and P2.

Measure	Effect	Contrast	Details	F	η^2
N1	S	f vs. p	-1.7 vs. 0.0	21.08***	.243
		c vs. f/p	-1.2 vs. -0.9	12.72**	.012
	L	l vs. r	-1.0 vs. -0.8	4.61*	.039
		m vs. l/r	-1.1 vs. -0.9	5.86*	.039
	S x Cond	Cz vs. Fz/pz	Low: -1.1 vs. -0.4		
			Med: -1.1 vs. -1.2		
			High: -1.4 vs -1.0	4.48*	.009
	L x Cond	m vs. l/r	Low: -1.0 vs. -0.5		
			Med: -1.2 vs. -1.1		
			High: -1.1 vs. -1.1	5.14**	.063
	Stim x Cond	Go vs. Nogo	Low: -1.1. vs. -0.2		
			Med: -1.2 vs. -1.1		
			High: -0.6 vs. -1.7	6.55**	.187
P2	S	f vs. p	2.3 vs. 5.4	51.47***	.430
	L	l vs. r	3.4 vs. 4.3	27.89***	.193
	Stim	Go vs. Nogo	4.6 vs. 3.4	12.58**	.146
	L x Stim	l vs. r	Go: 3.8 vs. 5.1		
			Nogo: 3.1 vs. 3.6	16.88***	.127
		m vs. l/r	Go: 4.8 vs. 4.4		
			Nogo: 3.4 vs. 3.3	5.60*	.030
	Cond	Low vs. High	3.3 vs. 5.4	5.29*	.085
	Stim x Cond	Go vs. Nogo	Low: 5.1 vs. 5.8		
			Med: 4.1 vs. 2.3		
			High: 4.5 vs. 2.1	8.34**	.193
	S x Stim x Cond	f vs. p	Low: Go, 3.5 to 6.2; Nogo, 3.7 to 7.2		
			Med: Go, 2.3 to 5.5; Nogo, 0.7 to 3.8		
			High: Go, 2.5 to 6.7; Nogo, 1.3 to 3.0	4.89*	.128

* = < .05, ** = < .01, ***= < .001

Details column represents mean amplitude in μV. Abbreviations for this and subsequent tables in this study: Cond, Condition: Low/Medium/High task difficulty. Low, Low task difficulty condition. Med, Medium difficulty condition, High, High difficulty condition. Stim, Stimulus type: Go/NoGo. Lateral (L) abbreviations: l, mean left hemisphere (F3, C3, P3); r, mean right hemisphere (F4, C4, P4); l/r, mean of the left and right hemispheres (F3, C3, P3, F4, C4, P4); m, mean of the midline (Fz, Cz, Pz). Sagittal (S) abbreviations: f, mean frontal (F3, Fz, F4); p, mean parietal (P3, Pz, P4); c, mean central (C3, Cz, C4); f/p, mean of frontal and parietal (F3, Fz, F4, P3, Pz, P4). Lateral by Sagittal (L x S) interactions: sites (e.g. f4) represent position on scalp (for e.g. frontal right hemisphere); f3/p3, mean of frontal and parietal left hemisphere; f4/p4, mean of frontal and parietal right hemisphere; fz/pz, mean of frontal and parietal midline; f3/f4, mean of frontal left and right hemispheres; p3/p4, mean of parietal left and right hemispheres; c3/c4, mean of central left and right hemispheres; f3f4/p3p4, mean of frontal and parietal left and right hemispheres.

Across the scalp, the P2 showed a Go > Nogo effect. On the Lateral dimension, both the right > left and midline > hemispheres effect was larger for the Go than Nogo stimuli, highlighting an enhanced Go relative to the Nogo P2 in the right hemisphere.

Globally, the P2 component was the largest in the Low condition and decreased linearly with increasing time pressure (i.e. L > M > H). Importantly, between stimuli (i.e. Go vs. Nogo), the Low condition showed a small Nogo > Go effect, while the Medium and High conditions displayed the opposite pattern – highlighting a reduction in the Nogo P2 with increasing task difficulty (see Figure 3.5). This effect was most apparent in posterior regions, with the Low condition showing a larger Posterior > Frontal effect for Nogo compared to Go (parietal vs. frontal difference: Nogo 3.5 vs. Go 2.7 μV), which was relatively equipotential for the Medium (Nogo 3.1 vs. Go 3.2 μV), and reversed for the High condition (Nogo 1.7 vs. Go 4.2 μV; see Figure 6 top panel).

In summary, the analyses of the early ERP potentials to Go/Nogo stimuli showed increased Nogo N1 amplitudes across the scalp with increasing task difficulty. However, the Nogo P2 declined with time pressure, showing the smallest amplitudes over posterior regions in the High condition.

3.3.4.3 N2

N2 (mean latency 272 ms) peaked earlier for Go (269 ms) than Nogo stimuli (276 ms; $F = 5.15$, $p = .007$, $\eta 2 = .085$), and decreased linearly with task difficulty, being shorter for the High (265 ms), than Medium (270 ms) and Low conditions (282 ms; $F = 10.24$, $p = .002$, $\eta 2 = .152$),

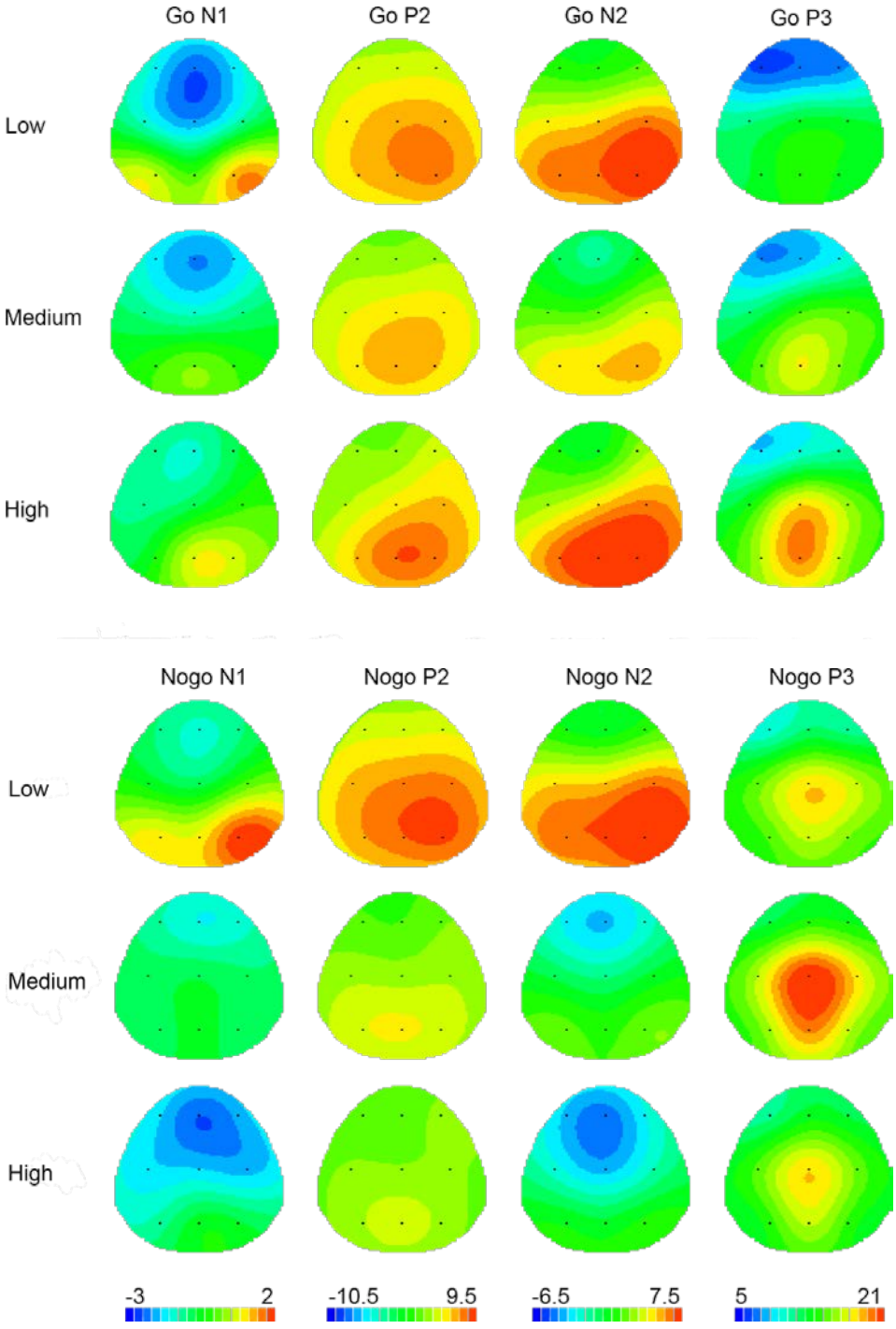


Figure 3-4. Topographic maps for each ERP component to Go (top panel) and Nogo (bottom panel) stimuli separately. Scale values represent the ends of the colour scale in μV for each component. Darkest blue = negativity, red = positivity.

The N2 showed a frontal maximum, and was larger in the left than right hemisphere, and greatest in the midline (see Table 3.3). N2 amplitude was larger to Nogo than Go stimuli, with the left > right effect being greater for the Go than Nogo N2, due mainly to an enhanced midline > hemispheres effect for the Nogo N2.

Table 3-3. Significant results for the N2 components.

Measure	Effect	Contrast	Details	F	η^2
N2	S	f vs. p	- 0.8 vs. 4.6	158.43***	.687
	L	l vs. r	1.6 to 2.8	46.49***	.242
		m vs. l/r	1.6 vs. 2.2	16.98***	.102
	Stim	Go vs. Nogo	3.5 vs. 0.4	46.86***	.343
	L x Stim	l vs. r	Go: 2.9 vs. 4.5		
			Nogo: 0.3 vs. 1.1	14.10***	.111
		m vs. l/r	Go: 3.3 vs. 3.7		
			Nogo: -0.2 vs. 0.7	19.43***	.079
	Cond	Low vs. High	4.1 vs. 1.1	9.22**	.139
		Med vs. High/Low	0.9 vs. 2.6	3.97*	.065
	Stim x Cond	Go vs. Nogo	Low: 4.0 vs. 4.1		
			Med: 2.5 vs. -0.8		
			High: 4.2 vs. -2.0	16.22***	.238
	S x Stim x Cond	f vs. p	Low: Go, 0.9 to 6.5; Nogo, 0.6 to 6.8		
			Med: Go, -0.4 to 5.2; Nogo, -3.3 to 1.6		
			High: Go, 1.1 to 7.2; Nogo, -3.9 to 0.4	3.25*	.075
		c vs. f/p	Low: Go, 4.7 to 3.7; Nogo, 5.1 to 3.7		
			Med: Go, 2.7 to 2.4; Nogo, -0.7 to -0.9		
			High: Go, 4.3 to 4.2; Nogo, -2.8 to -1.8	6.81**	.043

* = < .05, ** = < .01, ***= < .001

Linear and quadratic interactions revealed that N2 amplitude (i.e. Go + Nogo) increased with increasing task difficulty (i.e. H > M > L), which was characterised by a rapid rise from Low to Medium, but a relatively equipotential component for the Medium/High conditions. Notably, the Nogo > Go effect increased linearly with task difficulty (i.e. H > M > L), highlighting an augmented Nogo N2 across the scalp particularly for the High condition (see Figure 3.5). As shown in Figure 6, the High condition displayed an enhanced Nogo > Go N2 effect in parietocentral regions compared to the Medium/Low conditions. This is evidenced by a reduced frontal > parietal gradient (parietal vs. frontal difference: Nogo 4.3, Go 6.1 μV) and an increased central > frontal/parietal effect (central vs. frontal/parietal difference: Nogo 1.0, Go 0.1 μV) to Nogo compared to Go stimuli for the

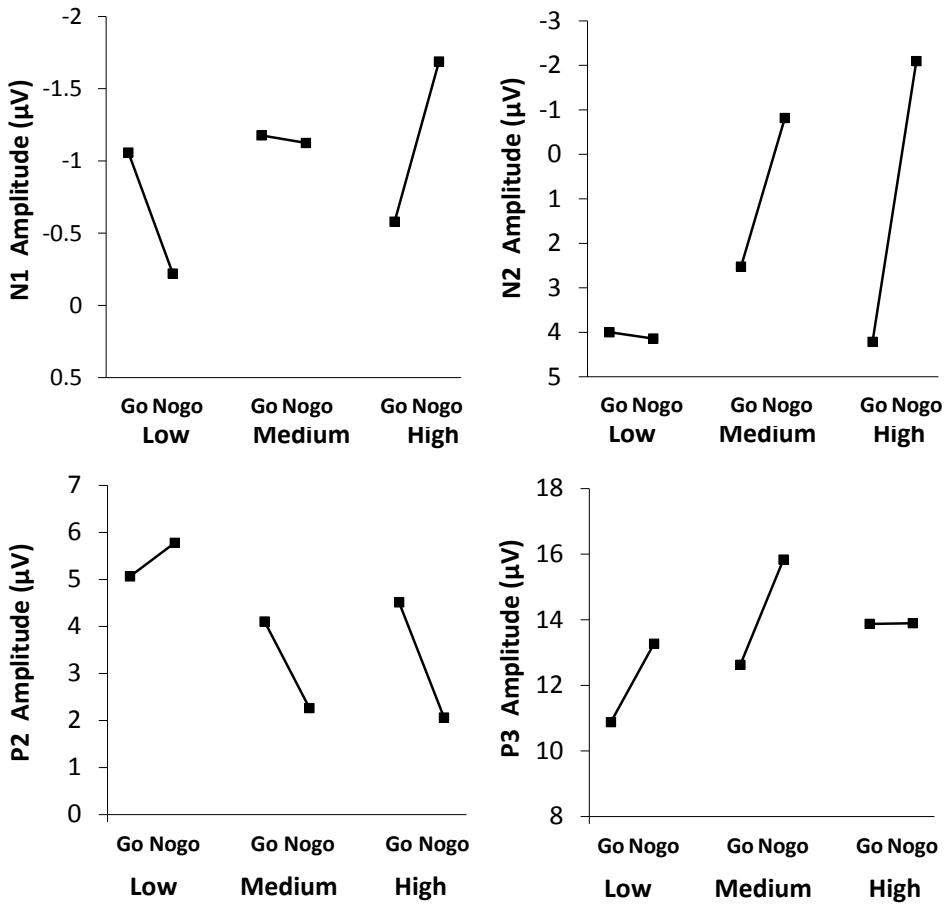


Figure 3-5. Go vs. Nogo amplitude across the scalp, by task difficulty condition, for the N1 (top left panel), P2 (top right panel), N2 (bottom left) and P3 (bottom right panel).

High condition, an effect which was reduced in the Medium (P vs. F diff.: Nogo 4.9, Go 5.6 μV; c vs. f/p: Nogo, 0.3, Go 0.3 μV) and relatively equipotential for the Low condition (P vs.F diff.: Nogo 5.8, Go 5.6 μV; c vs. f/p: Nogo, 1.4, Go 1.0 μV). The association between inhibition performance and the Nogo > Go N2 effect was evaluated by calculating Pearson's correlation between Nogo errors and the N2 effect (Nogo N2 – Go N2 at Fz, with larger negative scores indicating a larger Nogo > Go N2 effect). Results indicated an association between poorer inhibitory performance and larger Nogo N2 amplitudes (r = -.41, p = .001).

3.3.4.4 P3

P3 (mean latency 381.6 ms) peaked later for Nogo (401.8 ms) than Go stimuli (373.4 ms; F = 42.56, p < .001, η2 = .372). This effect differed between conditions: with the P3 peaking much later for Nogo than Go stimuli for the High (Go vs. Nogo difference: 52 ms) than the Medium (Go vs. Nogo difference: 15 ms) and Low conditions (Go vs. Nogo difference: 17 ms; F = 7.41, p = .001, η2 = .130).

The P3 showed parietocentral and right midline maxima (see Table 3.4) in the Sagittal and Lateral dimensions, respectively. P3 amplitude was globally larger to Nogo than Go stimuli. A reduced parietal > frontal gradient (parietal vs. frontal difference: Nogo 3.6, Go 7.1 μV) and an increased central > frontal/parietal effect in Nogo compared to Go stimuli (central vs. frontal/parietal difference: Nogo 2.8, Go 1.8 μV), highlighted a more anterior P3 to Nogo relative to Go stimuli. In addition, while the right > left effect was reduced for Nogo relative to Go stimuli, the midline hemisphere effect was increased.

Globally, the Nogo > Go P3 effect increased from the Low (Go vs. Nogo difference: 2.5 μV) to the Medium condition (Go vs. Nogo difference: 3.2 μV), contrasting with the

High, which showed little difference between stimulus types (Go vs. Nogo difference: 0.0 μV; Figure 5). The distribution of the Nogo > Go P3 effect also differed between conditions:

Table 3-4. Significant results for the P3 components.

Measure	Effect	Contrast	Details	F	η^2
P3	S	f vs. p	9.8 vs. 15.1	121.23***	.792
		c vs. f/p	14.8 vs. 12.5	113.89***	.202
	L	l vs. r	12.1 vs. 13.2	26.71***	.117
		m vs. l/r	14.4 vs. 12.7	99.73***	.381
	Stim	Go vs. Nogo	12.1 vs. 14.3	13.57**	.176
	S x Stim	f vs. p	Go: 8.0 vs. 15.1		
			Nogo: 11.6 vs. 15.2	54.34***	.376
		c vs. f/p	Go: 13.3 vs. 11.5		
			Nogo: 16.2 vs. 13.4	24.33***	.049
	L x Stim	l vs. r	Go: 11.0 vs. 12.4		
			Nogo: 13.2 vs. 14.0	5.24*	.038
		m vs. l/r	Go: 13.0 vs. 11.7		
			Nogo: 15.8 vs. 13.6	28.07***	.141
	Stim x Cond	Go vs. Nogo	Low: 10.8 vs. 13.3		
			Med: 12.6 to 15.8		
			High: 13.9 vs. 13.9	3.34*	.086
	S x Stim X Cond	f vs. p	Low: Go, 6.3 to 12.2; Nogo, 10.3 to 14.2		
			Med: Go, 8.4 to 16.0; Nogo, 12.6 to 16.9		
			High: Go, 9.4 to 17.0; Nogo, 11.8 to 14.4	3.35*	.046
		c vs. f/p	Low: Go, 11.1 to 9.3; Nogo, 15.3 to 12.3		
			Med: Go, 13.5 to 12.2; Nogo, 18.0 to 14.8		
			High: Go, 15.3 to 13.2; Nogo, 15.5 to 13.1	4.41*	.018
	L x Stim X Cond	m vs. l/r	Low: Go, 10.2 to 9.7; Nogo, 14.3 to 12.8		
			Med: Go, 13.3 to 12.3; Nogo, 17.6 to 14.9		
			High: 15.3 to 13.2: Nogo, 15.4 to 13.1	6.84**	.069

* = < .05, ** = < .01, *** = < .001

the Nogo relative to the Go P3 showed a more anterior focus for the Medium (parietal vs. frontal difference: Nogo 4.2, Go 7.6 μV; central vs. frontal/parietal difference: Nogo 3.2, Go 1.3 μV) than the Low condition (parietal vs. frontal difference: Nogo 4.2, Go 6.0 μV; central vs. frontal/parietal difference: Nogo 1.5, Go 3.0 μV), with this effect being reduced for the High condition (parietal vs. frontal difference: Nogo 2.6, Go 7.6 μV; central vs. frontal/parietal difference: Nogo 2.2, Go 2.1 μV). This effect highlights a reduction in centroparietal Nogo P3 activity for the High condition (see Figure 6). Similarly, on the Lateral dimension, a midline > hemispheres effect for Nogo relative to Go stimuli increased slightly from the Low (Mid. vs. Hem. diff.: Nogo 1.5, Go 0.5 μV) to the Medium condition

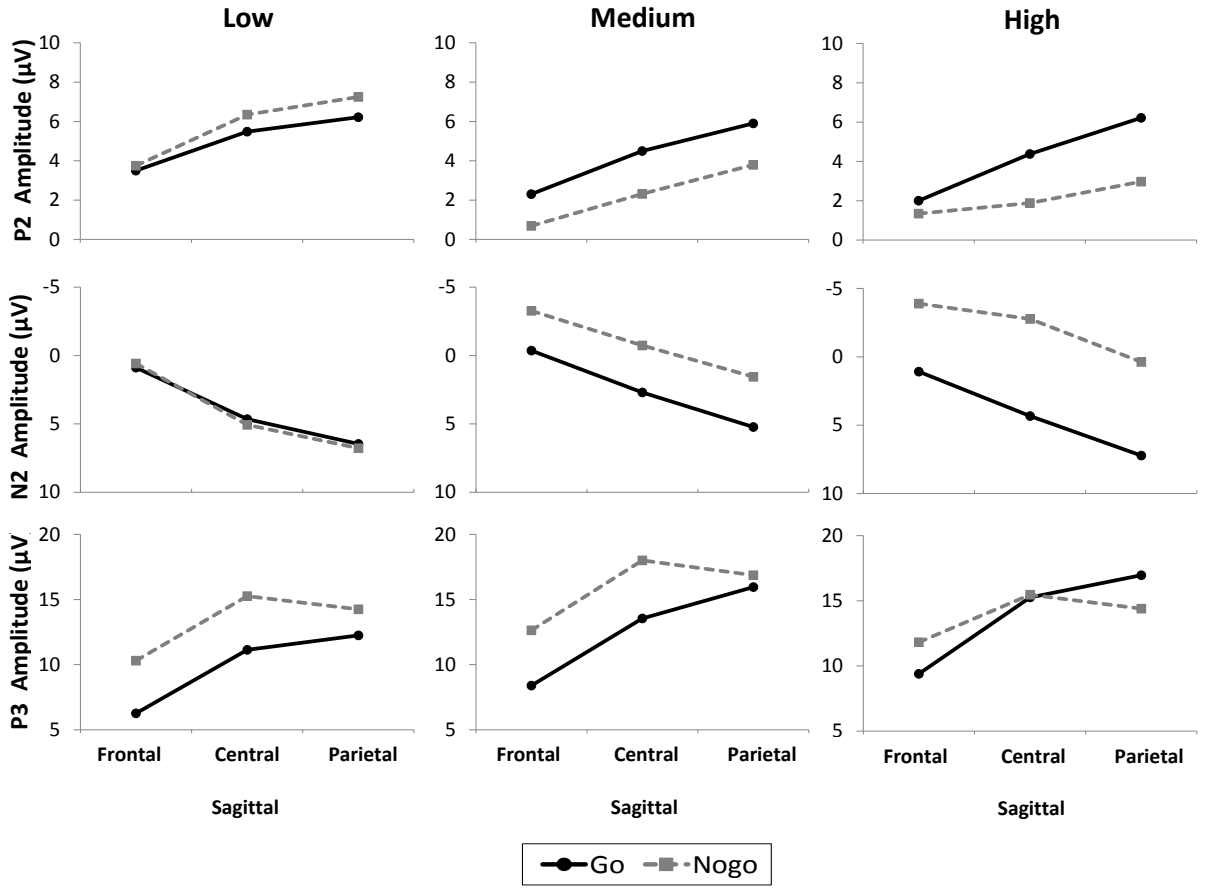


Figure 3-6. The Stimulus x Sagittal x Condition interactions for P2 (top panel), N2 (middle panel) and P3 amplitude (bottom panel). Note: Frontal= mean of F3, Fz, F4; Central = mean of C3, Cz, C4; Parietal = mean of P3, Pz, P4.

(Mid. vs. Hem. diff.: Nogo 2.7, Go 1.0 μV), but was reduced for the High (Mid. vs. Hem. diff.: Nogo 2.3, Go 2.1 μV).

In summary, the Nogo > Go N2 effect increased incrementally and peaked earlier as a function of task difficulty, with the largest amplitudes and shortest latencies in the High condition. By contrast, while the Nogo > Go P3 effect increased from Low to the Medium condition, it was significantly reduced for the High condition. Differences in the distribution for the Nogo > Go P3 effect were most apparent frontocentrally between the Low and Medium conditions, while the High showed a reduction in Nogo P3 activity in the centroparietal region.

3.4 Discussion

The primary aim of this study was to examine the influence of varying task difficulty, by the use of reaction time deadline, on the behavioural and ERP indices of inhibitory control during performance of the Go/Nogo task. In addition, we investigated whether the effect of task difficulty would also extend to the early ERP potentials, task-related arousal and perceived effort.

3.4.1 Task Performance

Our results indicate that task performance was significantly affected by variations in task difficulty. Specifically, Go and Nogo errors incrementally increased with each increase in task difficulty (i.e. RTD reduction: Table 3.1), with the greatest number of errors in the High condition. Importantly, modulations in task difficulty were also reflected by concurrent increases in perceived effort (Figure 3.2), consistent with the idea that greater effortful

control is required when the need to inhibit is high (Jodo & Kayama, 1992). Since previous research has either not utilised graded task difficulty levels (for e.g. Band et al., 2003; Smith et al., 2006), or did not report task performance data (Jodo & Kayama, 1992), these results provide clear self-report and behavioural evidence that Go/Nogo task difficulty can be incrementally increased by the use of RTDs.

3.4.2 SCL Arousal

Arousal level did not differ among conditions and did not appear to be related to task difficulty or performance in the present study. Combined with the findings of cumulative increases in Go/Nogo errors with increasing task difficulty, this SCL result differs from previous work suggesting that arousal is dependent on the difficulty level of a given task (Yerkes & Dodson, 1908). It is interesting to note, however, that arousal level was not completely static among conditions, with a tendency for arousal to show a Low/High > Medium effect – in line with previous work suggesting increased arousal levels during slow/fast, relative to medium speeds of presentation (Sanders, 1983). Alternatively, a more complete explanation might be in regard to the use of skin conductance level as a measure of arousal in the current research. In a series of studies, Barry and colleagues (e.g. Barry et al., 2005) experimentally differentiated between 'arousal', referring to the current energetic state of an individual, and 'activation', which refers to the task-related mobilisation of arousal. Notably, arousal was not found to be related to any of the performance variables, but instead, task-related activation significantly determined improvements in both reaction time and errors. Recent work by this group has also reported the classic inverted-U relationships between task-related activation and performance in a variety of tasks (VaezMousavi & Osanlu, 2008; VaezMousavi et al., 2009). Thus, it might be advantageous in future research to employ measures of task-related *activation* to more thoroughly explore the influence of task difficulty on arousal/activation.

3.4.3 Early ERP Findings

Although the primary aim of this study was to investigate the influence of a task difficulty manipulation on the inhibition-related ERP components of the N2 and P3, we report significant condition effects for the early exogenous potentials of the N1 and P2. Specifically, while the Low condition showed a Go > Nogo N1 effect across the scalp, this effect was reversed and increased with task difficulty, to show a large Nogo > Go effect for the High condition (see Figure 3.4 for head maps and Figure 3.5 for Go vs. Nogo plots). Previous examinations linking N1 and RT have produced mixed results: Bahramali, Gordon, & Li (1998) and Karlin et al., (1971) reported a larger N1 with fast responses, while Starr, Sandroni, and Michalewski (1995) found no significant differences. The N1 component is generally thought to represent the initial sensory extraction of, and attention to stimuli (Näätänen & Picton, 1987a), while previous investigators have interpreted an increased N140 to NoGo stimuli as reflecting an early manifestation of inhibitory processing (Nakata et al., 2004). Therefore, an enhanced Nogo N1 may reflect the greater visual resources required for inhibitory processing as a function of task difficulty - potentially indicating that the early extraction of stimulus information can be modulated by task demands (Miller et al., 2011), with implications for information processing at later stages (Smith et al., 2004).

While typically considered an exogenous component, the functional significance of the P2 in Go/Nogo tasks has yet to be resolved (Benikos & Johnstone, 2009; Wiersema et al., 2006). In discrimination paradigms, the P2 is thought to be involved in the protection against interference from irrelevant stimuli (Garcia-Larrea et al., 1992), giving the imperative stimulus a clear path for further processing (Oades, 1998). Ross and Tremblay (2009) posit that enhanced parietal P2 amplitudes reflects the physiological processes associated with improved task performance – an interpretation in line with reports of larger P2s with concurrent reductions in reaction time (Johnstone et al., 2005; Tonga et al., 2009) and

commission errors (Johnstone et al., 2005; Kenemans et al., 1993; Smid et al., 1999). In line with this, the Low condition showed a slightly larger Nogo than Go P2; in contrast to the Medium and High conditions, which displayed a large reduction in Nogo P2 amplitude primarily in posterior regions. Since larger P2s have also been linked to deliberately initiated actions (Kühn et al., 2009), it is possible that with sufficient time to respond, participants in the Low condition were more able to appropriately respond to Go/Nogo stimuli. In contrast, despite the enhanced activation of the Nogo N1, increased task difficulty in the High conditions could have reduced the ability of these participants to suppress extraneous stimuli and inhibit responses. These results are consistent with previous research suggesting that although the primary emphasis in the response inhibition literature has been the N2/P3 complex, earlier waveform components such as the N1 and P2 may play an important role in inhibition success (Roche et al., 2005b; Thomas et al., 2009). It thus seems reasonable to suggest that the Nogo P2 reductions seen in this study are largely due to task difficulty effects, and could be linked, in part, to impairments in inhibitory processing and declines in performance.

3.4.4 Inhibition-related ERP components

Across conditions, we replicated the well-known inhibition-related effects of increased N2 amplitudes and a more anterior P3 to Nogo relative to Go stimuli (Eimer, 1993; Kenemans et al., 1993; Oddy et al., 2005). Go N2 peaked earlier than the Nogo N2 (Jodo & Kayama, 1992), while the reverse was found for the P3 (i.e. Nogo P3 > Go P3 latency; Fallgatter & Strik, 1991; Salisbury et al., 2004). Finally, the current study also reports globally enhanced N2 amplitudes with increasing task difficulty, in line with previous research linking larger N2 peaks with faster responses (Bahramali et al., 1998; Starr et al., 1995).

3.4.4.1 N2

The Nogo > Go N2 effect was larger (Figure 3.5) and occurred earlier with each increase in task difficulty, as has been reported in previous studies (Band et al., 2003; Falkenstein, 2006). Since previous research by Jodo & Kayama (1992) did not report behavioural data, this study demonstrates that graded increases in task difficulty (via RTD) are reflected by incremental amplitude increases and reductions in Nogo N2 latency. In a frequently cited study, Falkenstein et al. (1999) reported that the Nogo N2 was larger and earlier in good compared to poor inhibitors (as measured by the number of commission errors), interpreted as due to a stronger and earlier inhibition process by the good inhibitors. In contrast, the present study reports the opposite effect (i.e. shorter latencies and increased Nogo N2 amplitudes) for the high difficulty condition, which showed the greatest number of inhibition errors. Given the significant correlation indicating an inverse relationship between Nogo N2 amplitude and inhibition performance, this argues against the interpretation of the Nogo N2 as pre-motor index of inhibitory control (e.g. Kok, 1999). Recently, however, evidence linking the N2 to response conflict has been accumulating (Smith, Johnstone & Barry, 2007, 2008; Smith et al., 2010). The conflict theory of N2 predicts increased competition between Go and Nogo representations on correct trials when participants are required to emphasise speed over accuracy (van Veen & Carter, 2002b). Thus, it might be that variations in the amplitude N2 reflect incremental increases in response conflict with task difficulty, rather than inhibitory control.

It is noteworthy to report that the Nogo N2 also appeared to change its distribution with enhanced difficulty, displaying an increased Nogo > Go N2 effect at centroparietal regions for the High condition (Figure 3.6). A prominent review of the N2 has suggested that it does not reflect a single underlying process, but rather a family of sub-components related to cognitive control (Folstein & Van Petten, 2008). In line with this, it may be that this

Condition x Site interaction is suggestive of different neural generators of the N2 for each condition (Johnson, 1993). According to Kok (2001), changes in cognitive processing are a common effect of task difficulty manipulations. Therefore, it may be that different neural generators of the N2 are differentially sensitive to task difficulty in the Go/Nogo task, potentially leading to alterations in its distribution.

3.4.4.2 P3

The Nogo > Go P3 effect increased from the Low to the Medium condition, with little difference found between the stimulus types for the High condition. A more anterior NoGo than Go P3 is considered to be reflective of inhibitory processing by some researchers (Bekker et al., 2005f; Kok et al., 2004; Smith & Douglas, 2011), and via the use of three task difficulty levels, the results from the present study appear to support this idea. That is, the larger Nogo than Go P3 for the Medium than Low condition (primarily at frontocentral regions) may be reflective of an increased requirement for inhibitory processing with increasing task difficulty. Beyond this point, however, task difficulty seems to overwhelm the response inhibition mechanism, leading to reductions in the Nogo P3 effect. Indeed the findings of longer Nogo P3 latency and 25% commission errors for the High as opposed to 11.1% commission errors for the Medium condition, is consistent with this interpretation. Studies investigating workload (for a review see Kok, 1997) and semantic categorisation (Maguire et al., 2009; Maguire et al., 2011) have reported similar reductions in P3 amplitude with increasing task difficulty

However, it is interesting to note that the distribution of the Nogo P3 revealed amplitude reductions for the High condition at centroparietal regions (see Figure 3.6). Thus it may argued that the relative decline of the Nogo P3 during high task difficulty may not be solely due to variations in inhibitory processing given that, (a) it is not a frontal change, (b)

frontal Nogo P3 amplitude does not appear to differ substantially between the Medium and High conditions (Figure 6), and (c) previous research has shown a clear relationship between frontal lobe activation and inhibitory processing (e.g. Rubia et al., 2001). Reduced Nogo P3 amplitudes over centroparietal regions with increasing task difficulty may thus be better explained in terms of a decrease in the ability to evaluate inhibition success (e.g. Beste et al., 2010). That is, although ISIs were kept consistent between conditions, participants in the High condition may have perceived that too little time was available to adequately monitor the inhibition outcome, leading to reductions in the centroparietal Nogo P3. It can also be argued that the functional interpretation of the Nogo P3 is dependent on the scalp topography (Tekok-Kilic et al., 2001; Vallesi, 2011), and that two distinct processes are contributing to the differences between conditions: a response inhibition process which produces the more anterior Nogo than Go P3for the Low and Medium conditions, and an inhibition monitoring process that is reflected by the centroparietal reductions for the High condition. However, this notion requires further investigation.

This investigation is not without limitations. Future studies could consider the use of a within-subjects design, which would add statistical power and reduce the error variance between conditions. In addition, due to the use of a psychology undergraduate population, all three task difficulty conditions contained many more females than males. While the issue of gender effects has not been well-studied in the Go/Nogo context, recent research by Yuan and colleagues (2008) has reported that women showed shorter latencies and larger amplitudes for deviant-related P2, N2 and P3 components. Accordingly, the use equal number of males and females might be useful in future research to further clarify the effect of task difficulty on inhibitory performance and processing.

3.4.5 Conclusions

In summary, this study reports that task difficulty in the Go/Nogo task can be effectively manipulated by varying RTDs. In the context of declines in task performance and the absence of arousal effects, incremental amplitude increases and reductions in latency were seen for the Nogo N2, potentially indicating enhanced response conflict with greater Go/Nogo task demands. In contrast, the NogoP3 effect was reduced with increasing task difficulty, suggesting that reductions in RTD may serve to impair inhibition-related processing or monitoring. Finally, our data also imply that the inhibitory control may not be solely manifested by modulations in the N2 and P3, but that differential processing of the N1 and the P2 may also influence Go/Nogo task performance. These findings have real-world significance in light of a growing body of literature examining techniques for training inhibitory control as a way to ameliorate inhibitory control deficits seen in disorders such as ADHD. Importantly, mixed results in this line of research have been suggested to be partly due to a lack of optimal task difficulty manipulation. Thus, taken together, this study provides useful baseline behavioural and ERP data for appropriately manipulating task difficulty in Go/Nogo tasks, and potentially offers a constructive avenue for researchers attempting to design effective inhibition training paradigms.

Several important research questions remain open in the training of inhibitory control: (a) Does the manipulation of task difficulty augment the training of inhibitory control?; (b) If so, how is this reflected by changes in the underlying neural processes?; (c) What role do energetic factors (e.g. task-related arousal, perceived effort) play in the process of the training? Therefore, the next study explored these questions using the same task design of study 1 while participants practiced the task over the course of a single training session.

Chapter 4 - Study 2: Short-term training in the Go/Nogo Task: Behavioural and Neural Changes Depend on Task Demands

Published as:

Benikos, N., Johnstone, S. J. & Roodenrys, S. J. (2013b). Short-term training in the Go/Nogo Task: Behavioural and Neural Changes Depend on Task Demands. *International Journal of Psychophysiology, 87* (3), 301-310.

Abstract

Neural activity underlying executive functions is subject to modulation as a result of increasing cognitive demands and practice. In the present study, we examined these modulatory effects by varying task difficulty, as manipulated by reaction time deadline (RTD), on inhibitory control during a single Go/Nogo training session (8 blocks; 70% Go). Sixty adults were randomly assigned to one of three task difficulty conditions: High (n = 20), Medium (n = 20) and Low (n = 20), with RTDs of 300, 500 or 1000 ms, respectively. Task performance, Event-related potentials (ERPs) and task-related arousal (as indexed by Skin Conductance Level) were examined for training effects. Results indicated that improvements in behavioural Go/Nogo proficiency were optimised during conditions of moderate rather than low or high inhibitory demands. An across-session increase in task-related arousal did not differ between conditions, indicating a generalised increase in the mobilisation of mental resources with time-on-task. In contrast, training-related changes in ERPs were dependent on task demands such that the Low task difficulty condition showed an enhanced centroparietal Nogo P2, while a training-induced augmentation in the Nogo > Go P3 effect was greater in the High than Medium condition. The High condition also showed the greatest reduction in the Nogo N1. Although further research is needed in this area, these findings implicate the potentially key role of task difficulty in training inhibitory control and suggest that practice-related changes are reflected by qualitative changes in brain activity.

4.1. Introduction

Everyday functioning requires the ability to deliberately inhibit dominant, automatic, or prepotent responses (Dagenbach & Carr, 1994; Dempster & Corkill, 1999). Localised to fronto-striatal networks (Aron et al., 2007; Aron et al., 2004), inhibitory control is crucial for the proper performance of many other higher-order cognitive functions, including working memory (Hester et al., 2004), task switching (Monsell, 2003) and action monitoring (Cooper & Shallice, 2000). Unfortunately, this capacity is susceptible to impairment with deficits linked to diverse spheres of atypical functioning, from excess consumption of food (Blumenthal & Gold, 2012) and alcohol (Wiers et al., 2007), to several psychiatric and neurological disorders, such as Attention-deficit/Hyperactivity disorder (ADHD; Smith et al., 2004) and Huntington's disease (Beste et al., 2008).

Intensive research over the last two decades has revealed that the neural mechanisms which underlie executive functions are amenable to training and experience (for a review see Kelly & Garavan, 2005), superseding the traditionally held belief that the human adult brain is hard-wired and resistant to change (Buonomano & Merzenich, 1998a; Kelly et al., 2006; Raskin et al., 2011). Consequently, fundamental research investigating the training-induced alterations in these abilities may not only determine the extent to which neuroplastic changes are available to healthy adults (Kelly & Garavan, 2005; Kelly et al., 2006), but also aid in remediating atypical neural processes (Kelly et al., 2006; Kujal & Näätänen, 2010). However, despite a recent upsurge of positive findings regarding the training of other executive functions (e.g. working memory, attention, task switching; for reviews see Cramer et al., 2011; Green & Bavelier, 2008; Kujal & Näätänen, 2010), the literature investigating the training of inhibitory control has been mixed.

For example, some studies report direct training-related improvements in inhibitory performance (Dowsett & Livesey, 2000; Schapkin et al., 2007; Thorell et al., 2009; Verbruggen & Logan, 2008), while others have found more indirect effects, such as a reduction in the consumption of food and alcohol after participants were trained to inhibit food and alcohol cues embedded in Go/Nogo and Stop-Signal tasks (Houben, 2011; Houben et al., 2011; Veling et al., 2011). Despite this, several other investigations have reported no significant change (Jodo & Inoue, 1990; Kelly et al., 2006; Rueda et al., 2005; Tomporowski, 2003), or even declines in performance with repeated exposure (Kato et al., 2009; Manuel et al., 2010), and no transfer to untrained tasks (Manuel et al., 2010; Thorell et al., 2009). In sum, despite some studies showing promising results, the question of how to reliably attain training-induced improvements in inhibitory control is still not clear - highlighting the fragmentary nature of our current understanding, and pointing to the need for further work in this area.

In a complementary line of research, a number of previous working memory (WM) training studies have consistently demonstrated improvements in cognition (Chein & Morrison, 2010; McNab et al., 2009) and overt behaviour post-training (Klingberg et al., 2005; Klingberg et al., 2002). Notably, these studies highlighted that a key ingredient of productive training was the enhancement of task difficulty (Klingberg, 2010; Lindqvist & Thorell, 2009; Thorell et al., 2009), while the training of WM at low levels of capacity does not lead to a substantial improvement (for a combined WM and inhibition training study see Johnstone et al., 2010; Klingberg et al., 2005; Klingberg et al., 2002). Similarly, variations in task difficulty also appear to be important for the training of other cognitive abilities (e.g. attention, perception; Kelley & Yantis, 2009; Wang et al., 2010). While we have previously demonstrated that Go/Nogo task difficulty can be successfully manipulated via reaction time deadline (RTD; Benikos et al., 2013a), whether different variations in RTD can augment the training of prepotent response inhibition has yet to be systematically investigated. Previous research has either not manipulated task difficulty (e.g. Jodo & Inoue, 1990), or have used

auto-adaptive difficulty manipulations (Manuel et al., 2010), leaving the question as to the *optimal* difficulty level required for learning in the Go/Nogo task open. Thus, the primary aim of the present study was to investigate the effect of varying degrees of task difficulty (i.e. Low, Medium and High) during the training of the Go/Nogo task, rather than simply assuming optimal learning at a single level.

Although variations in task performance offer a global measure of training-related changes in inhibitory control, they do little to provide an insight into the underlying neural mechanisms. In contrast, Event-related potentials (ERPs) allow a detailed examination of these processes, with ERP amplitude and latency sensitive to neuroplastic changes in brain activity (Kujal & Näätänen, 2010; Lillard & Erisar, 2011). Among the most commonly investigated ERPs in the Go/Nogo task are the Nogo N2, a frontally maximal negative component peaking around 200 ms after the onset of inhibition-evoking stimuli (Johnstone et al., 2005; Randall & Smith, 2011), and the Nogo P3, a positive component that has a more anterior topography than the Go P3, and peaks approximately 300 ms post-stimulus (Randall & Smith, 2011; Smith & Douglas, 2011). The link between the N2 and P3 to inhibitory processing is the subject of debate (Bruin et al., 2001; Nieuwenhuis et al., 2003). Some argue that the inhibition process is best reflected by the N2 (Falkenstein et al., 1999; Kok, 1986), while others suggest instead that the P3 is the more likely candidate (Randall & Smith, 2011; Smith & Douglas, 2011; Smith et al., 2006; Smith et al., 2007; Smith et al., 2008; Smith et al., 2010).

The literature investigating the effect of inhibition training on neural activity has been varied in regard to methodologies and outcomes. Jodo and Inoue (1990) found that Go reaction time and Nogo P3 latency were significantly shortened after six days of practice (200 trials per day) - in line with previous theoretical viewpoints suggesting more efficient processing with training (Neubauer & Fink, 2009). However, given that no results for Nogo errors were reported, a link between more efficient inhibitory performance and the Nogo P3

is unable to be made. Schapkin and colleagues (2007) found a reduction in Nogo errors, with a corresponding increase in the Nogo N2 after the first three daily training sessions (~200 trials per day) of a three week training protocol, which they interpreted as a practice-related strengthening of the inhibition mechanism (for a similar finding using fMRI see Kelly et al., 2006). No further change was reported by the conclusion of the training. Finally, more efficient early low-level processing has been suggested by Manuel and colleagues (2010), who found a reduction in left parietal activity to Nogo stimuli at 61-104 ms following thirty minutes of Go/Nogo task practice (528 trials total).

In sum, the literature does not appear to paint a straightforward picture of the neural changes that should be expected as a result of training inhibitory control. Furthermore, the above mentioned studies had a variety of shortcomings. First, it has been suggested that response inhibition may not be solely manifested by variations in the N2 and P3, but that earlier components in the waveform such as the N1 and P2 play a crucial role in determining inhibition success (Roche et al., 2005b; Thomas et al., 2009). Yet these components have not been investigated in the context of inhibition training. Secondly, previous work has generally only employed Pre/Post designs (Jodo & Inoue, 1990; Kelly et al., 2006b), which do little in the way of understanding the time-course of training effects. For optimal paradigm design it would be advantageous to isolate the time required to elicit positive training effects (Cramer et al., 2011). Finally, most studies have typically only included eleven or fewer participants (Jodo & Inoue, 1990; Manuel et al., 2010; Schapkin et al., 2007), making the generalisability of their findings and brain-behaviour correlations difficult to assess.

4.1.2 The Present Study

The primary aim of the present study was to examine the effect of varying task difficulty, as manipulated by RTD, on the training of inhibitory control using task

performance and inhibition-related ERPs. Participants were divided into one of three Go/Nogo task difficulty conditions: Low (1000 ms), Medium (500 ms) and High (300 ms). Since previous Go/Nogo studies have demonstrated ceiling effects in task performance using Low difficulty RTDs (e.g. Johnstone et al., 2005; Smith et al., 2006), and that High task difficulty generally results in performance declines (e.g. Benikos et al., 2013a), it was hypothesised that training outcomes would be optimised for the Medium task difficulty condition, with concurrent enhancements in the Nogo N2 and P3. A further focus of this study was on the potential contribution of early sensory processing to the training of inhibitory control, as indicated by the N1 and P2. While no specific predictions were made for these components, any differences found would be explored. Finally, a criticism of training paradigms manipulating task difficulty is the lack of consideration of state factors, such as task-related effort and arousal (Cramer et al., 2011; Green & Bavelier, 2008; Slagter et al., 2011). Given that these variables may be critical modulators of behaviour and task performance (e.g. Slagter et al., 2011; Tang & Posner, 2009; Yerkes & Dodson, 1908), participants provided perceived effort ratings and we recorded skin conductance level (SCL) - a well-established measure of central nervous system arousal (Barry & Sokolov, 1993).

4.2. Method

4.2.1 Participants

A total of 69 adults enrolled in the present study to fulfil an undergraduate course requirement, with three being excluded according to the selection criteria. To be included in the study, participants were required to refrain from caffeine for 2 hours prior to testing and have not taken any psychotropic substances (prescription or illegal) for 24 hours prior to testing, or no more than once a month in the previous six months. Participants were also screened for neurological disorders and all reported normal or corrected-to-normal vision.

The remaining 66 participants were randomly assigned to one of three conditions: Low, Medium or High task difficulty. Of these, data from 4 participants were rejected either due to excessive eye artefact (3 participants, leaving an insufficient number of correct and artefact –free trials available for averaging) or to faulty recording equipment (1 participant). A further two people were excluded, with one being unable to complete the testing session due to an unrelated emergency, and another for failing to perform the task properly by adopting a strategy of disregarding accuracy on Nogo trials in order to respond within the RTD. Therefore, 20 participants each were included in the final analyses for the Low (17 females, 3 males, mean age 21.23, SD 4.12), Medium (14 females, 6 males, mean age 21.5, SD 5.89) and High condition (14 females, 6 males, mean age 21.4, SD 3.32). There were no differences in age ($F(2,57) = 0.13$, $p = .877$) or gender ($\chi^2(2) = 0.53$, $p = .766$) between conditions. All but 5 of the 60 participants were right-handed. The research protocol was approved by the joint University of Wollongong and Illawarra Area Health Service Human Research Ethics Committee.

4.2.2 Task

Stimuli were delivered using Presentation (Version 11.0; Neurobehavioral Systems, Albany, CA, USA). Each trial began with a central fixation cross (+) presented for a variable interval of 500-1000 ms (M = 750 ms), followed by the Go/Nogo stimulus presented in the centre of the screen for 200 ms. A blank screen then replaced the stimulus for a variable blank period of 1250 – 1750 ms (M = 1500 ms). Within this period, participants in the High, Medium and Low task difficulty conditions were required to respond by a button press with their right hand (irrespective of handedness) to Go stimuli within 300, 500 or 1000 ms, respectively, or to refrain from responding to Nogo stimuli. Performance feedback was provided via the subsequent fixation cross: correct responses were followed by a white

fixation cross, while a red fixation cross was displayed after incorrect responses (i.e. presses to Nogo stimuli during the variable blank period, omissions and responses outside the RTD). Only presses to the Go stimulus within the predefined response window were regarded as correct.

Participants first completed an initial practice block of 30 trials (50% Nogo). In line with previous behavioural studies demonstrating improvements in inhibitory control using a single training session (Kelly et al., 2006b; Verbruggen & Logan, 2008), participants completed eight experimental blocks (30% Nogo) of 100 trials each. In order to minimise habituation of the visual ERP response (particularly the P3 component, e.g. see Ravden & Polich, 1998), the selection of shapes used to represent Go and Nogo stimuli were selected from a pool of eight 2D shapes (i.e. triangle, cross, hexagon, diamond, ellipse, rectangle, star or circle). Go/Nogo shape selection was changed from block to block. Presentation of shape stimuli were counterbalanced using a Latin square design (Bradley, 1958), and Go/Nogo response assignment counterbalanced across participants. Stimuli measured approximately 3 x 3 cm and were presented on a 15" computer monitor, with participants' seated one metre away. Each block lasted approximately 3.5 minutes. In order to equate training session length between conditions, the rest period between blocks was set at 1.5 minutes for all participants. Total session time including the practice and training blocks was approximately 43 minutes.

4.2.3 Procedure

Participants were given an outline of the testing procedure and familiarised with the laboratory equipment before informed consent was given. The experimenter emphasised that participants could withdraw at any time without penalty. They were then asked to complete a short screening questionnaire to assess vision problems, medication/psychotropic substance

use, and neurological disorders. Participants were then fitted with EEG and skin conductance recording equipment, and seated in a dimly-lit sound-attenuated and electrically-shielded testing booth. An incandescent light in the booth was dimmed for the duration of the training session. An initial 3 min baseline recording was conducted while participants were asked to sit quietly with eyes closed. Participants were then presented with a modified Go/Nogo task and were instructed that they would see one of two shapes, one representing the Go stimulus, and the other representing the Nogo stimulus. They were asked to press the button before the pre-determined RTD with the thumb of their right hand (irrespective of handedness) to Go stimuli, and to refrain from responding to Nogo stimuli. Participants were asked to "do their best" to avoid the incorrect feedback, and were encouraged to keep as still as possible and to minimise eye movements during the testing blocks. Go/Nogo shape assignment was shown on the screen and verbally confirmed by the participant prior to each block. At the end of each block, mean Go RT, the percentage of Go and Nogo errors were displayed for participants to review. They were then asked to rate their perceived level of effort irrespective of their task performance with the question "How much effort did you use to complete that block?" and responded by a 5-point Likert scale ranging from: 1 = Very little, 2 = Moderate effort, and 5 = Everything I had[1]. Prior to the first rating a basic example was shown to the participant to ensure understanding. Participants were given a timed break at the end of each block and asked to continue on.

[1] Although participants were instructed to rate their perceived effort irrespective of their task performance, knowledge of their performance may still have influenced their ratings.

4.2.4 Electrophysiological recording

The continuous scalp electroencephalogram (EEG) was recorded from 19 sites (Fp1, Fp2, F3, F4, F7, F8, Fz, C3, C4, Cz, P3, P4, Pz, T3, T4, T5, T6, O1, O2) using an electrode cap containing tin electrodes fitted according to the international 10-20 system (Jasper, 1958). A ground electrode located between Fpz and Fz, and all electrodes were referenced to linked ears. EOG was measured vertically with two tin cup electrodes, 1 cm above and below the left eye. Impedance was kept below 3 kΩ for EOG and reference electrodes, and below 5 kΩ for cap electrodes. EEG and EOG signals were amplified 19 times and sampled at 500 Hz, with bandpass down 3 db at 0.1 and 100 Hz via a NuAmps system (Compumedics Limited, Melbourne, Australia). Prior to processing, the EEG data were digitally filtered using a low-pass filter 3 db down at 30 Hz.

4.2.5 Skin Conductance recording

Electrodermal activity was recorded using two Ag/AgCl electrodes placed on the distal phalanges of the third and fourth digits of the left hand. Recording electrodes were filled with electrode paste (0.05 M NaCl in an inert viscous ointment base) and secured using velcro straps and tape. A constant voltage device (UFI Bioderm model 2701) set at 0.5V was used. This system separately recorded tonic DC-coupled SCL, AC-coupled skin conductance response (SCR), measured in microsiemens (μS) but only SCL is reported here.

4.2.6 Data Quantification

The ERP epoch was defined as 100 ms pre-stimulus to 900 ms post-stimulus onset. Epochs were excluded if they contained activity greater than ± 100 μV at any non-frontal site. EOG artefact reduction was carried out based on vertical EOG (Semlitsch et al., 1986). ERPs were averaged across epochs for correct responses only. This resulted in a minimum of 18 artefact-and-error-free Nogo trials being included in each average. To ensure compatibility within-subjects, the number of epochs available for averaging was determined for Nogo stimuli initially, with Go epochs restricted to the same number, being selected randomly from the total available. Grand average ERP waveforms for Go and Nogo stimuli were displayed in order to define the components latency range. Latency at all sites was locked to the peak latency at the site of maximum amplitude, with amplitude for all 9 electrodes taken at the same post-stimulus latency (Picton et al., 2000; Spencer et al., 2001). ERP component peaks were quantified using automatic peak-picking software which identified the largest positive or negative deflections within the predefined latency range, relative to the 100 ms pre-stimulus baseline period. Peak latency ranges and sites were as follows: N1 (100 -160 ms Fz), P2 (180-240 ms Pz), N2 (200-280 ms Fz), P3 (280-520 ms Pz). Skin conductance level was taken as the average value (in μS) for each 30 sec period over the 3.5 min duration of each block of the Go/Nogo task.

4.2.7 Statistical analyses

The error rate (Go omission errors, Go RTD errors and Nogo errors) was calculated as the number of incorrect responses divided by the total number of trials. The Go/Nogo performance data were participant to Condition [Low (L) vs. Medium (M) vs. High (H)] x Time [Block 1 (b1) vs. Block 4 (b4) vs. Block 8 (b8)] mixed design ANOVAs, with repeated measures on the within-subjects factors. Planned orthogonal contrasts were used to analyse

differences within Time and between conditions using Linear (b1 vs. b8) and Quadratic (mean of b1/b8 vs. b4) contrasts.

Primary analyses of the ERP data were restricted to the sites F3, Fz, F4, C3, Cz, C4, P3, Pz and P4. Go and Nogo data were subject to a Condition (L vs. M vs. H) x Lateral (Left vs. Midline vs. Right) x Sagittal (Frontal vs. Central vs. Parietal) x Stimulus (Go vs. Nogo) x Time (b1 vs. b4 vs. b8) ANOVAs. Planned orthogonal contrasts, which allow insight into training-related changes in the topographic distribution of each component**,** were performed on the within-subjects factors. The Sagittal factor compared the frontal region (mean of F3, Fz and F4) with the posterior region (mean of P3, Pz and P4), and their mean with the central region (mean of C3, Cz and C4). The Lateral factor compared activity in the left hemisphere (mean of F3, C3 and P3) with that in the right hemisphere (mean of F4, C4 and P4), and their mean with the midline region (mean of Fz, Cz and Pz). Finally, the Time factor compared block 1 to block 8 (Linear contrast), and their mean with block 4 (Quadratic). The analyses for component peak latency excluded site contrasts. As these contrasts were planned with no more of them than the degrees of freedom for each effect, no Bonferroni type adjustment to α were necessary (Tabachnick & Fidell, 1996). Also, single degrees of freedom contrasts are not affected by violations of symmetry assumptions common in repeated measures analyses, and thus do not require Greenhouse–Geisser-type corrections. As these analyses are carried out over a substantial number of variables, each may be considered to constitute a separate experiment. It should be noted that this increases the frequency of type 1 errors, however, as this is an increase in frequency, rather than probability, it cannot be ‘controlled’ by adjustment of alpha levels (Howell, 2009). All ERP statistics have (1,58) degrees of freedom unless otherwise indicated. Outliers in the data (i.e. values exceeding ± 2.5 standard deviations from the mean) were corrected for by replacing with the series mean (< 1.1% for any task performance or ERP variable). Data were normalised using the vector scaling method (McCarthy & Wood, 1985), and only

interactions with topography that remained significant in the normalised data are reported here.

4.3. Results

4.3.1 Manipulation check, perceived effort and SCL

Participants' perceived effort was greater in the High (M = 3.87) than the Medium (M = 3.57) and Low (M = 3.20) conditions (i.e. H > M > L; Linear: $F = 6.13$, $p = .016$, $\eta 2 = .096$). Similarly, there were incremental increases in Nogo errors (see Figure 1d) with each decrease in RTD, with the greatest overall percentage of errors in the High condition (Linear: $F = 77.70$, $p < .001$, $\eta 2 = .577$). Combined, these results suggest that three task difficulty levels were established, with greater perceived effort and declines in inhibitory performance with shorter RTDs. Across the session, the Time main effect (Linear: $F = .031$, $p = .862$) and the Time x Condition interaction (Linear: $F = .031$, $p = .970$) for perceived effort were not significant. SCL increased from the beginning (11.6 µS) to the end of the training session (13.1 µS; Linear: $F = 23.20$, $p < .001$, $\eta 2 = .289$), but this effect did not differ between conditions (Linear: $F = 2.08$, $p = .134$).

4.3.2 Task Performance

As seen in Figure 4.1a, Go reaction time (RT) decreased with training showing the largest decline in the Low condition (Linear: $F = 3.32$, $p = .043$, $\eta 2 = .032$). Go omission (Linear, $F = 3.41$, $p = .040$, $\eta 2 = .051$) and Go RTD errors (Linear, $F = 20.84$, $p < .001$, $\eta 2 = .198$; Quad: $F = 5.87$, $p = .005$, $\eta 2 = .059$) decreased early in the session (i.e. by block 4) for the Medium and High conditions - with the greatest declines for the High condition (see

Figure 4.1b and c). By contrast, Go RTD errors and Go omission errors appeared to be at ceiling for the Low condition and did not modulate over the course of training.

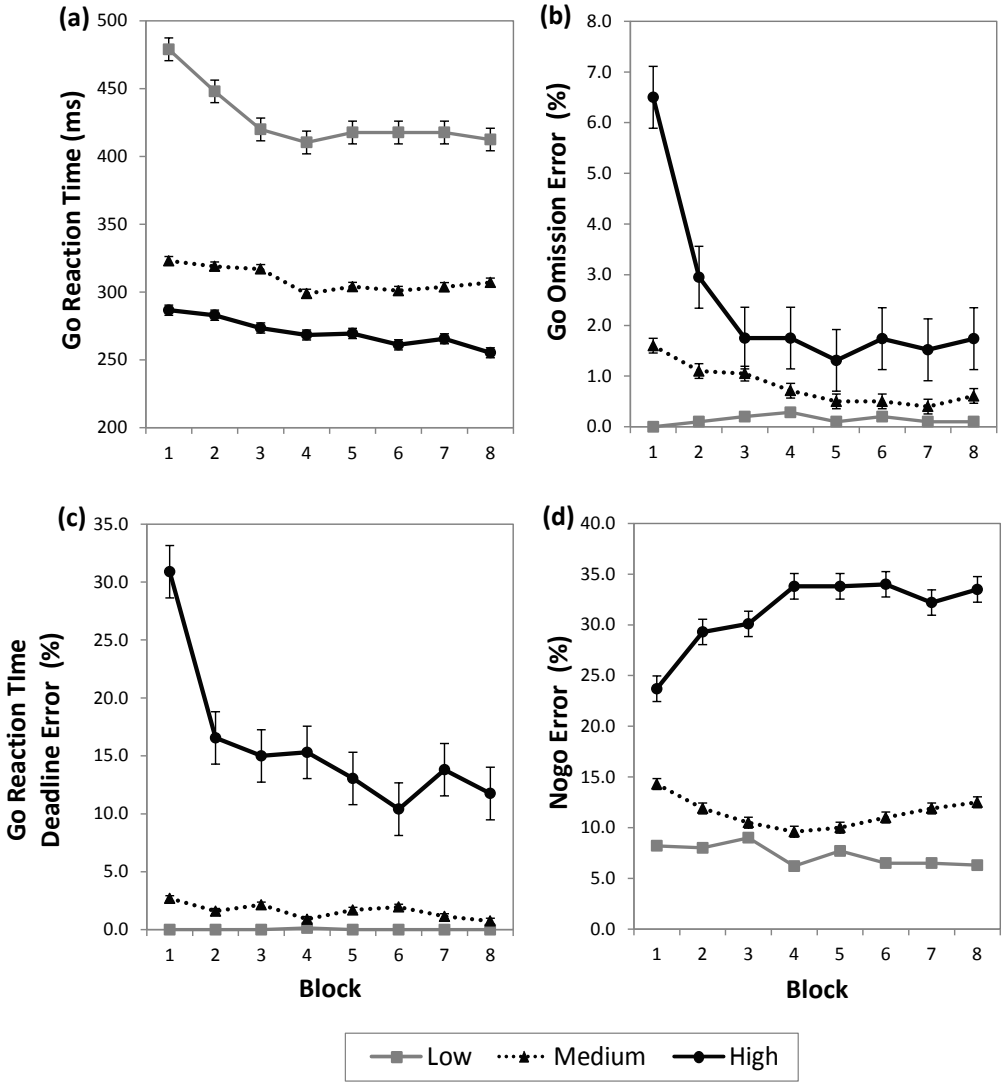


Figure 4-1. Task performance indices for each difficulty condition over the training session including (a) Go reaction time, (b) Go Omission, (c) Go reaction time deadline, and (d) Nogo errors. Error bars represent standard error of the mean. Note: Data for all eight blocks is included for display purposes, but only block 1, 4 and 8 were considered in the statistical analyses.

As seen in Figure 4.1d, Nogo errors showed different training effects with task difficulty. While Nogo errors increased sharply from block 1 to block 4 and plateaued thereafter for High condition, the Medium and Low condition remained relatively stable across the session (Linear: $F = 4.04$, $p = .023$, $\eta 2 = .124$; Quadratic: $F = 4.84$, $p = .011$, $\eta 2 = .145$). A further within Condition analysis of Nogo errors confirmed no change for the Low (Linear: $F = 2.05$, $p = .169$) or Medium condition (Linear: $F = 0.24$, $p = .632$), but a significant increase for the High (Linear: $F = 4.39$, $p = .050$, $\eta 2 = .188$). To clarify whether the facilitation of Go RT with training resulted in a speed-accuracy trade-off (SAT), we correlated the training-related change (i.e. b8 - b1) in Go RT and Nogo errors separately for each condition. This analyses was not significant for either the Low ($r = -.104$, $p = .664$) or Medium condition ($r = -.074$, $p = .758$), but it was for the High ($r = -.467$, $p = .038$). Given that Nogo errors remained stable for the Low and Medium conditions, declines in Go RT with training represent an improvement in behavioural Go/Nogo proficiency. This result is similar to Manuel et al. (2010).

4.3.3 Event- related Potentials

Figure 4.2 presents grand mean ERPs to Go/Nogo stimuli across conditions (top left panel) and for each condition separately (remaining three panels) for blocks 1, 4 and 8. ERP latency data is presented in Table 4.1. As the primary aim of this study was the effect of varying task difficulty on the training of inhibitory control, and as a large body of literature has been devoted to descriptions of the topography of the various ERP components, reporting of the results will focus on effects and interactions involving Time and Condition.

The waveforms were characterised by an N1-P2 complex, most apparent at frontal and central sites, followed by an N2 component at about 270 ms primarily in the

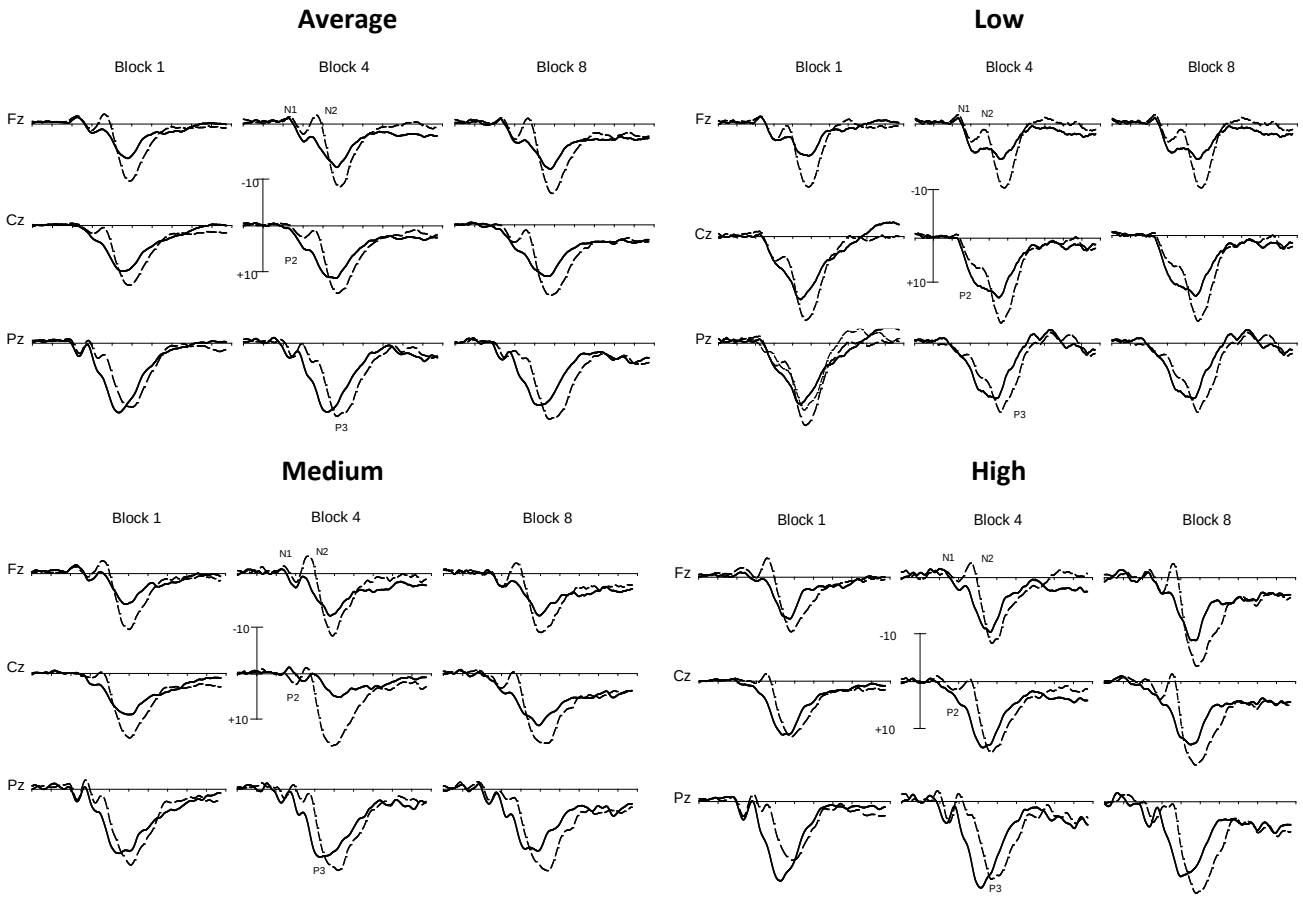


Figure 4-2. Grand mean ERPs for blocks 1, 4 and 8 to Go (solid line) and Nogo (dashed line) across condition (top left panel) and for each task difficulty condition separately (remaining three panels). ERPs are shown at three midline sites only. Note: x-axis ticks = 100 ms; stimulus onset at y-axis (scale: ± 10 μV) shown at Cz.

Table 4-1. Mean latency (in ms) for Go/Nogo stimuli between each task difficulty condition for blocks 1, 4 and 8 (Standard deviations in parentheses).

ERP	Block 1			Block 4			Block 8		
	Low	Medium	High	Low	Medium	High	Low	Medium	High
Go									
N1	139.0	146.2	142.9	134.3	142.8	127.8	129.8	142.7	130.6
	(12.7)	(20.0)	(25.5)	(32.1)	(20.3)	(23.4)	(21.0)	(25.1)	(28.2)
P2	233.3	221.3	225.9	226.7	225.0	212.4	214.4	233.2	209.1
	(22.5)	(16.8)	(23.3)	(37.4)	(21.2)	(37.1)	(30.2)	(31.6)	(46.3)
N2	282.8	267.1	262.0	265.9	260.8	243.2	254.7	272.8	264.1
	(23.3)	(19.1)	(18.8)	(46.0)	(21.2)	(35.8)	(38.3)	(37.7)	(40.6)
P3	368.9	398.1	355.7	350.3	358.0	337.1	324.1	378.1	352.8
	(40.6)	(34.2)	(29.6)	(46.7)	(48.8)	(27.3)	(34.4)	(49.9)	(42.7)
Nogo									
N1	141.0	144.9	149.1	136.1	141.3	135.7	133.0	145.2	130.1
	(20.4)	(15.6)	(21.5)	(25.0)	(17.1)	(26.4)	(16.7)	(22.6)	(16.7)
P2	232.2	226.6	221.0	223.2	229.2	205.4	233.2	226.3	208.1
	(25.8)	(14.6)	(16.7)	(28.1)	(20.3)	(27.4)	(23.5)	(23.8)	(18.3)
N2	285.8	274.4	270.1	266.6	271.9	251.8	274.1	272.8	257.1
	(22.4)	(18.8)	(17.5)	(24.8)	(17.7)	(32.8)	(24.4)	(22.4)	(15.4)
P3	382.7	418.6	400.4	366.2	418.4	392.6	379.9	419.3	383.9
	(35.2)	(21.0)	(22.7)	(39.9)	(34.5)	(46.8)	(42.5)	(30.3)	(41.6)

frontocentral region. The P3 is evident as a large positivity which peaks approximately 300-400 ms post-stimulus and is largest parietally.

4.3.3.1 N1

N1 latency (Mean 138.5 ms) declined linearly across the training session (see Table 4.1; Linear: $F = 13.94$, $p < .001$, $\eta 2 = .196$). A Time x Condition effect approached significance (Linear: $F = 3.11$, $p = .052$, $\eta 2 = .098$) indicating that the N1 latency reduction was greater for the High (b1 vs. b8 diff.: 15.5 ms) than the Low (b1 vs. b8 diff.: 8.6 ms) and Medium conditions (b1 vs. b8 diff.: 1.5 ms).

Table 4.2 summarises the following effects and provides means. N1 amplitude reduced linearly from the beginning until the end of the session. Interestingly, training differentially modulated Go/Nogo N1 amplitudes between conditions (Stimulus x Condition x Time interaction), in that a Go > Nogo N1 effect, which was larger for the Low than Medium condition in block 1, reduced across the training session to be almost equipotential for both conditions by block 8; contrasting with the High condition, that displayed a training-related reduction in the Nogo relative to Go N1 (see Figure 3).

Table 4-2. Significant results for the N1 and P2 components.

Measure	Effect	Contrast	Details	F	η^2
N1	T	Linear: b1 vs. b8	-1.0 vs. -0.3	6.95*	.063
		Quadratic: b4 vs. b1/b8	-0.3 vs. -0.6	3.65*	.024
	T x Stim x Cond	Linear: Go vs. Nogo	Low: b1, -0.9 vs. -0.1; b8, -0.1 vs. -0.2		
			Medium: b1, -1.2 vs. -1.1; b8, -0.4 vs. -0.2		
			High: b1 -0.7 vs. -1.6; b8, -0.9 vs. 0.0	3.83**	.048
P2	Stim	Go vs. Nogo	5.4 to 3.5	37.56***	.375
	T	Linear: b1 vs. b8	3.6 vs. 5.1	7.60**	.073
	T x S x Stim x Cond	Linear: f vs. p	Low: b1, Go, 3.9 to 6.7 vs. Nogo, 3.1 to 6.2;		
			b8, Go, 5.4 to 7.6 vs. Nogo, 3.7 to 8.2		
			Medium: b1, Go, 2.2 to 4.9 vs. Nogo, 0.6 to 4.0;		
			b8, Go, 3.6 to 7.5 vs. Nogo, 2.2 to 3.5		
			High: b1, Go, 1.7 to 7.3 vs. Nogo, 1.4 to 4.2;		
			b8: Go, 3.5 to 6.7 vs. Nogo, 2.8 to 2.1	4.37*	.022

* = < .05, ** = < .01, *** = < .001

Note: For this and subsequent tables, details column represents mean amplitude in μV. Cond, Condition: Low/Medium/High task difficulty. Low, Low task difficulty condition. Medium, Medium difficulty condition, High, High difficulty condition. Stim, Stimulus type: Go/NoGo. T, Time; Linear: Linear contrast comparing block 1 to block 8; Quadratic: Quadratic contrast comparing the average of block 1/8 and block4; b1, block 1; b1/b8, average of block 1 and 8; b8, block 8. Sagittal (S) abbreviations: f, mean frontal (F3, Fz, F4); p, mean parietal (P3, Pz, P4); c, mean central (C3, Cz, C4); f/p, mean of frontal and parietal (F3, Fz, F4, P3, Pz, P4).

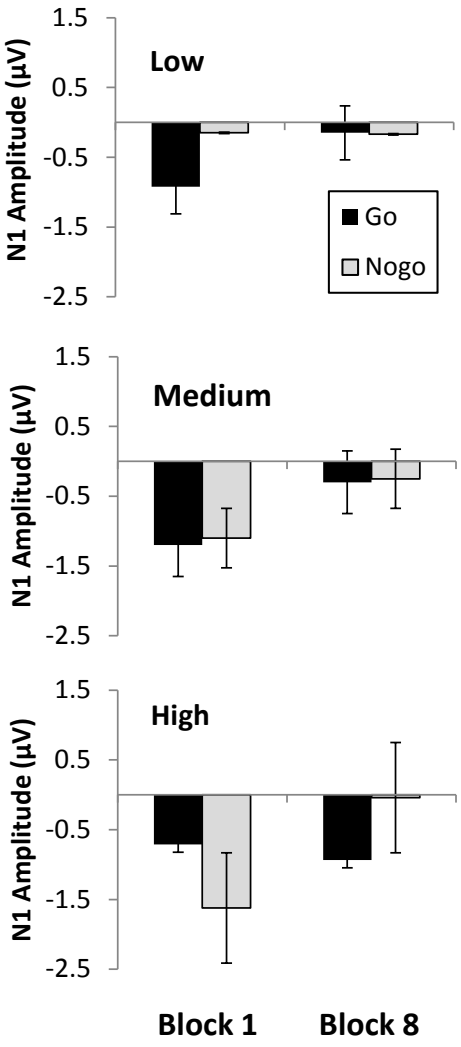


Figure 4-3. Stimulus x Condition x Time interaction for Go and Nogo N1 amplitude.

4.3.3.2 P2

P2 latency (Mean 222.7 ms) declined across the training session (Table 4.1; Linear: F = 6.26, p = .015, η2 = .053). This reduction was greater for the High (b1 vs. b8 diff.: 21.4 ms) than Low condition (b1 vs. b8 diff.: 6.8 ms), in contrast to the Medium condition that displayed a slightly longer P2 by the end of the session (b1 vs. b8 diff.: + 2.2 ms; Linear: F = 3.96, p = .025, η2 = .059).

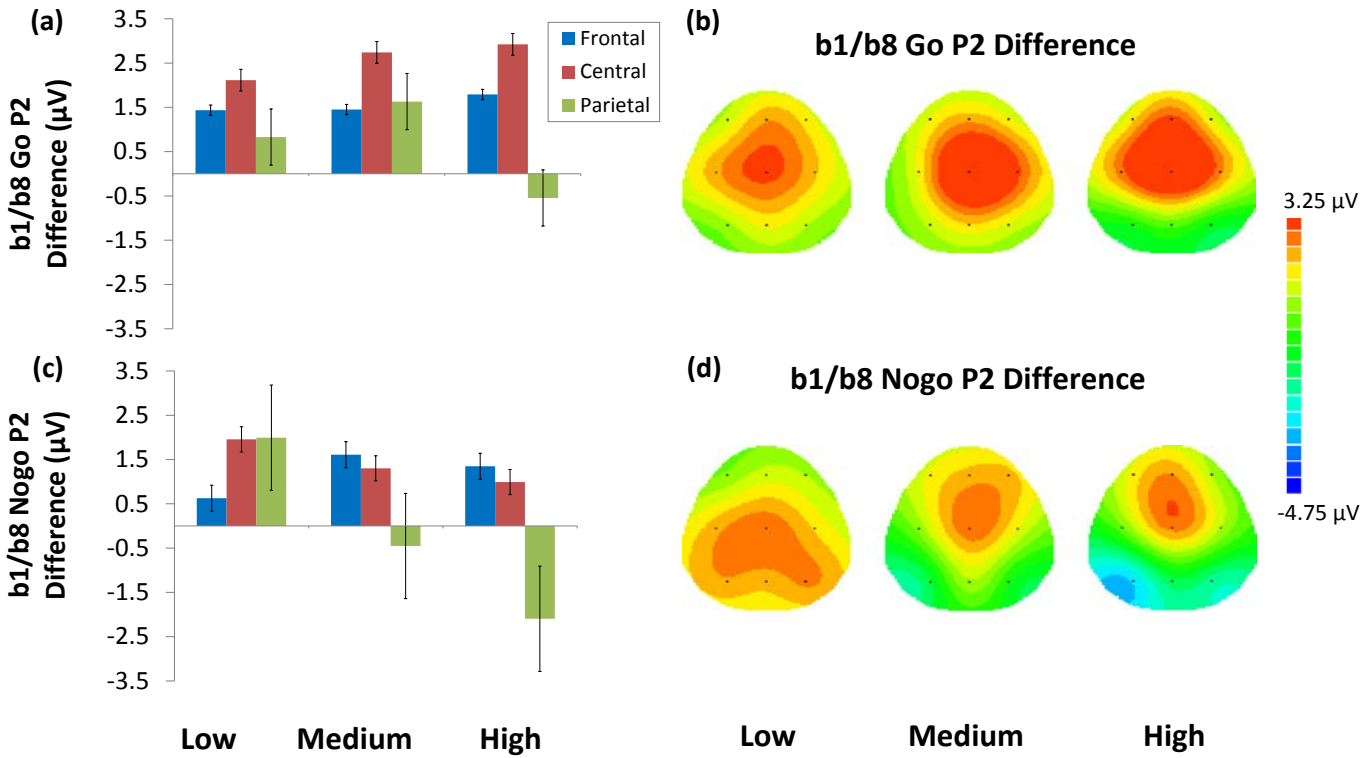


Figure 4-4. Mean change in the (a) Go P2 and (c) Nogo P2 from block 1 to block 8 across the Sagittal dimension. Error bars represent standard error of the mean. Topographic maps for the mean change in voltage distribution from block 1 to block 8 for the (b) Go P2 and (d) Nogo P2. Scale values represent the ends of the colour scale in µV for each component. Darkest blue = negativity, red = positivity.

P2 showed a Go > Nogo effect (see Table 4.2). The amplitude of the P2 increased linearly with training. As evidenced by significant Time x Sagittal x Stimulus x Conditions interactions, Go and Nogo P2 topography differed between conditions: for the Go P2, a central >frontal/parietal effect increased linearly with task difficulty (i.e. H > M > L), suggestive of an anterior shift of the Go P2 focus with training, particularly apparent in the Medium and High conditions (Figure 4.4a and b). For Nogo P2 the Medium and High conditions displayed a more anterior Nogo P2 with training, the Low condition showed the opposite pattern, with enhanced Nogo P2 activity at centroparietal regions (Figure 4.4c and d). Simple effects analyses confirmed a significant Sagittal x Time x Condition effect to Go (Quad: $F = 3.60$, $p = .032$, $\eta 2 = .011$) and Nogo stimuli (Linear: $F = 5.58$, $p = .006$, $\eta 2 = .055$).

4.3.3.3 N2

N2 (Mean 266.5 ms) peaked later to Nogo (269.2 ms) than Go stimuli (263.7 ms; $F = 6.09$, $p = .017$, $\eta 2 = .097$). Linear ($F = 7.96$, $p = .007$, $\eta 2 = .122$) and quadratic ($F = 8.51$, $p = .005$, $\eta 2 = .130$) effects indicated that while the N2 latency declined rapidly from block 1 (273.7 ms) to block 4 (260.1 ms), it began to increase slightly by block 8 (265.9 ms). Training effects for N2 latency also differed between conditions, showing a large decline for the Low (b1 vs. b8 diff.: 19.9 ms), but little change for the High (b1 vs. b8 diff: 5.4 ms), and Medium conditions (b1 vs. b8 difference: 2.0 ms; $F = 5.49$, $p = .007$, $\eta 2 = .161$).

Globally, N2 amplitude was larger to Nogo than Go stimuli (see Table 3 for effect summaries and means). Overall, N2 amplitude decreased across the training session. Moreover, a Time x Stimulus interaction showed that the Nogo > Go N2 effect increased linearly from block 1 to block 8. However, inspection of the means (see Table 3 and Figure 5) shows that it was the Go N2, and not the Nogo N2 that declined across the session. Follow-up analyses confirmed a significant reduction across the session for the Go N2 (Linear: ($F = 11.57$, $p = .001$,

η2 = .095), but not the Nogo N2 (Linear: $F = 0.00$, $p = .995$). Against predictions, these effects did not differ between conditions.

Table 4-3. Significant results for the N2 and P3 components.

Measure	Effect	Contrast	Details	F	η^2
N2	Stim	Go vs. Nogo	4.1 vs. 0.0	133.00***	.634
	T	Linear: b1 vs. b8	1.6 vs. 2.6	4.36**	.043
	T x Stim	Linear: b1 vs. b8	Go, 3.3 vs. 0.0; Nogo: 5.2 vs. 0.0	9.88**	.071
	T x S x Stim	Linear: c vs. f/p	b1: Go, 3.6 vs. 3.1, Nogo, 0.1 vs. -0.1		
			b8: Go, 6.2 vs. 4.7, Nogo, 0.0 vs. -0.1	20.7***	.030
P3	Stim	Go vs. Nogo	12.7 vs. 15.7	36.71***	.378
	S x Stim	f vs. p	Go: 8.4 vs. 15.2; Nogo: 12.7 vs. 16.4	57.28***	.405
		c vs. f/p	Go: 14.4 vs. 11.8; Nogo: 17.9 VS. 14.6	13.89***	.029
	T	b1 vs. b8	13.0 vs. 15.0	15.23***	.129
	T x Sim x Cond	Go vs. Nogo	Low: b1, 9.9 vs. 12.9; b8, 13.1 vs. 14.9		
			Medium: b1, 12.5 vs. 15.6; b8, 11.8 vs. 16.7		
			High: b1, 13.7 vs. 13.6; 14.1 vs. 19.7	6.39*	.049
	T x S x Stim x Cond	Linear: f vs. p;	Low: b1,Go, 6.4 vs. 12.2; Nogo, 9.8 vs. 13.9		
			b8, Go, 15.4 vs. 11.9; Nogo, 12.6 vs. 15.0		
			Medium: b1,Go, 8.3 vs. 15.9; Nogo, 12.1 vs. 17.0		
			b8, Go, 7.7 vs. 14.4; Nogo, 13.3 vs. 17.3		
			High: b1,Go, 9.3 vs. 16.6; Nogo, 11.5 vs. 14.3		
			b8, Go, 10.5 vs. 15.6; Nogo, 17.3 vs. 19.5	4.95*	.028
		Quadratic: c vs. f/p	Low: b1,Go, 11.2 vs. 9.3; Nogo, 17.8 vs. 14.5		
			b8, Go, 15.4 vs. 11.9; Nogo, 17.0 vs. 13.8		
			Medium: b1,Go, 13.5 vs. 12.1; Nogo, 12.1 vs. 17.0		
			b8, Go, 13.4 vs. 11.0; Nogo, 19.4 vs. 15.3		
			High: b1,Go, 15.2 vs. 13.0; Nogo, 15.1 vs. 12.9		
			b8, Go, 16.3 vs. 13.1; Nogo, 22.3 vs. 18.4	3.92*	.007

* = < .05, ** = < .01, ***= < .001

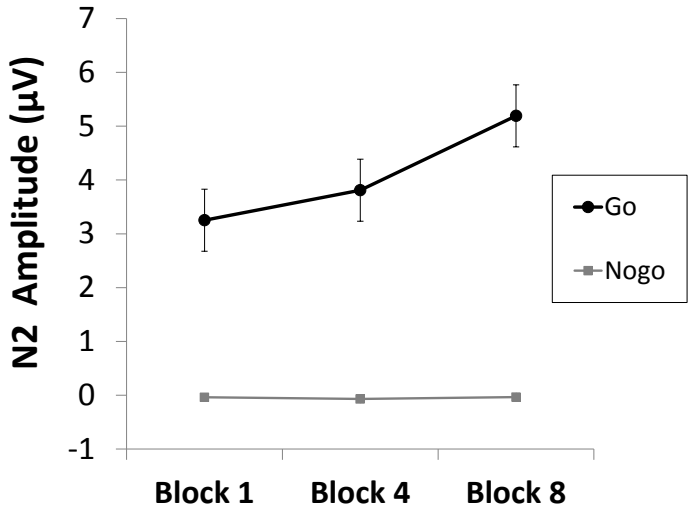


Figure 4-5. Go and Nogo N2 amplitude across the training session.Error bars represent standard error of the mean.

4.3.3.4 P3

The P3 (Mean 376.9 ms) peaked later for Nogo (395.8 ms) than Go stimuli (358.1 ms; $F = 64.64$, $p < .001$, $\eta 2 = .531$). While Nogo P3 latency remained relatively stable across the session for each condition, Go P3 latency showed the greatest training-related declines for the Low (b1 vs. b8 diff: 44.7 ms) compared to the Medium (b1 vs. b8 diff: 19.9 ms) and High conditions (b1 vs. b8 diff: 2.9 ms; $F = 4.68$, $p = .014$, $\eta 2 = .138$).

The P3 was larger to Nogo than Go stimuli (see Table 4.3 for effect summaries and means), with a smaller parietal > frontal gradient (parietal vs. frontal difference: Nogo 3.7 μV, Go 6.8 μV) and an increased central > frontal/parietal effect in Nogo compared to Go stimuli (central vs. frontal/parietal difference: Nogo 3.3 μV, Go 2.6 μV). These effects highlighted the anteriorisation of P3 to Nogo relative to Go stimuli.

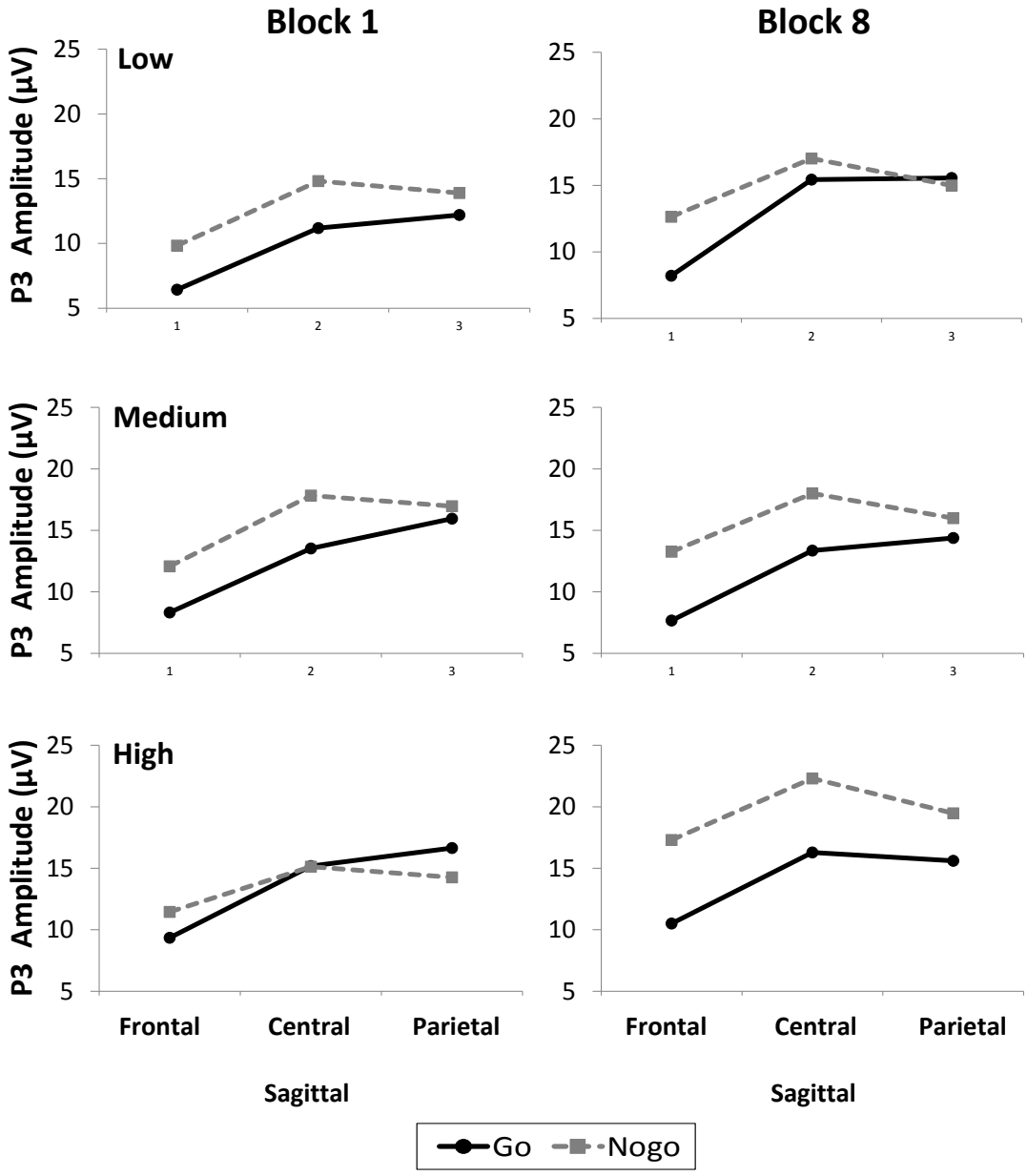


Figure 4-6. Time x Stimulus x Sagittal x Condition interaction for P3 amplitude.

P3 amplitude increased with training. The Nogo > Go P3 effect (across the scalp) was reduced for the Low condition by block 8 (Go vs. Nogo diff.: b1, 3.0 vs. b8, 1.8 μV), while the High condition (Go vs. Nogo diff.: b1, 0.0 vs. b8, 5.6 μV) showed a significantly larger training-induced increase in the Nogo > Go P3 effect than the Medium condition (Go vs. Nogo diff.: b1, 3.1 vs. b8, 4.9 μV). Time x Sagittal x Stimulus x Condition interactions indicated that

this effect was most apparent over central regions (Figure 4.6), as indicated by more anterior Nogo than Go P3 for the High than the Medium and Low conditions.

4.4. Discussion

The questions of how to reliably attain training-induced improvements in inhibitory control and the supporting neural mechanisms remains unresolved. Therefore, using task performance and neural markers of inhibitory processing, the primary focus of the present research was to investigate the effect of varying task difficulty during the short-term training of the Go/Nogo task. In addition, we also aimed to determine whether the early evoked potentials and state differences (as indexed by task-related arousal and perceived effort) would be modulated by training.

4.4.1 Task Performance

Performance findings revealed that the Go/Nogo training was significantly influenced by variations in task difficulty. Both the Low and Medium conditions showed considerable reductions in Go RT along with no change in Nogo accuracy; suggesting a training-related improvement in inhibitory control, given that accuracy was maintained in the context of faster responding (for a similar finding see Manuel et al., 2010). The relationship between fast Go responding and an increased requirement for inhibition on Nogo trials is well-established (Falkenstein et al., 2000; Falkenstein et al., 1999; Lindqvist & Thorell, 2009; Manuel et al., 2010; Smith et al., 2006). When responses grow progressively faster on average, the relative strength of inhibition must increase in order to overcome the fast Go response (Smith et al., 2006). Moreover, given that Go RT was much faster overall for the Medium than Low condition (in addition to large improvements in Go RTD errors and Omission errors for the Medium condition), it appears that moderate task difficulty leads to greater enhancements in Go/Nogo

proficiency. Together with the finding that the High condition showed a significant decline in inhibitory performance, these findings are in line with previous behavioural reports suggesting that learning is likely to be enhanced when a task remains relatively challenging but not overly difficult (Ahissar & Hochstein, 2004), and provide novel evidence for the appropriate use of RTDs in optimising the short-term training of inhibitory control.

4.4.2 Task-related arousal

In order to investigate the role of state factors during the training session we examined task-related arousal and perceived effort. While perceived effort did not significantly vary over the training session, all three conditions showed a linear increase in arousal. Based on their review of this literature, Dawson et al. (1990) have suggested that elevations in skin conductance reflects the effortful mobilisation of mental resources directed towards a task (for similar conclusions see Larue et al., 2011; Naccache et al., 2005; Thomas et al., 2009). The enhancement of task-related arousal could therefore be related to the increased efforts of participants to maintain an alert state throughout the training session irrespective of task difficulty condition. However, it should be noted that other factors including mood and fatigue have been shown to influence not only SCL (e.g. Eason et al., 1965; Geldreich, 1939; Hajcak et al., 2004; Jacobs et al., 1994), but also performance on Go/Nogo tasks (Kato et al., 2009; Kato et al., 2012; Scholz et al., 2009; Schulz et al., 2007; Smallwood et al., 2009). From this perspective, it may be useful in future studies to include additional state measures to further clarify the effect of these energetic factors during cognitive training.

4.4.3 Early ERP components

Interestingly, training differentially modulated Go/Nogo N1 amplitudes between conditions. Participants in the Low and Medium conditions showed relatively similar N1

amplitudes to Go and Nogo stimuli by the end of training, while those in the High condition displayed a reduced Nogo relative to Go N1. The N1 ERP component is sensitive to the sensory attributes of stimuli and is modulated by attention (Näätänen & Picton, 1987a). Similarly, Bekker et al. (2005a) has also suggested that N1 amplitudes may index an attentional switch that is determinative for subsequent inhibitory control. Together with the performance data, these findings point to differential focusing on task requirements for each of the three difficulty conditions over the course of the training session. That is, in the context of improved Go/Nogo proficiency, it would seem that participants in both the Low and Medium conditions applied a more balanced approach in attending to Go and Nogo stimuli. By contrast, training seems to have led to a reduction in attentional resources being directed towards Nogo stimuli in the High condition, possibly due to these participants focusing primarily on the Go stimulus in order to respond within the strict RTD (Johnstone et al., 2005). Such a reduction in attention to the Nogo stimuli may, in part, explain the increased errors on Nogo stimuli with training in this group.

Notably, training resulted in different changes in P2 topography between the task difficulty conditions: the Medium and High condition showed a more anterior P2 to both Go and Nogo stimuli, contrasting with the Low condition which displayed an enhanced centroparietal Nogo compared to the Go P2 (see Figure 4.4 c and d). These differences were apparent in the vector-scaled data suggesting a training-induced shift in the neural generators of these components (Johnson, 1993). Moreover, although the P2 component is generally thought to index the appropriate classification of stimuli (Oades, 1998), its functional significance may have dissociable meanings according to scalp location. A more anterior P2 may index greater relevance of task stimuli (Potts, 2004; Potts et al., 1996), whereas larger parietal P2s have been reported during easy perceptual learning paradigms, paralleled by improvements in performance (Ding et al., 2003; Qu et al., 2010; Song et al., 2002; Song et al., 2005). Thus, a more anterior Go and Nogo P2 for the Medium and High conditions implies greater stimulus processing and evaluation of these stimuli with training, possibly due to the faster overall Go RT for these conditions. By contrast, the increased Nogo P2 over centroparietal sites for the Low condition

may index an early perceptual learning effect that is linked to more automated bottom-up processing in a relatively easy task, as implied by inhibition performance at ceiling for this condition.

Consistent with this notion, Verbruggen and Logan (2008) posit that Go/Nogo task practice leads to the emergence of automatic inhibition, where learned associations between stimuli and withholding a response reduce the need for top-down executive control. In this context, it may be that enhanced Nogo P2 amplitudes for well-learned or easy tasks reflects the automated inhibition of Nogo stimuli, freeing top-down mechanisms from further processing. In contrast, more difficult tasks appear to show a reduced P2 at parietal sites, potentially signalling the need for greater top-down inhibitory control at later processing stages (Dimoska & Johnstone, 2007; Dimoska & Johnstone, 2008).

4.4.4 Inhibition-related ERP components

N2 amplitude and latency decreased across the session regardless of condition, in line with previous research (Ding et al., 2003; Song et al., 2002). Interestingly, however, further interactions highlighted that this decline was primarily due to reduction of the Go, but not the Nogo N2. The N2 component is thought to represent a controlled mismatch detection process (Näätänen & Picton, 1986; Snyder & Hillyard, 1976), and is therefore related to stimulus discrimination (Johnstone et al., 2001; Johnstone et al., 1996; Ritter et al., 1983). Attenuated cortical responses to repeated stimuli have typically been interpreted as an early manifestation of learning-induced neural plasticity (see Garrido et al., 2008; Race et al., 2010; Summerfield et al., 2011). Thus, reduced Go N2 amplitudes across training blocks may suggest more efficient stimulus discrimination with training. Moreover, Neubauer and Fisk (2009) have proposed that greater neural efficiency might arise when training with tasks of low difficulty. If this is the case, the finding of the larger training-induced decline in N2 latency for the Low than Medium/High conditions is in accord with this interpretation.

Against predictions, training-related variations in task performance were not accompanied by an increase in the Nogo N2 (see Figure 4.4). While consistent with some previous reports investigating the effect of repetition (Falkenstein et al., 2002; Kato et al., 2009), it is in contrast to others suggesting enhancements in this component concurrent with improvements in Go/Nogo proficiency (for a discussion see Manuel et al., 2010; Schapkin et al., 2007). Our previous work, which considered the effect of decreasing RTDs (Benikos et al., 2013a), found that faster Go RTs resulted in incremental increases in Nogo N2 amplitude, interpreted in terms of enhanced response conflict (see also Nieuwenhuis et al., 2003; Randall & Smith, 2011). From this perspective, it may be argued that the stable Nogo N2 in the present study reflects a reduction in the relative level of response conflict, given that all three conditions showed declines in Go RT.

Nonetheless, it is interesting to note that the only inhibition training study which reported changes in Nogo N2 amplitude, found this effect after three days of training (Schapkin et al., 2007), while Luu and colleagues (2007) have suggested that changes in the N2 may only be apparent during the later stages of learning. Thus, combined with the fact that participants were presented with fewer Nogo than Go stimuli over the course of the training session (i.e. 30% vs. 70%), the equivalent Nogo N2 may be due to the slower time course of learning for this component.

While little change was seen across the session for the Low condition, the Nogo > Go P3 effect increased as a function of task difficulty particularly over central regions; showing a greater training-induced augmentation for the High than Medium condition (Figure 4.5). Since previous research has reported no significant change (e.g. Jodo & Inoue, 1990; Johnstone et al., 2010; Schapkin et al., 2007), this result is the first to suggest that increased task difficulty may be required to elicit training-related enhancements in the Nogo P3. Does this effect represent a strengthening of a top-down inhibition mechanism? We have previously shown that increased inhibition difficulty results in reduced Nogo P3 amplitudes. An implication here is that P3

amplitude is inversely related to inhibitory load. On this basis, it could be suggested that conditions like practice which tend to reduce task difficulty result in increased Nogo P3 amplitudes (for a similar interpretation regarding memory load see Kok, 1997). Similarly, the training-induced increase in Nogo P3 for the Medium condition accompanied by enhanced Go/Nogo proficiency may be interpreted in this manner. Moreover, despite increased Nogo errors, the greatest Nogo P3 for the High condition may not completely rule-out a practice-based interpretation of this effect; given that Nogo errors plateaued by block 4 for this condition, while the Nogo P3 continued to increase until the conclusion of training. This suggests a continued adaption to the difficulty of the task and is perhaps unsurprising, considering the brief (42 min) experience participants had with the training and its high difficulty level (for a similar fMRI finding see Kelly et al., 2006b). While it may also be argued that a larger Nogo P3 over central regions could simply be due to greater monitoring of the inhibition outcome in order to limit the error rate (for a similar argument see Beste et al., 2010), this explanation is unlikely, given the location of this component over the pre-motor cortex and that central increases in the Nogo P3 have been suggested to reflect a motoric inhibition process unrelated to movement related potentials (Smith et al., 2007). Since previous training studies have reported that neural changes can precede behavioural changes (Atienza et al., 2002), and that training in higher-order executive functions can potentially transfer to untrained tasks (Dahlin et al., 2008b), an avenue for future research would be to investigate whether training-induced enhancements in Nogo P3 transfers to unpractised Go/Nogo stimuli. If larger Nogo P3s represent an enhancement in inhibitory control processes, this improvement would be expected to transfer to the untrained stimuli.

Finally, future studies could consider the influence of differences in IQ and potential learning capacity between training conditions. While previous research has generally reported no relationship between IQ and baseline inhibitory performance (Friedman et al., 2006), IQ is a potentially strong predictor of learning ability (Alloway & Alloway, 2010). Thus, it may be helpful for future research to include an index of IQ and potentially other individual differences

which potentially interact with training-related gains in inhibitory performance (e.g. impulsivity; Horn et al., 2003).

4.4.5 Conclusions

In summary, this study provides novel evidence for the differential effects of task difficulty on the training of inhibitory control. In particular, the behavioural effects of short-term training appear to be optimised during conditions of moderate rather than low or high inhibitory load. An across-session increase in task-related arousal did not differ between conditions, indicating a generalised increase in demand for mental resources with time-on-task. Moreover, taken together the findings of the present study are of relevance to the theoretical accounts of the effect of training on inhibition-related neural activity. While changes associated with training have typically either been linked to the reinforcement of top-down executive control processes, or to the emergence of automatic bottom-up forms of inhibitory control, our results imply that these effects may be dependent on task demands. Whereas conditions of Low task difficulty may primarily lead to early bottom-up perceptual learning as reflected by enhancements in the centroparietal Nogo P2, top-down changes, particularly in the Nogo P3 appear to be associated with enhanced task difficulty. Although further research is needed in this area, these findings implicate the potentially key role of task difficulty for researchers attempting to design effective inhibition training paradigms to ameliorate inhibitory control deficits as seen in disorders such as ADHD.

The findings presented here suggest an intriguing dissociation between exogenous and endogenous ERPs as a result of manipulating task demands during the training of inhibitory control. However, the present study was limited in several ways. First, RTDs were chosen in order to elicit faster responses and ensure that inhibition was increasingly more difficult. However, conditions of High time pressure may have been too difficult for participants to adapt

to within the time period available. A limited time window may prevent the identification of learning-related changes if performance has not reached asymptote levels (Poldrack, 2000). Instead, the manipulation of Nogo stimulus probability offers another method of varying Go/Nogo task difficulty without the use of such strict time pressure (e.g. Bruin & Wiers, 2002). A further limitation was the omission of a control condition that performed a different task, which may help to separate the training-dependent changes from training-independent changes in task performance and neural activity. Furthermore, a crucial issue in the field of skill acquisition is the generalizability of training-induced improvements. However, the question of whether training gains in inhibitory control can transfer to untrained stimuli remains open. To address these limitations, the next study examines the effect of varying task difficulty via stimulus probability and includes a non-inhibition training control condition. A final Go/Nogo test block employing untrained stimuli will also be included to assess whether training effects were stimulus-specific.

Chapter 5 - Study 3: Examining the effect of varying stimulus probability during the short-term training of inhibitory control

Abstract

The inhibition of responses is a core feature of cognitive control and can be defined as the process of deliberately suppressing a prepotent/ongoing actions or revisiting interference. This ability is subject to disruption, playing a prominent role in the development of several neurological and psychiatric disorders. Over recent times, there has been an unprecedented interest in investigating the fundamental nature of inhibitory control. However, whether this ability can be improved by training and the supporting neural mechanisms has received little attention. Thus, the primary aim of this study was to examine the effect of varying task difficulty, via stimulus probability, during the short-term training (8 blocks of 100 trials) of the Go/Nogo task. To this end, fifty four participants were randomly allocated to one of three training conditions: Standard Prepotency (SP; 70% Go; n = 18), High Prepotency (HP; 85% Go; n = 18) and Control (Go 30%; n = 18). After block 8, a final block containing previously untrained stimuli was used to assess if the training effects were stimulus-specific. In the absence of self-reported differences in motivation, workload and task-related arousal, all participants showed reductions in N1 and N2 amplitude, in addition to an anterior increase of the P2; indicative of generally more efficient processing of Go/Nogo stimuli with repeated task administration. Performance findings indicated the greatest gain in Go/Nogo proficiency for the HP than SP and Control conditions; an effect that was reflected by centrofrontal enhancement of the Nogo > Go P3. This effect was not stable with introduction of untrained stimuli. Unexpectedly, the SP condition showed little difference compared to the active controls in performance gains and the Nogo > P3 effect. However, further inspection of the present study's methodology indicated that the overall level of inhibitory load provided by RTDs appears to be the primary determinant of training success, rather than stimulus prepotency. Although

unanticipated, these results highlight key task design elements that should be employed in the design of future inhibition training paradigms.

5.1 Introduction

Effective goal-directed behaviour requires the ability to successfully inhibit cognitive and motor processes (Chambers et al., 2008; Clark, 1996; Nigg, 2000). Individual differences in inhibitory control not only influence how we respond to everyday events, such as stopping at traffic lights or suppressing inappropriate verbal behaviour, but also have important long-term implications (Casey et al., 2011; Moffitt et al., 2011). Poor inhibitory control during adolescence predicts later substance dependence (Nigg et al., 2006), with deficits in this ability observed in impulse control disorders (Chambers et al., 2008) such as attention-deficit/hyperactivity disorder (ADHD; Smith et al., 2004), substance abuse disorders (Bechara et al., 2006) and gambling disorders (Billieux et al., 2012; Brevers et al., 2012; Goudriaan et al., 2006; Grant et al., 2010)

Investigations of inhibitory processing frequently employ Go/Nogo paradigms in which participants are required to make speeded responses to one stimulus (Go), while withholding a response to another stimulus (Nogo). Two event-related potential (ERP) components have been related to the suppression of motor responses: the Nogo N2, which is maximal in frontal brain regions (Falkenstein et al., 1999), and peaks approximately 200 ms after stimulus onset; and also the P3 to Nogo stimuli which is typically larger in central or frontocentral regions compared to Go trials (termed the 'Nogo P3 anteriorisation' effect), occurring approximately 300 ms post-stimulus (e.g. Smith et al., 2013a).While several early studies supported the association between the Nogo N2 and inhibition (e.g. Falkenstein et al., 1999), it has generally been accepted as reflecting response conflict in recent years (for reviews see Folstein & Van Petten, 2008; Huster et al., 2013). The Nogo P3 has more consistently been interpreted as indexing the inhibition process (Smith, Johnstone & Barry, 2006, 2007, 2008; Smith et al., 2010), however, it has also been suggested to reflect an aftereffect of inhibition, such as the evaluation of inhibitory performance (Beste et al., 2008; Beste et al., 2010; Bruin et al., 2001).

In light of the importance of optimal inhibitory control for daily life and its role in clinical disorders, the possibility of developing effective inhibition training paradigms as an adjunct to existing rehabilitation methods offers a potentially promising avenue for the development of targeted remediation programs (Chambers et al., 2008; Dimoska-Di Marco et al., 2011; Markomichali et al., 2009). Moreover, given that atypical brain activity often accompanies inhibition deficits (for reviews Bari & Robbins, 2013; Chambers et al., 2008), it is important to uncover the underlying mechanisms behind performance improvements. While recently there has been unprecedented interest in the investigation of the neural basis of inhibitory control (for a review see Chambers et al., 2008), whether this ability can be improved with training and the supporting neural mechanisms has received little attention.

For instance, it has been suggested that training-induced changes in inhibitory control may lead to an enhancement of neural efficiency, with previous research reporting reductions in the EEG source activation of inhibition-related regions (e.g. right inferior frontal gyrus, rIFG; Manuel et al., 2013; Manuel et al., 2010) and reduction in the latency of the Nogo P3 (Benikos et al., 2013a; Jodo & Inoue, 1990). By contrast, it has also been suggested that training could lead to the strengthening of an underlying inhibition mechanism (Benikos et al., 2013a). However, here again, the manifestation of this effect has differed between studies, with reports of either increased Nogo N2 (Schapkin et al., 2007) or Nogo P3 amplitudes (Benikos et al., 2013a) , or greater activations in inhibitory control areas after training using fMRI (Kelly et al., 2006b). In particular, our previous work noted that variations in training difficulty may play an important role in eliciting training performance gains and neural changes (Benikos et al., 2013a). While performance improvements were optimised during conditions of moderate rather than low or high inhibitory load, the neural changes were dependent on task demands, such that the moderate condition displayed an enhanced Nogo P3, whereas the low difficulty training conditions showed an enhanced Nogo P2.

There are a number of possible reasons for the inconsistency of previous findings. First, it is increasingly accepted that a *necessary* component for optimal cognitive training paradigms is the manipulation of task difficulty (Lövdén et al., 2010). Previous inhibition training studies have either not manipulated task difficulty (e.g. Jodo & Inoue, 1990) or have varied widely in terms of difficulty type and intensity, including the use of perceptual difficulty (e.g. Millner et al., 2012), static (Benikos et al., 2013a) and adaptive reaction time deadlines (Manuel et al., 2013). A within-study comparison using different training task variants would help to clarify these findings (Jolles & Crone, 2012). Second, few previous inhibition training investigations have used a control condition, leaving them unable to differentiate training effects due to simple exposure to the task procedure (e.g. EEG capping, time in the recording booth) and expectancy effects (Shipstead et al., 2012). Control conditions may be boring and less motivating than the training conditions (Jolles & Crone, 2012; Markomichali et al., 2009; Shipstead et al., 2012), with differences in training outcomes simply due to lack of task engagement between conditions. The addition of self-report state measures may help to clarify these effects (Jolles & Crone, 2012). Finally, ERP components during auditory and visual single-session paradigms have been shown to habituate as a function of simple stimulus repetition (Ravden & Polich, 1998). Given that previous inhibition training studies have used the same stimuli throughout the training session (Manuel et al., 2013; Manuel et al., 2010), it is unclear whether reductions in neural activity are, at least in part, stimulus-specific and due to habituation effects.

5.1.1 The Present Study

Using ERP and behavioural measures, the current study examined the effect of varying task difficulty, via stimulus probability, during short-term Go/Nogo task training. To this end, we randomly allocated participants into one of three training conditions: Standard Prepotency (SP) with 70% Go stimuli, High Prepotency (HP) with 85% Go stimuli, and the Control condition (Control) with 30% Go stimuli. The literature has robustly reported that increased Go stimulus probabilities can be used to enhance response preparation, thereby increasing the

strength of inhibition required on Nogo trials (Bruin & Wiers, 2002; Donkers & van Boxtel, 2004; Enriquez-Geppert et al., 2010; Nieuwenhuis et al., 2003). In contrast, oddball-type tasks, where participants are required to respond to the Go (i.e., Target) stimulus on the minority of trials, and withhold that response to the remaining Nogo (or 'Standard') stimuli, are particularly suited for indexing attentional capacity (Barry et al., 2003; Smith et al., 2004). The use of the oddball task allowed consideration of a "low-dose'" control condition, which was similar to the training conditions, except for the variable being tested (i.e. inhibition difficulty, via stimulus prepotency). In order to provide a moderate time pressure where Go/Nogo training effects are optimised (Benikos et al., 2013a), each participant's mean Go RT from the practice block was used as the RTD for the experimental blocks. Moreover, setting a proper control condition involves consideration of additional factors that could potentially influence the outcome of training; such as motivation, arousal and workload (Green & Bavelier, 2008; Slagter et al., 2011; Tang & Posner, 2009; Yerkes & Dodson, 1908). Thus, participants provided perceived effort ratings and we recorded skin conductance level (SCL) - a well-established measure of central nervous system arousal (Barry & Sokolov, 1993). The current study also aimed to examine whether training gains in inhibitory control were driven primarily by the development of stimulus-response associations (Verbruggen & Logan, 2008). In line with previous behavioural studies demonstrating performance improvements using short term single-session training sessions, participants completed eight training blocks (e.g. Kelly et al., 2006b; Verbruggen & Logan, 2008), but we added a final test block using previously unseen Go/Nogo stimuli to test whether training gains were stimulus-specific.

5.2 Method

5.2.1 Participants

A total of 64 adults in the school of psychology enrolled in the present study as a means of attaining research participation credit, with four being excluded according to the selection criteria. To be included in this study, participants were required to refrain from caffeine for 2 hours prior to testing and have not taken any psychotropic substances (prescription or illegal) for 24 hours prior to testing, and no more than once a month in the previous six months. Participants were also screened for neurological disorders and reported normal or corrected-to-normal vision.

The remaining 60 participants were randomly assigned to one of three conditions: Control, SP or HP. A further 6 participants were excluded either due to excessive eye muscle artefact (2 participants) or technical problems with the recording equipment (4 participants). Therefore, the final analyses included 18 participants in each condition: Control (13 females, mean age 23.70, SD 5.78), SP (12 females, mean age 22.11, SD 5.28) and HP (11 females, mean age 21.58, SD 3.09). There were no differences in age ($F(2,51) = 0.92$, $p = .403$) or gender ($\chi 2(2) = 0.50$, $p = .779$) between conditions. All but 3 of the 54 participants were right-handed. The research protocol was approved by the joint University of Wollongong and Illawarra Area Heath Service Human Research Ethics Committee.

5.2.2 Task

A schematic of the Go/Nogo task can be seen in Figure 5.1, while Figure 5.2 presents the study design. Stimuli were generated using Presentation software (Version 11.0; Neurobehavioral Systems, Albany, CA) and presented centrally on a 15 inch LCD computer

monitor, with participants seated one metre from the screen. Each stimulus measured approximately 3 x 3 cm and participants responded with a response box using their right hand, irrespective of handedness.

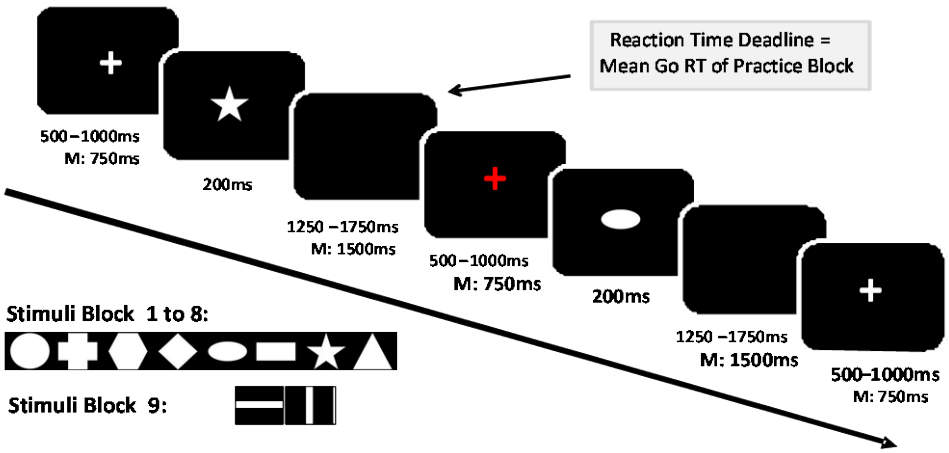


Figure 5-1. Schematic example of the using to Go (star) and Nogo (elipse) stimuli.

A trial began with a central fixation cross (+) presented for a variable interval of 500-1000 ms (M = 750 ms), followed by either the Go or Nogo stimulus for 200 ms. A blank screen then replaced the Go/Nogo stimulus for a variable blank period of 1250 – 1750 ms (M = 1500 ms). Within this period, participants were required to press the button press to Go stimuli within an individually tailored RTD (see below for further details), and to refrain from responding to Nogo stimuli. Performance feedback was provided via the subsequent fixation cross: correct responses were followed by a white fixation cross, while a red fixation cross was displayed after incorrect responses (i.e., presses to the Nogo stimuli during the variable blank period, omissions and responses outside the RTD). Only presses to the Go stimulus within the predefined response window were regarded as correct. Consistent with our previous research (Benikos et al., 2013a), the selection of shapes used to represent the Go and Nogo stimuli were selected from a pool of eight 2D shapes (i.e. circle, cross, hexagon, diamond, ellipse, rectangle, star or triangle; Figure 1) in order to minimise habituation of the visual ERP response (particularly the P3 component, e.g.

see Ravden & Polich, 1998). Furthermore, varying stimuli from block-to-block minimises consistent stimulus-response mappings (Verbruggen & Logan, 2008) and promotes the training of the underlying cognitive process (Dixon et al., 2009; Kelley & Yantis, 2009; for a review see Schmidt & Bjork, 1992). The presentation of shape stimuli was counterbalanced by using a Latin square design (Bradley, 1958) and the Go/Nogo response assignment was counterbalanced across participants.

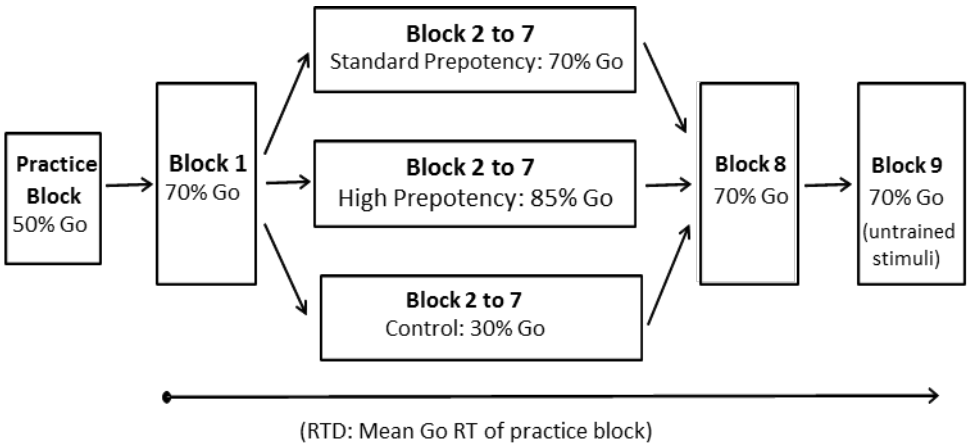


Figure 5-2. Study design including the changes in the percentage of Go trials for each condition across the training session. Note: a short break of ~10 minutes was included at the midpoint of testing.

Participants first completed a practice block of 30 trials (50% Nogo), followed by nine experimental blocks of 100 trials each - similar to previous single-session Go/Nogo investigations that have demonstrated training-related improvements in inhibitory control (Benikos et al., 2013a; Kelly et al., 2006b; Verbruggen & Logan, 2008). In order to provide a moderate time pressure, each participant's mean Go RT from the practice block was used as the RTD for the experimental blocks (Mean RTD: 434 ms). The percentage of Go stimuli was set differently for each condition during the training blocks (i.e. block 2 to 7): SP, 70% Go vs. HP, 85 % Go vs. Control, 30% Go (Figure 2). Secondly, to accurately compare potential training-

related changes in performance or ERPs, all participants completed blocks 1, 8 and 9 using the 70% Go prepotency. Finally, Go and Nogo stimuli were substituted with untrained stimuli, a horizontal or vertical bar during block (see Figure 5.1).

5.2.3 Procedure

Participants were familiarised with the laboratory equipment, before completing a short screening questionnaire designed to assess vision problems, medication/psychotropic substance use, handedness and neurological disorders. It was explained that they would be asked to undertake a training session where they would practice their ability respond to, and inhibit visual stimuli. It was emphasised that participation was entirely voluntary and that they could withdraw at any time without penalty. After providing written consent, participants were randomly allocated to either the Control, SP or HP condition. They were then fitted with the recording equipment and seated in a dimly-lit sound-attenuated electrically-shielded testing booth. An incandescent light in the booth was dimmed for the duration of the testing. Participants were then presented with the Go/Nogo task and instructed that they would see two shapes; one representing the Go stimulus, and the other representing the Nogo stimulus. They were required to press the button with the thumb of their right hand to the Go, but to refrain from responding to the Nogo stimulus. They were also asked to avoid the incorrect feedback and to “do your best” to improve task performance from the beginning until the end of the session. Go/Nogo shape assignment was shown on the screen and verbally confirmed by the participant prior to each block. Mean Go RT and the percentage of Go and Nogo errors were displayed for participants to review at the end of each block. Each block lasted approximately 3.5 min. Training session length was equated between the conditions by keeping the rest periods between the blocks at 1.5 min for all participants. A longer 10 minute break was provided half-way through the testing session. Total time performing the task, including the practice and training blocks, was approximately 48 min. Participants completed the self-report measures at

the conclusion of the training, and were informed of the training condition they had been assigned to.

5.2.4 Self-Report measures

Immediately following the testing session, participants completed a 14-item subset from the Dundee Stress State Questionnaire (DSSQ; Matthews et al., 2002; Matthews et al., 1999) to retrospectively assess motivation level (e.g., “I wanted to succeed on the task,” “I felt apathetic about my performance”). To examine whether the conditions differed in the degree of workload and overall task demand, we employed the NASA Task Load Index (NASA TLX; Hart & Staveland, 1988) using the following subscales: Mental Demand (‘‘How mentally demanding was the task?’’), Temporal Demand (‘‘How hurried or rushed was the pace of the task?’’), Perception of Performance (‘‘How successful were you in accomplishing what you were asked to do?’’), Effort (‘‘How hard did you have to work to accomplish your level of performance?’’), and Frustration (‘‘How insecure, discouraged, irritated, stressed, and annoyed were you?’’).

5.2.5 Electrophysiological recording

The continuous scalp electroencephalogram (EEG) was recorded from 19 sites (Fp1, Fp2, F3, F4, F7, F8, Fz, C3, C4, Cz, P3, P4, Pz, T3, T4, T5, T6, O1, O2) using an electrode cap containing tin electrodes fitted according to the international 10-20 system (Jasper, 1958). A ground electrode was located between Fpz and Fz, and all electrodes were referenced to linked ears. Vertical eye movement (vEOG) was measured using two tin cup electrodes placed 1 cm above and below the left eye. Impedance was kept below 3 kΩ for vEOG and reference electrodes, and below 5 kΩ for cap electrodes. EEG and vEOG signals were amplified 19 times and sampled at 500 Hz, with bandpass down 3 db at 0.1 and 100 Hz via a NuAmps system (Compumedics Limited, Melbourne, Australia).

5.2.6 Skin Conductance recording

Electrodermal activity was recorded using two Ag/AgCl electrodes placed on the distal phalanges of the third and fourth digits of the left hand. Recording electrodes were filled with electrode paste (0.05 M NaCl in an inert viscous ointment base) and secured using velcro straps and tape. A constant voltage device (UFI Bioderm model 2701) set at 0.5 V was used. This system separately recorded tonic DC-coupled skin conductance level (SCL) and AC-coupled skin conductance fluctuations (SCR), measured in microsiemens (μS), but only SCL is reported here.

5.2.7 Data quantification

Prior to processing, the EEG data were digitally filtered using a low-pass filter 3 db down at 30 Hz. The ERP epoch was defined as 100 ms pre-stimulus to 900 ms post-stimulus onset. Epochs were excluded if they contained activity greater than ± 100 μV at any non-frontal site. Eye movement artefact was corrected using the in-built procedure from Neuroscan (Semlitsch et al., 1986). ERPs were averaged across epochs for correct responses only, resulting in a minimum of 19 artefact-and-error-free Nogo trials being included in each average. Go epochs were averaged separately, chosen randomly from the available correct Go epochs to equal the number of Nogo epochs.

Grand average ERP waveforms for Go and Nogo stimuli were displayed in order to define each component's latency range. Latency was fixed across sites to the peak latency of the site of maximum amplitude (Picton et al., 2000; Spencer et al., 2001). ERP component peaks were quantified using automatic peak-picking software which identified the largest positive or negative deflections within the predefined latency range, relative to the 100 ms pre-stimulus baseline period. Peak latency ranges and sites were as follows: N1 (90 -150 ms, Fz), P2 (170-230 ms, Pz), N2 (220-280 ms, Fz), P3 (270-370 ms, Pz). Skin conductance level was taken as

the average value (in μS) for each 30 sec period over the approximate 3.5 min duration of each block of the Go/Nogo task.

5.2.8 Statistical analyses

Univariate analyses of variance (ANOVA) were used to analyse the self-report data with Condition (Control vs. SP vs. HP) as the between-subjects factor. To correct for skewed distributions, the Go RT data were normalized using the inverse of RT (computed as 1000 / (0 – RT); Ratcliff, 1993). The error rate indices (Go omission errors, RTD and Nogo errors) were calculated as the number of incorrect responses divided by the total number of presentations. Training task performance was analysed using a Condition (Control vs. SP vs. HP) x Time (Block 2 vs. 3 vs. 4 vs. 5 vs. 6 vs. 7) mixed repeated measures analysis of variance (ANOVA) using planned polynomial contrasts within Time and between Conditions. For blocks 1, 8 and 9, both SCL and task performance were analysed in a similar manner, but employed Repeated contrasts [i.e. block 1 (b1) vs. block 8 (b8); b8 vs. block 9 (b9)] to investigate the effects from before to after the training blocks, and with the introduction of untrained stimuli.

Primary analyses of the ERP data were restricted to nine sites (F3, Fz, F4, C3, Cz, C4, P3, Pz and P4) using Condition (Control vs. SP vs. HP) x Lateral (Left vs. Midline vs. Right) x Sagittal (Frontal vs. Central vs. Parietal) x Stimulus (Go vs. Nogo) x Time (b1 vs. b8 vs. b9) ANOVAs. Planned orthogonal contrasts within the Lateral factor compared activity in the left hemisphere (mean of F3, C3 and P3) with the right (mean of F4, C4 and P4), and the mean of these with activity in the midline region (mean of Fz, Cz and Pz). Contrasts within the Sagittal factor compared frontal activity (mean of F3, Fz and F4) with parietal (mean of P3, Pz and P4), and the mean of these with activity in the central region (mean of C3, Cz and C4). As above, differences within Time and between Conditions were assessed using Repeated contrasts (b1 vs. b8; b8 vs. b9). ERP component latencies were examined in the same manner as amplitudes but without the Sagittal factor. As these contrasts were planned with no more of them than the

degrees of freedom for each effect, no Bonferroni type adjustment to α were necessary (Tabachnick & Fidell, 1996). Also, single degrees of freedom contrasts are not affected by violations of symmetry assumptions common in repeated measures analyses, and thus do not require Greenhouse–Geisser-type corrections. It should be noted that this increases the frequency of type 1 errors, however, as this is an increase in frequency, rather than probability, it cannot be 'controlled' by adjustment of α levels (Howell, 2009). All ERP statistics have (1,51) degrees of freedom unless otherwise indicated. Outliers in the data (±2 SDs from the mean) were corrected for by replacing with the series mean. Data were normalised using the vector scaling method (McCarthy & Wood, 1985), and only interactions with topography that remained significant in the normalised data are reported here.

5.3 Results

5.3.1 Self-report measures

Table 5.1 outlines the means and standard deviations for the self-report measures. Participants reported comparable motivation levels in all three training conditions. Similarly, there was no difference on any of the subscales of the NASA-TLX, suggesting that participants in each condition experienced a similar degree of overall motivation and task workload throughout the experimental session.

Table 5-1. Means for self-the report measures. Standard deviations in parentheses.

Measure	Control	SP	HP	*F*	*p*	*η2*
NASA-TLX						
Mental	7.56 (1.85)	6.78 (2.18)	7.06 (1.59)	0.78	.463	.030
Physical	2.89 (2.17)	2.56 (2.31)	1.89 (1.71)	1.08	.347	.041
Temporal	6.78 (2.26)	6.00 (2.81)	6.28 (1.67)	0.53	.591	.020
Performance	6.67 (0.97)	7.05 (0.73)	6.50 (0.92)	1.89	.161	.069
Effort	7.62 (1.46)	6.83 (1.85)	7.28 (1.56)	1.03	.366	.039
Frustration	4,56 (2.31)	4.33 (2.59)	4.94 (2.38)	0.29	.748	.011
DSSQ						
Motivation	30.72 (9.92)	31.06 (8.05)	32.72 (10.45)	0.23	.797	.009

5.3.2 Task-related Arousal

SCL increased from the block 1 (12.30 µS) to block 8 (14.84 µS; $F = 32.86$, $p < .000$, $\eta 2 = .371$), with no change from block 8 to 9 (b9 = 14.81 µS; $F = 0.07$, $p = .795$, $\eta 2 = .000$). This effect did not differ between conditions (all *p values* $\geq .109$).

Training Data

5.3.3 RTD and training task difficulty check

The individually tailored RTD level did not differ between the control (437 ms), SP (439 ms) or HP condition (430 ms; $F = 0.14$, $p = .870$, $\eta 2 = .005$). The HP condition showed the fastest Go RTs overall (-2.71) compared to the SP (-2.54) and Control conditions (-2.32); Linear, $F = 20.19$, $p < .000$, $\eta 2 = .284$). Participants in the HP condition also displayed a much larger proportion of Nogo errors (32.4%) than the SP (14.0%), in contrast to the Control condition, which made very few Nogo errors (M = 2.1%; Linear, $F = 169.96$, $p < .000$, $\eta 2 = .768$).

5.3.4 Training Task Performance

Training task performance measures can be seen in Figure 5.3. Go RT showed different training-related changes between the conditions. While it showed a small linear reduction over the blocks for the Control condition, it showed a greater reduction in the HP than SP condition (Linear, $F = 4.95$, $p = .011$, $\eta 2 = .115$). Go RTD errors decreased early in the training session with no difference between conditions (Linear, $F = 9.82$, $p = .003$, $\eta 2 = .158$). In contrast, Go Omission errors showed no significant change (Linear, $F = 3.32$, $p = .074$, $\eta 2 = .065$).

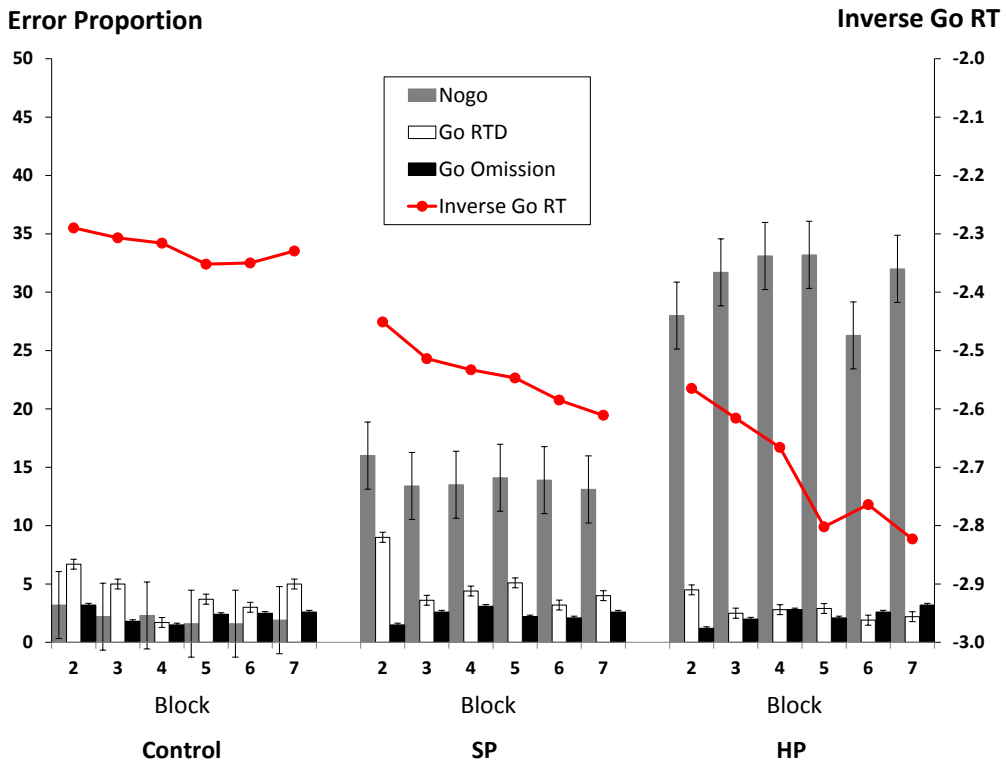


Figure 5-3. Go RT and mean error proportion (Go RTD, Omission and Nogo errors) across the training blocks for all three conditions.

For Nogo errors, neither the Time main effect (Linear, $F = 0.39$, $p = .534$, $\eta 2 = .007$) or the Time x Condition interaction (Linear; $F = 2.00$, $p = .146$, $\eta 2 = .072$) were significant. This result was confirmed by further within Condition analyses of Nogo errors showing no significant change over the blocks for either the Control (Linear, $F = 2.23$, $p = .153$, $\eta 2 = .111$), SP (Linear, $F = 0.79$, $p = .387$, $\eta 2 = .043$) or the HP condition (Linear, $F = 1.54$, $p = .232$, $\eta 2 = .083$). To clarify whether the improvement in Go RT was due to a speed-accuracy trade-off (SAT), we correlated the training-induced change in Go RT and Nogo errors (i.e. b7 minus b2). These analyses were not significant for either the Control ($r = .249$, $p = .318$), SP ($r = -.036$, $p = .888$) or HP condition ($r = -.048$, $p = .851$). In the context of stable inhibition performance, the largest training-related reduction in Go RT for the HP condition, represent an improvement in behavioural Go/Nogo task proficiency (Manuel et al., 2010).

Pre/Post Block Data

5.3.5 Pre/Post Task Performance

Go RT and mean error proportions for the block 1, 8 and 9 are displayed in Figure 5.4. Go RT decreased from blocks 1 to 8, showing the largest training-related decline for the HP relative to the SP and Control conditions ($F = 3.24$, $p = .047$, $\eta 2 = .057$), with little change from block 8 to 9 ($F = 0.33$, $p = .724$, $\eta 2 = .012$). This result was supported by a further comparison only including the Control and SP conditions, which found no difference in the Go RT decline from block 1 to 8 ($F = 0.23$, $p = .638$, $\eta 2 = .004$) or from block 8 to 9 ($F = 0.29$, $p = .594$, $\eta 2 = .008$). Go RTD errors decreased from block 1 to 8 ($F = 50.45$, $p < .000$, $\eta 2 = .497$), and remained relatively unchanged in block 8 to 9 ($F = 2.22$, $p = .142$, $\eta 2 = .051$). Go omission errors appeared to be at ceiling for all three conditions and did not differ from the b1 vs. b8 ($F = 0.40$, $p = .529$, $\eta 2 = .000$) or from block 8 to 9 ($F = 0.23$, $p = .632$, $\eta 2 = .000$).

Nogo errors remained relatively stable from block 1 to 8 ($F = 2.12$, $p = .151$, $\eta 2 = .039$) and from block 8 to 9 ($F = 3.12$, $p = .083$, $\eta 2 = .056$), with the Time x Condition effect not reaching significance (b1 vs. b8: $F = 0.47$, $p = .625$, $\eta 2 = .018$; b8 vs. b9: $F = 0.33$, $p = .722$, $\eta 2 = .013$). Similar to the training blocks, we correlated the change (i.e. b8 – b1) in Go RT and Nogo errors to investigate the possibility of a SAT with training. These analyses were not significant for either the Control (.404, $p = .097$), SP (.193, $p = .443$) or HP conditions (-.062, $p = .806$). There was no change in these results when considering performance between b1 to b9 (all $ps > .160$).

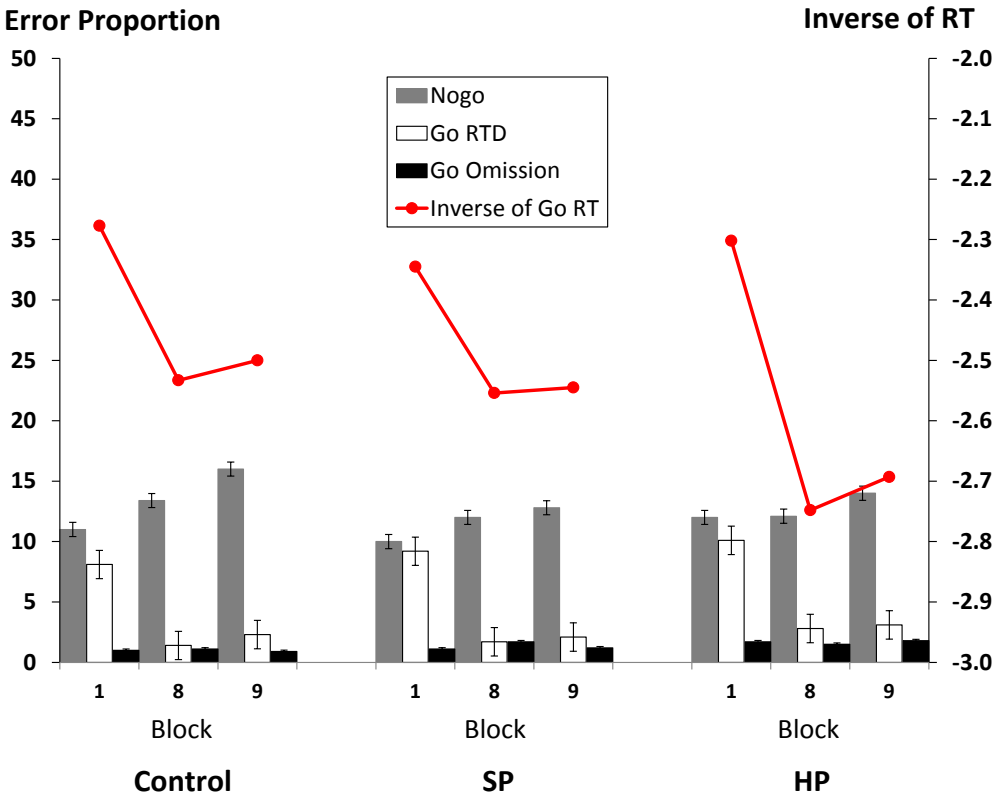
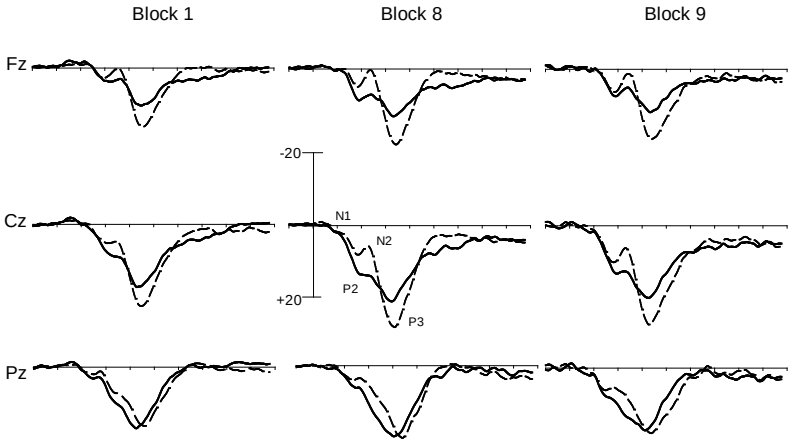


Figure 5-4. Means proportion of errors and inverse Go RT to Go/Nogo stimuli for block 1, 8 and 9.

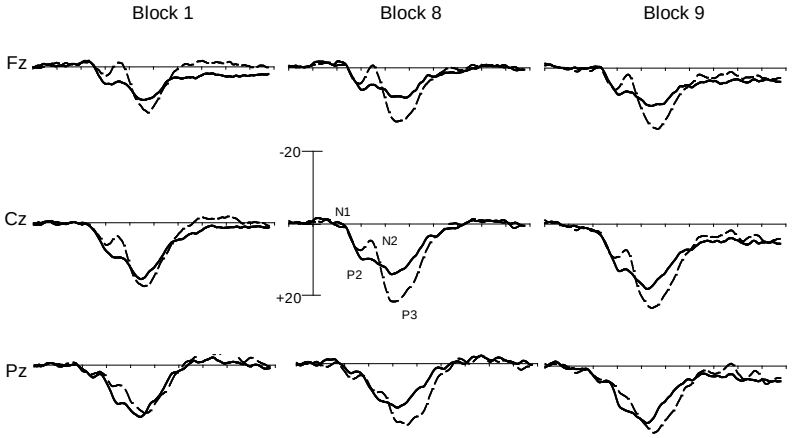
5.3.6 Event-related Potentials

To maintain the focus of the current study, the Results section only considers effects and interactions involving Stimulus type and Time. Figure 5.5 presents grand mean ERPs to Go/Nogo stimuli at midline sites for each condition for block 1, 8 and 9. There is a small frontal negative shift at about 100 ms, which appears to encompass the N1 component. This is followed by the P2 and N2 components, which are most apparent over frontocentral sites between 150 to 300 ms post-stimulus. The P3 can also be seen as a large positivity peaking approximately 300-500 ms, showing a clear frontocentral Nogo > Go effect, which appears to increase across the session.

(a) Control



(b) Standard Prepotency



(c) High Prepotency

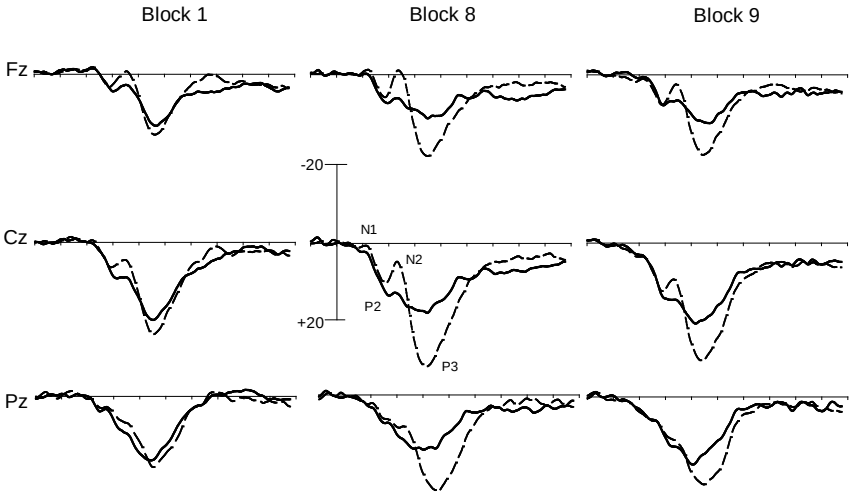


Figure 5-5. Grand mean ERPs for blocks 1, 8 and 9 to Go (solid line) and Nogo (dashed line) and each condition separately. ERPs are shown at three midline sites only. Note: x-axis ticks = 100 ms; stimulus onset at y-axis shown at Cz (scale: ± 20 μV).

5.3.6.1 N1

The N1 had a mean latency of 117 ms, peaking later for Nogo (120 ms) than Go stimuli (115 ms; $F = 8.44$, $p = .005$, $\eta 2 = .141$). N1 latency decreased from block 1 (121 ms) to 8 (116 ms; $F = 7.45$, $p = .009$, $\eta 2 = .127$), with little change from block 8 to 9 (115 ms; $F = 0.27$, $p = .606$, $\eta 2 = .005$).

Table 5.2 provides details for the following effects and provides means. N1 amplitude was larger to Nogo than Go responses, with this effect most apparent in the central region. Overall, N1 amplitude to Go/Nogo stimuli decreased from block 1 to block 8, with Time x Sagittal and Lateral interactions indicating focal reductions of N1 amplitude in central/parietal regions, and along the midline (see Figure 5.6). These effects remained stable b8 to b9 and did not interact with Condition.

Table 5-2. Significant results for the N1 and P2 component amplitudes including means.

Measure	Effect	Contrast	Details	*F*	η^2
N1	S x Stim	c vs. f/p	Go, 0.4 to 0.5 vs. Nogo, -0.2 to 0.3	19.79***	.269
	T	b1 vs. b8	-0.8 vs. 0.7	22.88***	.307
	T x S	c vs. f/p	b1, -1.2 to -0.6 vs. b8, 0.5 to 0.8	10.78**	.167
	T x L	m vs. l/r	b1, -1.2 to -0.6 vs. b8, 0.5 to 0.8	4.98*	.088
P2	Stim	Go vs. Nogo	8.7 vs. 7.3	44.20***	.444
	S x Stim	f vs. p	Go, 6.3 to 5.9 vs. Nogo, 9.5 to 6.5	16.57***	.241
	L x Stim	l vs. r	Go, 8.0 to 8.8 vs. Nogo, 5.9 to 6.2	7.60**	.129
	T	b1 vs. b8	5.5 vs. 8.4	53.80***	.510
		b8 vs. b9	b8 vs. 9.7	12.26**	.192
	T x S	f vs. p	b1, 3.4 to 6.8 vs. b8, 7.1 to 7.9	25.03***	.473
	T x L	l vs. r	b1: 4.8 to 5.6 vs. b8: 7.4 to 7.8	4.45*	.076

* = < .05, ** = < .01, *** = < .001

For this and subsequent tables, details column represents mean amplitude in μV. Abbreviations: Cond, Condition: SP, Standard Prepotency, HP, High Prepotency, Control, Control condition. Stim, Stimulus type: Go/NoGo. T, Time; b1, block 1; b8, block 8; b9, block 9. Lateral (L) abbreviations: l, mean of the left hemisphere (F3, C3, P3); r, mean of the right hemisphere (F4, C4, P4); l/r, mean of the left and right hemispheres (F3, C3, P3, F4, C4, P4); m, mean of the midline (Fz, Cz, Pz). Sagittal (S) abbreviations: f, mean frontal (F3, Fz, F4); p, mean parietal (P3, Pz, P4); c, mean central (C3, Cz, C4).

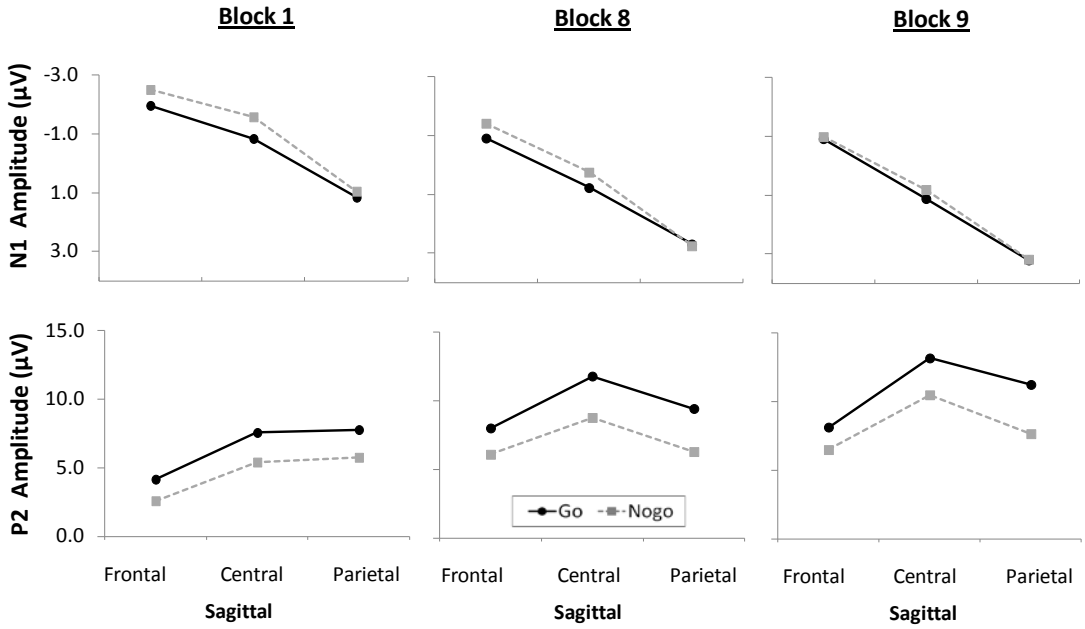


Figure 5-6. Go and Nogo amplitudes for the N1 (upper panel) and the P2 component (lower panel) for block 1, 8 and 9.

5.3.6.2 P2

The P2 (mean latency 205 ms) peaked earlier for Nogo (202 ms) than Go stimuli (208 ms; $F = 5.68$, $p = .021$, $\eta 2 = .098$). Overall, P2 latency reduced significantly from block 1 (214 ms) to block 8 (199 ms; b1 vs. b8; $F = 29.04$, $p < .000$, $\eta 2 = .341$), with no significant change from block 8 to 9 (203 ms; $F = 2.28$, $p = .137$, $\eta 2 = .040$).

The P2 was larger to Go than Nogo stimuli across the scalp, with this effect most apparent over parietal regions and along the midline (see Table 5.2). Across the scalp, Go/Nogo P2 amplitude increased from block 1 to block 8, and further still in block 9. Time x Sagittal and Time x Lateral interactions highlighted an anterior midline shift of the P2 focus for both Go and Nogo stimuli from block 1 to 8, with no significant change from block 8 to 9 (see Figure 6). There were no significant differences between conditions.

5.3.6.3 N2

N2 latency (mean latency 253 ms) reduced from block 1 (261 ms) to block 8 (248 ms; $F = 25.77$, $p < .000$, $\eta 2 = .313$), with little change in block 9 (251 ms; $F = 1.68$, $p = .201$, $\eta 2 = .030$).

The N2 showed a Nogo > Go effect, with this difference largest frontocentrally (see Table 5.3). Overall, N2 amplitude decreased from block 1 to 8, with little change in block 9 and no difference between the conditions.

5.3.6.4 P3

P3 (mean latency 337 ms) peaked later for Nogo (349 ms) than Go stimuli (327 ms; $F = 46.89$, $p < .000$, $\eta 2 = .477$). P3 latency reduced from block 1 (349 ms) to block 8 (332 ms; $F = 20.55$, $p < .000$, $\eta 2 = .286$), with little change in block 9 (331 ms; $F = 0.13$, $p = .719$, $\eta 2 = .003$).

Globally, P3 amplitude was larger to Nogo than Go stimuli (see Table 5.3). Stimulus x Sagittal and Lateral interactions revealed that this difference was largest at frontal and central leads, highlighting the Nogo P3 anteriorisation effect.

Overall (i.e. Go + Nogo), P3 amplitude increased from block 1 to 8, with little change in block 9. The Nogo > Go P3 effect showed different training-related changes between conditions: while controls showed a small frontocentral increase by block 8, the SP condition displayed a similar increase, as well as an increase in the centroparietal region. The HP condition displayed the largest increase in the Nogo > Go P3 effect, with this effect most apparent over centrofrontal regions. Interestingly, while the frontocentral Nogo > Go P3 effect reduced slightly for the Control and SP condition from block 8 to 9, HP condition showed a

Table 5-3. Effect summaries and means for the N2 and P3 component amplitudes

Measure	Effect	Contrast	Details	*F*	η^2
N2	Stim	Go vs. Nogo	8.2 vs. 4.2	97.63***	.655
	S x Stim	f vs. p	Go, 4.2 to 10.8 vs. Nogo, -0.2 to 7.8	10.85**	.158
		c vs. f/p	Go, 9.7 to 7.5 vs. Nogo, 4.9 to 3.8	22.66***	.272
	L x Stim	l vs. r	Go, 7.5 to 8.5 vs. Nogo, 4.0 to 4.4	8.65**	.145
		m vs. l/r	Go, 8.7 to 8.0 vs. Nogo, 4.1 to 4.2	29.42***	.359
	T	b1 vs. b8	4.5 vs. 6.6	20.4***	.335
P3	Stim	Go vs. Nogo	15.3 vs. 19.6	61.44***	.535
	S x Stim	f vs. p	Go, 11.1 to 17.0 vs. Nogo, 16.9 to 19.0	69.03***	.521
		c vs. f/p	Go, 17.7 to 14.0 vs. Nogo, 23.2 to 18.0	31.44***	.377
	L x Stim	m vs. l/r	Go, 16.6 to 14.6 vs. Nogo, 22.4 to 18.4	112.51***	.679
	T	b1 vs. b8	15.3 vs. 18.5	20.94***	.269
	T x Sim x Cond	Go vs. Nogo	Control: b1, 12.6 to 16.0 vs. b8, 18.0 to 21.5		
			SP: b1, 14.6 to 16.3 vs. b8, 13.8 to 19.3		
			HP: b1, 15.4 to 16.8 vs. b8, 15.4 to. 23.2	4.08*	.340
	T x S x Sim x Cond	f vs. p	Control: b1: Go, 9.1 to 14.5 vs. Nogo, 14.2 to 14.8;		
			b8: Go, 12.9 to 20.5 vs. Nogo, 19.6 to 19.5;		
			SP: b1, Go, 10.1 to 17.3 vs. b8, Nogo, 14.0 to 16.1		
			b8: Go, 9.7 to 15.5 vs. Nogo, 15.8 to 19.8;		
			HP: b1, Go, 11.5 to 16.8 vs. b8, Nogo, 14.5 to 16.0		
			b8: Go, 11.9 to 15.8 vs. Nogo, 19.3 to 23.0;	6.13**	.125
		f vs. p	Control: b8 vs. b9: Go, 11.0 to 16.8 vs. Nogo, 17.0 to 17.5		
			SP: b8 vs. b9: Go, 11.8 to 17.9 vs. Nogo, 17.3 to 21.6		
			HP: b8 vs. b9: Go, 11.6 to 17.7 vs. Nogo, 20.2 to 23.1	4.49*	.072

* = < .05, ** = < .01, *** = < .001

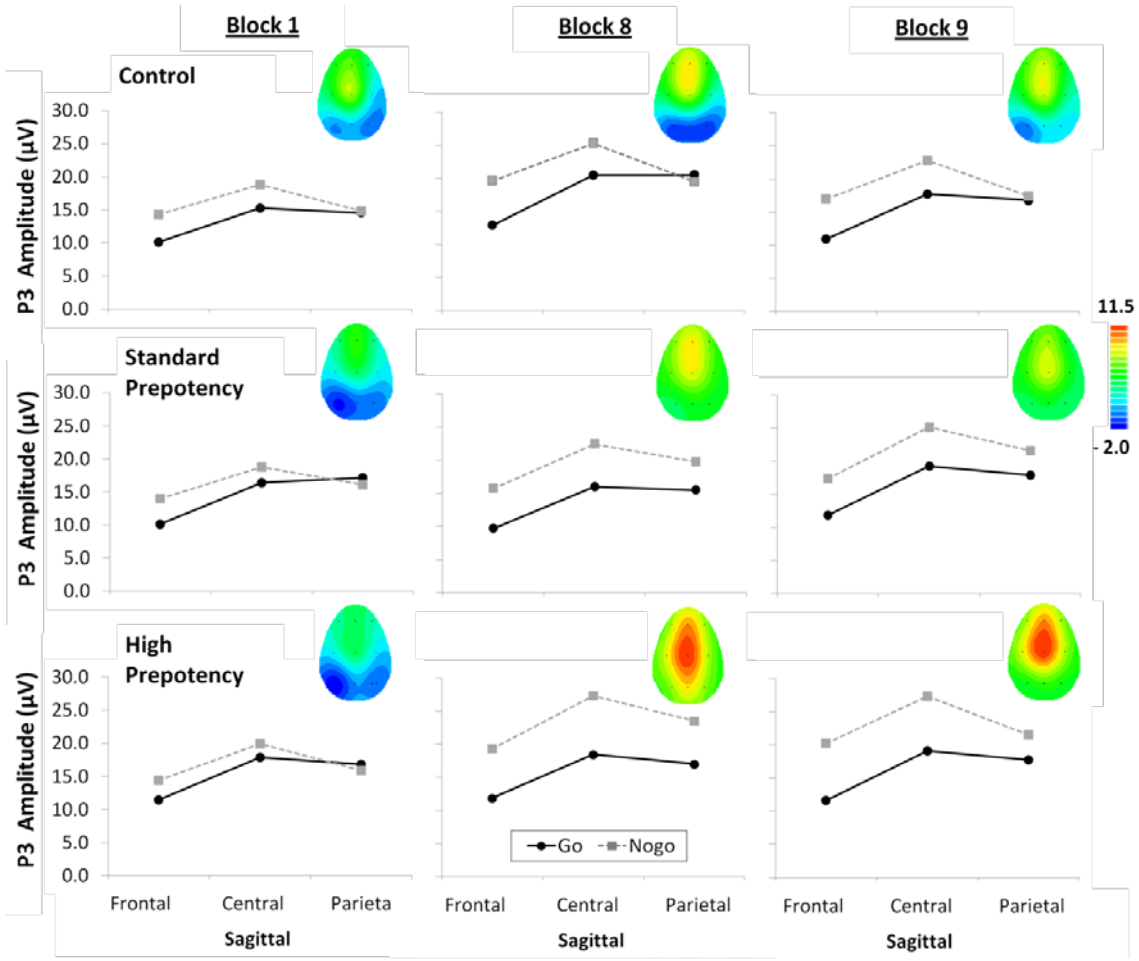


Figure 5-7. Time x Stimulus x Sagittal x Condition interaction for the Nogo > Go P3 effect, including Nogo minus Go topographic maps depicting the change in topography from block 1, 8 and 9. Scale values represent the ends of the colour scale in μV for. Darkest blue = negativity, red = positivity.

reduction in the Nogo P3 over centroparietal regions (see Figure 5.7 for plots and topographic maps).

5.4 Discussion

While inhibitory control has been extensively studied, the optimal task parameters required to elicit inhibition training task performance gains and the underlying neural mechanisms remain largely unresolved. The present study investigated whether increasing task difficulty (via stimulus prepotency) in two Go/Nogo training conditions (70% vs. 85% Go probability) would influence training effects. A control condition was included that trained participants using a low stimulus probability task to help rule-out factors unrelated to training. To investigate whether state variables differed between conditions, this study measured self-reported motivation and perceived workload, in addition to SCL as an objective measure of task-related arousal. Finally, to test whether training effects were stimulus-specific, we added a final test block using previously unseen Go/Nogo stimuli. There were a number of findings of note.

5.4.1 Performance and neural changes differing between conditions

First, training performance findings revealed that Go RT showed the greatest improvement in the HP compared to the SP and Control conditions, suggesting a greater training-related increase in Go/Nogo proficiency for the HP condition (Manuel et al., 2010). These results suggest that the training task difficulty manipulation was successful, and are also compatible with a number of previous studies reporting enhanced inhibition difficulty under conditions of frequent Go responding and rare Nogo trials (Bruin & Wiers, 2002; Enriquez-Geppert et al., 2010; Nieuwenhuis et al., 2003).

Second, performance findings between the Pre-and Post-training blocks (i.e. block 1 to 8) paralleled the training blocks, with the largest improvement in Go/Nogo proficiency seen again in the HP condition (Figure 5.4). Notably, consistent with previous research in this thesis (Benikos et al., 2013a), the change in performance for the HP condition was accompanied by an enhanced Nogo > Go P3 effect over centrofrontal regions compared to the SP and Control conditions (i.e. block 8; Figure 5.7). A more anterior Nogo than Go P3 has been suggested to reflect inhibitory processing (e.g. Randall & Smith, 2011; Smith et al., 2013a; Smith & Douglas, 2011), and via the use of enhanced stimulus prepotency, these findings suggest a training-related strengthening of an underlying inhibition mechanism under conditions of enhanced task difficulty (Benikos et al., 2013a); potentially supporting the use of stimulus prepotency in future inhibition training investigations. However, it is interesting to note that the distribution of the Nogo P3 was not stable upon the introduction of untrained stimuli, such that the HP condition showed amplitude reductions particularly over centroparietal regions (Figure 5.7). In addition to the well-studied frontal network that has been linked to inhibitory control, further research has also implicated parietal areas (Chikazoe et al., 2007; Criaud & Boulinguez, 2013; Dosenbach et al., 2006; Garavan et al., 1999; Li et al., 2006; Manuel et al., 2010; Rubia et al., 2001; Swick et al., 2008, 2011; Watanabe et al., 2002). The role of parietal cortices has been attributed to the regulation of motor planning (Rushworth et al., 1997; Watanabe et al., 2002) and to movement preparation (Decety et al., 1992; Deiber et al., 1996), rather than to inhibitory control. Moreover, previous work in this thesis has shown that increased Go/Nogo task difficulty led to centroparietal reductions in amplitude of the Nogo P3 (Benikos et al., 2013a). Therefore, given the continued faster Go RT overall for the HP than SP/Control conditions in block 9, it could be that introduction of new stimuli, which possessed no previously learned motor preparation or planning processes, was more difficult for HP participants to respond to, reflected by reductions in the centroparietal Nogo P3.

Third, unexpectedly, the Control and SP condition showed comparable changes in Go/Nogo proficiency and the Nogo > Go P3 anteriorisation effect. This finding initially goes against those of our previous study (Benikos et al., 2013a) which reported a greater improvement in Go/Nogo performance during conditions of moderate than high/low task demands using a 70/30 Go/Nogo split; but are in line previous inhibition training studies reporting negative reports of "true" training effects for inhibitory control (Enge et al., 2014; Thorell et al., 2009). Similarly, previous working memory (WM) training research has observed performance gains for training compared to passive groups, but not for active controls (Shipstead et al., 2012). It appears on first look, that the potential benefits from training inhibitory control by varying task difficulty may be limited (Enge et al., 2014).

However, I am reluctant to interpret this as a negative finding given a further inspection of the current study's methodology. To ensure that participants were matched as closely as possible on expectancy and effort for the training tasks, the study protocol imposed the same *relative* RTD for all participants. While this approach appears to be supported by the finding of no condition differences in self-reported motivation, workload or task-related arousal, it is possible that some of the condition-specific training effects were clouded due to this procedure. That is, despite the different Go probabilities between the Control and SP (30% vs 70%), further analyses showed that the decline in Go RT was equivalent; suggesting that the difference in Go probability was not the key determinant of training-related performance changes. Rather, the overall level of time pressure induced by the RTD appears to have elicited the intended training effects. Future research should instead focus on using adaptive RTDs, given that response activation likely differs between participants, and that previous cognitive training research in the WM domain has shown that adaptive task difficulty leads to greater performance gains (for a review see Klingberg, 2010).

5.4.2 Neural changes shared between conditions

Finally, there were a number of neural changes that occurred irrespective of training condition. Consistent with our previous study (Benikos et al., 2013a), and those from the general training literature (Ross & Tremblay, 2009; Tremblay et al., 2014), N1 amplitude reduced across the training session, while the P2 increased over anterior regions to both Go and Nogo stimuli (Wang et al., 2010). The N1 is typically understood to signify the initial sensory extraction of, and attention to stimuli (Näätänen & Picton, 1987a). Recent research reports that the anterior P2 is only present to task-relevant stimuli (Potts, 2004), and that P2 amplitude increases with stimulus repetition, regardless of changes in performance (Tremblay et al., 2014). In addition, despite showing a Nogo > Go effect, the N2 component reduced across the training session, compatible with some previous research (Ding et al., 2003; Song et al., 2002), but not others (Schapkin et al., 2007). The present study, together with those of previous research, suggest that the Nogo N2 represents variations in response conflict (e.g.van Veen & Carter, 2002b), whereas, the Go N2 is related to stimulus discrimination (e.g. Johnstone et al., 1996). In combination, the reduced amplitudes of the N1 and N2, in addition to anterior increase in the P2 component, may represent more efficient attentional control with repeated task administration, and not directly related to performance changes between the conditions.

5.4.3 Limitations

Although the current study provided some interesting results, there are a number of limitations that need to be taken into account for future research. First, as previously mentioned, the task for the control condition may have been too similar to that of the training conditions. Instead, the control task could be modified by requiring participants to count target stimuli in an oddball paradigm. Without the requirement of a motor response

this task would load on stimulus classification rather than inhibitory processing (e.g. Smith et al., 2004), while still equating participants for non-training related effects such as arousal, time-on-task and sustained attention. Second, the present study conducted the post-training assessment directly after training. As argued by Persson and colleagues (2013), cognitive resources are subject to resource depletion much like a fatigued muscle after a training session, and that "true" training gains should only be apparent after a period of recovery. Future research should conduct a post-training testing session at a later date to gain a more accurate measure of post-training performance and ERP changes.Thirdly, the stimuli used in the transfer block were very similar to those employed in the training blocks. If inhibitory control training is to be useful for remediation purposes, training-induced improvements should be shown to transfer to different inhibition domains (e.g. action withholding, action cancellation, interference control). Thus the use of multiple pre/post inhibition tasks would help to clarify these effects. Fourthly, only a static level of task difficulty was used throughout this study. In the WM domain, adaptive task difficulty leads to greater training gains (for a review see Klingberg, 2010). The use of adaptive RTD based on Go/Nogo performance may be of value in future studies. Finally, increasing stimulus prepotency in the current study did not appear to add any further benefit compared to the more standard 70/30 Go vs. Nogo approach. However, inhibition task difficulty could also be modulated by using a combined Go/Nogo stop-signal task (Enriquez-Geppert et al., 2010). Indeed, Go/Nogo and stop-signal tasks are thought to differentially modulate inhibitory processing, with enhanced task difficulty seen in the stop-signal task (Johnstone et al., 2007).

5.4.4 Conclusion

To conclude, in the context of no condition differences in self-reported motivation workload and task-related arousal, the effect of enhanced stimulus prepotency during the short-term training of inhibitory control appeared to show the greatest improvements in task

performance, accompanied by top-down augmentation of the Nogo > Go P3 effect over centrofrontal sites. However, further inspection of the present study's methodology indicated that the overall level of inhibitory load provided by RTDs is the primary determinant of training success, rather than stimulus prepotency. Although unexpected this result highlights key task design elements that should be employed in the design of future inhibition training paradigms.

Several important issues to the optimal design of effective inhibition training paradigms were raised by the results of the present study. These issues relate to (a) the choice of control condition, (b) the timing of the post-training assessment, (c) the use of multiple inhibition tasks to accurately assess training-related changes in inhibitory control, (d) the notion of static versus adaptive training task difficulty levels, and (e) the use of combined inhibitory control tasks. Therefore the next study aimed to address these issues by adding a number of important task design features to clarify task difficulty effects on inhibitory control training.

Chapter 6 - Study 4: Training-induced improvements in inhibitory control

Submitted for publication:

Benikos, N., Johnstone, S. J. & Roodenrys, S. J. (submitted). Training-induced improvements in inhibitory control.

Abstract

Inhibitory control - the ability to suppress automatic and ongoing responses or to resist interference – is a fundamental feature of adaptive functioning. Deficits in inhibitory control have been implicated in the development of several psychiatric and neurological disorders. Despite a recent upsurge of positive findings regarding the training of other executive functions, whether inhibitory control can be trained and the underlying neural mechanisms remains unclear. Here we examine behavioural and electrophysiological evidence for the effects of two different training approaches. In the present study, fifty-four adults were randomly assigned to one of three conditions, Go/Nogo training (NG; n = 18), Go/Nogo-Stop training (NG-ST; n = 18), or a control oddball counting task (CON; n = 18), and completed a single training session (8 blocks). Task parameters were manipulated to maintain task difficulty at a moderate level as performance improved in both the NG and NG-ST training. Pre- and post-training performance was compared to assess improvements in inhibitory control using a Go/Nogo task (GNG), in addition to a Stop-signal (SS) and an Eriksen-flanker (ERIKSEN) task to measure near-transfer. During all tasks event-related potentials (ERPs) were recorded. Relative to the controls, the inhibition training conditions showed similar improvements in the active inhibition of responses during the GNG and SS tasks, with ERP analyses showing an overlapping frontocentral increase in the Nogo and SS P3 component; suggesting a top-down augmentation and near-transfer of inhibitory processes. These effects, howver, did not extend to the interference inhibition domain, with no performance or ERP effects seen for the ERIKSEN task. Across conditions, early ERP components revealed decreased N1 and increased P2 amplitudes in the GNG and SS, with

little change in the early ERIKSEN components. Overall, these findings suggest that adaptively manipulating task difficulty can lead to improvements in actively inhibiting stimuli in untrained tasks, leading to quantitative changes in brain activity; but that these effects are dependent on the whether the training and Pre/Post tasks engage overlapping processing components and brain regions.

6.1 Introduction

Inhibitory control – the ability to deliberately suppress a response, stop an ongoing response or to resist interference – is an essential feature of effective everyday behaviours (Barkely, 1997; Chambers et al., 2008; Clark, 1996; Nigg, 2000). Individual differences in inhibitory control also predict important long-term outcomes (e.g. socio-economic status, physical health, criminal conviction; Casey et al., 2011; Moffitt et al., 2011) and are consistently linked to impulse control disorders, including addiction (Luijten et al., 2013), obsessive-compulsive (OCD; Bannon et al., 2002) and attention-deficit/hyperactivity disorder (ADHD; Smith et al., 2004).

Considering the ubiquity and importance of effective inhibitory control for optimal functioning and the role its disruption plays in clinical disorders, the development of inhibition training paradigms constitutes an important treatment development goal (Chambers et al., 2008; Dimoska-Di Marco et al., 2011; Markomichali et al., 2009). However, previous research has produced variable results. For instance, some report training-related gains in inhibitory performance (Benikos et al., 2013a; Ditye et al., 2012; Dowsett & Livesey, 2000; Enge et al., 2014; Schapkin et al., 2007; Thorell et al., 2009; Tomporowski, 2003; Verbruggen & Logan, 2008), whereas others report no change (Guerrieri et al., 2012; Jodo & Inoue, 1990; Kelly et al., 2006b; Rueda et al., 2005; Tomporowski, 2003), performance declines (Manuel et al., 2010) and no transfer to untrained tasks (Enge et al., 2014; Manuel et al., 2010; Thorell et al., 2009). Further studies have instead suggested that inhibition training leads to more indirect effects, with participants showing post-training reductions in the consumption of alcohol (Bowley et al., 2013; Houben et al., 2012; Houben et al., 2011; Jones et al., 2013; Jones et al., 2011; Jones & Field, 2013), excessive food intake (Houben, 2011; Houben et al., 2011), and the frequency of risky gambling behaviours (Verbruggen et al., 2012; Verbruggen et al., 2013);

despite little evidence of performance improvements. Yet, these effects may be attributed more to reduced approach motivation (Houben et al., 2012) and/or the development of automatic affective associations for task-related cues (Houben et al., 2012; for a review see Jones et al., 2013) - rather the strengthening of an underlying inhibition mechanism.

A number of methodological issues in previous inhibition training studies present challenges for the generalisation and replication of their findings (cf. Jolles & Crone, 2012). First, most previous trials have not employed a control condition, leaving them unable to differentiate the pre-to-post changes due to simple exposure or more general procedural effects from actual training effects (e.g. Manuel et al., 2013; Manuel et al., 2010; Millner et al., 2012; Schapkin et al., 2007). A second related issue, is that the implementation of a control condition also involves consideration of additional factors that could potentially influence inhibition training outcomes such as baseline levels of impulsivity (Dimoska & Johnstone, 2007), task-related-arousal (Benikos et al., 2013a), motivation (Padmala & Pessoa, 2010) and workload (for discussions see Green & Bavelier, 2008; Slagter et al., 2011). Third, the general cognitive training literature robustly reports that effective training protocols depend on the maintenance of a constant task difficulty level by individually adjusting task parameters to compensate for performance improvements (e.g. Klingberg, 2010; Lövdén et al., 2010; Thorell et al., 2009). However, previous work has either not manipulated task difficulty (Houben et al., 2011; Jones et al., 2011), or has used varying task difficulty parameters in terms of type and intensity, including perceptual difficulty (Millner et al., 2012), static (Benikos et al., 2013a) and adaptive reaction time deadlines (RTD; Manuel et al., 2013); leaving it unclear as to the *optimal* task difficulty parameters required to elicit training gains. It would be therefore be advantageous to directly compare different variants of training approaches within the same study protocol to isolate the central parameters required for successful training outcomes. Finally, previous trials (e.g. Berkman et al., 2014; Kelly et al., 2006b; Manuel et al., 2013; Manuel et al., 2010) have employed the

same task during training and the assessment of training effects, with no measure of whether training gains transferred to non-trained tasks. Given the key applied goal that inhibition training gains should extend to real-world improvements in cognitive functioning and behavioural control, future studies should include further tasks pre/post training tasks to test the extent of transfer.

Although changes in inhibitory performance provide an overall index of training effectiveness, they do not offer insight into their neural bases. By contrast, event-related potentials (ERPs) allow a detailed examination of the temporal and spatial properties of neural activity underlying inhibitory control (for a review see Huster et al., 2013) and can index functional neuroplastic changes in brain activity (Kujal & Näätänen, 2010). Two characteristic components of the ERP, the N2 and P3, that occur between 200 and 500 ms post-stimulus, have typically been investigated in tasks indexing inhibitory control; from withholding planned/ongoing responses in Go/Nogo (GNG) and Stop-signal (SS) tasks, to resisting interference from distractors in the Eriksen-flanker task (ERIKSEN; Eriksen & Eriksen, 1974). The functional significance of the N2 and P3 to inhibition-evoking stimuli is debated in the literature (for a review see Huster et al., 2013). Early on leading researchers interpreted the N2 are reflecting the inhibition process (e.g. Falkenstein et al., 1999), but the theory that the N2 represents the advent of response conflict (i.e. whenever multiple incompatible representations are activated; Botvinick et al., 2004) has gained ground in recent years to become the dominant theory of the N2 (for reviews see Folstein & Van Petten, 2008; Huster et al., 2013). By contrast, evidence linking the P3 to motor inhibition in SS and GNG tasks has been accumulating in recent years (Dimoska & Johnstone, 2008; Dimoska et al., 2006; Johnstone et al., 2007; Randall & Smith, 2011; Smith & Douglas, 2011; Smith et al., 2006, 2008; Smith et al., 2010). However, rather than the inhibition mechanism itself, it has also been argued that the P3 represents instead an aftereffect of inhibition, such as the evaluation of the inhibitory process (Band & van Boxtel, 1999; Bruin

et al., 2001; Dimoska et al., 2006; Jonkman et al., 1999); particulalrly in the Eriksen-Flanker task (e.g. Johnstone & Galletta, 2013)

To-date the literature investigating the neural changes associated with training inhibitory control training has been small and inconsistent (for a recent review see Spierer et al., 2013). Previous studies employing fMRI (Berkman et al., 2014) and EEG source analysis (Manuel et al., 2013; Manuel et al., 2010) have reported reduced activations in inhibition-related regions; compatible with theoretical interpretations suggesting more efficient processing following training (Neubauer & Fink, 2009). By contrast, further research has proposed that, rather than reduced activity, inhibition training results in a strengthening of an underlying inhibition network (Benikos et al., 2013a; Schapkin et al., 2007), with enhanced activations in inhibitory control regions seen using fMRI (Kelly et al., 2006b) and greater GNG ERP amplitudes being reported by previous research (Benikos et al., 2013a; Schapkin et al., 2007). In particular, study 2 noted that variations in training difficulty may be a key predictor of training effects, such that task performance improvements were optimised during conditions of moderate rather that low or high inhibitory load (Benikos et al., 2013a). Further, training-induced improvements in the moderate condition were accompanied by an enhanced frontal Nogo P3, compatible with theory that training leads to the augmentation of a top-down inhibition mechanism.

6.1.1 The Present Study

Using task performance and ERP measures, the current study tested the effect of two brief adaptive training procedures on inhibitory control in adults. The design improved on previous studies in a number of important ways. First, we compared two different inhibition training paradigms: a standard GNG training condition (NG; 30% GO trials), and another which added STOP trials into the GNG training (NG-ST; 15 % Nogo and 15% stop-signals).

This second type of trial is regarded as a more challenging type of inhibition than a NOGO trial on a GNG task (Johnstone et al., 2007). In low probability GNG tasks (e.g. 30% Nogo), where a prepotency is built towards response execution, responses are likely to inhibited relatively early during response preparation. By contrast, in the SS task, ongoing responses need to be stopped at variable stages of processing; from early preparation, up to the point of actual execution. Consequently, these differences result in greater inhibitory load in the SS task, with additional emphasis on response execution in the GNG task. Second, task difficulty level was adaptively manipulated to induce performance improvements. For NG training this was achieved by adaptively reducing the reaction time deadline (RTD); for the NG-ST, both RTD and the Stop-signal delay (SSD; the time between the presentation of the go and stop signal). Third, a control condition (CON) was included which trained participants on a standard oddball paradigm (30% Go) that required them to count the stimuli presented. Fourth, task-related arousal was recorded (Barry et al., 2005) and participants completed self-report measures of impulsivity and energetic input/output (i.e. motivation, task workload) to assess the impact of training, relative to the control condition.. Fifth, we tested near-transfer by having participants complete a post-training assessment on non-trained GNG and SS tasks, in addition to a third outcome measure that tapped a different form of inhibitory control - interference control, as measured by an ERIKSEN task. The post-training assessment was conducted 3 to 5 days after the training to preclude the possibility of fatigue effects clouding the results (e.g. Kato et al., 2009). Many have argued that the transfer of training effects is possible only to the degree that training and transfer tasks involve overlapping neural networks or share common sub-components (e.g. Dahlin et al., 2008a). Imaging evidence suggests that tasks indexing prepotent response inhibition, action cancellation and interference control share a common underlying inhibition network including the right inferior frontal gyrus (rIFG) and the pre-supplementary area (pre-SMA) (for a review see Huster et al., 2013; Swick et al., 2008, 2011), which may help to facilitate transfer effects between the three tasks. At the same time, even such apparently closely related tasks as the GNG and SS are known to be innervated by different neurotransmitter

systems, suggesting that they employ dissociable neuro-cognitive processes (Eagle et al., 2008). Recent research contrasting patterns of brain activation using a hybrid SS, GNG and ERIKSEN tasks has indicated that interference control relies primarily on a parieto-frontal response selection network, compared to more frontal-striatal activity elicited for action withholding/cancellation (Sebastian et al., 2012; Sebastian et al., 2013). If this is the case, NG or NG-ST training gains would not be expected to transfer to the ERIKSEN task.

Building on previous studies it was hypothesised that training outcomes would be optimised in the two active training conditions compared to controls. Specifically, it was predicted that there would be an improvement on the GNG task between pre- and post-training for NG and NG-ST relative to the control condition in terms of a reduction in the number of NOGO errors and stop signal reaction time (SSRT; i.e., greater inhibitory control with training). Second, it was hypothesised that this effect would be larger for the NG-ST than the NG task alone, given the combined inhibitory load experienced during training for this condition. Third, it was also hypothesised that these effects would transfer to the ERIKSEN task to the degree that cognitive processes overlapped with the training tasks. Fourthly, it was predicted that behavioural improvements would be accompanied by an enhancement of inhibition-related P3 component for each task, whereas reduced response conflict would reflected by attenuated N2 amplitudes. While no specific predictions were made for the early ERP components, given that inhibitory control may not be solely manifested by modulations in the N2 and P3, but that earlier waveforms such as the N1 and P2 component play an important role for inhibition success (Bekker et al., 2005b; Roche et al., 2005a), any differences found would be explored.

6.2 Method

6.2.1 Participants

Sixty adult students initially enrolled in this study as a means of attaining research participation course credits. To be included, participants were required to refrain from caffeine for two hours prior to testing and from any psychotropic substances (prescription or illegal) for 24 hours prior to testing, and/or no more than once a month in the previous six months. Participants were excluded is they had experienced an epileptic seizure, serious head injury, period of unconsciousness or any psychiatric condition. Two participants failed to meet the inclusion criteria. The remaining 58 participants were randomly assigned to one of three training conditions: NG, NG-ST and CON. Data from four participants was excluded. One failed to complete the full study protocol and three encountered technical difficulties. Therefore there were 18 participants in each condition; NG (13 females; M: 21.50 yrs, SD: 5.67); NG-ST (13 females; M: 20.85 yrs, SD: 5.39) and CON (13 females; M: 21.49 yrs, SD: 6.60). There were no differences in age $F(2,51) = 0.45$, $p = .638$, $\eta 2 = .017$) between the conditions. Forty-nine of the participants were right-handed. The research protocol was approved by the joint University of Wollongong and Illawarra Area Heath Service Human Research Ethics Committee.

6.2.2 Study Protocol and Tasks

The experiment was conducted over two sessions (Figure 6.1). At the beginning of both sessions participants were given an outline of the testing procedure and familiarised with the laboratory equipment before providing informed consent. The experimenter emphasised that participants could withdraw at any time without penalty. Participants

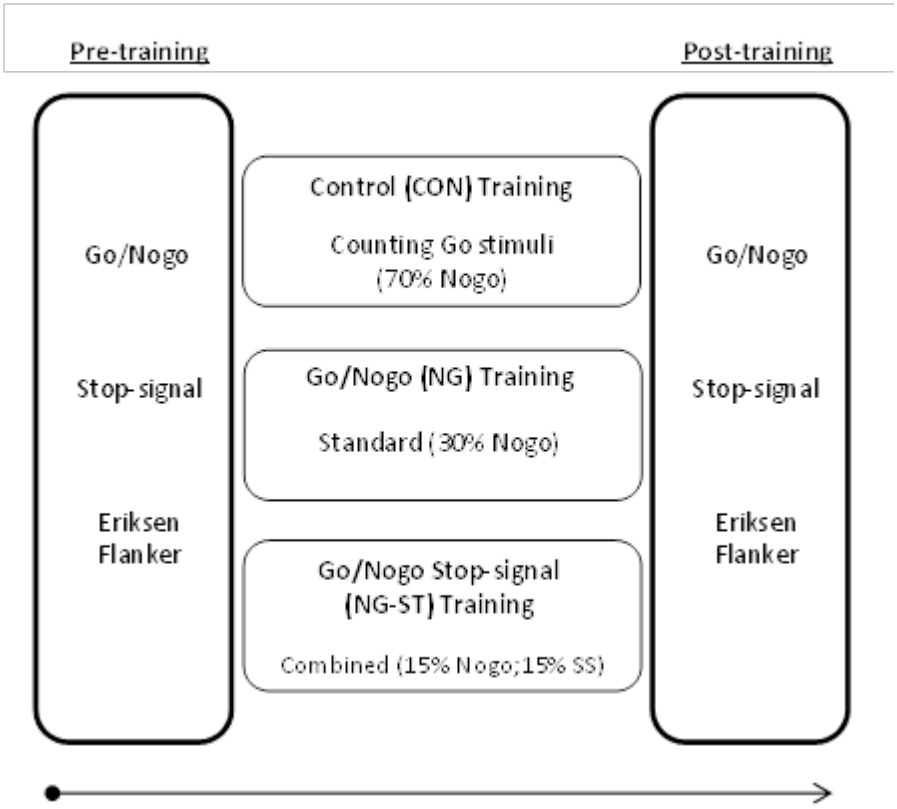


Figure 6-1. Schematic depiction of the experimental design and procedure. Participants completed the same task battery at pre-and post-training. The post-training assessment was conducted during a separate session which took place 3-5 days later at the same time of day. Training consisted of 8 blocks with a 10 minute break at the midpoint of testing.

completed a short screening questionnaire to assess vision problems, medication and psychotropic substance use, handedness and neurological disorders and the Barratt Impulsivity Scale (BIS-11; Patton et al., 1995). Participants' were then fitted with the EEG equipment and seated in a dimly lit sound-attenuated and electrically-shielded testing booth. An incandescent light in the booth was dimmed for the duration of the experiment. An initial 3 minute baseline recording was conducted while participants were asked to sit quietly while

focusing on a fixation cross. They were then asked to close their eyes for a further 3 minute recording.

All tasks were programmed using Presentation software (Version 11.0; Neurobehavioral Systems, Albany, CA, USA). Stimuli were presented centrally on a 15 inch computer monitor at eye-level. Participants were seated one metre from the screen. For all tasks, trial-by-trial performance feedback was provided via the subsequent fixation cross: correct responses were followed by a white fixation cross, while a red fixation cross was displayed after incorrect responses (i.e. responses outside of the RTD or incorrect choice). At the end of each block, reaction time (RT) and the percentage of correct responses were displayed for 10 s.

Pre/Post-training assessments

The same tasks were presented pre-and post-training. The post-training assessment was conducted in session two which took place three to five days after training at the same time of day as the first session. There were no differences in the number of days between the sessions for the three conditions (NG - M: 3.94, SD: 1.31; NG-ST - M: 4.00, SD: 1.97; or CON - M: 3.94, SD: 1.31; $F(2,51) = 0.02$, $p = .978$, $\eta 2 = .001$)). The order of the tasks was counterbalanced between participants. Overall the battery took approximately 40 minutes to complete.

GNG task: GO and NOGO stimuli were either a horizontal or vertical bar, measuring approximately 5.0 x 1.5 cm presented in white on black background. Stimulus type was counterbalanced between participants. The trial sequence began with a fixation cross (+) presented for a variable interval of 500-1000 ms (M = 750 ms), followed by either the GO or NOGO stimulus for 200 ms. A blank screen then replaced the stimuli for a variable period of 1250 –750 ms (M = 1250 ms). To prevent ceiling effects and to ensure a sufficient level of task difficulty (Benikos et al., 2013), participants were required to respond

within a 450 ms reaction time deadline (RTD), or to refrain from responding to NOGO stimuli, with performance feedback provided via the subsequent fixation cross (as described above). Participants responded with their right hand irrespective of handedness. Only presses to the GO stimulus within the predefined response window were regarded as correct. After an initial practice block of 30 trials (50% NOGO), all participants completed one experimental block of 100 trials (30% NOGO). The key performance measure used to assess training effects was the percentage of NOGO errors.

SS task: Participants were required to perform a binary-choice RT task including two visual Go stimuli: the letters "T" and "O". These letters were presented sequentially in the centre of the screen (white Courier font on black background, approximately 2 cm high x 1.5 cm wide), each with a 50% probability. Each trial began with a central fixation cross (+) presented for a variable interval of 500-1000 ms (M = 750 ms), followed by the Go stimulus for 200 ms. A blank screen then replaced the stimulus for a variable blank period of 1250 – 1750 ms (M = 1250 ms). Within this period, all participants were required to respond with their left index finger to one Go target, and the right index finger to the other Go target, using the "Z" and "/" keys on a computer keyboard, respectively. Incorrect feedback was displayed for Go binary-choice errors and presses to the stop-signal. Go response assignment was balanced across participants. The stopping component of the task consisted of visual "Stop" sign which replaced the Go stimulus at the pre-defined stop-signal delay (30% of trials) and instructed participants to inhibit their response on the primary RT task. The SSD was varied relative to each participant's go reaction time (Go RT) from the preceding practice block (i.e. Go RT- 80, Go RT- 160, Go RT- 240, Go RT- 320, Go RT - 400 and Go RT- 480 ms; Logan & Burkell, 1986). All participants began the task by completing a practice block (50 trials), which included fixed SSDs of either 100, 200, 300, 400 or 500 ms after the onset of the Go stimulus, followed by the experimental block of 140 trials. The latency of the stop process, i.e., stop-signal reaction time (SSRT) was used to assess training effects.

FLANKER: Target stimuli consisted of either a central left-or-right pointing arrow (i.e. "<" or ">"), indicating a left or right button press. Targets were either presented alone, or were flanked on both sides by either two equals signs on neutral trials (NEUTRAL i.e. "= = < = =" or "= = > = ="), arrows pointing in the same direction as the target on congruent trials (CONGRUENT i.e. "< < < < <" or "> > > > >"), or arrows pointing in the opposite direction for incongruent trials (INCONGRUENT i.e. "< < > < <" or "> > < > >"). All stimuli were presented with equal probability. Each trial began with a central fixation cross (+) for a variable interval of 500-1000 ms (M = 750 ms), followed by the target stimulus for 200 ms, and a variable blank period of between 1250 – 1750 ms (M = 1250 ms). Within in this period, participants were required to respond within a 500 ms RTD. Participants' responded with their left index finger for left-pointing target arrows, and right index finger for right-pointing arrows using the "Z" and "/" keys of a computer keyboard, respectively. Target choice errors and presses outside the RTD were followed by incorrect feedback as indicated by the red fixation cross. Following a practice block of 28 trials, all participants performed one experimental block of 140 trials (32 of each stimulus type). The key performance measures used to assess training effects were the incongruency effects for errors and RT (i.e. INCONGRUENT versus the CONGRUENT trials).

Training Tasks

Participants were given a 15 minute break at the conclusion of the pre-training session and offered a drink or healthy snack. They were then randomly assigned to one of the three training conditions: NG, NG-ST or CON. Participants were encouraged to "do their best" to respond quickly and accurately and improve from block to block if possible. After a practice block, participants completed eight blocks of training, with a short break of 10 minutes during the midpoint of testing. In order to equalise the training session length between conditions, the rest period between blocks was set at 1.5 min for all participants. To

examine whether the conditions differed in the degree of task-related arousal, motivation and workload, skin conductance level was recorded (Barry & Sokolov, 1993) and participants completed a14-item subset from the Dundee Stress State Questionnaire (DSSQ; Matthews et al., 2002; Matthews et al., 1999) and the NASA Task Load Index at the conclusion of the training blocks (NASA TLX; Hart & Staveland, 1988). Total training time was approximately 43 min. At the conclusion of the study participants were debriefed and given a movie voucher ($15 AUD).

NG: In line with our previous research GO and NOGO stimuli were selected from a pool of eight 2D shapes presented in white on black background (i.e. triangle, cross, hexagon, diamond, ellipse, rectangle, star and circle; as used in Benikos et al., 2013ad). The selection of shapes was changed from block to block in order minimise the possibility of consistent stimulus-response mappings (Verbruggen & Logan, 2008), to promote the top-down process of inhibition, and enhance the likelihood of transfer effects (Dixon et al., 2009; Kelley & Yantis, 2009; for a review see Schmidt & Bjork, 1992). Prior to each block, GO/NOGO shape assignments were shown on screen and verbally confirmed by the participant. All stimuli measured approximately 3 x 3 cm and were completely counterbalanced within and between participants. Participants received performance feedback via the fixation cross and an RT/accuracy report was provided visually on screen at the conclusion of each block. All participants completed eight training blocks of 100 trials each, generally compatible with previous behavioural studies demonstrating task performance improvements in inhibitory control using single session training paradigms (Benikos et al., 2013ad; Kelly et al., 2006b; Manuel et al., 2013; Manuel et al., 2010; Verbruggen et al., 2012; Verbruggen & Logan, 2008; Woolard et al., 2010). Trial parameters were the same as the GNG outcome measure. Difficulty level was adapted every 20 trials. If accuracy to GO/NOGO trials exceeded 90%, the RTD was decreased by 50 ms; if performance dropped below 90%, it was increased by 50 ms. After a practice block of 20

trials, the RTD was set at 750 ms for the first block. For each subsequent block, the RTD was set to the last level attained at the end of the preceding block.

NG-ST: The same training cues and task parameters were used as for the NG training except that the 30% non-GO trials were divided into 15% NOGO trials and 15% STOP trials. These GNG-STOP trials began with the presentation of the GO stimulus, but on 15% of trials after a variable delay, the GO stimulus changed to a red colour; indicating participants' had to withdraw their response. During practice block (20 trials), the RTD was set to 750 ms and fixed SSDs (i.e. 100, 200, 300 and 400 ms) were used. For all training blocks, the RTD was set to the last level reached during the preceding block. SSD was also varied relative to the participants Go RT from the previous block: Go RT – 0, Go RT – 150, Go RT – 300, Go RT – 450 (Dimoska et al., 2006).

CON: This condition employed an oddball task where the pattern of response prepotency was reversed compared to the training conditions. GO stimuli were presented infrequently (30%). Participants were instructed to covertly count the number of GO stimuli in each block (e.g. Smith et al., 2008). To avoid anticipation of the number of GO stimuli, participants were told that the number of GO trials varied from block-to-block, while the total number of trials was always 100. Participants' reported a GO stimulus count to the experimenter at the end of each block. If they matched against the count generated, participants received positive feedback from the experimenter (e.g. "well done, keep it up!"), if not they were told "try to do better next time".

6.2.3 Electrophysiological Recording

The continuous scalp electroencephalogram (EEG) was recorded from 19 sites (Fp1, Fp2, F3, F4, F7, F8, Fz, C3, C4, Cz, P3, P4, Pz, T3, T4, T5, T6, O1, O2) using an electrode

cap containing tin electrodes fitted according to the international 10-20 system (Jasper, 1958). A ground electrode located between Fpz and Fz, and all electrodes were referenced to linked ears. EOG was measured vertically with two tin cup electrodes, 1 cm above and below the left eye. Impedance was kept below 3 kΩ for EOG and reference electrodes and below 5 kΩ for cap electrodes. EEG and EOG signals were amplified 19 times and sampled at 500 Hz, with bandpass down 3 db at 0.1 and 100 Hz via a NuAmps system (Compumedics Limited, Melbourne, Australia). Prior to processing, the EEG data were digitally filtered using a low-pass filter 3 dB down at 30 Hz.

6.2.4 Data Quantification

ERP Components

The ERP epoch was defined as 100 ms pre-stimulus to 900 ms post-stimulus onset. An ocular artefact reduction procedure were based on the vEOG channel (Semlitsch et al., 1986). Epochs were excluded if they contained activity greater than ± 100 μV at any non-frontal site. ERPs were averaged across epochs for correct responses. To ensure compatibility within- participants for each task, the number of epochs available for averaging was initially determined for the inhibition-evoking stimuli (i.e. successful NOGO, STOP, INCONGRUENT), with GO, failed-STOP[2] and CONGRUENT epochs restricted to the same number, being randomly selected from the total available. Repeated measures ANOVA confirmed that there was no difference between conditions in the number of epochs analysed for the different tasks [$F(2,51) = 3.27$, $p = .077$] or between the pre and-post assessments [$F(2,51) = 0.39$, $p = .538$]. In order to define the pre and-post training task ERP latency range, grand average waveforms were displayed for each trial type. Peaks were

[2] Due to the short interval between the onset of Go stimuli and Stop-signals, the ERP responses to the Stop-signals included overlap from the preceding Go stimulus, distorting the final ERP averages. To correct for this, sub-averages of the successful and failed Stop-signals were calculated by sorting them into the six SSDs s and then averaged (Johnstone et al., 2007).

quantified using automatic peak-picking software (Neuroscan v4.4) which identified the largest positive or negative deflections within the predefined latency range, relative to the 100 ms pre-stimulus baseline period. Latency was fixed across sites to the peak latency of the site of maximum amplitude (Picton et al., 2000; Spencer et al., 2001). In the GNG task the search parameters were N1 (90-140 ms; locked to Fz), P2 (150-270 ms; Pz), N2 (240-380 ms; Fz), P3 (380-500 ms; Pz). For the SS task the latency ranges were N1 (90-165; Fz), P2 (140-220; Pz), N2 (170-280; Fz) and P3 (250-500; Cz). For the Flanker task the ranges included N1 (90-150; Fz), P2 (140-220 ms; Cz), N2 (170-280 ms; Fz), P3 (250-500 ms; Cz).

6.2.5 Statistical Analysis

Self-report, task-related arousal, and motivation

Differences between the conditions for the BIS-11 and NASA-TLX was investigated using Univariate ANOVA with Condition as the between subjects factor. The DSSQ Motivation scale was assessed by comparing post-training performance for Condition (NG vs. NG-ST vs. CON) as the between subject variable, with pre-training data used as a covariate. Planned orthogonal contrasts within Condition compared CON participants, against the two training conditions (i.e. mean of NG vs. NG-ST vs. CON) and then the two training conditions against each other (NG vs. NG-ST). These contrasts examined whether altered motivation from Pre- to-Post training, and whether the combined inhibition training of the NG-ST showed any further difference from the NG condition.

Training task performance

Training performance for the NG and NG-ST condition were subject to a Condition [NG vs. NG-ST] × Time [Block 1 vs. Block 8] mixed design ANOVAs, with repeated

measures on the within-subjects factors. The training adaptive paradigm aimed to keep constant the number of errors across sessions and so analysis was restricted to RT data. Given the differential nature of task performance (i.e. no access to RT data), training performance for the CON condition was considered separately.

Pre- vs. post-training changes for task performance

GNG, STOP and FLANKER tasks were assessed by comparing post-training performance for Condition (NG vs. NG-ST vs. CON) as the between subject variable with pre-training data used as a covariate. Planned orthogonal contrasts within Condition compared CON participants, against the two training conditions (i.e. mean of NG vs. NG-ST vs. CON) and then the two training conditions against each other (NG vs. NG-ST); allowing determination of whether the training produced an effect, and whether the combined inhibition training of the NG-ST condition had any additional benefit on task performance.

Pre- vs. post-training changes for ERP Components

Pre- to post-training considered each task separately using a mixed design ANOVA including (NG vs. NG-ST vs. CON) as the between-subjects factor, with trial type [GO vs. NOGO] / [Successful stop (SI) vs. Unsuccessful stop (UI)] / [INCONGRUENT vs. CONGRUENT] as a within-subject factor. In addition two other within-subject factors were included to capture Lateral (Left vs. Midline vs. Right) x Sagittal (Frontal vs. Central vs. Parietal) effects. Analyses of the ERP data were restricted to nine sites F3, Fz, F4, C3, Cz, C4, P3, Pz and P4, an approach established in previous studies (for e.g. Broyd et al., 2005; Dimoska & Johnstone, 2008; Smith et al., 2004, 2006; Smith et al., 2007; Smith et al., 2008; Thomas et al., 2009; Thomas et al., 2007) which reduces the number of statistical comparisons made while optimally allowing for differences in the hemispheric and anterior-posterior gradient dimensions (Picton et al., 2000). Planned orthogonal contrasts within the

Lateral factor compared activity in the left hemisphere (mean of F3, C3 and P3) with the right (mean of F4, C4 and P4), and the mean of these with activity in the midline region (mean of Fz, Cz and Pz). Contrasts within the Sagittal factor compared frontal activity (mean of F3, Fz and F4) with parietal (mean of P3, Pz and P4), and the mean of these with activity in the central region (mean of C3, Cz and C4). A further ANOVA compared Lateral x Sagittal x Task x Time x Condition to examine whether the components overlap and the magnitude of training effects between conditions. As these contrasts were planned with no more of them than the degrees of freedom for each effect, no Bonferroni type adjustment to α were necessary (Tabachnick & Fidell, 1996). Also, single degrees of freedom contrasts are not affected by violations of symmetry assumptions common in repeated measures analyses, and thus do not require Greenhouse–Geisser-type corrections. It should be noted that this increases the frequency of type 1 errors, however, as this is an increase in frequency, rather than probability, it cannot be 'controlled' by adjustment of α levels (Howell, 2009). Data were normalised using the vector scaling method (McCarthy & Wood, 1985), and only interactions with topography that remained significant in the normalised data are reported here. The normality of the data distributions was examined and outliers in the data (i.e., values exceeding ±2.5 standard deviations from the mean) were corrected by replacing them with the series mean (≤ 3.4% for any task performance or ERP variable). All statistics have (1,52) degrees of freedom unless otherwise indicated.

6.3 Results

6.3.1 Self-report Measures and task-related arousal

Table 6.1 outlines the results for the BIS-11, NASA-TLX and Motivation scales.

Table 6-1. Self-report scores for each condition. Standard deviation in parentheses.

Measure	Control	GNG	GNG-SS	*F*	*p*	η^2
Barratt (BIS-11)						
Attentional	10.33 (2.20)	10.61 (2.50)	11.11 (2.17)	0.53	.591	.020
Motor	20.89 (4.11)	20.61 (4.07)	21.56 (3.63)	0.27	.763	.011
Non-planning	6.50 (1.79)	6.61 (1.58)	6.39 (1.29)	0.09	.914	.004
Total	37.72 (6.76)	37.83 (5.88)	39.06 (5.41)	0.27	.765	.010
NASA-TLX						
Mental demand	6.67 (1.28)	7.50 (1.89)	6.33 (1.53)	2.58	.086	.092
Physical demand	2.50 (1.95)	2.44 (2.26)	2.06 (2.21)	0.23	.795	.009
Temporal demand	6.83 (1.79)	6.83 (2.26)	6.28 (2.14)	0.43	.652	.017
Performance	6.72 (1.18)	6.39 (1.65)	6.30 (1.46)	2.01	.145	.073
Effort	7.00 (2.17)	7.00 (1.41)	6.94 (0.87)	0.01	.993	.000
Frustration	4.39 (2.36)	5.06 (2.86)	5.00 (1.97)	0.42	.659	.016
DSSQ						
Motivation	41.75 (6.30)	41.06 (6.21)	39.50 (4.59)	1.12	.333	.043

Analysis of the BIS-11 revealed no group difference in any of the self-reported impulsivity scales. Participants in all three conditions reported a similar degree of task-related motivation, demand (i.e. mental, physical and temporal) and experienced a comparable level of perceived effort, frustration and expectations about their performance. Given that there were no baseline differences in impulsivity or differential training-induced motivational/energetic effects between the conditions, these factors were not considered to have impacted the task performance and ERP results discussed below.

SCL (i.e. task-related arousal) increased from the beginning (10.8 uS) until the end of the end of training session (14.4 uS; Linear: $F = 29.97$, $p < .000$), indicating a training-related increase in task-related arousal across the session (Benikos et al., 2013a). The effect did not differ between conditions (all ps > .54)

6.3.2 Training task performance

NG vs. NG-ST-training: As seen in Figure 6.2, Go RT was faster overall for the NG than NG-ST ($F = 5.38$, $p = .026$, $\eta 2 = .137$). A main effect of Time indicated that both Go RT (Linear; $F = 32.56$, $p < .000$, $\eta 2 = .489$) and the average RTD level (Linear; $F = 56.07$, $p < .000$, $\eta 2 = .137$) decreased significantly from the beginning to the end of the training session, suggesting improved overall task proficiency with training for both conditions. However, this effect did not differ between the NG and NG-ST conditions (Time x Condition: Linear; Go RT: $F = 0.66$, $p = .798$, $\eta 2 = 001$; Linear; Go RTD: $F = 1.14$, $p = .292$, $\eta 2 = .013$).

CON-training: Counting performance for the CON group was excellent, with participants successfully reporting, on average, 99.2 % (SD =1.27%) of all target stimuli across the training blocks. Moreover, there was no significant change in counting accuracy from the beginning (99.6 %; SD =1.09%) until the end of the training blocks (99.2%; SD =1.45%), suggesting consistently high task engagement ($F(1,17) = 1.00$, $p = .331$, $\eta 2 = .056$)

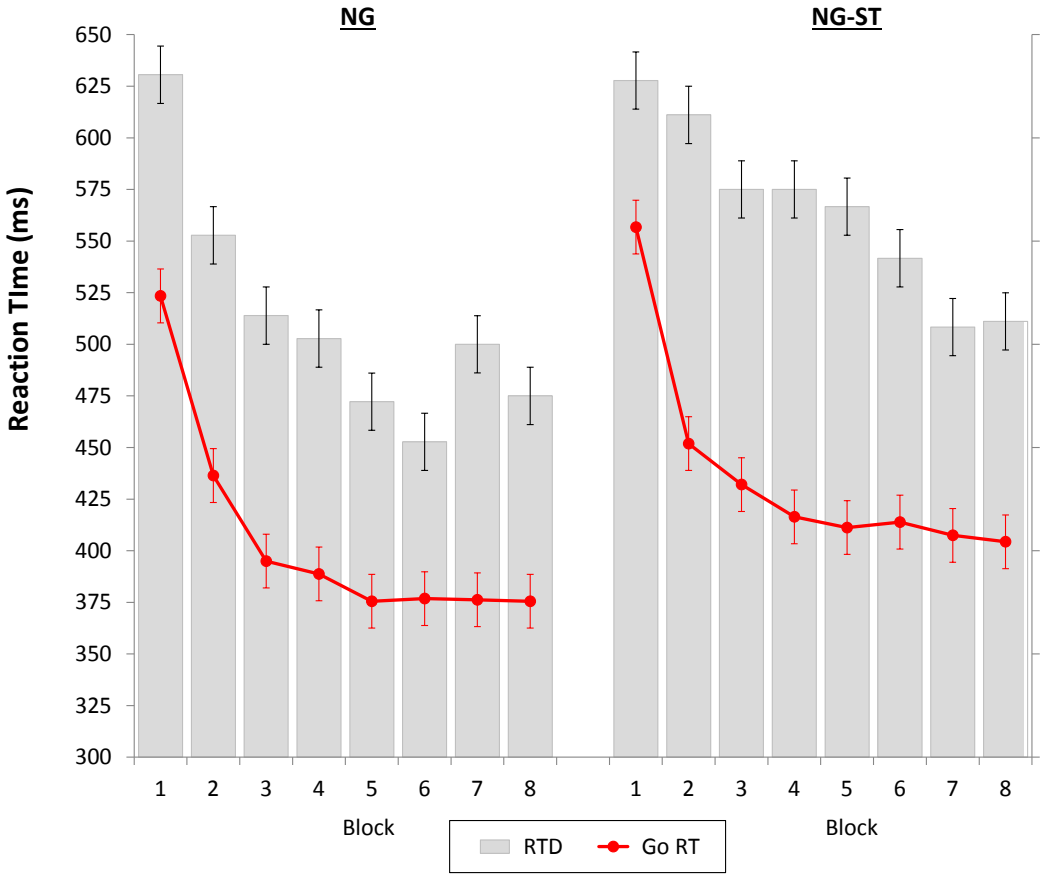


Figure 6-2. Task performance measures across the training blocks for the NG (left) and NG-ST conditions (right). Error bars represent standard error of the mean.

6.3.3 Pre- vs. post-training changes for task performance

There were no baseline differences for the pre-training tasks in performance or ERP variables (all ps > .109). Training-related changes in task performance are depicted in Figure 6.3.

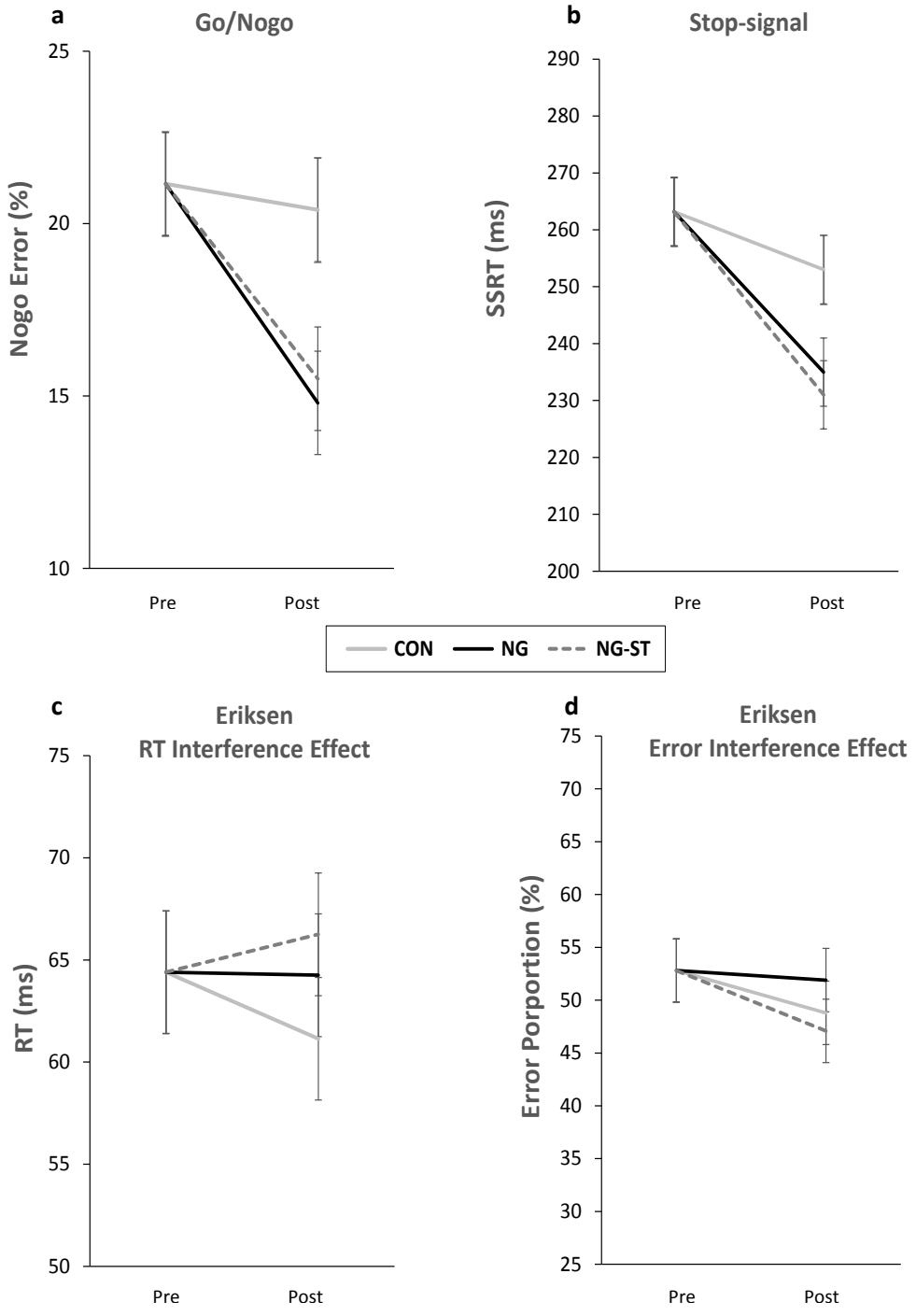


Figure 6-3. Task performance for the untrained GNG, SS and FLANKER task between the conditions, Nogo errors (panel a), SSRT (panel b). The interference effect for Eriksen interference effect for RT (panel c) errors (panel d). RT and errors was calculated as the difference between INCONGRUENT and CONGROUS conditions. Pre-training values represent the mean used in the covariate analysis. Error bars represent standard error of the mean.

GNG task – Using pre-training performance as covariate, there was a significantly larger post-training decrease in the percentage of Nogo errors in the training conditions (NG + NG-ST: 15.3%) compared to the CON (20.4%: $F = 5.75$, $p = .020$, $\eta 2 = .103$). However, planned comparisons revealed no difference between the NG and NG-ST conditions (Figure 6.3a; $F = 0.00$, $p = .940$, $\eta 2 = .000$).

SS task – SSRT decreased significantly (with pre-training as a covariate) for the training (NG + NG-ST: 233 ms) compared to the CON condition (250 ms; $F = 4.66$, $p = .036$, $\eta 2 = .085$). There were no differences between the NG and NG-ST conditions (Figure 6.3b; $F = 0.22$, $p = .638$, $\eta 2 = .004$).

ERIKSEN task- Using pre-train performance as a covariate, there were no significant post-training differences between the training (NG + NG-ST: 67 ms) and CON in the interference RT effect (61 ms; $F = 0.93$, $p = .340$, $\eta 2 = .018$) and the interference error effect (NG + NG-ST: 49% vs. CON: 48%; $F = 2.27$, $p = .138$, $\eta 2 = .044$). No differences were found between the NG and NG-ST condition (see Figure 6.3c and d; RT Inference: $F = 0.73$, $p = .397$, $\eta 2 = .014$; Error Inference: $F = 1.31$, $p = .259$, $\eta 2 = .025$).

6.3.4 Pre- vs. post-training changes for ERP Components

The Results section will focus on effects and interactions involving Stimulus type and Time. Figure 4, 5 and 6 presents grand mean ERPs to GNG, SS and FLANKER stimuli at pre- and post-training.. For all three tasks, there is a small frontal negative shift at about 100 ms followed by a positive potential at approximately 200 ms, which appears to encompass the N1 and P2 components. This is followed by the N2 and P3 components, which peak at about 150 to 300 ms and 300-500 ms post-stimulus, respectively. In particular,

the Nogo and SS P3 appears to show a clear training-related increase, with little change seen in the P3 in the ERIKSEN.

6.3.4.1 GNG

Pre- and post-training grand mean ERP waveforms for the GNG task are presented in Figure 6.4.

N1peaked at 112 ms and was largest in the frontocentral region [Frontal (F): -0.9 uV > Parietal (P): 1.3 uV; F = 68.48, p < .000, $\eta 2$ = .569; Central (C): -0.3 uV > Frontal/Parietal (F/P): 0.2 uV; F = 22.22, p < .000, $\eta 2$ = .297]. A main effect of Time indicated that N1 amplitude showed a global reduction from pre- to post-training (-0.2 vs. 0.3 uV; F = 5.66, p = .021, $\eta 2$ = .096). There were no significant Time x Condition interactions (all ps > .330).

P2 peaked at 219 ms. The P2 showed shorter latency to Go (215 ms) than Nogo stimuli (221 ms; F = 7.26, p = .010, $\eta 2$ = .122), and displayed a Go > Nogo effect (5.5 vs. 4.1 uV; F = 12.84, p = .001, $\eta 2$ = .189). The P2 was maximal in the central region (C: 5.8 uV > F/P: 4.3 uV; F = 69.58, p < .000, $\eta 2$ = .574). Overall, P2 peaked earlier (222 vs. 214 ms; F

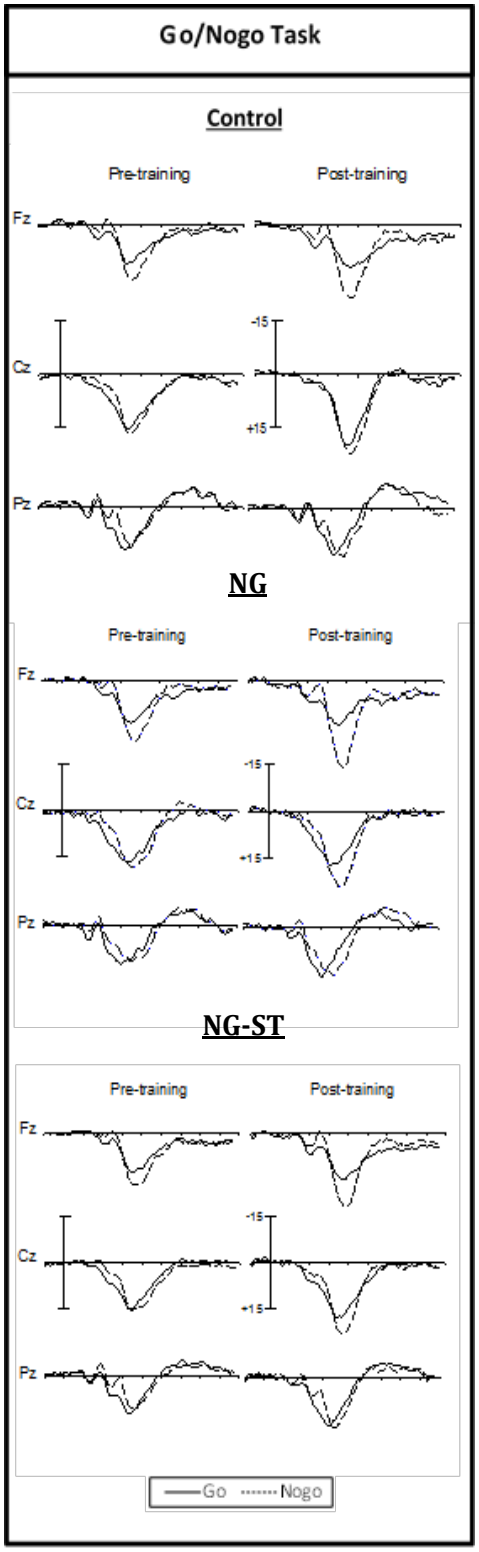


Figure 6-4. Pre- and post-training grand means for the GO/NOGO training at midline sites across for each condition separately. Note: For this and subsequent figures, x-axis ticks = 100 ms; stimulus onset at y-axis shown at Cz.

= 9.30, p = .004, $\eta 2$ = .144) and increased in amplitude from pre- to post-training (4.3 vs. 5.3 uV; F = 7.28, p = .009, $\eta 2$ = .123). There were no significant Time x Condition interactions (all ps > .238).

N2 (mean latency 259 ms) amplitude showed a Nogo > Go effect (F = 73.72, p < .000, $\eta 2$ = .578), with this difference largest centrally (C, Go/Nogo diff : 4.5 uV >F/ P, Go/Nogo diff: 3.7 uV; F = 14.40, p < .000, $\eta 2$ = .216). Overall, the N2 component peaked later (257 vs. 261 ms; F = 3.92, p = .052, $\eta 2$ = .071) and decreased in amplitude from pre- to post-training (3.9 vs. 4.9 uV; F = 7.92, p = .007, $\eta 2$ = .134). No Time x Condition interactions were significant (all ps > .124).

The P3 (mean 358 ms) peaked later to Nogo (369 ms) than Go stimuli (348 ms; F = 53.60, p < .000, $\eta 2$ = .503), and showed a Nogo > Go effect (17.6 > 14.2 uV; 14. F = 74.17, p < .000, $\eta 2$ = .583). A smaller parietal > frontal gradient effect in Nogo compared to Go stimuli (parietal vs. frontal difference: Nogo – 3.1 vs. Go 2.2 uV), highlighted the Nogo > Go anteriorisation effect (F = 70.55, p < .000, $\eta 2$ = .571).

Overall, the P3 component (Go + Nogo) increased in amplitude with training (14.5 vs. 17.3 uV; F = 19.92, p < .000, $\eta 2$ = .272). Notably, the conditions showed different training-related effects (Stimulus x Sagittal x Time x Condition interaction): while the CON condition showed little change in the Nogo > Go P3 anteriorisation effect post-training (Nogo minus Go diff, Pre: 5.4 uV vs. Post: 4.9 uV), both the NG training (Nogo minus Go diff, Pre: 5.4 uV vs. Post: 7.2 uV) and the NG-ST (Nogo minus Go diff, Pre: 5.4 uV vs. Post: 9.5 uV) showed large training-induced increases (see Figure 6.5 for plots; F = 4.27, p = .019, $\eta 2$ = .135). A further ANOVA comparing the NG and NG ST participants showed that the enhancement in Nogo > Go P3 anteriorisation effect did not differ between the two training conditions (F = 2.15, p =.152, $\eta 2$ = .272; see Figure 6.9 for topographic maps).

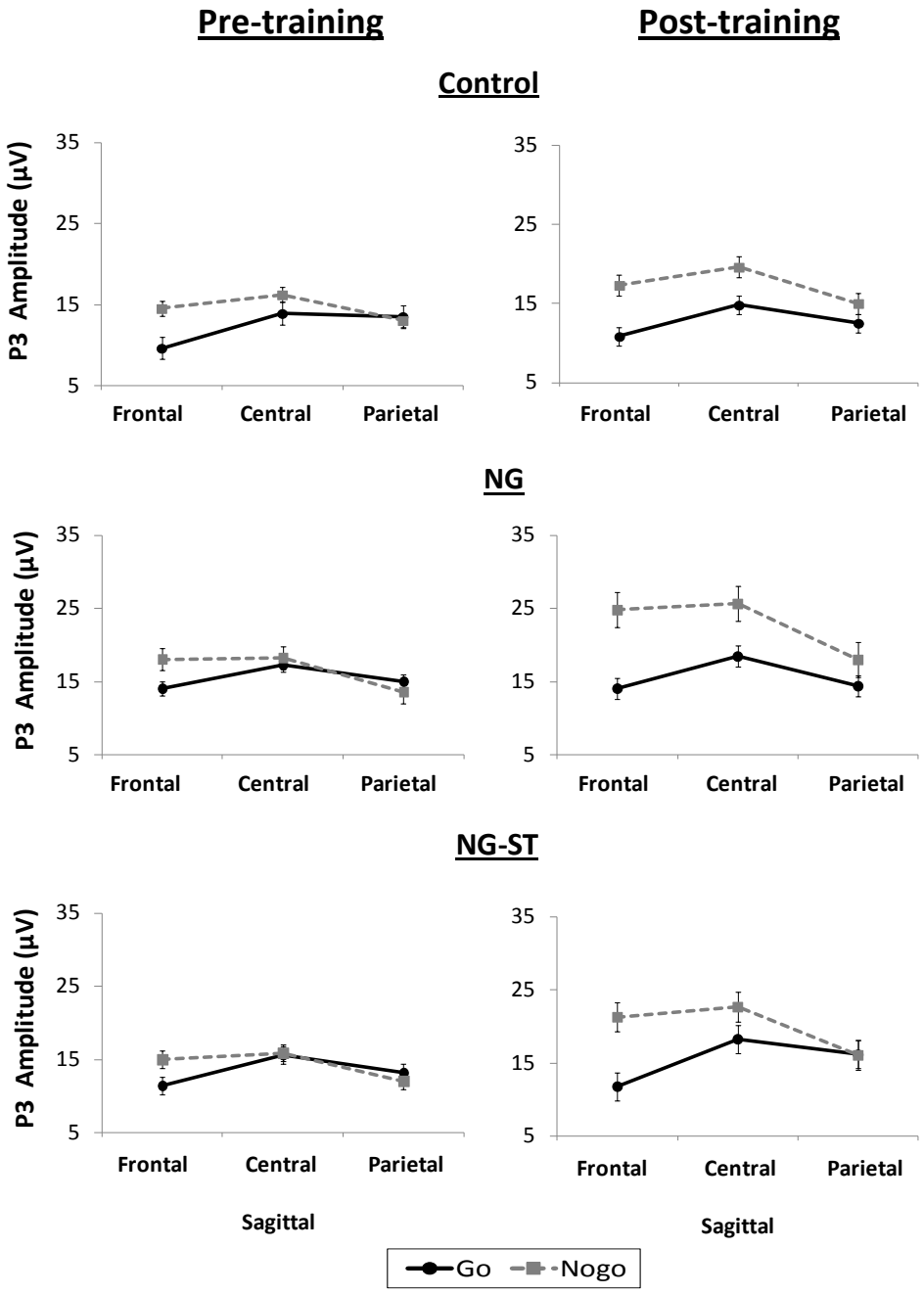


Figure 6-5. Time x Stimulus x Sagittal x Condition P3 interaction for the GNG task.

6.3.4.2 STOP-SIGNAL

Pre- and post-training grand mean ERP waveforms for the SS task are presented in Figure 6.6.

N1 (mean127 ms) was largest in the frontal region (F: -2.5 uV > P: .06 uV; F = 74.45, p < .000, $\eta 2$ = .584) and showed a Successful Inhibition (SI) > Failed Inhibition (FI) effect (-1.7 > 0. uV; F = 4.05, p = .050, $\eta 2$ = .069). A main effect of Time indicated that N1 amplitude showed a global reduction from pre to post-training (-1.5 vs. -0.8 uV; F = 4.40, p = .041, $\eta 2$ = .079). No Time x Condition interactions were significant (ps > .72).

P2 (mean172 ms) peaked earlier on FI (168 ms) than SI trials (176 ms; F = 5.58, p = .022, $\eta 2$ = .099) and was maximal in the centroparietal region [P: 3.1 uV > F: 2.2 uV; F = 5.27, p = .026, $\eta 2$ = .091; C: 3.6 uV > F/P: 2.7 uV; F =

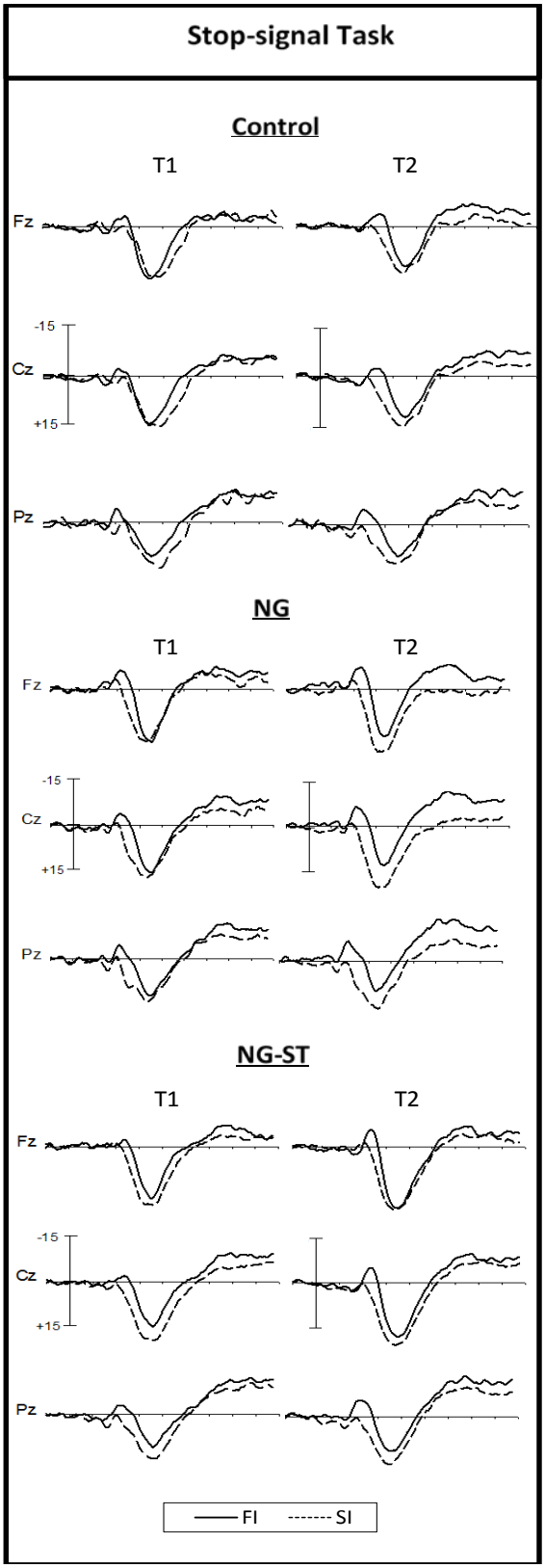


Figure 6-6. Pre- and post-training grand means for the STOP-SIGNAL task at midline sites across for each condition separately.

36.72, $p < .000$, $\eta 2 = .412$). Across the scalp, the P2 tended to increase in amplitude from pre- to post-training (2.6 uV vs. 3.3 uV*;* $F = 3.48$, $p = .068$, $\eta 2 = .086$). There were no Time x Condition interactions (all ps > .312).

N2 (mean 222 ms) peaked later on FI (277 ms) than SI trials (207 ms; $F = 97.46$, $p <..000$, $\eta 2 = .654$) and was largest in the frontal region (F: -5.1 uV > P: -3.1 uV .06; $F = 82.17$, $p < .000$, $\eta 2 = .609$). A main effect of Stimulus revealed N2 amplitude was larger across the scalp for FI than SI trials (-6.5 vs. -1.7 uV; $F = 82.17$, $p < .000$, $\eta 2 = .609$). No Time or Time x Condition effects were significant (all ps > .545).

P3 (mean 361 ms) peaked later on FI (368 ms) than SI trials (354 ms; $F = 7.74$, $p = .008$, $\eta 2 = .129$) and was maximal in the frontocentral region (F: 15.0 uV > P: 13.3 uV; $F = 13.43$, $p = .001$, $\eta 2 = .193$; C: 16.7 uV > F/P: 14.2 uV; $F = 104.43$, $p < .000$, $\eta 2 = .665$). The P3 was larger on SI than the FI trials across the scalp (16.5 vs. 13.4 uV; $F = 27.58$, $p < .000$, $\eta 2 = .351$). An increased central > fronto/parietal effect on SI compared FI trials (central vs. parietal difference: SI: 3.0 uV vs. FI 1.9 uV), highlighted that this effect was largest at centrofrontal regions *(*$F = 6.39$, $p = .015$, $\eta 2 = .107$).

A Stimulus x Sagittal x Time x Condition interaction (see Figure 6.7 for plots and Figure 6.9 for headmaps) indicated that the centrofrontal SI > FI P3 effect showed differential training effects between the conditions: while little change was seen for the Control condition (Central FI minus SI diff, Pre: 0.2. uV vs. Post: 0.2 uV), the NG-ST (Central FI minus SI diff, Pre: 2.2. uV vs. Post: 2.7 uV) and the NG condition showed a comparable increase over central regions (Central FI minus SI diff, Pre: 2.3. uV vs. Post: 2.5 uV; $F = 4.49$, $p = .016$, $\eta 2 = .150$).

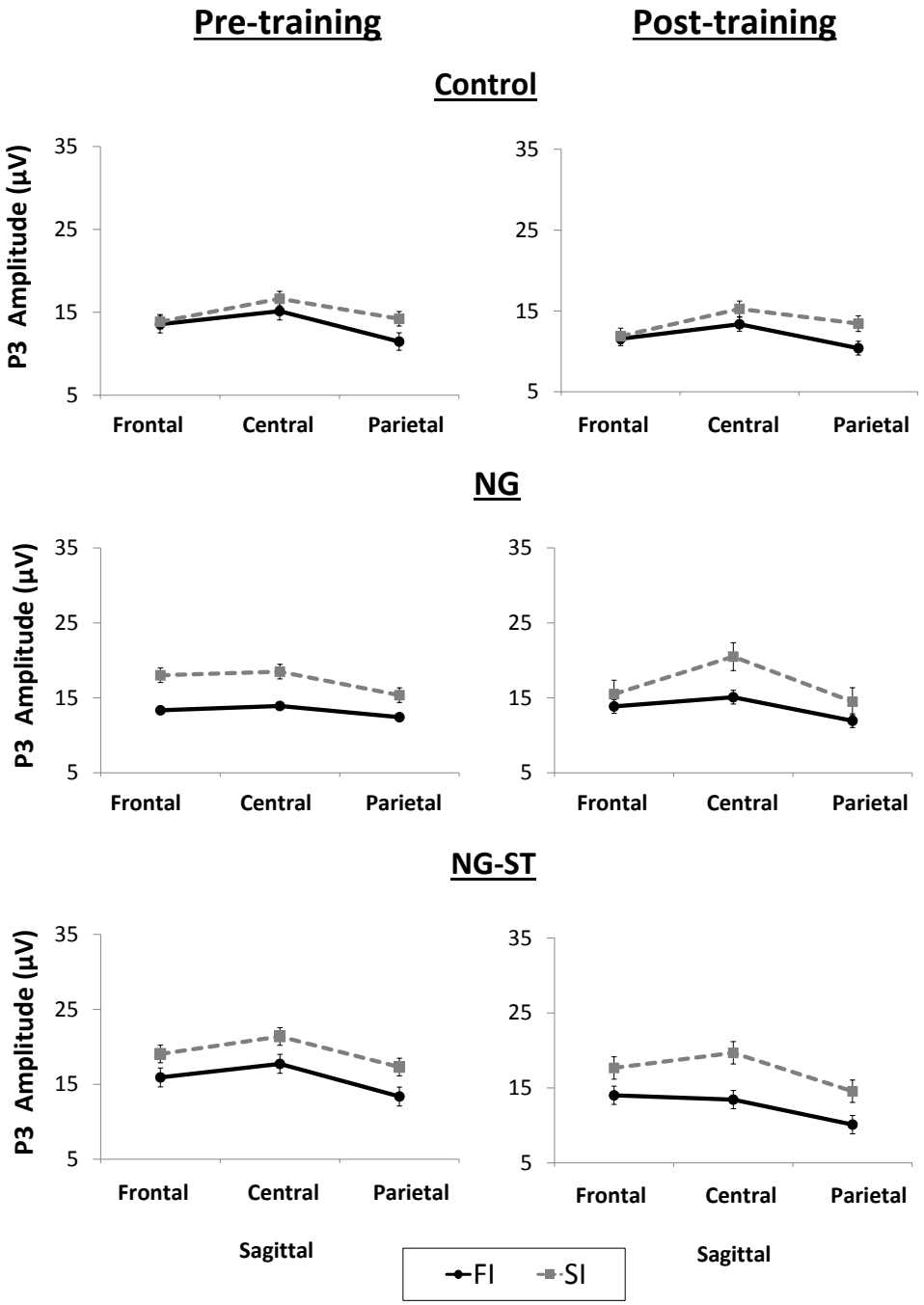


Figure 6-7. Time x Stimulus x Sagittal x Condition P3 interaction for the SS task.

6.3.4.3 ERIKSEN

Pre- and post-training grand mean ERP waveforms for the ERIKSEN task are presented in Figure 6.8.

N1 peaked at 110 ms and was largest in the central region (C: -0.9 μV > F/P: 0.0 μV; $F = 41.08$, $p < .000$, $\eta 2 = .444$]. A Time main effect revealed that N1 amplitude reduced in the frontal region from pre- to post-training (-0.6 vs. 0.0 μV; $F = 4.82$, $p = .033$, $\eta 2 = .079$. No Time x Condition effects were not significant (all ps > .215).

P2 (mean 145 ms) was maximal in the centroparietal region (F/P: 4.0 μV > C: 3.2 μV; $F = 23.13$, $p < .000$, $\eta 2 = .307$). No Time x Condition effects were significant (*ps* > .215).

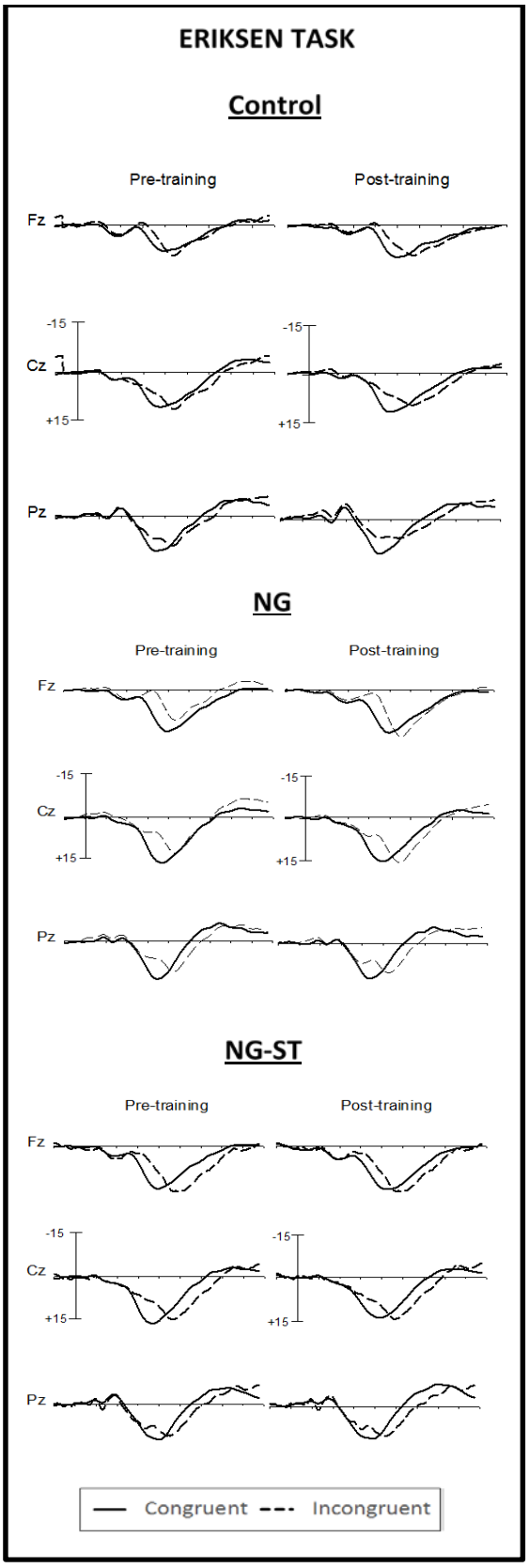


Figure 6-8. Pre- and post-training grand means for the ERIKSEN task at midline sites across for each training condition separately.

The N2 (mean 280 ms) peaked later to incongruent than congruent stimuli (272 vs. 288 ms; $F = 9.83$, $p = .003$, $\eta 2 = .160$) and was also tended to show an Incongruent > Congruent amplitude effect (1.4 vs. 2.6 μV; $F = 3.97$, $p = .052$, $\eta 2 = .071$). No Time x Condition effects were significant (*ps* > .082).

The P3 (mean 438 ms) peaked later to incongruent than congruent stimuli (411 vs. 458 ms; $F = 63.76$, $p < .000$, $\eta 2 = .535$) and was largest in the frontocentral region (F: 22.0 uV > P: 16.5 uV; $F = 18.00$, $p < .000$, $\eta 2 = .261$; C: 20.0 uV > F/P: 19.4 uV; $F = 4.02$, $p = .050$, $\eta 2 = .073$). Overall, P3 amplitude increased with training (18.8 vs. 20.5 μV; $F = 5.55$, $p = .022$, $\eta 2 = .095$). No Time x Condition effects were significant (ps > .364).

6.3.5 ERP Overlap Analysis Difference Waves

In order to investigate the overlap in components and the potential inhibition-related mechanisms to the training-related transfer between the GNG, SS and ERIKSEN tasks, we conducted a repeated measures ANOVA with the factors Task (GNG, Nogo minus Go; SS, SI minus FI; ERIKSEN, INCON minus CON). Difference waves allow for the optimal isolation of the underlying processes related to task performance (Luck, 2004; Luck, 2014). The main effect of Task (see Figure 6.9) was significant in the P3 time range. P3 amplitude showed a centrofrontal maximum for the SS task and a frontocentral maximum for GNG task ($F = 8.18$, $p = .006$, $\eta 2 = .138$), contrasting with ERIKSEN that showed a centroparietal maxima ($F = 13.59$, $p = .001$, $\eta 2 = .210$). These results indicated that although the topographic distribution of the P3 differs between the GNG and SS tasks, there is substantial overlap. Transfer is more likely by promoted between these two tasks in comparison to the ERIKSEN, which showed a parietocentral maxima.

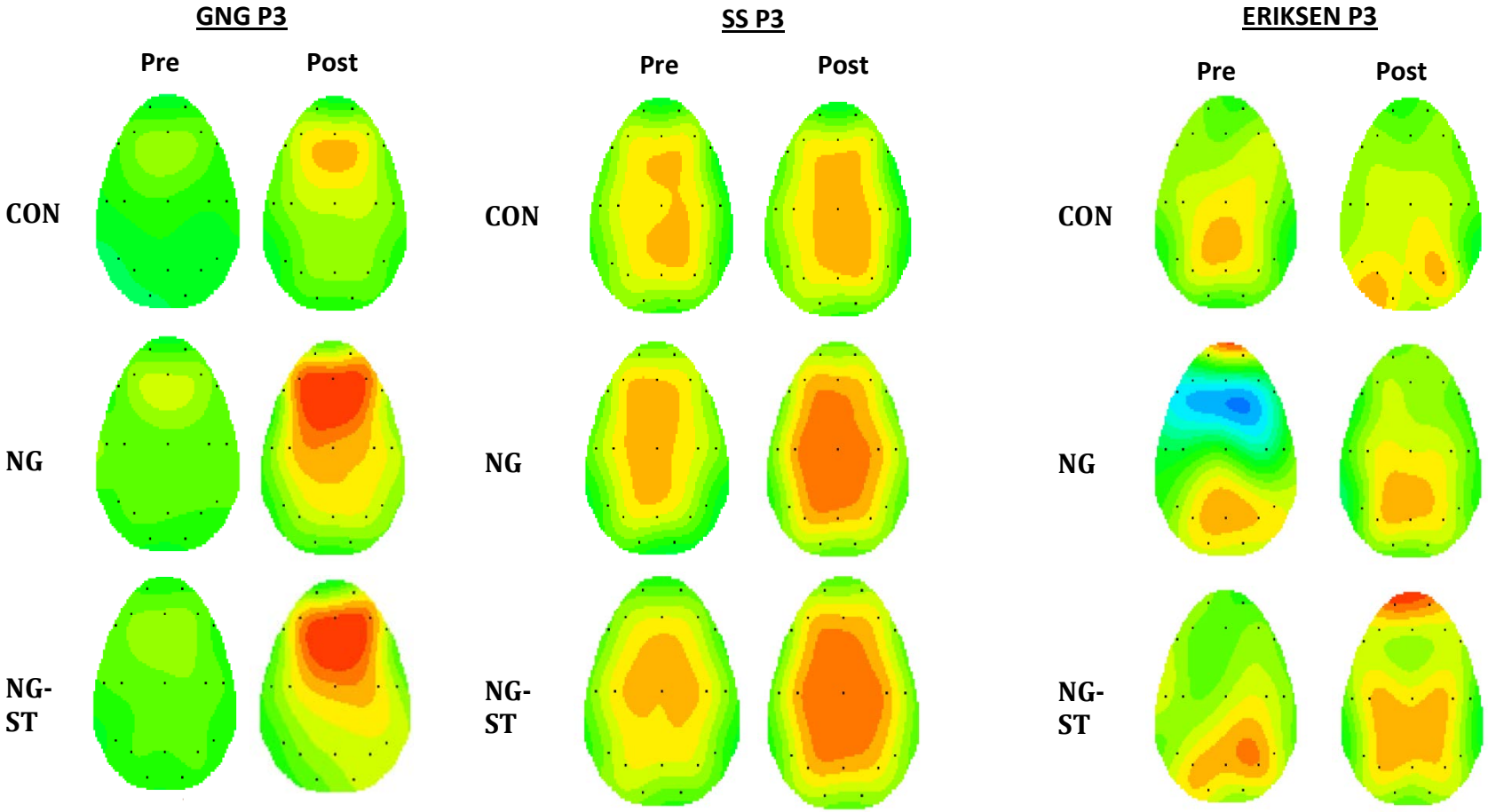


Figure 6-9. Pre- and post-training grand means each Pre/Post task for the difference wave for the GNG (Nogo minus Go; left panel), SS (SI minus FI; middle panel) and ERIKSEN (Incongruent minus Congruent; left panel).

6.4 Discussion

Although inhibitory control has been extensively studied, the extent to which it can be improved with training and the underlying neural processes remains unresolved. Thus, the primary aim of this study was to investigate the behavioural and electrophysiological effects of short term inhibitory control training by comparing two inhibition training conditions; one designed to index prepotent response inhibition (i.e. standard GNG task) with a novel training paradigm that combined prepotent response inhibition with the suppression of an ongoing response, using stop-signals (NG-ST task); both were evaluated in comparison to an active counting oddball training control condition. Task difficulty was adaptively manipulated by RTD for both training tasks and objective (i.e. task-related arousal) and self-report measures were taken to investigate the role of energetic/workload factors between the training conditions. It was also of interest to test whether, and to what extent, the training led to near-transfer on untrained inhibitory control measures (SS and ERIKSEN). Several important findings emerged.

Findings revealed that the training conditions significantly improved over the course of the training session (Figure 6.2), with both the NG and NG-ST participants showing a significant reduction in mean RT (in addition to decreased RTD level). Indicative of an overall training-related improvement in task performance, given that when responses grow faster on average, the relative strength of the inhibition mechanism must increase to successfully inhibit the fast go response (Jodo & Kayama, 1992).These results are in line with those of the general cognitive training literature demonstrating the utility of adaptive task-difficulty manipulations (e.g. Klingberg, 2010; Klingberg et al., 2005) and that inhibition performance can be reliably improved using relatively brief single-session protocols (Benikos et al., 2013a; Houben, 2011; Houben et al., 2012; Houben et al., 2011;

Jones et al., 2013; Verbruggen et al., 2012; Verbruggen et al., 2013; Verbruggen & Logan, 2008; Woolard et al., 2010).

Compatible with the training data, positive training effects were also evident between the conditions in the GNG task assessed post-training, with the NG and NG-ST participant's displaying a larger post-training reduction in Nogo errors compared to the CON (Figure 6.3). However, the type of training did not modulate training gains, with both the NG and NG-ST showing almost identical reduction in Nogo errors. Nonetheless, it is notable that behavioural changes for the GNG and NG-ST conditions were also reflected at the electrophysiological level. The frontocentral Nogo > Go P3 effect displayed a similar training-induced augmentation in the NG and NG-ST compared to CON condition (Figure 6.5). This result is consistent with our previous research suggesting that augmented frontocentral Nogo P3 amplitudes represent a training-related strengthening of a top-down inhibitory control mechanism that is dependent on task demands (Benikos et al., 2013a). Moreover, in a recent review, Jones and colleagues (2013) suggested that training-related changes in inhibitory control may simply represent short-lived fluctuations triggered by environmental triggers and/or motivational factors, and not actual gains in the capacity to inhibit responses. Indeed, while previous research using single-session GNG and SS training paradigms have reported behavioural improvements post-training, such reductions in excessive alcohol consumption (Bowley et al., 2013; Jones & Field, 2013) and risky gambling behaviours (Verbruggen et al., 2013), these effects appear transient, and were not evident at follow-up sessions conducted from as early as two hours (Verbruggen et al., 2013) or up to one week post-training (Bowley et al., 2013; Jones & Field, 2013). By contrast, in the context of no condition differences in task-related arousal, self-reported motivation or workload, our results provide novel evidence that brief but intensive training leads to relatively stable behavioural improvements, given the training conditions showed improvements in behavioural and neural changes on average 4 days after testing.

ERP overlap analysis indicated that the GNG and SS P3 activated comparable inhibition-related topographies over frontocentral scalp regions (Benikos et al., 2013a; Dimoska & Johnstone, 2007); contrasting with the ERIKSEN task, which displayed increased amplitudes over centropareital regions (Johnstone et al., 2009a). These effects remained in the vector-scaled data suggesting that the Eriksen P3 component had a unique source compared to the GNG/SS tasks (Johnson, 1993). It has been hypothesised that near-transfer will occur only to the degree that the training and transfer tasks initially engage overlapping processes or brain circuits (Dahlin et al., 2008a). From this perspective, these results suggest that GNG and SS task share similar underlying mechanisms and may be more likely to show near-transfer. By contrast, the ERIKSEN task appears to rely on different neural resources, making the possibly training transfer from GNG training less likely.

Compatible with this idea, the NG and NG-ST conditions showed near-transfer to the untrained SS task, with reductions in SSRT and a similar central enhancement in the Stop P3 relative to the CON condition. This result corroborates previous reports of improved SSRT with practice (Berkman et al., 2014; although see Cohen et al., 2013; Ditye et al., 2012; Manuel et al., 2013; Verbruggen & Logan, 2008), with this study showing the first evidence that behavioural and neural changes can transfer to a SS task that was not specifically trained. In line with the ERP overlap analysis, several previous fMRI studies comparing activations between GNG and SS tasks suggest that these tasks rely on overlapping brain regions, including the right lateralized IFG, pre-SMA, anterior insula, anterior cingulate cortex (ACC) and the parietal regions (Bari & Robbins, 2013; Chambers et al., 2008; Eagle et al., 2008; Sebastian et al., 2012; Sebastian et al., 2013; Swick et al., 2008, 2011). Combined, our results suggest that training-related near-transfer is possible due to the high degree of overlap in the neural circuitry between the SS and GNG tasks.

Despite near-transfer effects being seen between the GNG and SS tasks, there was no transfer to the ERIKSEN task, either in terms of performance or ERP measures. Recent neuroimaging research has suggested that withholding and cancelling responses shares significant mutual activation with interference inhibition in the same underlying inhibition network (e.g. rIFG, pre-SMA;Sebastian et al., 2013). From this perspective, near-transfer would be possible after training. There are a number of possible explanations for this finding. First, as outlined in the introduction, regions highly involved in response selection, including the parietal cortex, are activated to a greater degree during interference control than action withholding or cancellation (Blasi et al., 2006; Sebastian et al., 2012; Sebastian et al., 2013). Given the lack of overlap at the scalp level, the response selection circuits may be too specific and modular in comparison to the inhibition network, making transfer unlikely to occur. An alternative hypothesis is that action withholding, cancellation and interference control represent different subcomponents of inhibition that manifest differentially within the inhibition process (Johnstone et al., 2009a; Johnstone et al., 2007; Sebastian et al., 2012). For example, while the P3 to inhibition-evoking stimuli has reliably been linked to response inhibition in GNG and SS tasks (Enriquez-Geppert et al., 2010; for a review see Huster et al., 2013; Johnstone et al., 2007), the ERIKSEN P3 may reflect stimulus evaluation and not likely to show transfer effects in the ERP (Johnstone & Galletta, 2013). From this perspective, it could be argued that the Eriksen N2, which has been suggested to reflect response conflict would be a more likely candidate (Van Veen & Carter, 2002a; van Veen & Carter, 2002b. It might be expected that reduced response conflict would lead to greater cognitive control and performance (Millner et al., 2012). Despite this, the Eriksen N2 amplitude did not vary with Time or between the conditions. Finally, given the single-session employed in the present study, it may be that the training was too brief to elicit reliable transfer effects in the ERIKSEN task.

As noted above, little difference was found for the performance and ERP variables between the NG and NG-ST conditions. Although it was hypothesised that combining action

withholding and cancellation could potentially enhance training effects (Enriquez-Geppert et al., 2010), it appears that the addition of stop-signals does not enhance the training response. Rather, as suggested in the previous study (study 3), the speed of the average Go response appears to be the key determinant of optimising training gains, with the added benefit that it can be adaptively manipulated and tailored to an individual's ability level. The adaptive manipulation of RTDs in GNG tasks appears to be the "first line" task difficulty manipulation employed by future inhibition training research. Moreover, this finding underlines the importance of a direct comparison of training methodologies within the same study to isolate the key variables associated with performance gains. However, this result does not preclude use of separate GNG and SS tasks in future research. It might be that the training of both forms of inhibition produces optimal training gains (for a similar suggestion see Jones et al., 2013). Therefore future research should employ separate multi-task training designs to investigate this possibility further.

Compatible with study 3, there were several neural changes that occurred irrespective of training condition or task type. N1 amplitude reduced across the training session, while the P2 increased for both the GNG and SS tasks (Wang et al., 2010). The N1 has been suggested to reflect early sensory attention towards task stimuli (Näätänen & Picton, 1987a). The P2 is enhanced to task-relevant stimuli (Potts, 2004) and with stimulus repetition, regardless of changes in performance (Tremblay et al., 2014). Together, the reduced amplitudes of the N1 and increases in the P2 component for the GNG and SS tasks might reflect more efficient task-related attentional control with repeated task administration.

In contrast to the N1 and P2, the N2 showed different effects between tasks; showing a training-related attenuation for the GNG, but no changes in the SS or ERIKSEN task. The N2 has been increasingly linked to response conflict in recent years (Van Veen & Carter, 2002a; van Veen & Carter, 2002b). Therefore, amplitudes attenuations potentially represent reduced response conflict elicited by the task. Perhaps then, given that all

participants trained using a variant of a two-stimulus RT task (e.g. oddball, GNG), the across condition attenuation in the N2, but not SS or ERIKSEN N2, may reflect reduced conflict for the task structure they had more experience with, compared with the additional task requirements of the SS or ERIKSEN. Finally, no change was seen in the early potentials in the ERIKSEN, in line with behavioural results showing little transfer to the interference inhibition domain.

6.4.1 Summary and integration

The results of the present research provide novel evidence that the manipulation of task difficulty (via RTDs) helps to optimize the short-term training and transfer of inhibitory control. Note that these effects were not due to differences between conditions to task-related arousal, motivation/task workload or simple repetition of stimuli, and that they remained stable post-training.

The results also have importance to the understanding of the neural changes that should be expected from the training of inhibitory control. Although the current literature suggests that executive functions are subject to plastic changes, the underlying neural mechanisms remain largely unresolved (for reviews see Kelly & Garavan, 2005; Kelly et al., 2006b; Spierer et al., 2013). Potential patterns of training-induced neural changes may form three broad categories: (a) enhanced activation, possibly reflecting more coherent activation of the related brain units; (b) decreased neural responding that may index enhanced neural efficiency; or (c) functional reorganisation/redistribution of the underlying neural processes, possibly due to the adoption of a new task strategy (Kelly & Garavan, 2005; Kelly et al., 2006b; Tremblay et al., 2014).

To-date no evidence of functional reorganisation/redistribution of neural responses has been reported in the context of inhibition training, but there is evidence of performance improvements in inhibitory control being accompanied by a decrease in source activation strength of the inhibition-related regions such as the IFG, striatal areas (Manuel et al., 2013) and left parietal regions (Manuel et al., 2010). However, these results are unclear given that they were attained using the same stimuli throughout a single-session training protocol and that they included no control condition. Neural responding has been shown to habituate with simple repetition of stimuli (Ravden & Polich, 1998). Additionally the imaging literature indicates that fatigue results in reduced activations in regions implicated in response inhibition (Persson et al., 2013). Accordingly, the question of whether reduced activations are, at least in part, stimulus-specific (or due to fatigue) and not related to the improvement of inhibitory capacity remains open.

In contrast, the findings of our previous research (Benikos et al., 2013ad), and those of the present study, consistently indicate that enhanced frontocentral P3 amplitudes reflect training-induced improvements in inhibitory control; an effect, that is greater compared to active control conditions, is not linked to energetic task performance factors, is stable over several days and shows near-transfer to SS tasks. Moreover, these findings are also in line with several previous investigations linking the frontal P3 and inhibitory control. For example, the frontal P3 predicts better response inhibition capacity (Fallgatter & Strik, 1999) and inhibition performance (Benikos et al., 2013a), while the opposite is also true, with reduced frontal P3 amplitude being seen in situations of reduced inhibition capacity, such as with fatigue (Kato et al., 2009), sleep deprivation (Qi et al., 2010) and in psychopathological disorders characterised by inhibition deficits, such as ADHD (Fallgatter et al., 2005).

The training protocols used here have focused on the manipulation of task difficulty in order to tax top-down inhibitory processing; a process, which may make it more likely for training to transfer to untrained conditions or tasks supported by the same higher-order

fronto-basal brain network (Spierer et al., 2013). Based on these findings, I propose that the top-down augmentation of inhibitory control is dependent on task demands and is reflected by increased activation of the frontal P3 inhibition process, potentially via more coherent activation of an underlying inhibition mechanism.

6.4.2 Limitations and future directions

This study is not without limitations. First, cognitive training studies have been criticised for allowing an ambiguous interpretation or generalisation of the results due to the omission of appropriate control groups (Shipstead et al., 2012). Although we included a control group that matched the training participants for lab time, self-reported and objective energetic variables, the inclusion of an additional training condition that trained participants using a static GNG RTD would have provided a further comparison and validation of the reported changes in performance and ERP variables (Enge et al., 2014). Second, Houben (2011) demonstrated that that the effectiveness of inhibition training was dependent on participant's initial level of inhibitory control, such that only those with high levels of impulsivity showed training-induced behavioural changes. The current study included a high-functioning and healthy university sample, but future research could consider a study sample of high vs. low levels of impulsivity or a clinical sample with known inhibition deficits (e.g. older adults, ADHD). Third, the training data presented here provided proof of principle for the relatively short-term effects of manipulating task difficulty during the training of inhibitory control. However, it remains unclear whether these effects would be enhanced with further training, and how "expert" performance would present in neural activity. Inhibition automaticity has been infrequently studied, but would provide a clearer picture of what performance and neural changes should be expected of inhibition training (Cohen et al., 2013). Therefore, future studies should consider increasing the number of training sessions over a number of weeks using a pre/post/follow-up design (Berkman et al.,

2014). Finally, we did not assess IQ in the present study. While it may be assumed that the use of high functioning university sample that were randomly assigned to each condition limited the impact of IQ differences between conditions, future research should include an IQ measure to rule-out this possibility.

6.4.3 Conclusions

In summary, the current study provides new evidence that the use of adaptive task difficulty while training inhibitory control shows near-transfer to untrained tasks; both in terms of performance and neural changes. It was suggested that positive training-induced improvements in inhibitory performance are reflected by top-down strengthening of a frontal inhibition mechanism. However, these effects are limited to closely related inhibitory domains and further avenues for future research were suggested.

Chapter 7 - General discussion and future directions

7.1 Summary and general discussion

This thesis aimed to clarify the key experimental parameters required to elicit positive training-induced gains during the short-term training of inhibitory control, with a further focus on identifying the resultant changes in its putative electrophysiological correlates.

The four studies in this thesis examined (a) the effect of incremental increases in Go/Nogo task difficulty (via RTD) on performance and the inhibition-related ERPs (N2 and P3), with a lesser focus on early processing (i.e. N1, P2 components) and energetic factors (perceived effort, task-related arousal; Study 1); (b) if the task difficulty effects found in Study 1 would be modulated by single-session short-term training (Study 2); (c) whether a different method of manipulating Go/Nogo task difficulty – stimulus probability - would enhance training performance outcomes/changes in the ERP components, and if they would show stable post-training changes upon the presentation of untrained stimuli (Study 3); (d), if a hybrid Go/Nogo/Stop-signal task would serve to improve the training and transfer effects in performance and processing to untrained tasks over and above a standard Go/Nogo task, and finally (e) whether the changes in task performance and ERPs would be stable after the initial training session approximately 3 to 4 days later (Study 4). Therefore, this thesis offered the first systematic investigation into the key experimental parameters aimed to improve inhibitory performance and investigated the underlying neural mechanisms.

In the first study, a Go/Nogo task with 70% Go probability was used to ensure that prepotent response inhibition was elicited. Under the assumption that greater Go/Nogo task

difficulty occurs when Go response times are reduced (via shorter RTDs), a between-subjects manipulation of task difficulty revealed reduced RTs, along with incremental increases in Nogo errors, with each RTD reduction. In support of this approach, participants reported greater perceived effort with enhanced task difficulty. At the neural level, the Nogo N2 displayed shorter latencies and increased amplitudes with increasing task difficulty; in support of the response conflict model of the N2 which suggests increased competition between Go and Nogo stimuli when participants are required to emphasise speed over accuracy. By contrast, the Nogo P3 effect was reduced in the High compared to the Medium difficulty condition. Given the increased proportion of Nogo errors in the High condition, this effect was interpreted in terms of reduced capacity of these participants to successfully inhibit or monitor their responses on Nogo trials. Analysis of the early ERPs showed that Nogo N1 was enhanced in the High condition, while the Nogo P2 was increased in the Low relative to the other conditions, suggesting that in addition to the typical inhibition-related ERP components (i.e. N2, P3), that the early ERP components of the N1 and P2 also reflect important processing stages related to task performance.

In combination these results provided valuable baseline evidence that Go/Nogo task difficulty could be successfully varied, but importantly it supported the application of RTDs for use in inhibition training paradigms. The Nogo N2 did not appear to accurately reflect an underlying inhibitory control mechanism, while the frontal Nogo P3 effect did. However, the results also suggested that consideration of the early N1 and P2 components may provide a more complete picture of what is to be expected after Go/Nogo task training.

Study 2 used the three task difficulty levels established in Study 1 and investigated whether short term training (i.e. a single session of 8 blocks) resulted in training-related improvements in inhibitory performance and processing. It was hypothesised that training using Medium compared to Low or High task difficulty levels would result in the greatest training-induced changes in task performance, given that training effects are likely to be

enhanced when a task remains relatively challenging but not overly difficult (Ahissar & Hochstein, 2004). In the absence of condition differences in perceived effort or task-related arousal, Go/Nogo proficiency was optimised during the Medium condition. Changes in the ERP components were also dependent on task demands, such that the Low difficulty condition showed an enhanced Nogo P2 and a greater reduction in the Nogo N1. By contrast, a larger frontocentral Nogo P3 was seen in the High than the Medium condition. These findings suggested that automatic inhibition leads to pre-attentional training effects as manifested by enhanced Nogo P2 amplitudes when training is relatively easy. By contrast, when the demands of top-down inhibition are increased, training results in the enhancement of the frontal Nogo P3 effect. Although training-induced changes have typically been associated with the reinforcement of top-down executive control processes or to the emergence of automatic bottom-up forms of inhibitory control, the results of Study 2 implied that these effects may be dependent on task demands. These findings suggested an interesting dissociation between exogenous and endogenous ERPs as a result of manipulating task demands during the training of inhibitory control.

However, the results of Study 2 opened up many questions regarding the optimal manipulation of task difficulty to enhance inhibition training gains. While RTDs were chosen to elicit faster responses and ensure that inhibition was increasingly more difficult, the High task difficulty condition showed a decline in performance. It was argued that such strict time pressure clouded the training effects and the examination of a different manipulation of task difficulty would further clarify the results.

Study 3 investigated whether increasing Go/Nogo task difficulty by varying Go stimulus probability would augment the positive effects of Go/Nogo task training, by placing greater demand on the inhibitory process during training. An oddball training task (stimulus probability 30%) was included as a control condition. All conditions (Control, Standard, and

High prepotency) were subject to the same RTD based on the RT of the common practice block. Expected condition differences during the training blocks were seen suggesting three levels of task difficulty were successfully achieved. In the absence of self-reported differences in motivation, workload, task-related arousal, or differences in the early ERP components (i.e. N1 and P2), the High Probability condition showed the greatest training-induced improvement of Go/Nogo task proficiency. This result remained unchanged with the presentation of previously untrained Go/Nogo stimuli. Compatible with the results of Study 2, and in line with the interpretation that it reflects an underlying inhibitory control mechanism, the largest training-related enhancement in the frontocentral Nogo P3 anteriorisation effect was found in the high stimulus prepotency condition. Unexpectedly, the SP and Control condition showed little difference in performance and early (N1, P2) and late (N2, P3) components with training. However, given that the same RTD was imposed on all participants, it was suggested that the primary determinant of training success was the overall RTD imposed, rather than stimulus prepotency. Overall, stimulus prepotency does not appear to be an effective modulator of training performance or ERP changes in the Go/Nogo task.

Building on the previous findings in this thesis, Study 4 looked to further clarify the effect of task difficulty on inhibitory control training by the use of adaptive RTDs. Employing a combined Go/Nogo/Stop-signal task, Study 4 assessed whether the combination of prepotent inhibition and the cancellation of responses would augment the transfer of training using multiple inhibition paradigms (Go/Nogo, Stop-signal, Eriksen flanker). It was also crucial to investigate whether any improvements would be transient, given that previous research has suggested that the positive effects of inhibition training paradigms are short-lived (Jones et al., 2013; Verbruggen et al., 2013; Verbruggen & Logan, 2008). An active oddball control condition was compared against the two training conditions that differed in task difficulty manipulation: adaptive RTD Go/Nogo training and another that trained on a combined Go/Nogo Stop-signal task (with adaptive RTDs and stop-signals).

No conditions differences in self-reported motivation, workload or arousal were found suggesting that any differences in performance or ERP components were primarily related to training effects. The training conditions (i.e. NG, NG-ST) showed similar post-training improvements in Go/Nogo task performance compared to the Control condition. Notably, training transferred to the Stop-signal task, with ERP analyses showing overlapping frontocentral increases in the Nogo and SS P3 component; suggesting that inhibition training can show near transfer, reflected by changes in the ERP. However, these effects did not extend to the interference inhibition domain.

Study 4 was designed to further investigate the degree to which inhibition training effects are dependent on task demands. The two training conditions showed a clear improvement in Go/Nogo performance compared to the Control condition, which was reflected by an enhanced frontal Nogo P3 effect; potentially indicting more coherent firing of an underlying inhibition mechanism after training. Moreover, given the overlapping nature of the Go/Nogo and Stop-signal task over centrofrontal regions, this appeared to result in the transfer of training effects, whereas no transfer effects were seen to the Eriksen task. It was suggested that the degree to which tasks show overlapping brain activation appears to limit the ability of training to transfer to untrained tasks.

The results from these studies convey several important points about the nature of inhibitory control tasks required to elicit training gains and how they are reflected in ERP components linked to inhibitory control. These are dealt with in turn, in addition to the limitations of the research and future suggestions.

7.2 Optimising training-related changes in inhibitory performance

The idea behind increasing task difficulty with training is to evoke improvements in inhibitory control by keeping the task challenging throughout the training phase, thereby maximizing performance gains (Lövdén et al., 2010; Schmiedek et al., 2013). The results presented in this thesis indicate that task demands are a key modulator of training-induced performance changes in inhibitory control. Study 1 showed that task demands (via shorter RTDs) showed reliable manipulation of inhibitory performance, with greater difficulty resulting in an increased proportion of inhibition errors. Study 2 built on these results by demonstrating that task demands elicited very different training-related performance changes; Low task difficulty elicited early automatic forms of inhibition (as manifested by the Nogo P2), whereas Medium inhibition difficulty shows the greatest gains in Go/Nogo proficiency. By contrast, High inhibition difficulty showed decreased Go/Nogo proficiency. In Study 3, and based on previous research (e.g. Bruin & Wiers, 2002), it was hypothesized that increases in Go stimulus probability would enhance training-induced changes in task difficulty independently of imposing strict RTDs (as seen in High difficulty condition in Study 2). However, the results showed that only the imposition of High Go stimulus prepotency (which yielded faster reaction times and greater inhibitory load) resulted in a greater augmentation in Go/Nogo proficiency post-training. Crucially, further investigation of this study's methodology suggested that the overall determinant of inhibition training success was the actual speed of the Go process.

To further probe the specific parameters required to elicit training-related gains in inhibitory performance, Study 4 explored whether combining two inhibition abilities in a hybrid Go/Nogo/Stop-signal task (i.e. prepotent response inhibition, and inhibition of an ongoing/activated response) might enhance training gains compared to a standard prepotent inhibition task (Go/Nogo). It was shown that the main determinant of inhibition training gains was the speed of the Go response. It appears that only increasing time pressure results

in improvements of inhibitory control. Although previous research has manipulated task difficulty by using variations in perceptual difficulty (Miller et al., 2011; Millner et al., 2012), it can be questioned whether this elicits training-related changes in an underlying inhibition mechanism or simply taxes perceptual processes. Previous research has shown that simply varying the perceptual difficulty does not tax inhibitory control, but rather stimulus-responses associations specific to a task that do not generalise to other domains (Millner et al., 2012; Spierer et al., 2013). If inhibition training is to be useful for enhancing cognitive function in typically developing individuals and those displaying deficits in inhibitory control, it needs to be shown that inhibition-related gains in performance are independent of extraneous processes. Variations in perceptual difficulty do not meet this criterion. Furthermore, the results of this thesis showed that the intended training effects were independent of context-related effects such as fatigue, workload or arousal. Training-related gains in performance and processing appear to be independent of energetic factors and reflect true gains in cognitive capacity (Enge et al., 2014)

7.3 Training-related changes of inhibition-related components

A major aim of this thesis was to examine the effect of training on the inhibition-related components of the ERP, N2 and P3. If training-induced improvements in inhibitory performance are found, they should be reflected by changes in the putative markers of an underlying inhibition mechanism and therefore be informative regarding their functional significance.

7.3.1 Training-related changes in the early ERP components

7.3.1.1 The N1 component

The N1 component has been argued to represent an early attentional switch that is determinative for inhibition success (Dimoska & Johnstone, 2007; Dimoska & Johnstone, 2008). Against this hypothesis, the High task difficulty condition in Study 1 showed increased Nogo N1 amplitudes along with the highest proportion of Nogo errors. However, the N1 is also subject to habituation effects, such that it decreases with the repeated presentation of stimuli (Barry & Sokolov, 1993). Compatible with this interpretation, the Go/Nogo N1 reliably declined with time-on-task irrespective of task difficulty manipulation (Study 2, and 3). From the perspective that the N1 component reflects the early sensory extraction of, and attention to stimuli (Näätänen & Picton, 1987a), it appears that as participants learned the nature of the task stimuli, the underlying early attentional neural processes reduced over time. This is supported by the results of Study 4 where the Go/Nogo and Stop-signal N1 components reduced from pre- to post-training. By contrast, the Eriksen flanker N1 showed no significant training-related change. However, given that the participants' had little experience with the task structure of the flanker, it is perhaps not surprising that no significant change was seen. In combination, the results of this thesis suggest that the N1 component is indicative of early automatic attentional processes that do not appear to be an indicator of training-related improvements in inhibitory control.

7.3.1.2 The P2 component

In Study 1, centroparietal Nogo P2 amplitude was larger in the Low task difficulty condition compared to conditions of Medium or High difficulty. Similarly, the results of Study 2 showed that when Nogo stimuli were more effectively discriminated (i.e. when

RTDs were slower and therefore stimuli were more easily detectable), the Low condition showed a large training-related increase in P2 over centroparietal regions; whereas, the Go and the Nogo P2 showed similar anterior shifts for both the Medium and High difficulty conditions. In particular, the latter result was supported by Study 3. When task difficulty (as manipulated by RTD based on the practice trial RT) was applied equally to all conditions (Control, SP, HP), a training-related anterior increase in the Go and Nogo P2 was seen irrespective of condition. Study 4 showed a similar anterior augmentation for the Go/Nogo and Stop-signal task (with no difference in stimulus type) with training, but no difference in the Eriksen P2 component. This again is not surprising, given the little training experience participants had with the Eriksen task.

Although the functional significance of the P2 has yet to be determined, there is evidence that its interpretation may have dissociable meanings according to scalp topography. The P2 at centro-parietal regions indexes early visual processing, which is enhanced by easily detected and readily classified stimuli (Lindholm & Koriath, 1985; Luck & Hillyard, 1994c) and displays training-related enhancements concurrent with performance improvements in the perceptual learning literature (e.g. Tonga et al., 2009; Tremblay, 2007). By contrast, the frontocentral (or more anterior) P2 reflects the activation of frontal regions associated with identification of task-relevant stimuli (Potts, 2004; Potts et al., 1996). Consistent with the notion that larger centro-parietal P2s index more easily classified stimuli, Verbruggen and Logan (2008) argued that practice on inhibitory control tasks results in the advent of automatic inhibition, where learned stimulus-response associations between activating and withholding a response reduce the need for top-down executive control. In line with this view, enhanced Nogo P2 amplitudes to well-learned tasks may reflect the automated inhibition of the Nogo stimuli, freeing top-down mechanisms from further processing (Study 2). By contrast, Cohen and colleagues (1992) conceptualised automatic versus controlled processes as a continuum, with the amount of training being a key indicator of whether automatic responses will be elicited. As a result, more anterior P2s may

indicate further stimulus processing and evaluation of stimuli with training, which occurs before automatic processes are put in place. Given the relatively brief training and increased task difficulty in Study 2 (Medium and High conditions), 3 and 4, it suggests that automatic processing at the P2 stage did not have sufficient time to emerge. Thus, it would be of benefit for future research to investigate the effect of longer-term inhibitory control training to further isolate the role of the P2.

7.3.2 Training-related changes in the inhibition-related components

7.3.2.1 The N2 component

In tasks indexing inhibitory control, larger amplitudes of the N2 component have typically been considered to be a marker of an inhibition process (see section 1.5.1). In all the studies in this thesis, the N2 effect (i.e. larger amplitudes to inhibition-evoking compared to other stimuli) was significant, with topographic maps revealing a frontal focus, consistent with previous research linking frontal brain regions and inhibitory processing (Aron, 2011; Aron et al., 2007; Aron et al., 2004; Smith et al., 2008; Smith et al., 2010; Sonuga‐Barke et al., 1992; Xue et al., 2008).

However, the results from this thesis argue against an inhibitory interpretation for N2. The Nogo N2 effect was incrementally enhanced with increasing task difficulty in Study 1. Although this effect could be interpreted as reflecting the greater need for inhibitory control with increasing task demands, further analyses indicated an inverse relationship between the Nogo N2 effect and inhibition performance, such that increased Nogo errors were associated with larger Nogo N2 amplitudes. Given the training-induced improvements in Go/Nogo proficiency in Study 2 for the Medium task difficulty condition, it might be expected that the Nogo N2 effect would increase with training (Schapkin et al., 2007). Instead there was no change in the Nogo N2, only the Go N2 reduced; potentially indicating

a decreased requirement for stimulus discrimination (Johnstone et al., 1996). In Study 3, both Go and Nogo N2 amplitude reduced with training irrespective of condition. In Study 4, the N2 displayed different training-related effects between tasks, showingacross-condition attenuation to Go/Nogo stimuli post-training, but no change in the Stop N2. This was in the context of larger reductions in SSRT for the training (i.e. NG, NG-ST) compared to the control condition. Thus, the findings of this thesis suggest that the N2 does not appear to act in a way consistent with this component reflecting inhibitory control.

An increasingly influential interpretation of the N2 to inhibition-evoking stimuli is that it reflects response conflict (Van Veen & Carter, 2002a; van Veen & Carter, 2002b). This view holds that N2 magnitude indicates the level of conflict between competing response representations whenever two (or more) incompatible representations are simultaneously activated (Nieuwenhuis et al., 2003). From this perspective, the prepotent tendency to respond on Go trials competes with the need for inhibition on Nogo trials and results in increased response conflict and an enhanced Nogo N2 component. This can also be seen in the Stop-signal task, where response activation competes with the recently activated stop-signal cue. In the Eriksen flanker task, competing response tendencies are driven by presentations of Incongruent as compared to Congruent flankers. Larger N2 amplitudes are seen in failed compared to successful inhibition trials in the Stop-signal task (e.g. Dimoska & Johnstone, 2008) and to Incongruent flanker trials compared to Congruent or Neutral trials (e.g. Gehring et al., 1992; Johnstone & Galletta, 2013). If this is the case, an increased Nogo N2 with greater Go/Nogo task difficulty can be interpreted in terms of greater response conflict when participants emphasise speed over accuracy (Study 1). In relation to training-related Go/Nogo N2 attenuations across conditions (Study 3), it could be that repeated presentation of the Nogo stimulus enabled participants to more effectively respond to the requirements of the task – driven, at least in part, by a reduction in response conflict. A key tenant of the conflict model is that it is response-related (e.g. Randall & Smith, 2011); that is, the degree to which response conflict is experienced depends on the nature of the

response required, and as such, can be modulated by task demands. Thus, the conflict model can also explain the results of Study 4 that showed N2 attenuations to the Go/Nogo, but not the Stop-signal or Eriksen task post-training. Given that all participants trained using a variant of a two-stimulus RT task (e.g. oddball, GNG), the Go/Nogo N2 attenuations likely reflects reduced response-related conflict to the specific task demands participants had more experience with, compared with the additional task requirements of the SS and Eriksen flanker tasks (tasks they had little *direct* experience with).

If it is accepted that the N2 component represents response conflict, it is puzzling why the Nogo N2 showed no training-related change across conditions in Study 2, compared to the relatively reliable attenuations for both the Go and Nogo N2 seen in Study 3 and 4. As noted earlier in this thesis, the N2 component might not reflect a unitary process, but rather a "family" of sub-components. For example, Folstein and Van Petten (2008) argue that an N2 component related to cognitive control (encompassing inhibition and conflict monitoring) overlaps temporally with two other N2 components linked to stimulus mismatch and novelty. In partial support of this idea, it was found that Nogo N2 appeared to change its distribution with enhanced difficulty, displaying an increased Nogo > Go N2 effect at centro-parietal regions for the High condition in Study 2. Kok (2001) has suggested that variation in task difficulty changes the underlying cognitive processing related to task performance. If so, further replication of these findings using decomposition methods such as principal component (PCA; Dien, 2010) or independent component analysis (ICA; Makeig et al., 1997) would help to uncover these effects. It seems clear from the results of this thesis that training-related modulation of the N2 component to inhibition-related stimuli does not reflect changes to an underlying inhibitory control mechanism.

7.3.2.2 The P3 component

If it is recognized that the N2 component does not reflect training-related changes in inhibitory control, perhaps the P3 is a marker of this process.

In Study 1, the frontocentral Nogo P3 accurately reflected the success of inhibitory control, such that it was reduced under conditions of High task difficulty (where Nogo inhibition errors increased substantially) compared to Medium or Low task difficulty RTD conditions. In Study 2, the Medium task difficulty condition showed the greatest increase in Go/Nogo proficiency overall and also displayed a larger frontocentral Nogo P3 compared to the Low condition (which showed little change in performance and the frontocentral Nogo P3 effect). Although the High task difficulty condition showed an even larger increase in the Nogo P3 effect, this result does not rule-out a training-related interpretation for this component given that Nogo errors plateaued by block 4 for this condition, while the Nogo P3 continued to increase until the conclusion of training - suggesting a continued adaptation to the difficulty of the task (Kelly et al., 2006b). In Study 3, the only condition to show enhanced training-induced improvement in Go/Nogo proficiency, the High stimulus probability condition, displayed an attendant frontocentral increase in the Nogo P3 effect. Note this effect remained even when presenting participants with previously untrained stimuli, suggesting that it reflects a reliable training-induced modulation of the underlying neural processes. However, it could also be argued that this effect was transient and simply represents a short term carryover effect (Jones et al., 2013; Jones & Field, 2013; Verbruggen et al., 2013). Study 4 was designed to address this issue. It was shown that an augmented frontocentral Nogo P3 was still present, on average, 3.5 days after the single training session, concurrent with a reduction in Nogo errors (irrespective of whether stop-signals were presented during training). Moreover, this effect showed near-transfer to an untrained Stop-signal task, with similar frontocentral increases were seen at post-training in the context of a reduction in SSRT. This thesis provides the first evidence that the inhibition-related frontal

P3 component reliably reflects training-related improvements in inhibitory control. Given that Go/Nogo and Stop-signal inhibition processing overlapped over frontocentral regions, this result also supports previous suggestions that transfer is most likely to occur in tasks that elicit activation of similar brain regions (Dahlin et al., 2008a; Dahlin et al., 2008b). This was reinforced by the finding that the P3 in the Eriksen flanker task showed a more parietal distribution, suggesting different underlying neural processes - precluding the chance of transfer (Sebastian et al., 2012; Sebastian et al., 2013).

The findings of this thesis provide fundamental baseline research which suggests that (a) the inhibition-related P3 component accurately reflects inhibition performance and processing, (b) training-related performance improvements coincide with enhanced magnitudes of this component, and (c) given similar and overlapping neural processing, the P3 shows near-transfer to untrained inhibitory control tasks. Based on these results, it appears that the top-down augmentation of inhibitory control is dependent on training task demands and is reflected by increased activation of the frontal P3 inhibition process, potentially via more coherent activation of an underlying inhibition mechanism.

7.4 Future directions

It may be argued that training gains seen in relatively short training paradigms would have shown limited generalisation of training and transfer effects in the current thesis. However, it should be pointed out that Verbruggen and Logan (2008) have shown reliable training gains in Go/Nogo and Stop-signal tasks and that Study 4 showed overlap at neural level between these tasks in Study 4. However, these results were intended to provide proof-of-principle towards some of the key parameters for training inhibitory control. The inhibition training literature has been so clouded with different training paradigms, time

schedules, outcome measures and proposed mechanisms of changes that it is difficult to isolate if or how this process can be trained.

Overall, the results of this thesis suggest that inhibitory control is malleable and subject to plastic changes, suggesting that further research in this area may be useful in improving this ability and potentially ameliorating deficits. However, the puzzle of whether the training of inhibitory control results in tangible benefits has yet to be resolved. There are several areas of research that would be useful in order to explore this issue.

Training with adaptive task difficulty appears to result in key performance and neural changes in trained and non-trained tasks. Firstly, this implies that enhancing task difficulty results in the improvement and transfer of inhibitory control processes - possibly by increasing underlying cognitive capacity (Markomichali et al., 2009). However, proof-of-principle does not extend to viability. Further research needs to show that improved capacity in performance and neural processes extends long-term and ultimately to non-trained abilities (i.e. far transfer) that influence everyday life (e.g. IQ, clinical measures of disinhibition, class room performance etc.). It has also been suggested that performance and neural changes with training should only extend to those that have an initial deficit in inhibitory control (Enge et al., 2014; Houben et al., 2012). Given the promising results of the methodology used in this thesis, an important next step will be to investigate whether these results extend to different clinical and sub-clinical groups characterised by impulse control deficits (e.g. children with ADHD, excess gambling and alcohol).

Understanding whether and how inhibitory control can be trained is crucial since it could potentially improve the rehabilitation of inhibition-related pathologies by optimizing behavioural interventions via a targeted rehabilitation protocol. Many studies have demonstrated that patients suffering from inhibition-related disorders (e.g. ADHD) showed deficient inhibitory performance on various tasks including the Go/Nogo and the Stop Signal

tasks. Training on these abilities may act as an adjunct to therapy which might help to ameliorate these deficits.

In conclusion, the aim of this thesis was to investigate he key task parameters required for training gains in inhibitory controls, as indexed by performance and neural measures. Results determined that a key parameter for optimised training-related effects is the adaptive modulation of task difficulty via RTDs. It is suggested that top-down training-induced improvements in inhibitory control are reflected by increased magnitude of the frontal P3 component and that transfer to untrained tasks is most likely when training and untrained tasks index similar processes and brain regions.

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Appendix A- Contribution of candidate and co-authors

Nicholas P. Benikos was primarily responsible for all aspects of the research and the initial drafts of each section. The co-authors contributed to the design and analyses of the studies, and commented on drafts and made minor editing corrections to the manuscripts. In consultation with the thesis supervisors, a journal style format was chosen to allow more rapid dissemination of the findings. Clear linking statements have added between studies to highlight the progression of the overall research program. Copyright permission for the published chapters has been attained from the relevant journal.

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Appendix B – Published articles

Benikos, N., Johnstone, S. J. & Roodenrys, S. J. (2013a). Varying task difficulty in the Go/Nogo task: the effects of inhibitory control, arousal, and perceived effort on ERP components. *International Journal of Psychophysiology, 87* (3), 262-272.

International Journal of Psychophysiology 87 (2013) 262–272

Contents lists available at SciVerse ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Varying task difficulty in the Go/Nogo task: The effects of inhibitory control, arousal, and perceived effort on ERP components

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ARTICLE INFO

Article history:
Received 28 September 2011
Received in revised form 3 August 2012
Accepted 9 August 2012
Available online 17 August 2012

Keywords:
Task difficulty
Inhibition
N2
P3
Arousal
Effort
ERPs
Time pressure

ABSTRACT

Similar to other executive functions, inhibitory control is thought to be a dynamic process that can be influenced by variations in task difficulty. However, little is known about how different task parameters alter inhibitory performance and processing as a task becomes more difficult. The aim of this study was to investigate the influence of varying task difficulty, via manipulation of reaction time deadline (RTD), on measures of inhibitory control, perceived effort, and task-related arousal (indexed by skin conductance level). Sixty adults completed a visual Go/Nogo task (70% Go) after being randomly assigned to one of three task difficulty conditions: High, Medium and Low, with RTDs of 300, 500 or 1000 ms, respectively. Results revealed incremental increases in Go/Nogo errors and greater perceived effort with increasing difficulty. No condition differences were found for arousal, but the amplitude of the Nogo N2 increased and peaked earlier with increasing task difficulty. In contrast, the Nogo P3 effect was reduced in the High condition compared to the Low and Medium conditions. Finally, the amplitude of N1 and P2 showed differential effects, with Nogo N1 increasing with task difficulty, while the Nogo P2 decreased. This study provides valuable baseline behavioural and ERP data for appropriately manipulating difficulty (via RTD) in Go/Nogo tasks — highlighting the potential key role of not only the N2 and P3, but also the N1 and P2 components for task performance.

1. Introduction

Inhibitory control refers to the ability to successfully suppress thoughts, behaviour and irrelevant stimuli (Aron et al., 2004). Crucial for the proper functioning of many other cognitive capacities (Clark, 1996), inhibitory control is an important, but often unnoticed, feature of everyday life: Its effective execution potentially means the difference between safely crossing a busy road or endangering oneself to oncoming traffic.

Among the most commonly employed paradigms used to investigate inhibitory processing is the Go/Nogo task, which requires participants to respond to a frequently presented Go stimulus, while withholding a response to a rare Nogo stimulus. Event-related potentials (ERPs) to Go/Nogo tasks typically contain two inhibition-related components: an augmented N2 for Nogo relative to Go stimuli, primarily at frontal sites (e.g. Falkenstein et al., 1999; Fallgatter and Strik, 1991; Oddy et al., 2005), and a more anterior focus for the Nogo P3, where P3 is larger for Nogo than Go stimuli at frontal and central leads. The Nogo N2 has been suggested to reflect the pre-motor 'need' for inhibition (Kok, 1986), but more recent research has instead linked the N2 to response conflict (Donkers and van Boxtel, 2004; Nieuwenhuis et al., 2003). By contrast, the Nogo P3 has primarily been related to motor inhibition in recent years (Smith et al., 2006, 2007, 2008, 2010). But further work has also suggested that it may not be linked to inhibition itself, but more to the evaluation of the inhibitory process (Band and van Boxtel, 1999; Bruin et al., 2001). Notably, both components appear to be modulated by different neurobiological pathways (Beste et al., 2008, 2010) supporting the idea that they reflect different inhibition-related sub-processes.

Like other executive functions, inhibitory control is assumed to be a dynamic process that should be influenced by variations in task difficulty. However, relatively little is known about how different experimental parameters affect the behavioural and neural underpinnings of this ability (Beste et al., 2010; Lindqvist and Thorell, 2009; Thorell et al., 2009). There are a number of key reasons why it is important to study the influence of task difficulty on inhibitory control. Firstly, from a clinical perspective, the nature of inhibition deficits can only be ascertained if the paradigms employed are sufficiently difficult to differentiate performance between clinical subjects and healthy controls (Beste et al., 2010; Lindqvist and Thorell, 2009). Further, variations in task difficulty, in and of themselves, have been linked to differences in neural activation, leading to inconsistencies in the Go/Nogo literature (for a meta-analysis see Simmonds et al., 2008). Baseline ERP data are required to clarify these effects. Finally, the possibility of developing targeted inhibition training paradigms as an adjunct to existing rehabilitation programmes may offer a potentially useful aid for individuals suffering from deficits in inhibitory control (for e.g. attention-deficit/hyperactivity

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http://dx.doi.org/10.1016/j.ijpsycho.2012.08.005

disorder, ADHD; Johnstone et al., 2010; Thorell et al., 2009). Training outcomes in these studies may be enhanced if the approach taken is based on fundamental research into the optimal way to manipulate inhibition difficulty. Thus, studying how task difficulty influences inhibitory control is important from both a 'pure science' and applied perspective, and is the major aim of this study.

Previous research examining the influence of task difficulty on inhibition-related ERP components has been varied with respect to methodologies and findings. Jodo and Kayama (1992) manipulated task difficulty with reaction time deadline, asking one group of participants to respond within 300 ms of the Go signal, and another to respond within 500 ms. They reported an enhancement of the Nogo N2 only in the fast responders. Although this effect was interpreted as being due to increased inhibition difficulty, this was unable to be confirmed since no behavioural results for inhibitory performance were reported. In a subsequent investigation, Band et al. (2003) divided participants into one of two instructional conditions: a speed condition, where subjects were required to respond as fast as possible, and a balance condition, where speed as well as accuracy was emphasised. The speed of response was found to modulate both inhibitory performance and ERPs, with increased Nogo errors and Nogo N2 for the speed condition. In contrast to these reports, Smith et al. (2006), who separated participants into 'fast' and 'slow' responders via median split post-hoc, reported no differences for the N2.

Furthermore, despite clear effects being reported for the N2, the Go/Nogo literature examining the influence of task difficulty on the P3 is limited. Previous investigations have either not considered the P3 (Band et al., 2003; Jodo and Kayama, 1992), or have used a 50/50 Go/Nogo split (Jodo and Kayama, 1992; Smith et al., 2006) which may not reliably induce prepotent response inhibition, depending on the paradigm (e.g. Braver et al., 2001; Tekok-Kilic et al., 2001). Moreover, these studies have generally only employed two difficulty levels (i.e. low vs. high). Given that both theoretical viewpoints (e.g. Cognitive-energetic model; Sanders, 1983) and experimental findings (Wodka et al., 2009) have suggested performance improvements only during moderate rather than easy/hard difficulty levels, the use of the three task difficulty conditions in the present study allows examination of a range of effects, rather than simply assuming linear changes. Thus, one aim of this study was to extend previous research by clarifying the effect of task difficulty (as manipulated by reaction time deadline: RTD) on not only the N2, but also the P3, using a 70/30 Go/Nogo split and three difficulty conditions (Low, Medium and High).

Although the main focus of this study was the influence of task difficulty on inhibitory processing, the measurement of skin conductance level (SCL) — a well-established measure of central nervous system (CNS) arousal (Barry and Sokolov, 1993) — allows examination of the effect of arousal level on inhibitory performance and processing. A review of the literature suggests that arousal may amplify or improve task performance (for a discussion see VaezMousavi et al., 2007), which may be characterised by an inverted-U relationship, where moderate levels of physiological arousal result in optimal performance, with a deterioration in performance seen during low- or high-arousal levels (Yerkes and Dodson, 1908). Additionally, as initially proposed by Yerkes and Dodson (1908), optimal arousal levels may depend on the difficulty of a given task. In line with the findings of Yerkes and Dodson (1908) are results showing that inhibition performance was optimised only at moderate inter-stimulus intervals (ISIs; Wodka et al., 2009). Further work by Barry et al. (2007) has reported that increased arousal, via caffeine ingestion, resulted in not only increased SCL, but also concurrent improvements in Go/Nogo performance. However, findings from research using similar tasks have been mixed, showing no relationship between arousal and performance (Barry et al., 2005; VaezMousavi et al., 2009, 2007). The paucity of errors in the previous studies may help to explain these results, and as such, the manipulation of task difficulty would ensure greater errors and help to more thoroughly explore the arousal/performance link.

In sum, this study sought to extend previous research by examining the behavioural and neural effects of varying task difficulty, via RTD, on inhibitory processing. To this end, we used a modified version of the Go/Nogo task that required the inhibition of a prepotent response during three task difficulty conditions: Low (1000 ms), Medium (500 ms) and High (300 ms). As mentioned above, the Nogo N2 and Nogo P3 have been associated with different aspects of response inhibition so the ERP analyses focused on these components. While no specific predictions were made for the early ERP components, given the potential modulatory effects of task difficulty on early stimulus processing (e.g. Miller et al., 2011), any differences found would be explored. Moreover, participants provided perceived effort ratings and we recorded skin conductance to assess the contribution of arousal on performance and processing.

2. Method

2.1. Participants

A total of 69 adults enrolled in the present study to fulfil an undergraduate course requirement, with three being excluded according to the selection criteria. To be included in the study, participants were required to refrain from caffeine for 2 h prior to testing and have not taken any psychotropic substances (prescription or illegal) for 24 h prior to testing, or no more than once a month in the previous six months. Participants were also screened for neurological disorders and all reported normal or corrected-to-normal vision.

The remaining 66 participants were randomly assigned to one of three conditions: Low, Medium or High task difficulty. Of these, data from 6 subjects were rejected either due to excessive eye artefact (3 participants), technical problems (2 participants) or for failure to perform the task properly (1 participant). Therefore, 20 participants each were included in the final analyses for the Low (Low: 17 females, 3 males, mean age 21.23, SD 4.12), Medium (14 females, 6 males, mean age 21.5, SD 5.89) and High condition (14 females, 6 males, mean age 21.4, SD 3.32). All but 5 of the 60 participants were right-handed. The research protocol was approved by the joint University of Wollongong and Illawarra Area Heath Service Human Research Ethics Committee.

2.2. Task

Stimuli were generated using Presentation (Version 11.0; Neurobehavioral Systems, Albany, CA, USA). Each trial began with a central fixation cross (+) presented for a variable interval of 500–1000 ms (M = 750 ms), followed by the Go/Nogo stimulus presented in the centre of the screen for 200 ms. A blank screen then replaced the stimulus for a variable blank period of 1250–1750 ms (M = 1250 ms). Within this period, participants in the High, Medium and Low task difficulty conditions were required to respond via a button press to Go stimuli within 300, 500 or 1000 ms, respectively (see Fig. 1), or to refrain from responding to Nogo stimuli. Performance feedback was provided via the following fixation cross, which remained white for correct response, but changed to a red colour for incorrect responses. Incorrect responses (i.e. presses to Nogo stimuli during the variable blank period, omissions and responses outside the RTD) were recorded in order to calculate error rates. Only presses to the Go stimulus within the predefined response window were regarded as correct.

After an initial practice block of 30 trials (50% Nogo), all participants completed eight experimental blocks (30% Nogo) of 100 trials each. Only the data from the first two blocks is reported here. Target Go/Nogo stimuli for each block were selected from a pool of eight shapes (i.e. triangle, cross, hexagon, diamond, ellipse, rectangle, star and circle; see Fig. 1) and were presented on a 15 inch computer monitor, with participants seated

1 m from the screen. The stimuli measured approximately 3×3 cm on the screen. Presentation of shape stimuli was counterbalanced using a Latin square design (Bradley, 1958), with Go/Nogo response assignment counterbalanced across subjects. Total task time was approximately 43 min.

2.3. Procedure

Participants were given an outline of the testing procedure and familiarised with the laboratory equipment before informed consent was given. The experimenter emphasised that participants could withdraw any time without penalty. They were then asked to complete a short screening questionnaire to assess vision problems, medication/psychotropic substance use, and neurological disorders. Subjects were then fitted with EEG and skin conductance recording equipment, and seated in a dimly-lit sound-attenuated and electrically-shielded testing booth. An incandescent light in the booth was dimmed for the duration of the experiment. An initial 3 min baseline recording was conducted while participants were asked to sit quietly with eyes closed. Subjects were then presented with a modified Go/Nogo task and were instructed that they would see either of two shapes, one representing the Go stimulus, and the other representing the Nogo stimulus. They were asked to press the button before the pre-determined RTD with the thumb of their right hand to Go stimuli, and to refrain from responding to Nogo stimuli. Performance feedback was provided by the following fixation cross, which changed from a white to red colour on incorrect trials (i.e. Go responses exceeding the RTD and presses to Nogo stimuli) and remained white on correct trials. Participants were asked to "do their best" to avoid the incorrect feedback, and were encouraged to keep as still as possible and to minimise eye movements during the testing blocks. Go/Nogo shape assignment was shown on the screen and verbally confirmed by the participant prior to each block. After a short practice block, all participants completed the experimental blocks. At the end of each block, mean Go RT, the percentage of Go and Nogo errors were displayed for subjects to review. They were then asked to rate their perceived level of effort with the question "How much effort did you use to complete that block?" and responded by a 5-point Likert scale ranging from: 1 = Very little, 2 = Moderate effort, and 5 = Everything I had. Prior to the first rating a basic example was shown to the subject to ensure understanding. Participants were given a short break at the end of each block and asked to continue on.

2.4. Electrophysiological recording

The continuous scalp electroencephalogram (EEG) was recorded from 19 sites (Fp1, Fp2, F3, F4, F7, F8, Fz, C3, C4, Cz, P3, P4, Pz, T3, T4, T5, T6, O1, O2) using an electrode cap containing tin electrodes fitted according to the international 10–20 system (Jasper, 1958). A ground electrode located between Fpz and Fz, and all electrodes were referenced to linked ears. EOG was measured vertically with two tin cup electrodes, 1 cm above and below the left eye. Impedance was kept below 3 kΩ for EOG and reference electrodes, and below 5 kΩ for cap electrodes. EEG and EOG signals were amplified 19 times and sampled at 500 Hz, with bandpass down 3 dB at 0.1 and 100 Hz via a NuAmps system (Compumedics Limited, Melbourne, Australia). Prior to processing, the EEG data were digitally filtered using a low-pass filter 3 dB down at 30 Hz.

2.5. Skin conductance recording

Electrodermal activity was recorded using two Ag/AgCl electrodes placed on the distal phalanges of the third and fourth digits of the left hand. Recording electrodes were filled with electrode paste (0.05 M NaCl in an inert viscous ointment base) and secured using velcro straps and tape. A constant voltage device (UFI Bioderm model 2701) set at 0.5 V was used. This system separately recorded tonic DC-coupled SCL and AC-coupled skin conductance fluctuations (skin conductance response; SCR), measured in microsiemens (μS). Only SCL is reported here.

2.6. Data quantification

The ERP epoch was defined as 100 ms pre-stimulus to 900 ms post-stimulus onset. Epochs were excluded if they contained activity greater than ±100 μV at any non-frontal site. EOG artefact reduction was carried out based on vertical EOG (Semlitsch et al., 1986). ERPs were averaged across epochs for correct responses only. This resulted in a minimum of 32 artefact-and-error-free Nogo trials being included in each average. Go epochs were averaged separately, chosen randomly from the available correct Go epochs to equal the number of Nogo epochs. Grand average ERP waveforms for Go and Nogo stimuli were displayed in order to define the component latency range. Latency was fixed across sites to the peak latency of the site of maximum amplitude (Picton et al., 2000; Spencer et al., 2001). ERP component peaks were quantified using automatic peak-picking software which identified the largest positive or negative deflections within the predefined latency range, relative to the 100 ms pre-stimulus baseline period. Peak latency ranges and sites were as follows: N1 (100–160 ms Fz), P2 (180–240 ms Pz), N2 (200–280 ms Fz), and P3 (280–520 ms Pz). Skin conductance level was taken as the average value (in μS) for each 30 s period over the 3.5 min duration of each block of the Go/Nogo task.

2.7. Statistical analyses

The error rate (Go omission errors, RTD and Nogo errors) was calculated as the number of responses divided by the total number of presentations. Univariate analysis of variance (ANOVA) was used to analyse task performance perceived effort and skin conductance level data with Condition (Low vs. Medium vs. High) as the between-subjects factor. Planned polynomial (Linear, Quadratic) contrasts were used to analyse differences within Condition.

Primary analyses of the ERP data were restricted to the sites F3, Fz, F4, C3, Cz, C4, P3, Pz and P4. Go and Nogo data were subject to a Condition [Low (L) vs. Medium (M) vs. High (H)] × Lateral (Left vs. Midline vs. Right) × Sagittal (Frontal vs. Central vs. Parietal) × Stimulus (Go vs. Nogo) ANOVA, with repeated measures on the within-subjects factors. Differences within Condition were assessed using polynomial contrasts (Linear, Quadratic). Analyses for component latency omitted the site contrasts. Planned orthogonal contrasts, which allow insight into the topographic distribution of each component, were performed on the within-subjects factors. The Lateral factor compared activity in the left hemisphere (mean of F3, C3 and P3) with the right (mean of F4, C4 and P4), and the mean of these with activity in the midline region (mean of Fz, Cz and Pz). Contrasts within the Sagittal factor compared frontal activity (mean of F3, Fz and F4) with parietal (mean of P3, Pz and P4), and the mean of these with activity in the central region (mean of C3, Cz and C4). As these contrasts were planned with no more of them than the degrees of freedom for each effect, no Bonferroni type adjustment to α was necessary (Tabachnick and Fidell, 1996). Also, single degrees of freedom contrasts are not affected by violations of symmetry assumptions common in repeated measures analyses, and thus do not require Greenhouse–Geisser-type corrections. As these analyses are carried out over a substantial number of variables, each may be considered to constitute a separate experiment. It should be noted that this increases the frequency of type 1 errors, however, as this is an increase in frequency, rather than probability, it cannot be 'controlled' by adjustment of levels (Howell, 2009). All ERP statistics have (1,58) degrees of freedom unless otherwise indicated. Outliers in the data were corrected for by replacing with the series mean. Data were normalised using the vector scaling method (McCarthy and

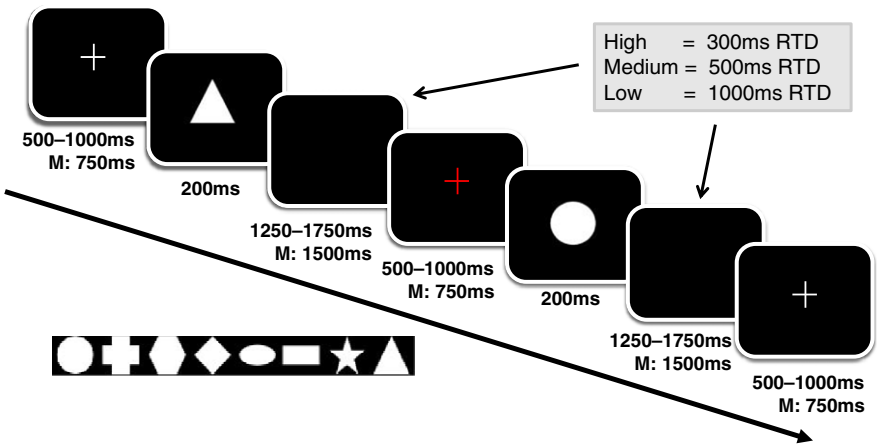

Fig. 1. Schematic presentation of each task difficulty condition to Go (triangle) and Nogo (circle) stimuli.

Wood, 1985), and only interactions with topography that remained significant in the normalised data are reported here.

3. Results

3.1. Manipulation check and perceived effort

As can be seen in Fig. 2, participants' perceived effort was greater in the High than Medium and Low conditions (Linear: $F=6.64$, $p=.013$, $\eta^2=.104$), suggesting that the difficulty manipulation was successful, with greater perceived effort seen with each increase in task difficulty.

3.2. Task performance

Means and standard deviations of RT and errors are summarised in Table 1. Consistent with our experimental manipulation, RT to Go stimuli decreased with each RTD reduction (L>M>H; Linear: $F=403.55$, $p<.001$, $\eta^2=.787$), with the steepest drop from the Low to Medium conditions (Quad: $F=52.02$, $p<.001$, $\eta^2=.101$).

Both Go RTD and omission errors (Go Om) showed linear (Go RTD: $F=222.93$, $p<.001$, $\eta^2=.673$; Go Om: $F=38.80$, $p<.001$, $\eta^2=.382$), and quadratic trends (Go RTD: $F=51.31$, $p<.001$, $\eta^2=.155$; Go Om: $F=4.17$, $p=.046$, $\eta^2=.043$), highlighting a steep increase in Go errors with increasing task difficulty, particularly apparent for the High condition. Inhibition performance showed a similar pattern, with incremental increases in Nogo errors with increasing task difficulty (i.e. H>M>L), with the greatest percentage of errors seen in the High condition (Linear: $F=45.62$, $p<.001$, $\eta^2=.423$; Quad: $F=5.15$, $p=.027$, $\eta^2=.048$).

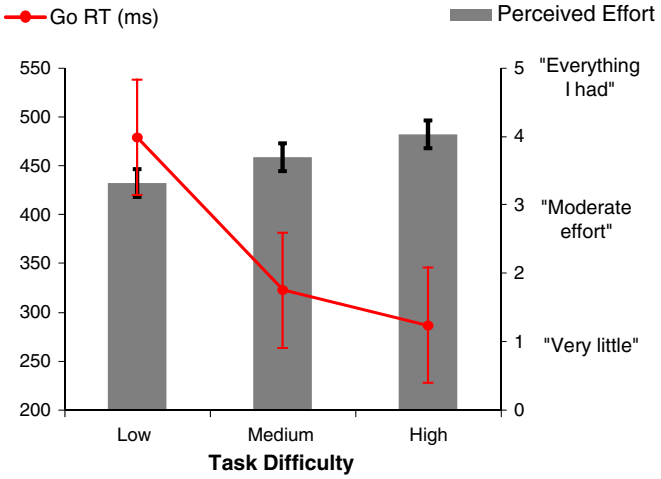

Fig. 2. Reaction time and perceived effort ratings for each task difficulty condition. Error bars represent standard error of the mean.

3.3. Skin conductance level

While SCL appeared to show a quadratic trend among task difficulty conditions (i.e. H/L>M), no significant differences were found between the High (12.49 μS), Medium (10.80 μS) or Low conditions (12.17 μS; Quad: $F=1.90$, $p=.174$).

3.4. Event related potentials

Fig. 3 presents grand mean ERPs to Go and Nogo stimuli across groups (top left panel) and for each condition separately (remaining three panels), with scalp distribution maps for each component in Fig. 4. The waveforms are characterised by an N1–P2 complex, most apparent at frontal and central sites. An N2 component is apparent at about 270 ms primarily in the frontocentral region. Evident at approximately 300–400 ms post-stimulus, the P3 is a large positivity which peaks parietally for the Go condition and central-frontally for the Nogo condition.

3.4.1. N1

N1 peaked at 143.7 ms, with no condition differences for latency (Low = 138.9 ms, Medium = 144.5 ms, High = 147.7 ms).

The general topography of the N1 (i.e. across stimulus and condition) showed a frontocentral maximum, with a left-midline focus (see Table 2 for effect summaries and means). Between task difficulty conditions and across stimulus, the central>frontoparietal difference was reduced with increasing task difficulty (i.e. L>M>H),

Table 1
Summary statistics for task performance measures for each task difficulty condition.

	Task difficulty		
	Low	Medium	High
RT (ms)			
Go RT	479.0	323.0	286.6
SDRT	87.4	67.4	57.7
Error rate (%)			
Go RTD	0.0	2.7	30.9
Go omission	0.7	1.6	5.0
Nogo errors	7.4	11.1	25.0

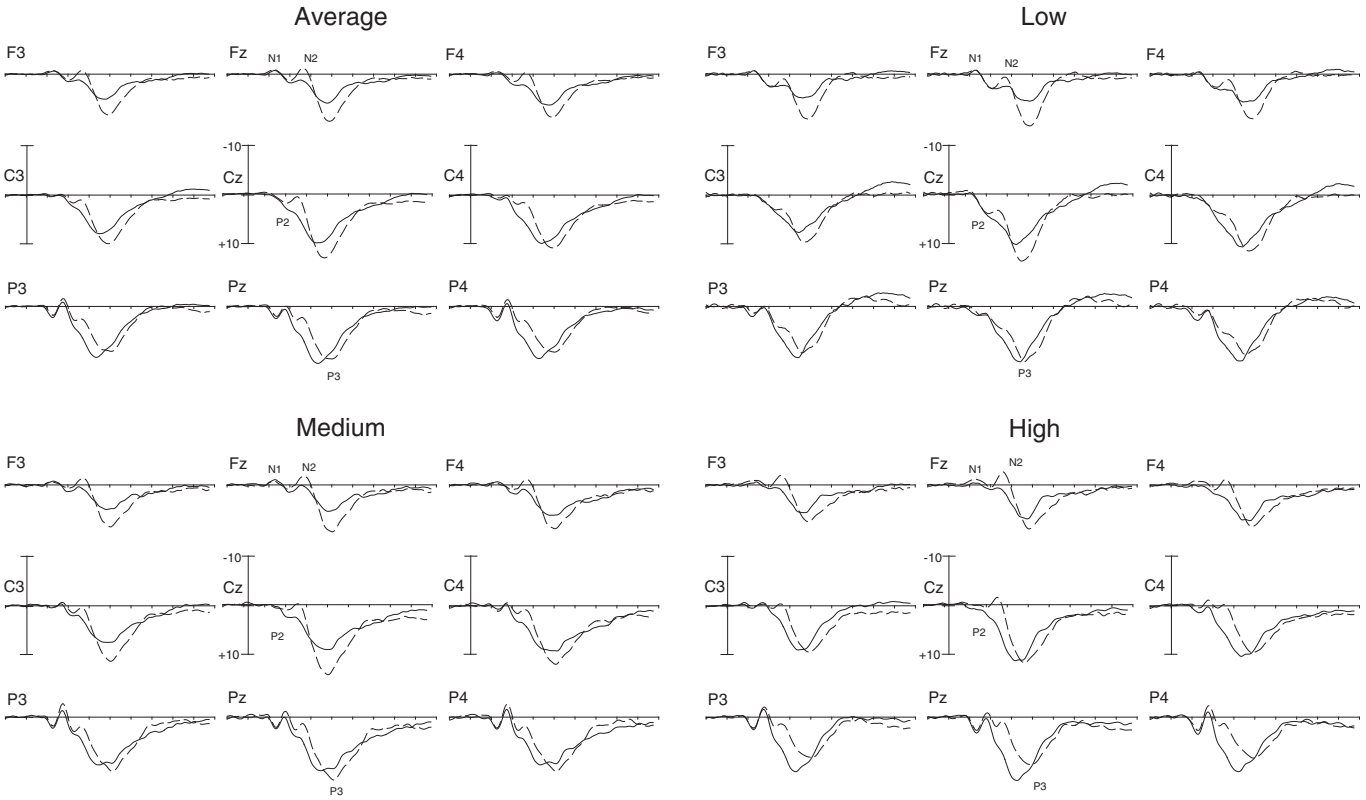

Fig. 3. Grand mean ERPs to Go (solid line) and Nogo (dashed line) across condition (top left panel) and for each task difficulty condition separately (remaining three panels) at nine scalp locations.

highlighting a larger N1 amplitude in posterior regions for the Medium/High, relative to the Low condition. On the Lateral dimension, the Low condition showed a large midline > hemispheres effect, in contrast to the Medium and High conditions, which displayed little hemispheric variation.

Notably, there was a significant difference for the N1 to Go vs. Nogo stimuli among the conditions. The Low condition showed a clear Go > Nogo N1, while this effect was reduced to be almost equipotential for the Medium condition, and reversed for the High condition (i.e. Nogo > Go N1; see Fig. 4 for head maps and Fig. 5, top left panel, for Go vs. Nogo comparisons).

3.4.2. P2

P2 peaked at 226.1 ms, with no condition differences in latency (Low = 231.7 ms, Medium = 224.1 ms, High = 222.4), showed a parietal maxima, with a right > left effect also reaching significance (see Table 2 for effect summaries and means). Across the scalp, the P2 showed a Go > Nogo effect. On the Lateral dimension, both the right > left and midline > hemisphere effect was larger for the Go than Nogo stimuli, highlighting an enhanced Go relative to the Nogo P2 in the right hemisphere.

Globally, the P2 component was the largest in the Low condition and decreased linearly with increasing time pressure (i.e. L > M > H). Importantly, between stimuli (i.e. Go vs. Nogo), the Low condition showed a small Nogo > Go effect, while the Medium and High conditions displayed the opposite pattern — highlighting a reduction in the Nogo P2 with increasing task difficulty (see Fig. 5). This effect was most apparent in posterior regions, with the Low condition showing a larger Posterior > Frontal effect for Nogo compared to Go (parietal vs. frontal difference: Nogo 3.5 vs. Go 2.7 μV), which was relatively equipotential for the Medium (Nogo 3.1 vs. Go 3.2 μV), and reversed for the High condition (Nogo 1.7 vs. Go 4.2 μV; see Fig. 6 top panel).

In summary, the analyses of the early ERP potentials to Go/Nogo stimuli showed increased Nogo N1 amplitudes across the scalp with increasing task difficulty. However, the Nogo P2 declined with time pressure, showing the smallest amplitudes over posterior regions in the High condition.

3.4.3. N2

N2 (mean latency 272.9 ms) peaked earlier for Go (269.8 ms) than Nogo stimuli (276.1 ms; $F = 5.15$, $p = .007$, $\eta^2 = .085$), and decreased linearly with task difficulty, being shorter for the High (265.6 ms), than Medium (270.5 ms) and Low conditions (282.7 ms; $F = 10.24$, $p = .002$, $\eta^2 = .152$).

The N2 showed a frontal maximum, and was larger in the left than right hemisphere, and greatest in the midline (see Table 3). N2 amplitude was larger to Nogo than Go stimuli, with the left > right effect being greater for the Go than Nogo N2, due mainly to an enhanced midline > hemispheres effect for the Nogo N2.

Linear and quadratic interactions revealed that N2 amplitude (i.e. Go + Nogo) increased with increasing task difficulty (i.e. H > M > L), which was characterised by a rapid rise from Low to Medium, but a relatively equipotential component for the Medium/High conditions. Notably, the Nogo > Go effect increased linearly with task difficulty (i.e. H > M > L), highlighting an augmented Nogo N2 across the scalp particularly for the High condition (see Fig. 5). As shown in Fig. 6, the High condition displayed an enhanced Nogo > Go N2 effect in parietocentral regions compared to the Medium/Low conditions. This is evidenced by a reduced frontal > parietal gradient (parietal vs. frontal difference: Nogo 4.3, Go 6.1 μV) and an increased central > frontal/parietal effect (central vs. frontal/parietal difference: Nogo 1.0, Go 0.1 μV) to Nogo compared to Go stimuli for the High condition, an effect which was reduced in the Medium (P vs. F diff.: Nogo 4.9, Go 5.6 μV; c vs. f/p: Nogo, 0.3, Go 0.3 μV) and relatively equipotential for the Low condition (P vs. F diff.: Nogo 5.8,

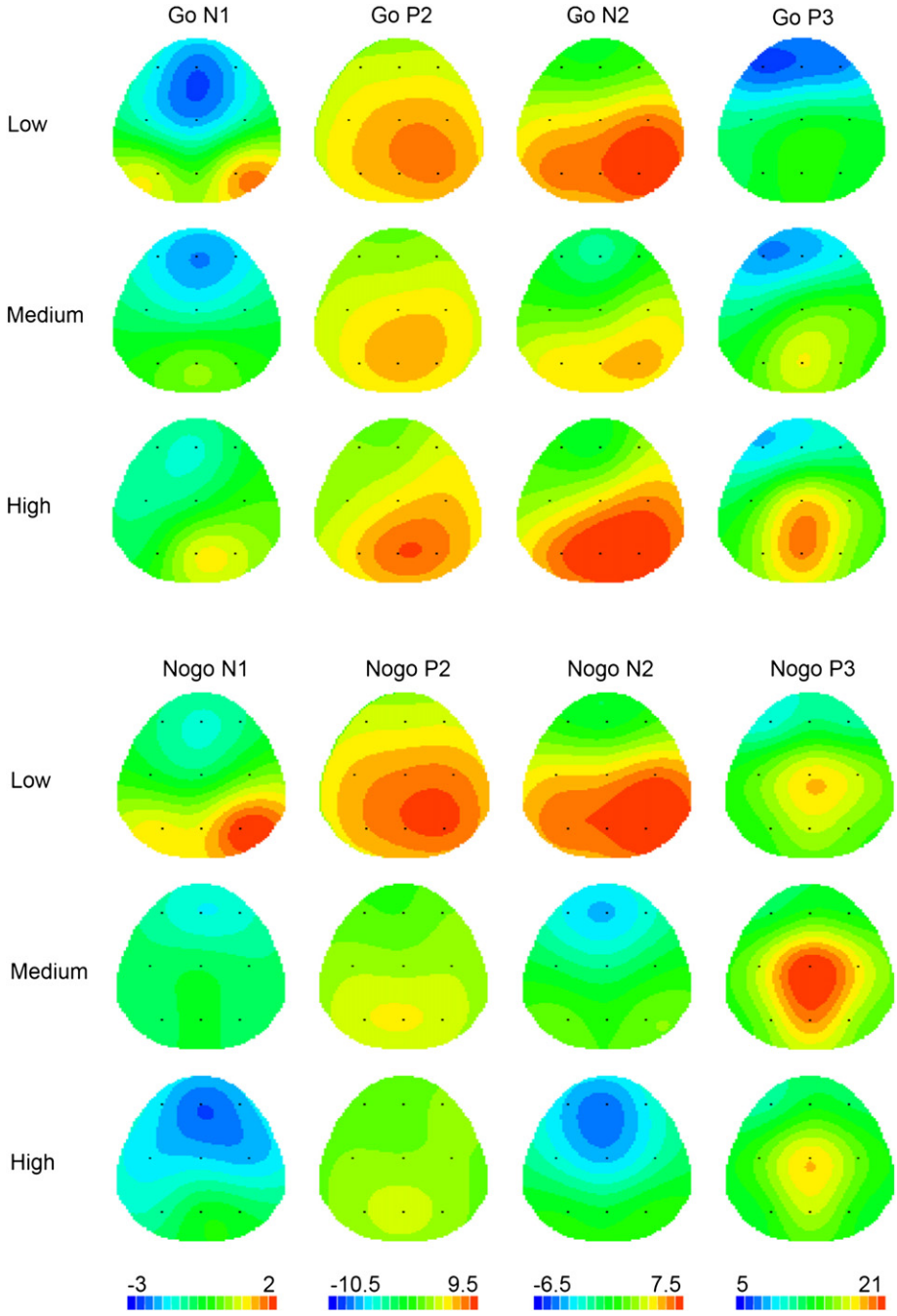

Fig. 4. Topographic maps for each ERP component to Go (top panel) and Nogo (bottom panel) stimuli separately. Scale values represent the ends of the colour scale in μV for each component. Darkest blue = negativity, red = positivity.

Go 5.6 μV; c vs. f/p: Nogo, 1.4, Go 1.0 μV). The association between inhibition performance and the Nogo > Go N2 effect was evaluated by calculating Pearson's correlation between Nogo errors and the N2 effect (Nogo N2–Go N2 at Fz, with larger negative scores indicating a larger Nogo > Go N2 effect). Results indicated an association between poorer inhibitory performance and larger Nogo N2 amplitudes ($r = -.41$, $p = .001$).

3.4.4. P3

P3 (mean latency 381.6 ms) peaked later for Nogo (401.8 ms) than Go stimuli (373.4 ms; $F = 42.56$, $p < .001$, $\eta^2 = .372$). This effect differed between conditions: with the P3 peaking much later for Nogo than Go stimuli for the High (Go vs. Nogo difference: 52 ms) than the Medium (Go vs. Nogo difference: 15 ms) and Low conditions (Go vs. Nogo difference: 17 ms; $F = 7.41$, $p = .001$, $\eta^2 = .130$).

The P3 showed parietocentral and right midline maxima (see Table 4) in the Sagittal and Lateral dimensions, respectively. P3 amplitude was globally larger to Nogo than Go stimuli. A reduced parietal > frontal gradient (parietal vs. frontal difference: Nogo 3.6, Go 7.1 μV) and an increased central > frontal/parietal effect in Nogo compared to Go stimuli (central vs. frontal/parietal difference: Nogo 2.8, Go 1.8 μV), highlighted a more anterior P3 to Nogo relative to Go stimuli. In addition, while the right > left effect was reduced for Nogo relative to Go stimuli, the midline hemisphere effect was increased.

Globally, the Nogo > Go P3 effect increased from the Low (Go vs. Nogo difference: 2.5 μV) to the Medium condition (Go vs. Nogo difference: 3.2 μV), contrasting with the High, which showed little

Table 2
Significant results for the early ERP components, the N1 and P2.

Measure	Effect	Contrast	Details	F	η^2
N1	S	f vs. p	−1.7 vs. 0.0	21.08***	.243
		c vs. f/p	−1.2 vs. −0.9	12.72**	.012
	L	l vs. r	−1.0 vs. −0.8	4.16*	.039
		m vs. l/r	−1.1 vs. −0.9	5.86*	.039
	S × Cond	Cz vs. Fz/pz	Low: −1.1 vs. −0.4		
			Med: −1.1 vs. −1.2		
			High: −1.4 vs −1.0	4.48*	.009
	L × Cond	m vs. l/r	Low: −1.0 vs. −0.5		
			Med: −1.2 vs. −1.1		
			High: −1.1 vs. −1.1	5.14**	.063
	Stim × Cond	Go vs. Nogo	Low: −1.1. vs. −0.2		
			Med: −1.2 vs. −1.1		
			High: −0.6 vs. −1.7	6.55**	.187
P2	S	f vs. p	2.3 vs. 5.4	51.47***	.430
	L	l vs. r	3.4 vs. 4.3	3.46*	.193
	Stim	Go vs. Nogo	4.6 vs. 3.4	12.58**	.146
	L × Stim	l vs. r	Go: 3.8 vs. 5.1		
			Nogo: 3.1 vs. 3.6	16.88*	.127
		m vs. l/r	Go: 4.8 vs. 4.4		
			Nogo: 3.4 vs. 3.3	5.60*	.030
	Cond	Low vs. High	3.3 vs. 5.4	5.29*	.085
	Stim × Cond	Go vs. Nogo	Low: 5.1 vs. 5.8		
			Med: 4.1 vs. 2.3		
			High: 4.5 vs. 2.1	8.34**	.193
	S × Stim × Cond	f vs. p	Low: Go, 3.5 to 6.2; Nogo, 3.7 to 7.2		
			Med: Go, 2.3 to 5.5; Nogo, 0.7 to 3.8		
			High: Go, 2.5 to 6.7; Nogo, 1.3 to 3.0	4.89*	.128

* = <.05, ** = <.01, *** = <.001.
Details column represents mean amplitude in μV. Abbreviations for this and subsequent tables in this study: Cond, Condition: Low/Medium/High task difficulty. Low, Low task difficulty condition. Med, Medium difficulty condition. High, High difficulty condition. Stim, Stimulus type: Go/NoGo. Lateral (L) abbreviations: l, mean left hemisphere (F3, C3, P3); r, mean right hemisphere (F4, C4, P4); l/r, mean of the left and right hemispheres (F3, C3, P3, F4, C4, P4); m, mean of the midline (Fz, Cz, Pz). Sagittal (S) abbreviations: f, mean frontal (F3, Fz, F4); p, mean parietal (P3, Pz, P4); c, mean central (C3, Cz, C4); f/p, mean of frontal and parietal (F3, Fz, F4, P3, Pz, P4). Lateral by Sagittal (L × S) interactions: sites (e.g. f4) represent position on scalp (for e.g. frontal right hemisphere); f3/p3, mean of frontal and parietal left hemisphere; f4/p4, mean of frontal and parietal right hemisphere; fz/pz, mean of frontal and parietal midline; f3/f4, mean of frontal left and right hemispheres; p3/p4, mean of parietal left and right hemispheres; c3/c4, mean of central left and right hemispheres; f3f4/p3p4, mean of frontal and parietal left and right hemispheres.

difference between stimulus types (Go vs. Nogo difference: 0.0 μV; Fig. 5). The distribution of the Nogo > Go P3 effect also differed between conditions: the Nogo relative to the Go P3 showed a more anterior focus for the Medium (parietal vs. frontal difference: Nogo 4.2, Go 7.6 μV; central vs. frontal/parietal difference: Nogo 3.2, Go 1.3 μV) than the Low condition (parietal vs. frontal difference: Nogo 4.2, Go 6.0 μV; central vs. frontal/parietal difference: Nogo 1.5, Go 3.0 μV), with this effect being reduced for the High condition (parietal vs. frontal difference: Nogo 2.6, Go 7.6 μV; central vs. frontal/parietal difference: Nogo 2.2, Go 2.1 μV). This effect highlights a reduction in centroparietal Nogo P3 activity for the High condition (see Fig. 6). Similarly, on the Lateral dimension, a midline > hemispheres effect for Nogo relative to Go stimuli increased slightly from the Low (Mid. vs. Hem. diff.: Nogo 1.5, Go 0.5 μV) to the Medium condition (Mid. vs. Hem. diff.: Nogo 2.7, Go 1.0 μV), but was reduced for the High (Mid. vs. Hem. diff.: Nogo 2.3, Go 2.1 μV).

In summary, the Nogo > Go N2 effect increased incrementally and peaked earlier as a function of task difficulty, with the largest amplitudes and shortest latencies in the High condition. By contrast, while the Nogo > Go P3 effect increased from Low to the Medium condition, it was significantly reduced for the High condition. Differences in the distribution for the Nogo > Go P3 effect were most apparent frontocentrally between the Low and Medium conditions, while the High showed a reduction in Nogo P3 activity in the centroparietal region.

4. Discussion

The primary aim of this study was to examine the influence of varying task difficulty, by the use of reaction time deadline, on the behavioural and ERP indices of inhibitory control during performance of the Go/Nogo task. In addition, we investigated whether the effect of task difficulty would also extend to the early ERP potentials, task-related arousal and perceived effort.

4.1. Task performance

Our results indicate that task performance was significantly affected by variations in task difficulty. Specifically, Go and Nogo errors incrementally increased with each increase in task difficulty (i.e. RTD reduction: Table 1), with the greatest number of errors in the High condition. Importantly, modulations in task difficulty were also reflected by concurrent increases in perceived effort (Fig. 2), consistent with the idea that greater effortful control is required when the need to inhibit is high (Jodo and Kayama, 1992). Since previous research has either not utilised graded task difficulty levels (for e.g. Band et al., 2003; Smith et al., 2006), or did not report task performance data (Jodo and Kayama, 1992), these results provide clear self-report and behavioural evidence that Go/Nogo task difficulty can be incrementally increased by the use of RTDs.

4.2. SCL arousal

Arousal level did not differ among conditions and did not appear to be related to task difficulty or performance in the present study. Combined with the findings of cumulative increases in Go/Nogo errors with increasing task difficulty, this SCL result differs from previous work suggesting that arousal is dependent on the difficulty level of a given task (Yerkes and Dodson, 1908). It is interesting to note, however, that arousal level was not completely static among conditions, with a tendency for arousal to show a Low/High > Medium effect — in line with previous work suggesting increased arousal levels during slow/fast, relative to medium speeds of presentation (Sanders, 1983). Alternatively, a more complete explanation might be in regard to the use of skin conductance level as a measure of arousal in the current research. In a series of studies, Barry and colleagues (e.g. Barry et al., 2005) experimentally differentiated between 'arousal', referring to the current energetic state of an individual, and 'activation', which refers to the task-related mobilisation of arousal. Notably, arousal was not found to be related to any of the performance variables, but instead, task-related activation significantly determined improvements in both reaction time and errors. Recent work by this group has also reported the classic inverted-U relationships between task-related activation and performance in a variety of tasks (VaezMousavi and Osanlu, 2008; VaezMousavi et al., 2009). Thus, it might be advantageous in future research to employ measures of task-related *activation* to more thoroughly explore the influence of task difficulty on arousal/activation.

4.3. Early ERP findings

Although the primary aim of this study was to investigate the influence of a task difficulty manipulation on the inhibition-related ERP

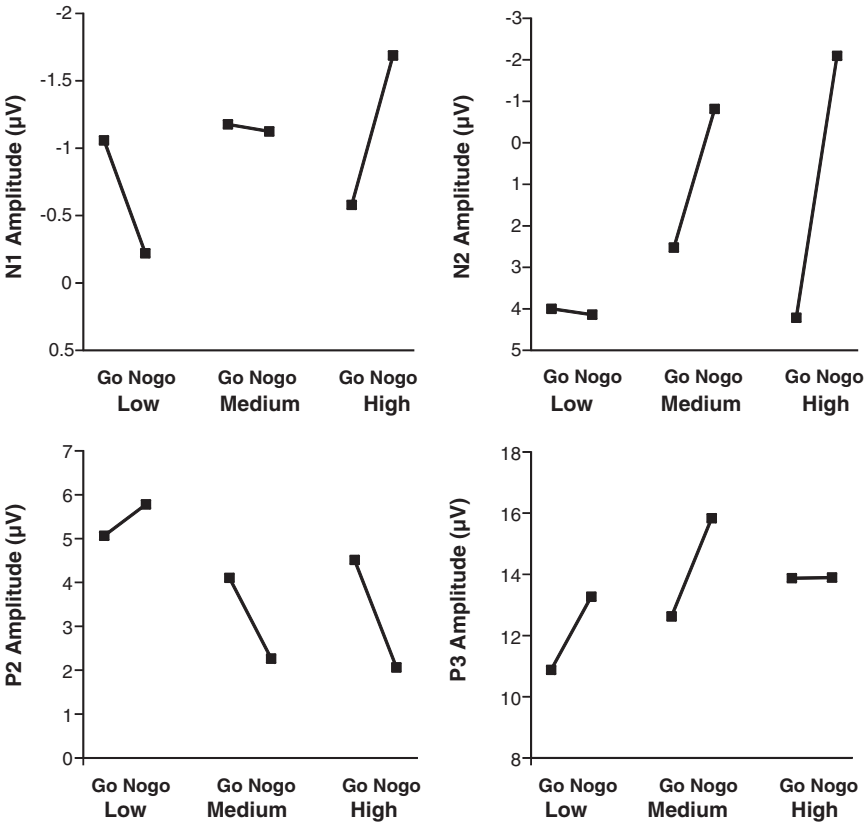

Fig. 5. Go vs. Nogo amplitude across the scalp, by task difficulty condition, for the N1 (top left panel), P2 (top right panel), N2 (bottom left) and P3 (bottom right panel).

components of the N2 and P3, we report significant condition effects for the early exogenous potentials of the N1 and P2. Specifically, while the Low condition showed a Go > Nogo N1 effect across the scalp, this effect was reversed and increased with task difficulty, to show a large Nogo > Go effect for the High condition (see Fig. 4 for head maps and Fig. 5 for Go vs. Nogo plots). Previous examinations linking N1 and RT

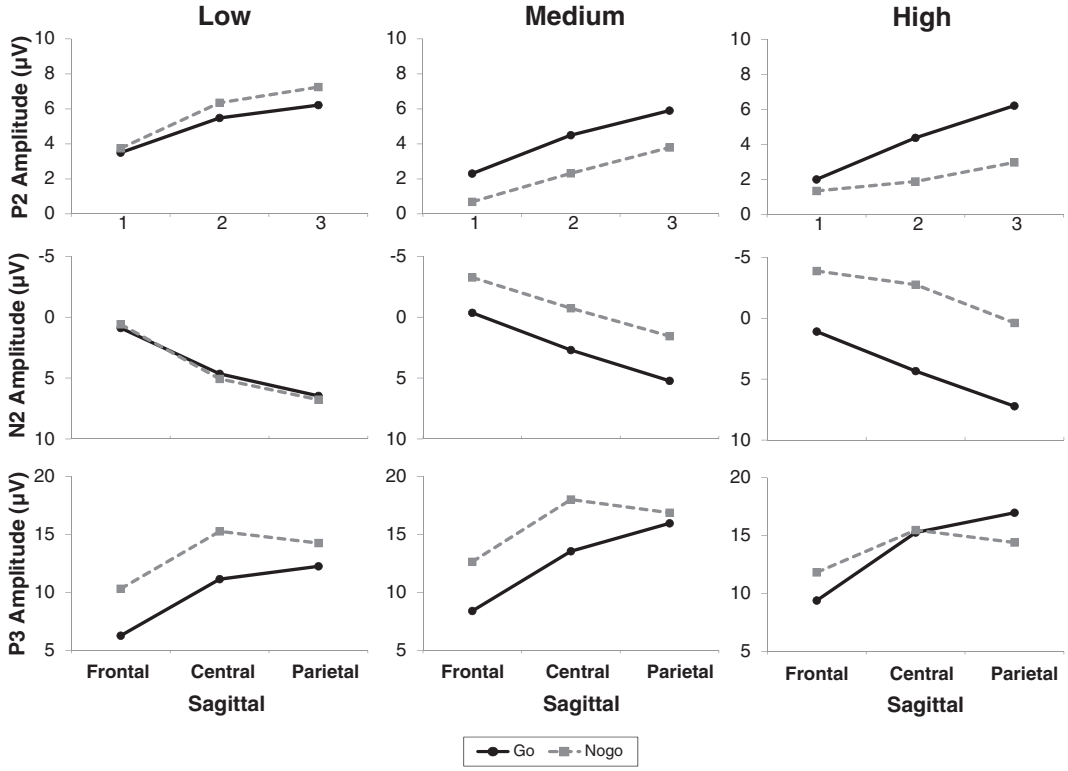

Fig. 6. The Stimulus × Sagittal × Condition interactions for P2 (top panel), N2 (middle panel) and P3 amplitude (bottom panel). Note: Frontal = mean of F3, Fz, F4; Central = mean of C3, Cz, C4; Parietal = mean of P3, Pz, P4.

Table 3
Significant results for the N2.

Measure	Effect	Contrast	Details	F	η^2
N2	S	f vs. p	−0.8 vs. 4.6	158.43***	.687
	L	l vs. r	1.6 to 2.8	46.49***	.242
		m vs. l/r	1.6 vs. 2.2	8.29***	.102
	Stim	Go vs. Nogo	3.5 vs. 0.4	46.49***	.343
	L × Stim	l vs. r	Go: 2.9 vs. 4.5		
			Nogo: 0.3 vs. 1.1	14.10***	.111
		m vs. l/r	Go: 3.3 vs. 3.7		
			Nogo: −0.2 vs. 0.7	19.43***	.079
	Cond	Low vs. High	4.1 vs. 1.1	9.22**	.139
		Med vs. High/Low	0.9 vs. 2.6	3.97*	.065
	Stim × Cond	Go vs. Nogo	Low: 4.0 vs. 4.1		
			Med: 2.5 vs. −0.8		
			High: 4.2 vs. −2.0	16.22***	.238
	S × Stim × Cond	f vs. p	Low: Go, 0.9 to 6.5; Nogo, 0.6 to 6.8		
			Med: Go, −0.4 to 5.2; Nogo, −3.3 to 1.6		
			High: Go, 1.1 to 7.2; Nogo, −3.9 to 0.4	3.25*	.075
		c vs. f/p	Low: Go, 4.7 to 3.7; Nogo, 5.1 to 3.7		
			Med: Go, 2.7 to 2.4; Nogo, −0.7 to −0.9		
			High: Go, 4.3 to 4.2; Nogo, −2.8 to −1.8	6.81**	.043

* = <.05, ** = <.01, *** = <.001.

Table 4
Significant results for the P3.

Measure	Effect	Contrast	Details	F	η^2
P3	S	f vs. p	9.8 vs. 15.1	121.23***	.792
		c vs. f/p	14.8 vs. 12.5	113.89***	.202
	L	l vs. r	12.1 vs. 13.2	26.71***	.117
		m vs. l/r	14.4 vs. 12.7	99.73***	.381
	Stim	Go vs. Nogo	12.1 vs. 14.3	13.57*	.176
	S × Stim	f vs. p	Go: 8.0 vs. 15.1		
			Nogo: 11.6 vs. 15.2	54.34***	.376
		c vs. f/p	Go: 13.3 vs. 11.5		
			Nogo: 16.2 vs. 13.4	24.33***	.049
	L × Stim	l vs. r	Go: 11.0 vs. 12.4		
			Nogo: 13.2 vs. 14.0	5.24***	.038
		m vs. l/r	Go: 13.0 vs. 11.7		
			Nogo: 15.8 vs. 13.6	28.07*	.141
	Stim × Cond	Go vs. Nogo	Low: 10.8 vs. 13.3		
			Med: 12.6 to 15.8		
			High: 13.9 vs. 13.9	3.34*	.086
	S × Stim × Cond	f vs. p	Low: Go, 6.3 to 12.2; Nogo, 10.3 to 14.2		
			Med: Go, 8.4 to 16.0; Nogo, 12.6 to 16.9		
			High: Go, 9.4 to 17.0; Nogo, 11.8 to 14.4	3.35*	.046
		c vs. f/p	Low: Go, 11.1 to 9.3; Nogo, 15.3 to 12.3		
			Med: Go, 13.5 to 12.2; Nogo, 18.0 to 14.8		
			High: Go, 15.3 to 13.2; Nogo, 15.5 to 13.1	4.41*	.018
	L × Stim × Cond	m vs. l/r	Low: Go, 10.2 to 9.7; Nogo, 14.3 to 12.8		
			Med: Go, 13.3 to 12.3; Nogo, 17.6 to 14.9		
			High: 15.3 to 13.2: Nogo, 15.4 to 13.1	6.84**	.069

* = <.05, ** = <.01, *** = <.001.

have produced mixed results: Bahramali et al. (1998) and Karlin et al. (1971) reported a larger N1 with fast responses, while Starr et al. (1995) found no significant differences. The N1 component is generally thought to represent the initial sensory extraction of, and attention to stimuli (Näätänen and Picton, 1987), while previous investigators have interpreted an increased N140 to NoGo stimuli as reflecting an early manifestation of inhibitory processing (Nakata et al., 2004). Therefore, an enhanced Nogo N1 may reflect the greater visual resources required for inhibitory processing as a function of task difficulty — potentially indicating that the early extraction of stimulus information can be modulated by task demands (Miller et al., 2011), with implications for information processing at later stages (Smith et al., 2004).

While typically considered an exogenous component, the functional significance of the P2 in Go/Nogo tasks has yet to be resolved (Benikos and Johnstone, 2009; Wiersema et al., 2006). In discrimination paradigms, the P2 is thought to be involved in the protection against interference from irrelevant stimuli (Garcia-Larrea et al., 1992), giving the imperative stimulus a clear path for further processing (Oades, 1998). Ross and Tremblay (2009) posit that enhanced parietal P2 amplitudes reflects the physiological processes associated with improved task performance — an interpretation in line with reports of larger P2s with concurrent reductions in reaction time (Johnstone et al., 2005; Tonga et al., 2009) and commission errors (Johnstone et al., 2005; Kenemans et al., 1993; Smid et al., 1999). In line with this, the Low condition showed a slightly larger Nogo than Go P2; in contrast to the Medium and High conditions, which displayed a large reduction in Nogo P2 amplitude primarily in posterior regions. Since larger P2s have also been linked to deliberately initiated actions (Kühn et al., 2009), it is possible that with sufficient time to respond, participants in the Low condition were more able to appropriately respond to Go/Nogo stimuli. In contrast, despite the enhanced activation of the Nogo N1, increased task difficulty in the High conditions could have reduced the ability of these participants to suppress extraneous stimuli and inhibit responses. These results are consistent with previous research suggesting that although the primary emphasis in the response inhibition literature has been the N2/P3 complex, earlier waveform components such as the N1 and P2 may play an important role in inhibition success (Roche et al., 2005; Thomas et al., 2009). It thus seems reasonable to suggest that the Nogo P2 reductions seen in this study are largely due to task difficulty effects, and could be linked, in part, to impairments in inhibitory processing and declines in performance.

4.4. Inhibition-related ERP components

Across conditions, we replicated the well-known inhibition-related effects of increased N2 amplitudes and a more anterior P3 to Nogo relative to Go stimuli (Eimer, 1993; Kenemans et al., 1993; Oddy et al., 2005). Go N2 peaked earlier than the Nogo N2 (Jodo and Kayama, 1992), while the reverse was found for the P3 (i.e. Nogo P3 > Go P3 latency; Fallgatter and Strik, 1991; Salisbury et al., 2004). Finally, the current study also reports globally enhanced N2 amplitudes with increasing task difficulty, in line with previous research linking larger N2 peaks with faster responses (Bahramali et al., 1998; Starr et al., 1995).

4.5. N2

The Nogo > Go N2 effect was larger (Fig. 5) and occurred earlier with each increase in task difficulty, as has been reported in previous studies (Band et al., 2003; Falkenstein, 2006; Jodo and Inoue, 1990). Since previous research by Jodo and Kayama (1992) did not report behavioural data, this study demonstrates that graded increases in task difficulty (via RTD) are reflected by incremental amplitude increases and reductions in Nogo N2 latency. In a frequently cited study, Falkenstein et al. (1999) reported that the Nogo N2 was larger and earlier in good compared to poor inhibitors (as measured by the number of commission errors), interpreted as due to a stronger and earlier inhibition process by the good inhibitors. In contrast, the

present study reports the opposite effect (i.e. shorter latencies and increased Nogo N2 amplitudes) for the high difficulty condition, which showed the greatest number of inhibition errors. Given the significant correlation indicating an inverse relationship between Nogo N2 amplitude and inhibition performance, this argues against the interpretation of the Nogo N2 as pre-motor index of inhibitory control (e.g. Kok, 1986). Recently, however, evidence linking the N2 to response conflict has been accumulating (Smith et al., 2010; Randall and Smith, 2011). The conflict theory of N2 predicts increased competition between Go and Nogo representations on correct trials when participants are required to emphasise speed over accuracy (van Veen and Carter, 2002). Thus, it might be that variations in the amplitude N2 reflect incremental increases in response conflict with task difficulty, rather than inhibitory control.

It is noteworthy to report that the Nogo N2 also appeared to change its distribution with enhanced difficulty, displaying an increased Nogo > Go N2 effect at centroparietal regions for the High condition (Fig. 6). A prominent review of the N2 has suggested that it does not reflect a single underlying process, but rather a family of sub-components related to cognitive control (Folstein and Van Petten, 2008). In line with this, it may be that this Condition × Site interaction is suggestive of different neural generators of the N2 for each condition (Johnson, 1993). According to Kok (2001), changes in cognitive processing are a common effect of task difficulty manipulations. Therefore, it may be that different neural generators of the N2 are differentially sensitive to task difficulty in the Go/Nogo task, potentially leading to alterations in its distribution.

4.6. P3

The Nogo > Go P3 effect increased from the Low to the Medium condition, with little difference found between the stimulus types for the High condition. A more anterior NoGo than Go P3 is considered to be reflective of inhibitory processing by some researchers (Bekker et al., 2005; Kok et al., 2004; Smith and Douglas, 2011), and via the use of three task difficulty levels, the results from the present study appear to support this idea. That is, the larger Nogo than Go P3 for the Medium than Low condition (primarily at frontocentral regions) may be reflective of an increased requirement for inhibitory processing with increasing task difficulty. Beyond this point, however, task difficulty seems to overwhelm the response inhibition mechanism, leading to reductions in the Nogo P3 effect. Indeed the findings of longer Nogo P3 latency and 25% commission errors for the High as opposed to 11.1% commission errors for the Medium condition, is consistent with this interpretation. Studies investigating workload (for a review see Kok, 1997) and semantic categorisation (Maguire et al., 2009, 2011) have reported similar reductions in P3 amplitude with increasing task difficulty.

However, it is interesting to note that the distribution of the Nogo P3 revealed amplitude reductions for the High condition at centroparietal regions (see Fig. 6). Thus it may be argued that the relative decline of the Nogo P3 during high task difficulty may not be solely due to variations in inhibitory processing given that, (a) it is not a frontal change, (b) frontal Nogo P3 amplitude does not appear to differ substantially between the Medium and High conditions (Fig. 6), and (c) previous research has shown a clear relationship between frontal lobe activation and inhibitory processing (e.g. Rubia et al., 2001). Reduced Nogo P3 amplitudes over centroparietal regions with increasing task difficulty may thus be better explained in terms of a decrease in the ability to evaluate inhibition success (e.g. Beste et al., 2010). That is, although ISIs were kept consistent between conditions, participants in the High condition may have perceived that too little time was available to adequately monitor the inhibition outcome, leading to reductions in the centroparietal Nogo P3. It can also be argued that the functional interpretation of the Nogo P3 is dependent on the scalp topography (Tekok-Kilic et al., 2001; Vallesi, 2011), and that two distinct processes are contributing to the differences between conditions: a response inhibition process which produces the more anterior Nogo than Go P3 for the Low and Medium conditions, and an inhibition monitoring process that is reflected by the centroparietal reductions for the High condition. However, this notion requires further investigation.

This investigation is not without limitations. Future studies could consider the use of a within-subjects design, which would add statistical power and reduce the error variance between conditions. In addition, due to the use of a psychology undergraduate population, all three task difficulty conditions contained many more females than males. While the issue of gender effects has not been well-studied in the Go/Nogo context, recent research by Yuan et al. (2008) has reported that women showed shorter latencies and larger amplitudes for deviant-related P2, N2 and P3 components. Accordingly, the use of equal number of males and females might be useful in future research to further clarify the effect of task difficulty on inhibitory performance and processing.

5. Conclusions

In summary, this study reports that task difficulty in the Go/Nogo task can be effectively manipulated by varying RTDs. In the context of declines in task performance and the absence of arousal effects, incremental amplitude increases and reductions in latency were seen for the Nogo N2, potentially indicating enhanced response conflict with greater Go/Nogo task demands. In contrast, the Nogo P3 effect was reduced with increasing task difficulty, suggesting that reductions in RTD may serve to impair inhibition-related processing or monitoring. Finally, our data also imply that inhibitory control may not be solely manifested by modulations in the N2 and P3, but that differential processing of the N1 and the P2 may also influence Go/Nogo task performance. These findings have real-world significance in light of a growing body of literature examining techniques for training inhibitory control as a way to ameliorate inhibitory control deficits seen in disorders such as ADHD. Importantly, mixed results in this line of research have been suggested to be partly due to a lack of optimal task difficulty manipulation. Thus, taken together, this study provides useful baseline behavioural and ERP data for appropriately manipulating task difficulty in Go/Nogo tasks, and potentially offers a constructive avenue for researchers attempting to design effective inhibition training paradigms.

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Benikos, N., Johnstone, S. J. & Roodenrys, S. J. (2013b). Short-term training in the Go/Nogo Task: Behavioural and Neural Changes Depend on Task Demands. *International Journal of Psychophysiology, 87* (3), 301-310.

International Journal of Psychophysiology 87 (2013) 301–312

Contents lists available at SciVerse ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Short-term training in the Go/Nogo task: Behavioural and neural changes depend on task demands

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ARTICLE INFO

Article history:
Received 26 July 2012
Received in revised form 1 December 2012
Accepted 4 December 2012
Available online 12 December 2012

Keywords:
Training
Practice
Task difficulty
ERPs
Inhibition
N2
P3
Arousal

ABSTRACT

Neural activity underlying executive functions is subject to modulation as a result of increasing cognitive demands and practice. In the present study, we examined these modulatory effects by varying task difficulty, as manipulated by reaction time deadline (RTD), on inhibitory control during a single Go/Nogo training session (8 blocks; 70% Go). Sixty adults were randomly assigned to one of three task difficulty conditions: High (n = 20), Medium (n = 20) and Low (n = 20), with RTDs of 300, 500 or 1000 ms, respectively. Task performance, Event-related potentials (ERPs) and task-related arousal (indexed by skin conductance level) were examined for training effects. Results indicated that improvements in behavioural Go/Nogo proficiency were optimised during conditions of moderate rather than low or high inhibitory demands. An across-session increase in task-related arousal did not differ between conditions, indicating a generalised increase in the mobilisation of mental resources with time-on-task. In contrast, training-related changes in ERPs were dependent on task demands such that the Low task difficulty condition showed an enhanced centroparietal Nogo P2, while a training-induced augmentation in the Nogo > Go P3 effect was greater in the High than Medium condition. The High condition also showed the greatest reduction in the Nogo N1. Although further research is needed in this area, these findings implicate the potential key role of task difficulty in training inhibitory control and suggest that practice-related changes are reflected by qualitative changes in brain activity.

1. Introduction

Everyday functioning requires the ability to deliberately inhibit dominant, automatic, or prepotent responses (Dagenbach and Carr, 1994; Dempster and Corkill, 1999). Localised to fronto-striatal networks (Aron et al., 2007, 2004), inhibitory control is crucial for the proper performance of many other higher-order cognitive functions, including working memory (Hester et al., 2004), task switching (Monsell, 2003) and action monitoring (Cooper and Shallice, 2000). Unfortunately, this capacity is susceptible to impairment with deficits linked to diverse spheres of atypical functioning, from excess consumption of food (Blumenthal and Gold, 2012) and alcohol (Wiers and Bartholow, 2007), to several psychiatric and neurological disorders, such as attention-deficit/hyperactivity disorder (ADHD; Smith et al., 2004) and Huntington's disease (Beste et al., 2008).

Intensive research over the last two decades has revealed that the neural mechanisms which underlie executive functions are amenable to training and experience (for a review see Kelly and Garavan, 2005), superseding the traditionally held belief that the human adult brain is hard-wired and resistant to change (Buonomano and Merzenich, 1998; Kelly et al., 2006b; Raskin et al., 2011). Consequently, fundamental research investigating the training-induced alterations in these abilities may not only determine the extent to which neuroplastic changes are available to healthy adults (Kelly et al., 2006a; Kelly and Garavan, 2005), but also aid in remediating atypical neural processes (Kelly et al., 2006a; Kujal and Näätänen, 2010). However, despite a recent upsurge of positive findings regarding the training of other executive functions (e.g., working memory, attention, task switching; for reviews see Cramer et al., 2011; Green and Bavelier, 2008; Kujal and Näätänen, 2010), the literature investigating the training of inhibitory control has been mixed.

For example, some studies report direct training-related improvements in inhibitory performance (Dowsett and Livesey, 2000; Schapkin et al., 2007; Thorell et al., 2009; Verbruggen and Logan, 2008), while others have found more indirect effects, such as a reduction in the consumption of food and alcohol after participants were trained to inhibit food and alcohol cues embedded in Go/Nogo and Stop-Signal tasks (Houben, 2011; Houben and Jansen, 2011; Houben et al., 2011; Veling et al., 2011). Despite this, several other investigations have reported no significant change (Jodo and Inoue, 1990; Kelly et al., 2006b; Rueda et al., 2005; Tomporowski, 2003), or even declines in performance with practice (Kato et al., 2009; Manuel et al., 2010), and no transfer to untrained tasks (Manuel et al., 2010; Thorell et al., 2009). In sum, despite some studies showing promising

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http://dx.doi.org/10.1016/j.ijpsycho.2012.12.001

results, the question of how to reliably attain training-induced improvements in inhibitory control is still not clear — highlighting the fragmentary nature of our current understanding, and pointing to the need for further work in this area.

In a complementary line of research, a number of previous working memory (WM) training studies have consistently demonstrated improvements in cognition (Chein and Morrison, 2010; McNab et al., 2009; Olesen et al., 2004) and overt behaviour post-training (Klingberg et al., 2005, 2002). Notably, these studies highlighted that a key ingredient of productive training was the enhancement of task difficulty (Klingberg, 2010; Lindqvist and Thorell, 2009; Thorell et al., 2009), while the training of WM at low levels of capacity does not lead to a substantial improvement (for a combined WM and inhibition training study see Johnstone et al., 2010; Klingberg et al., 2005, 2002). Similarly, variations in task difficulty also appear to be important for the training of other cognitive abilities (e.g., attention, perception; Kelley and Yantis, 2009; Wang et al., 2010). While we have previously demonstrated that Go/Nogo task difficulty can be successfully manipulated via reaction time deadline (RTD; Benikos et al., 2013), whether different variations in RTD can augment the training of prepotent response inhibition has yet to be systematically investigated. Previous research has either not manipulated task difficulty (e.g., Jodo and Inoue, 1990), or have used auto-adaptive difficulty manipulations (Manuel et al., 2010), leaving the question as to the *optimal* difficulty level required for learning in the Go/Nogo task open. Thus, the primary aim of the present study was to investigate the effect of varying degrees of task difficulty (i.e., Low, Medium and High) during the training of the Go/Nogo task, rather than simply assuming optimal learning at a single level.

Although variations in task performance offer a global measure of training-related changes in inhibitory control, they do little to provide an insight into the underlying neural mechanisms. In contrast, event-related potentials (ERPs) allow a detailed examination of these processes, with ERP amplitude and latency sensitive to neuroplastic changes in brain activity (Kujal and Näätänen, 2010; Lillard and Erisar, 2011). Among the most commonly investigated ERPs in the Go/Nogo task is the Nogo N2, a frontally maximal negative component peaking around 200 ms after the onset of inhibition-evoking stimuli (Johnstone et al., 2005; Smith, 2011), and the Nogo P3, a positive component that has a more anterior topography than the Go P3, and peaks approximately 300 ms post-stimulus (Randall and Smith, 2011; Smith and Douglas, 2011). The link between the N2 and P3 to inhibitory processing is the subject of debate (Bruin et al., 2001; Nieuwenhuis et al., 2003). Some argue that the inhibition process is best reflected by the N2 (Falkenstein et al., 1999; Kok, 1986), while others suggest instead that the P3 is the more likely candidate (Randall and Smith, 2011; Smith, 2011; Smith and Douglas, 2011; Smith et al., 2006, 2007, 2008; Smith et al., 2010).

The literature investigating the effect of inhibition training on neural activity has been varied in regard to methodologies and outcomes. Jodo and Inoue (1990) found that Go reaction time and Nogo P3 latency were significantly shortened after six days of practice (200 trials per day) — in line with previous theoretical viewpoints suggesting more efficient processing with training (Neubauer and Fink, 2009). However, given that no results for task performance were reported, a link between more efficient inhibitory performance and the Nogo P3 is unable to be made. Schapkin et al. (2007) found a reduction in Nogo errors, with a corresponding increase in the Nogo N2 after the first three daily training sessions (~200 trials per day) of a three week training protocol, which they interpreted as a practice-related strengthening of the inhibition mechanism (for a similar finding using fMRI see Kelly et al., 2006b). No further change was reported by the conclusion of the training. Finally, more efficient early low-level processing has been suggested by Manuel et al. (2010), who found a reduction in the left parietal activity to Nogo stimuli at 61–104 ms following 30 min of the Go/Nogo task practice (528 total trials).

In sum, the literature does not appear to paint a straightforward picture of the neural changes that should be expected as a result of training inhibitory control. Furthermore, the above mentioned studies had a variety of shortcomings. First, it has been suggested that response inhibition may not be solely manifested by variations in the N2 and P3, but that earlier components in the waveform such as the N1 and P2 play a crucial role in determining inhibition success (Roche et al., 2005; Thomas et al., 2009). Yet these components have not been investigated in the context of inhibition training. Secondly, previous work has generally only employed Pre/Post designs (Jodo and Inoue, 1990; Kelly et al., 2006a), which do little in the way of understanding the time-course of training effects. For optimal paradigm design it would be advantageous to isolate the time required to elicit positive training effects (Cramer et al., 2011). Finally, most studies have typically only included eleven or fewer participants (Jodo and Inoue, 1990; Manuel et al., 2010; Schapkin et al., 2007), making the generalisability of their findings and brain–behaviour correlations difficult to assess.

1.1. The present study

The primary aim of the present study was to examine the effect of varying task difficulty, as manipulated by RTD, on the training of inhibitory control using task performance and inhibition-related ERPs. Participants were divided into one of three Go/Nogo task difficulty conditions: Low (1000 ms), Medium (500 ms) and High (300 ms). Since previous Go/Nogo studies have demonstrated ceiling effects in task performance using Low difficulty RTDs (e.g., Johnstone et al., 2005; Smith et al., 2006), and that High task difficulty generally results in performance declines (e.g., Benikos et al., 2013), it was hypothesised that training outcomes would be optimised for the Medium task difficulty condition, with concurrent enhancements in the Nogo N2 and P3. A further focus of this study was on the potential contribution of early sensory processing to the training of inhibitory control, as indicated by the N1 and P2. While no specific predictions were made for these components, any differences found would be explored. Finally, a criticism of training paradigms manipulating task difficulty is the lack of consideration of state factors, such as task-related effort and arousal (Cramer et al., 2011; Green and Bavelier, 2008; Slagter et al., 2011). Given that these variables may be critical modulators of behaviour and task performance (e.g., Slagter et al., 2011; Tang and Posner, 2009; Yerkes and Dodson, 1908), participants provided perceived effort ratings and we recorded skin conductance level (SCL) — a well-established measure of central nervous system arousal (Barry and Sokolov, 1993).

2. Method

2.1. Participants

A total of 69 adults enrolled in the present study to fulfil an undergraduate course requirement, with three being excluded according to the selection criteria. To be included in the study, participants were required to refrain from caffeine for 2 h prior to testing and to have not taken any psychotropic substances (prescription or illegal) for 24 h prior to testing, or no more than once a month in the previous six months. Participants were also screened for neurological disorders and all reported normal or corrected-to-normal vision.

The remaining 66 participants were randomly assigned to one of the three conditions: Low, Medium or High task difficulty. Of these, data from 4 subjects were rejected either due to excessive eye artefact (3 participants, leaving an insufficient number of correct and artefact — free trials available for averaging) or to faulty recording equipment (1 participant). A further two people were excluded, with one being unable to complete the testing session due to an unrelated emergency, and another for failing to perform the task properly by adopting a

strategy of disregarding accuracy on Nogo trials in order to respond within the RTD. Therefore, 20 participants each were included in the final analyses for the Low (17 females, 3 males, mean age 21.23, SD 4.12), Medium (14 females, 6 males, mean age 21.5, SD 5.89) and High condition (14 females, 6 males, mean age 21.4, SD 3.32). There were no differences in age ($F(2,57)=0.13$, $p=.877$) or gender ($\chi^2(2)=0.53$, $p=.766$) between conditions. All but 5 of the 60 participants were right-handed. The research protocol was approved by the joint University of Wollongong and Illawarra Area Health Service Human Research Ethics Committee.

2.2. Task

Stimuli were delivered using Presentation software (Version 11.0; Neurobehavioral Systems, Albany, CA, USA). Each trial began with a central fixation cross (+) presented for a variable interval of 500–1000 ms (M = 750 ms), followed by the Go/Nogo stimulus presented in the centre of the screen for 200 ms. A blank screen then replaced the stimulus for a variable blank period of 1250–1750 ms (M = 1500 ms). Within this period, participants in the High, Medium and Low task difficulty conditions were required to respond by a button press with their right hand (irrespective of handedness) to Go stimuli within 300, 500 or 1000 ms, respectively, or to refrain from responding to the Nogo stimuli. Performance feedback was provided via the subsequent fixation cross: correct responses were followed by a white fixation cross, while a red fixation cross was displayed after incorrect responses (i.e., presses to the Nogo stimuli during the variable blank period, omissions and responses outside the RTD). Only presses to the Go stimulus within the predefined response window were regarded as correct.

Participants first completed an initial practice block of 30 trials (50% Nogo). In line with previous behavioural studies demonstrating improvements in inhibitory control using a single training session (Kelly et al., 2006b; Verbruggen and Logan, 2008), participants completed eight experimental blocks (30% Nogo) of 100 trials each. In order to minimise habituation of the visual ERP response (particularly the P3 component, e.g., see Ravden and Polich, 1998), the selection of shapes used to represent the Go and Nogo stimuli were selected from a pool of eight 2D shapes (i.e., triangle, cross, hexagon, diamond, ellipse, rectangle, star or circle). Go/Nogo shape selection was changed from block to block. The presentation of shape stimuli was counterbalanced by using a Latin square design (Bradley, 1958), and the Go/Nogo response assignment was counterbalanced across subjects. The stimuli measured approximately 3 × 3 cm and were presented on a 15″ computer monitor, with participants' seated 1 m away. Each block lasted approximately 3.5 min. In order to equate the training session length between conditions, the rest period between blocks was set at 1.5 min for all participants. Total session time including the practice and training blocks was approximately 43 min.

2.3. Procedure

Participants were given an outline of the testing procedure and familiarised with the laboratory equipment before informed consent was given. The experimenter emphasised that participants could withdraw at any time without penalty. They were then asked to complete a short screening questionnaire to assess vision problems, medication/psychotropic substance use, and neurological disorders. Subjects were then fitted with EEG and skin conductance recording equipment, and seated in a dimly-lit sound-attenuated and electrically-shielded testing booth. An incandescent light in the booth was dimmed for the duration of the training session. An initial 3 min baseline recording was conducted while participants were asked to sit quietly with eyes closed. Subjects were then presented with a modified Go/Nogo task and were instructed that they would see one of two shapes, one representing the Go stimulus, and the other representing the Nogo stimulus. They were asked to press the button before the pre-determined RTD with the thumb of their right hand (irrespective of handedness) to the Go stimuli, and to refrain from responding to the Nogo stimuli. Participants were asked to "do their best" to avoid the incorrect feedback, and were encouraged to keep as still as possible and to minimise eye movements during the testing blocks. The Go/Nogo shape assignment was shown on the screen and verbally confirmed by the participant prior to each block. At the end of each block, mean Go RT, the percentage of Go and Nogo errors were displayed for subjects to review. They were then asked to rate their perceived level of effort irrespective of their task performance with the question "How much effort did you use to complete that block?" and responded by a 5-point Likert scale ranging from: 1 = very little, 2 = moderate effort, and 5 = everything I had.[1] Prior to the first rating a basic example was shown to the subject to ensure understanding. Participants were given a timed break at the end of each block and asked to continue on.

2.4. Electrophysiological recording

The continuous scalp electroencephalogram (EEG) was recorded from 19 sites (Fp1, Fp2, F3, F4, F7, F8, Fz, C3, C4, Cz, P3, P4, Pz, T3, T4, T5, T6, O1, O2) using an electrode cap containing tin electrodes fitted according to the international 10–20 system (Jasper, 1958). A ground electrode located between Fpz and Fz, and all electrodes were referenced to linked ears. EOG was measured vertically with two tin cup electrodes, 1 cm above and below the left eye. Impedance was kept below 3 kΩ for EOG and reference electrodes, and below 5 kΩ for cap electrodes. EEG and EOG signals were amplified 19 times and sampled at 500 Hz, with bandpass down 3 dB at 0.1 and 100 Hz via a NuAmps system (Compumedics Limited, Melbourne, Australia). Prior to processing, the EEG data were digitally filtered using a low-pass filter 3 dB down at 30 Hz.

2.5. Skin conductance recording

Electrodermal activity was recorded using two Ag/AgCl electrodes placed on the distal phalanges of the third and fourth digits of the left hand. Recording electrodes were filled with electrode paste (0.05 M NaCl in an inert viscous ointment base) and were secured using velcro straps and tape. A constant voltage device (UFI Bioderm model 2701) set at 0.5 V was used. This system separately recorded tonic DC-coupled SCL, AC-coupled skin conductance response (SCR), measured in microsiemens (μS) but only SCL is reported here.

2.6. Data quantification

The ERP epoch was defined as 100 ms pre-stimulus to 900 ms post-stimulus onset. Epochs were excluded if they contained activity greater than ±100 μV at any non-frontal site. EOG artefact reduction was carried out based on vertical EOG (Semlitsch et al., 1986). ERPs were averaged across epochs for correct responses only. This resulted in a minimum of 18 artefact-and-error-free Nogo trials being included in each average. To ensure compatibility within-subjects, the number of epochs available for averaging was determined for the Nogo stimuli initially, with the Go epochs restricted to the same number, being selected randomly from the total available epochs. Grand average ERP waveforms for the Go and Nogo stimuli were displayed in order to define the component latency range. Latency at all sites was locked to the peak latency at the site of maximum amplitude, with the amplitude for all 9 electrodes taken at the same post-stimulus latency (Picton et al., 2000; Spencer et al., 2001). The ERP component peaks were quantified

[1] Although participants were instructed to rate their perceived effort irrespective of their task performance, knowledge of their performance may still have influenced their ratings.

using an automatic peak-picking software which identified the largest positive or negative deflections within the predefined latency range, relative to the 100 ms pre-stimulus baseline period. Peak latency ranges and sites were as follows: N1 (100–160 ms Fz), P2 (180–240 ms Pz), N2 (200–280 ms Fz), P3 (280–520 ms Pz). Skin conductance level was taken as the average value (in μS) for each 30 sec period over the 3.5 min duration of each block of the Go/Nogo task.

2.7. Statistical analyses

The error rate (Go omission errors, Go RTD errors and Nogo errors) was calculated as the number of incorrect responses divided by the total number of trials. The Go/Nogo performance data were subject to Condition [Low (L) vs. Medium (M) vs. High (H)] × Time [Block 1 (b1) vs. Block 4 (b4) vs. Block 8 (b8)] mixed design ANOVAs, with repeated measures on the within-subjects factors. Planned orthogonal contrasts were used to analyse differences within Time and between conditions by using Linear (b1 vs. b8) and Quadratic (mean of b1/b8 vs. b4) contrasts.

Primary analyses of the ERP data were restricted to the sites F3, Fz, F4, C3, Cz, C4, P3, Pz and P4. The Go and Nogo data were subject to a Condition (L vs. M vs. H) × Lateral (Left vs. Midline vs. Right) × Sagittal (Frontal vs. Central vs. Parietal) × Stimulus (Go vs. Nogo) × Time (b1 vs. b4 vs. b8) ANOVAs. Planned orthogonal contrasts, which allow insight into training-related changes in the topographic distribution of each component, were performed on the within-subjects factors. The Sagittal factor compared the frontal region (mean of F3, Fz and F4) with the posterior region (mean of P3, Pz and P4), and their mean with the central region (mean of C3, Cz and C4). The lateral factor compared activity in the left hemisphere (mean of F3, C3 and P3) with that in the right hemisphere (mean of F4, C4 and P4), and their mean with the midline region (mean of Fz, Cz and Pz). Finally, the Time factor compared block 1 to block 8 (Linear contrast), and their mean with block 4 (Quadratic). The analyses for the component peak latency excluded site contrasts. As these contrasts were planned with no more of them than the degrees of freedom for each effect, no Bonferroni type adjustment to α were necessary (Tabachnick and Fidell, 1996). Also, single degrees of freedom contrasts are not affected by violations of symmetry assumptions common in repeated measures analyses, and thus do not require Greenhouse–Geisser-type corrections. As these analyses are carried out over a substantial number of variables, each may be considered to constitute a separate experiment. It should be noted that this increases the frequency of type 1 errors, however, as this is an increase in frequency, rather than probability, it cannot be 'controlled' by the adjustment of alpha levels (Howell, 2009). All ERP statistics have (1.58) degrees of freedom unless otherwise indicated. Outliers in the data (i.e., values exceeding ±2.5 standard deviations from the mean) were corrected by replacing them with the series mean (<1.1% for any task performance or ERP variable). Data were normalised using the vector scaling method (McCarthy and Wood, 1985), and only interactions with topography that remained significant in the normalised data are reported here.

3. Results

3.1. Manipulation check, perceived effort and SCL

Participants' perceived effort was greater in the High (M = 3.87) than the Medium (M = 3.57) and Low (M = 3.20) conditions (i.e., H > M > L; Linear: $F = 6.13$, $p = .016$, $\eta^2 = .096$). Similarly, there were incremental increases in Nogo errors (see Fig. 1d) with each decrease in RTD, with the greatest overall percentage of errors in the High condition (Linear: $F = 77.70$, $p < .001$, $\eta 2 = .577$). Combined, these results suggest that three task difficulty levels were established, with greater perceived effort and declines in inhibitory performance with shorter RTDs. Across the session, the Time main effect (Linear: $F = .031$, $p = .862$) and the Time × Condition interaction (Linear: $F = .031$, $p = .970$) for perceived effort were not significant. SCL increased from the beginning (11.6 μS) to the end of the training session (13.1 μS; Linear: $F = 23.20$, $p < .001$, $\eta^2 = .289$), but this effect did not differ between conditions (Linear: $F = 2.08$, $p = .134$).

3.2. Task performance

As seen in Fig. 1a, the Go reaction time (RT) decreased with training showing the largest decline in the Low condition (Linear: $F = 3.32$, $p = .043$, $\eta^2 = .032$). Go omission (Linear, $F = 3.41$, $p = .040$, $\eta^2 = .051$) and Go RTD errors (Linear, $F = 20.84$, $p < .001$, $\eta^2 = .198$; Quad: $F = 5.87$, $p = .005$, $\eta^2 = .059$) decreased early in the session (i.e., by block 4) for the Medium and High conditions — with the greatest declines for the High condition (see Fig. 1b and c). By contrast, Go RTD errors and Go omission errors appeared to be at ceiling for the Low condition and did not modulate over the course of the training.

As seen in Fig. 1d, Nogo errors showed different training effects with task difficulty. While Nogo errors increased sharply from block 1 to block 4 and plateaued thereafter for High condition, the Medium and Low conditions remained relatively stable across the session (Linear: $F = 4.04$, $p = .023$, $\eta^2 = .124$; Quadratic: $F = 4.84$, $p = .011$, $\eta^2 = .145$). A further within Condition analysis of Nogo errors confirmed no change for the Low (Linear: $F = 2.05$, $p = .169$) or Medium condition (Linear: $F = 0.24$, $p = .632$), but a significant increase for the High (Linear: $F = 4.39$, $p = .050$, $\eta^2 = .188$). To clarify whether the facilitation of Go RT with training resulted in a speed-accuracy trade-off (SAT), we correlated the training-related change (i.e., b8–b1) in Go RT and Nogo errors separately for each condition. This analyses was not significant for either the Low ($r = -.104$, $p = .664$) or Medium condition ($r = -.074$, $p = .758$), but it was for the High ($r = -.467$, $p = .038$). Given that Nogo errors remained stable for the Low and Medium conditions, declines in Go RT with training represent an improvement in behavioural Go/Nogo proficiency. This result is similar to that of Manuel et al.'s (2010).

3.3. Event-related potentials

Fig. 2 presents grand mean ERPs to Go/Nogo stimuli across conditions (top left panel) and for each condition separately (remaining three panels) for blocks 1, 4 and 8. ERP latency data is presented in Table 1. As the primary aim of this study was to investigate the effect of varying task difficulty on the training of inhibitory control, and as a large body of literature has been devoted to descriptions of the topography of the various ERP components, reporting of the results will focus on effects and interactions involving Time and Condition.

The waveforms were characterised by an N1–P2 complex, most apparent at frontal and central sites, followed by an N2 component at about 270 ms primarily in the fronto-central region. The P3 is evident as a large positivity which peaks approximately at 300–400 ms post-stimulus and is the largest parietally.

3.4. N1

N1 latency (mean 138.5 ms) declined linearly across the training session (see Table 1; Linear: $F = 13.94$, $p < .001$, $\eta^2 = .196$). A Time × Condition effect approached significance (Linear: $F = 3.11$, $p = .052$, $\eta^2 = .098$) indicating that the N1 latency reduction was greater for the High (b1 vs. b8 diff.: 15.5 ms) than the Low (b1 vs. b8 diff.: 8.6 ms) and Medium conditions (b1 vs. b8 diff.: 1.5 ms).

Table 2 summarises the following effects and provides means. N1 amplitude reduced linearly from the beginning until the end of the session. Interestingly, training differentially modulated Go/Nogo N1

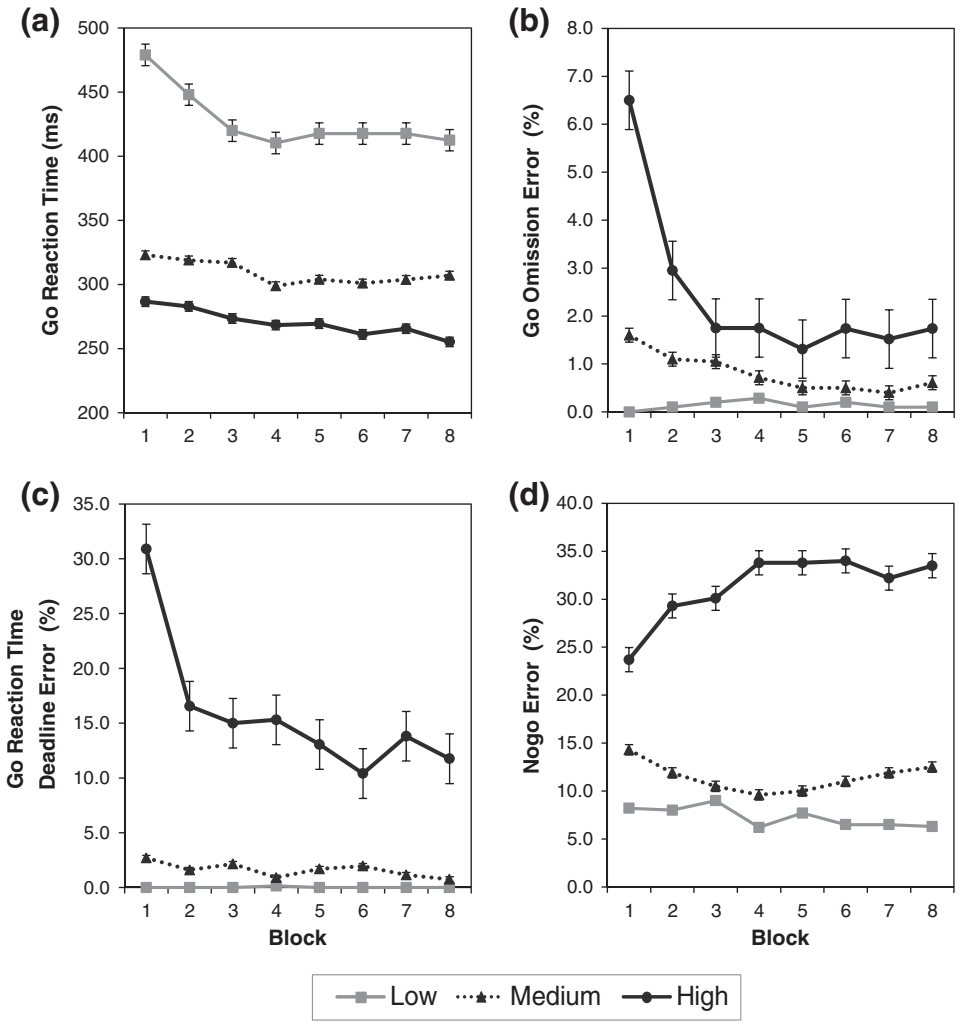

Fig. 1. Task performance indices for each difficulty condition over the training session including (a) Go reaction time, (b) Go omission, (c) Go reaction time deadline, and (d) Nogo errors. Error bars represent standard error of the mean. Note: Data for all eight blocks is included for display purposes, but only blocks 1, 4 and 8 were considered in the statistical analyses.

amplitudes between conditions (Stimulus × Condition × Time interaction), in that a Go > Nogo N1 effect, which was larger for the Low than Medium condition in block 1, reduced across the training session to be almost equipotential for both conditions by block 8; contrasting with the High condition, that displayed a training-related reduction in the Nogo relative to Go N1 (see Fig. 3).

3.5. P2

P2 latency (mean 222.7 ms) declined across the training session (Table 1; Linear: $F = 6.26$, $p = .015$, $\eta^2 = .053$). This reduction was greater for the High (b1 vs. b8 diff.: 21.4 ms) than the Low condition (b1 vs. b8 diff.: 6.8 ms), in contrast to the Medium condition that displayed a slightly longer P2 by the end of the session (b1 vs. b8 diff.: +2.2 ms; Linear: $F = 3.96$, $p = .025$, $\eta^2 = .059$).

P2 showed a Go > Nogo effect (see Table 2). The amplitude of the P2 increased linearly with the training. As evidenced by significant Time × Sagittal × Stimulus × Condition interactions, the Go and Nogo P2 topography differed between conditions: for the Go P2, a central > frontal/parietal effect increased linearly with task difficulty (i.e., H > M > L), suggestive of an anterior shift of the Go P2 focus with training, particularly apparent in the Medium and High conditions (Fig. 4a and b). For Nogo P2 the Medium and High conditions displayed a more anterior Nogo P2 with training, the Low condition showed the opposite pattern, with enhanced Nogo P2 activity at centroparietal regions (Fig. 4c and d). Simple effects analyses confirmed a significant Sagittal × Time × Condition effect to Go (Quad: $F = 3.60$, $p = .032$, $\eta^2 = .011$) and the Nogo stimuli (Linear: $F = 5.58$, $p = .006$, $\eta^2 = .055$).

3.6. N2

N2 (mean 266.5 ms) peaked later to Nogo (269.2 ms) than the Go stimuli (263.7 ms; $F = 6.09$, $p = .017$, $\eta^2 = .097$). Linear ($F = 7.96$, $p = .007$, $\eta^2 = .122$) and quadratic ($F = 8.51$, $p = .005$, $\eta^2 = .130$) effects indicated that while the N2 latency declined rapidly from block 1 (273.7 ms) to block 4 (260.1 ms), it began to increase slightly by block 8 (265.9 ms). The training effects for N2 latency also differed between conditions, showing a large decline for the Low (b1 vs. b8 diff.: 19.9 ms), but a little change for the High (b1 vs. b8 diff: 5.4 ms), and Medium conditions (b1 vs. b8 difference: 2.0 ms; $F = 5.49$, $p = .007$, $\eta^2 = .161$).

Globally, the N2 amplitude was larger to Nogo than the Go stimuli (see Table 3 for effect summaries and means). Overall, the N2 amplitude decreased across the training session. Moreover, a Time × Stimulus interaction showed that the Nogo > Go N2 effect increased linearly from block 1 to block 8. However, an inspection of the means (see Table 3 and Fig. 4) shows that it was the Go N2, and not the Nogo N2 that

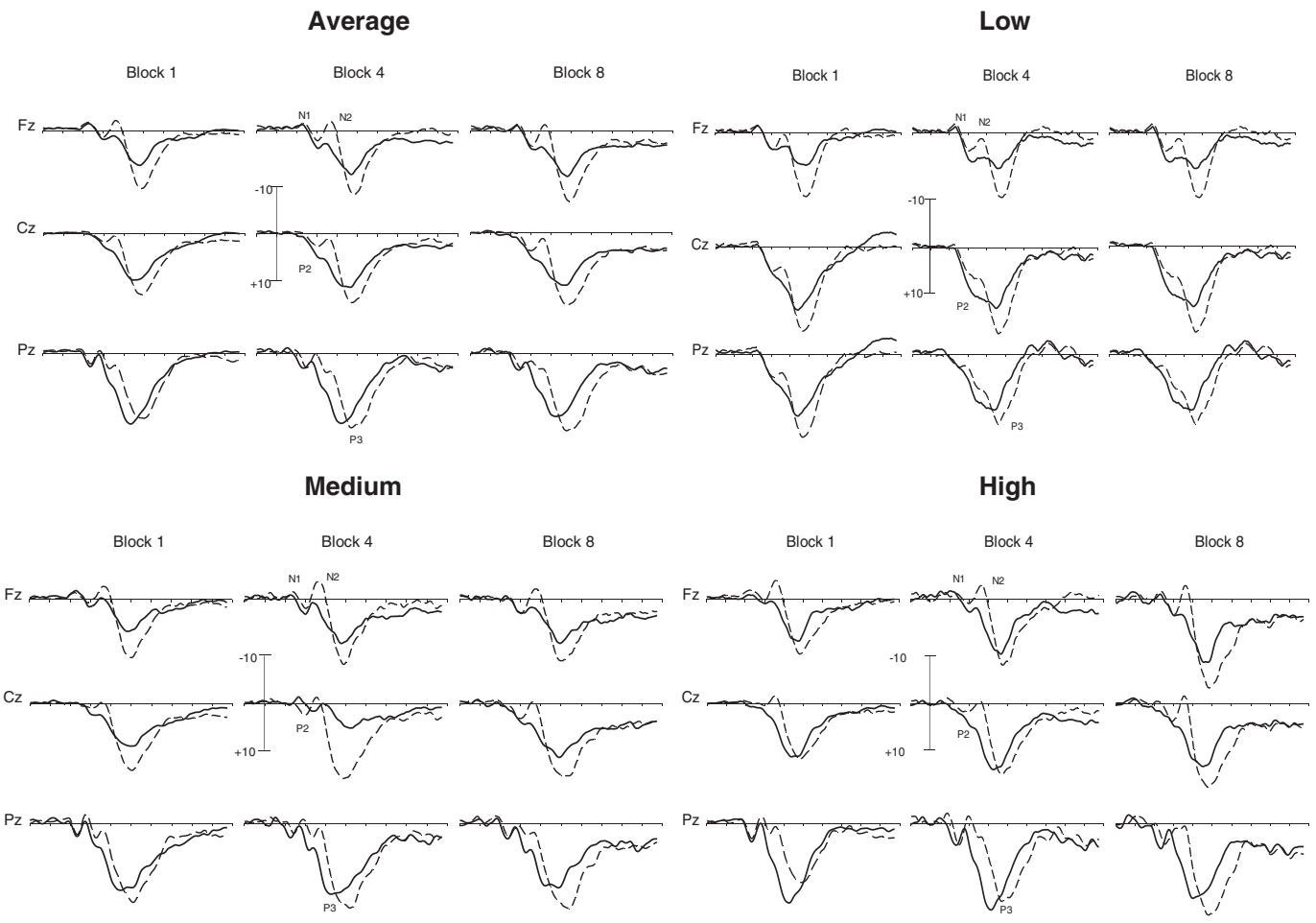

Fig. 2. Grand mean ERPs for blocks 1, 4 and 8 to Go (solid line) and Nogo (dashed line) across condition (top left panel) and for each task difficulty condition separately (remaining three panels). ERPs are shown at three midline sites only. Note: x-axis ticks = 100 ms; stimulus onset at y-axis (scale: ±10 μV) shown at Cz.

declined across the session. Follow-up analyses confirmed a significant reduction across the session for the Go N2 (Linear: $F = 11.57$, $p = .001$, $\eta^2 = .095$), but not the Nogo N2 (Linear: $F = 0.00$, $p = .995$). Against predictions, these effects did not differ between conditions.

3.7. P3

The P3 (mean 376.9 ms) peaked later for Nogo (395.8 ms) than the Go stimuli (358.1 ms; $F = 64.64$, $p < .001$, $\eta^2 = .531$). While Nogo P3 latency remained relatively stable across the session for each

Table 1
Mean latency (in ms) for Go/Nogo stimuli between each task difficulty condition for blocks 1, 4 and 8 (standard deviations in parentheses).

ERP	Block 1			Block 4			Block 8		
	Low	Medium	High	Low	Medium	High	Low	Medium	High
Go									
N1	139.0	146.2	142.9	134.3	142.8	127.8	129.8	142.7	130.6
	(12.7)	(20.0)	(25.5)	(32.1)	(20.3)	(23.4)	(21.0)	(25.1)	(28.2)
P2	233.3	221.3	225.9	226.7	225.0	212.4	214.4	233.2	209.1
	(22.5)	(16.8)	(23.3)	(37.4)	(21.2)	(37.1)	(30.2)	(31.6)	(46.3)
N2	282.8	267.1	262.0	265.9	260.8	243.2	254.7	272.8	264.1
	(23.3)	(19.1)	(18.8)	(46.0)	(21.2)	(35.8)	(38.3)	(37.7)	(40.6)
P3	368.9	398.1	355.7	350.3	358.0	337.1	324.1	378.1	352.8
	(40.6)	(34.2)	(29.6)	(46.7)	(48.8)	(27.3)	(34.4)	(49.9)	(42.7)
Nogo									
N1	141.0	144.9	149.1	136.1	141.3	135.7	133.0	145.2	130.1
	(20.4)	(15.6)	(21.5)	(25.0)	(17.1)	(26.4)	(16.7)	(22.6)	(16.7)
P2	232.2	226.6	221.0	223.2	229.2	205.4	233.2	226.3	208.1
	(25.8)	(14.6)	(16.7)	(28.1)	(20.3)	(27.4)	(23.5)	(23.8)	(18.3)
N2	285.8	274.4	270.1	266.6	271.9	251.8	274.1	272.8	257.1
	(22.4)	(18.8)	(17.5)	(24.8)	(17.7)	(32.8)	(24.4)	(22.4)	(15.4)
P3	382.7	418.6	400.4	366.2	418.4	392.6	379.9	419.3	383.9
	(35.2)	(21.0)	(22.7)	(39.9)	(34.5)	(46.8)	(42.5)	(30.3)	(41.6)

Table 2
Significant results for the N1 and P2 components.

Measure	Effect	Contrast	Details	F	η^2
N1	T	Linear: b1 vs. b8	−1.0 vs. −0.3	6.95*	.063
		Quadratic: b4 vs. b1/b8	−0.3 vs. −0.6	3.65*	.024
	T×Stim ×Cond	Linear: Go vs. Nogo	Low: b1, −0.9 vs. −0.1; b8, −0.1 vs. −0.2 Medium: b1, −1.2 vs. −1.1; b8, −0.4 vs. −0.2		
			High: b1 −0.7 vs. −1.6; b8, −0.9 vs. 0.0	3.83**	.048
P2	Stim	Go vs. Nogo	5.4 to 3.5	37.56***	.375
	T	Linear: b1 vs. b8	3.6 vs. 5.1	7.60**	.073
	T×S×Stim ×Cond	Linear: f vs. p	Low: b1, Go, 3.9 to 6.7 vs. Nogo, 3.1 to 6.2; b8, Go, 5.4 to 7.6 vs. Nogo, 3.7 to 8.2 Medium: b1, Go, 2.2 to 4.9 vs. Nogo, 0.6 to 4.0; b8, Go, 3.6 to 7.5 vs. Nogo, 2.2 to 3.5 High: b1, Go, 1.7 to 7.3 vs. Nogo, 1.4 to 4.2;		
			b8: Go, 3.5 to 6.7 vs. Nogo, 2.8 to 2.1	4.37*	.022

Note: For this and subsequent tables, detail column represents mean amplitude in μV. Cond, Condition: Low/Medium/High task difficulty. Low, low task difficulty condition. Medium, medium difficulty condition, High, high difficulty condition. Stim, stimulus type: Go/Nogo. T, time; Linear: linear contrast comparing block 1 to block 8; Quadratic: quadratic contrast comparing the average of block 1/8 and block4; b1, block 1; b1/b8, average of block 1 and 8; b8, block 8. Sagittal (S) abbreviations: f, mean frontal (F3, Fz, F4); p, mean parietal (P3, Pz, P4); c, mean central (C3, Cz, C4); f/p, mean of frontal and parietal (F3, Fz, F4, P3, Pz, P4).
* =<.05.
** =<.01.
*** =<.001.

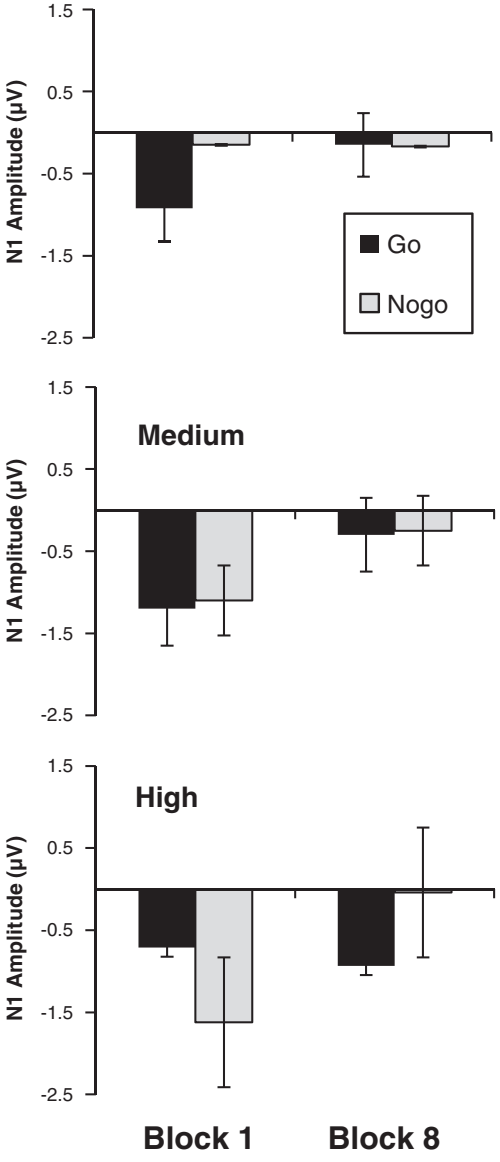

Fig. 3. Stimulus×Condition×Time interaction for Go and Nogo N1 amplitude.

condition, Go P3 latency showed the greatest training-related declines for the Low (b1 vs. b8 diff: 44.7 ms) compared to the Medium (b1 vs. b8 diff: 19.9 ms) and High conditions (b1 vs. b8 diff: 2.9 ms; $F=4.68$, $p=.014$, $\eta^2=.138$).

The P3 was larger to Nogo than the Go stimuli (see Table 3 for effect summaries and means), with a smaller parietal>frontal gradient (parietal vs. frontal difference: Nogo 3.7 μV, Go 6.8 μV) and an increased central>frontal/parietal effect in Nogo compared to the Go stimuli (central vs. frontal/parietal difference: Nogo 3.3 μV, Go 2.6 μV). These effects highlighted the anteriorisation of P3 to Nogo relative to Go stimuli.

P3 amplitude increased with training. The Nogo>Go P3 effect (across the scalp) was reduced for the Low condition by block 8 (Go vs. Nogo diff.: b1, 3.0 vs. b8, 1.8 μV), while the High condition (Go vs. Nogo diff.: b1, 0.0 vs. b8, 5.6 μV) showed a significantly larger training-induced increase in the Nogo>Go P3 effect than the Medium condition (Go vs. Nogo diff.: b1, 3.1 vs. b8, 4.9 μV). Time×Sagittal×Stimulus×Condition interactions indicated that this effect was most apparent over central regions (Fig. 6), as indicated by the more anterior Nogo than the Go P3 for the High than the Medium and Low conditions.

4. Discussion

The questions of how to reliably attain training-induced improvements in inhibitory control and the supporting neural mechanisms remain unresolved. Therefore, using task performance and neural markers of inhibitory processing, the primary focus of the present research was to investigate the effect of varying task difficulty during short-term training of the Go/Nogo task. In addition, we also aimed to determine whether the early evoked potentials and state differences (as indexed by task-related arousal and perceived effort) would be modulated by training.

4.1. Task performance

Performance findings revealed that the Go/Nogo training was significantly influenced by variations in task difficulty. Both the Low and Medium conditions showed considerable reductions in Go RT along with no change in Nogo accuracy; suggesting a training-related improvement in inhibitory control, given that accuracy was maintained in the context of faster responding (for a similar finding see Manuel et al.'s, 2010). The relationship between fast Go responding and an increased requirement for inhibition on Nogo trials is well-established (Band et al., 2003; Jodo and Kayama, 1992; Smith et al., 2006; Manuel et al., 2010; Falkenstein et al., 1999; Lindqvist and Thorell, 2009; Falkenstein et al., 2000). When responses grow progressively faster on average, the relative strength of inhibition must increase in order to overcome the fast Go response (Smith et al., 2006). Moreover, given

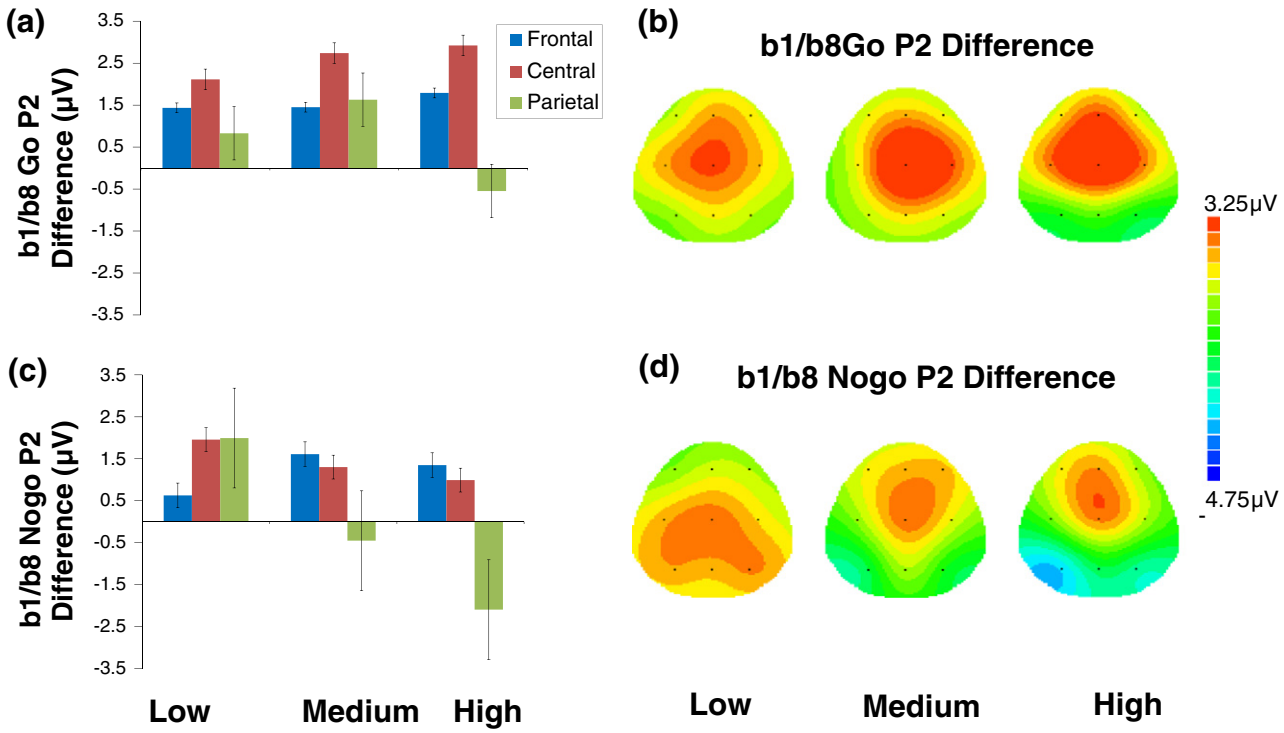

Fig. 4. Mean change in the (a) Go P2 and (c) Nogo P2 from block 1 to block 8 across the sagittal dimension. Error bars represent standard error of the mean. Topographic maps for the mean change in voltage distribution from block 1 to block 8 for the (b) Go P2 and (d) Nogo P2. Scale values represent the ends of the colour scale in μV for each component. Darkest blue = negativity, red = positivity.

that Go RT was much faster overall for the Medium than the Low condition (in addition to large improvements in Go RTD and Go Omission errors for the Medium condition.), it appears that moderate task difficulty leads to greater enhancements in Go/Nogo proficiency. Together with the finding that the High condition showed a significant decline in inhibitory performance, these findings are in line with previous behavioural reports suggesting that learning is likely to be enhanced when a task remains relatively challenging but not overly difficult (Ahissar and Hochstein, 2004), and provide novel evidence for the appropriate use of RTDs in optimising the short-term training of inhibitory control.

4.2. Task-related arousal

In order to investigate the role of state factors during the training session we examined task-related arousal and perceived effort. While perceived effort did not significantly vary over the training session, all three conditions showed a linear increase in arousal. Based on their review of this literature, Dawson et al. (1990) have suggested that elevations in skin conductance reflects the effortful mobilisation of mental resources directed towards a task (for similar conclusions see Johnstone et al., 2009; Larue et al., 2011; Naccache et al., 2005). The enhancement of task-related arousal could therefore be related to the increased efforts of participants to maintain an alert state throughout the training session irrespective of the task difficulty condition. However, it should be noted that other factors including mood and fatigue have been shown to influence not only SCL (e.g., Eason et al., 1965; Geldreich, 1939; Hajcak et al., 2004; Jacobs et al., 1994), but also performance on the Go/Nogo tasks (Kato et al., 2009, 2012; Scholz et al., 2009; Schulz et al., 2007; Smallwood et al., 2009). From this perspective, it may be useful in future studies to include additional state measures to further clarify the effect of these energetic factors during cognitive training.

4.3. Early ERP components

Interestingly, training differentially modulated the Go/Nogo N1 amplitudes between conditions. Participants in the Low and Medium conditions showed relatively similar N1 amplitudes to Go and Nogo stimuli by the end of the training, while those in the High condition displayed a reduced Nogo relative to Go N1. The N1 ERP component is sensitive to the sensory attributes of stimuli and is modulated by attention (Näätänen and Picton, 1987). Similarly, Bekker et al. (2005) has also suggested that N1 amplitudes may index an attentional switch that is determinative for subsequent inhibitory control. Together with the performance data, these findings point to differential focusing on task requirements for each of the three difficulty conditions over the course of the training session. That is, in the context of improved Go/Nogo proficiency, it would seem that participants in both the Low and Medium conditions applied a more balanced approach in attending to Go and Nogo stimuli. By contrast, training seems to have led to a reduction in attentional resources being directed towards Nogo stimuli in the High condition, possibly due to these participants focusing primarily on the Go stimulus in order to respond within the strict RTD (Johnstone et al., 2005). Such a reduction in attention to Nogo stimuli may, in part, explain the reduction in inhibition accuracy with training in this group.

Notably, the training resulted in different changes in P2 topography between the task difficulty conditions: the Medium and High conditions showed a more anterior P2 to both Go and Nogo stimuli, contrasting with the Low condition which displayed an enhanced centroparietal Nogo compared to the Go P2 (see Fig. 4c and d). These differences were apparent in the vector-scaled data suggesting a training-induced shift in the neural generators of these components (Johnson, 1993). Moreover, although the P2 component is generally thought to index the appropriate classification of stimuli (Oades, 1998), its functional significance may have dissociable meanings according to the scalp

Table 3
Significant results for the N2 and P3 components.

Measure	Effect	Contrast	Details	F	η^2
N2	Stim	Go vs. Nogo	4.1 vs. 0.0	133.00***	.634
	T	Linear: b1 vs. b8	1.6 vs. 2.6	4.36**	.043
	T×Stim	Linear: b1 vs. b8	Go, 3.3 vs. 0.0; Nogo: 5.2 vs. 0.0	9.88**	.071
	T×S×Stim	Linear: c vs. f/p	b1: Go, 3.6 vs. 3.1, Nogo, 0.1 vs. −0.1		
			b8: Go, 6.2 vs. 4.7, Nogo, 0.0 vs. −0.1	20.7***	.030
P3	Stim	Go vs. Nogo	12.7 vs. 15.7	36.71***	.378
	S×Stim	f vs. p	Go: 8.4 vs. 15.2; Nogo: 12.7 vs. 16.4	57.28***	.405
		c vs. f/p	Go: 14.4 vs. 11.8; Nogo: 17.9 vs. 14.6	13.89***	.029
	T	b1 vs. b8	13.0 vs. 15.0	15.23***	.129
	T×Sim ×Cond	Go vs. Nogo	Low: b1, 9.9 vs. 12.9; b8, 13.1 vs. 14.9		
			Medium: b1, 12.5 vs. 15.6; b8, 11.8 vs. 16.7		
			High: b1, 13.7 vs. 13.6; 14.1 vs. 19.7	6.39*	.049
	T×S×Stim ×Cond	Linear: f vs. p;	Low: b1,Go, 6.4 vs. 12.2; Nogo, 9.8 vs. 13.9		
			b8, Go, 15.4 vs. 11.9; Nogo, 12.6 vs. 15.0		
			Medium: b1,Go, 8.3 vs. 15.9; Nogo, 12.1 vs. 17.0		
			b8, Go, 7.7 vs. 14.4; Nogo, 13.3 vs. 17.3		
			High: b1,Go, 9.3 vs. 16.6; Nogo, 11.5 vs. 14.3		
			b8, Go, 10.5 vs. 15.6; Nogo, 17.3 vs. 19.5	4.95*	.028
		Quadratic: c vs. f/p	Low: b1,Go, 11.2 vs. 9.3; Nogo, 17.8 vs. 14.5		
			b8, Go, 15.4 vs. 11.9; Nogo, 17.0 vs. 13.8		
			Medium: b1,Go, 13.5 vs. 12.1; Nogo, 12.1 vs. 17.0		
			b8, Go, 13.4 vs. 11.0; Nogo, 19.4 vs. 15.3		
			High: b1,Go, 15.2 vs. 13.0; Nogo, 15.1 vs. 12.9		
			b8, Go, 16.3 vs. 13.1; Nogo, 22.3 vs. 18.4	3.92*	.007

* =<.05.
** =<.01.
*** =<.001.

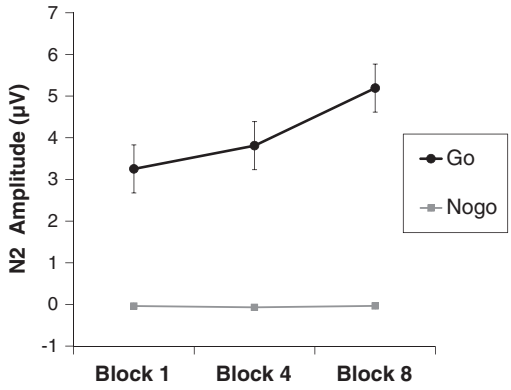

Fig. 5. Go and Nogo N2 amplitude across the training session. Error bars represent standard error of the mean.

location. A more anterior P2 may index greater relevance of task stimuli (Potts, 2004; Potts et al., 1996), whereas larger parietal P2s have been reported during easy perceptual learning paradigms, paralleled by improvements in performance (Ding et al., 2003; Qu et al., 2010; Song et al., 2002; Song et al., 2005). Thus, a more anterior Go and Nogo P2 for the Medium and High conditions implies greater stimulus processing and evaluation of these stimuli with training, possibly due to the faster overall Go RT for these conditions. By contrast, the increased Nogo P2 over centroparietal sites for the Low condition may index an early perceptual learning effect that is linked to more automated bottom-up processing in a relatively easy task, as implied by inhibition performance at ceiling for this condition.

Consistent with this notion, Verbruggen and Logan (2008) posit that Go/Nogo task practice leads to the emergence of automatic inhibition, where learned associations between the stimuli and withholding a response reduce the need for top-down executive control. In this context, it may be that enhanced Nogo P2 amplitudes for well-learned or easy tasks reflect the automated inhibition of the Nogo stimuli, freeing top-down mechanisms from further processing. In contrast, more difficult tasks appear to show a reduced P2 at parietal sites, potentially signalling the need for greater top-down inhibitory control at later processing stages (Dimoska and Johnstone, 2008; Smith et al., 2004).

4.4. Inhibition-related ERP components

N2 amplitude and latency decreased across the session regardless of condition, in line with previous research (Ding et al., 2003; Song et al., 2002). Interestingly, however, further interactions highlighted that this decline was primarily due to the reduction of the Go, but not the Nogo N2. The N2 component is thought to represent a controlled mismatch detection process (Näätänen and Picton, 1986; Snyder and Hillyard, 1976), and is therefore related to stimulus discrimination (Johnstone et al., 2001, 1996; Ritter et al., 1983). Attenuated cortical responses to repeated stimuli have typically been interpreted as an early manifestation of learning-induced neural plasticity (see Garrido et al., 2008; Race et al., 2010; Summerfield et al., 2011). Thus, reduced Go N2 amplitudes across training blocks may suggest more efficient stimulus discrimination with training. Moreover, Neubauer and Fink (2009) have proposed that greater neural efficiency might arise when training with tasks of low difficulty. If this is the case, the finding of the larger training-induced decline in N2 latency for the Low than Medium/High conditions is in accord with this interpretation.

Against predictions, training-related variations in task performance were not accompanied by an increase in the Nogo N2 (see Fig. 4). While consistent with some previous reports investigating the effect of repetition (Falkenstein et al., 2002; Kato et al., 2009), it is in contrast to others suggesting enhancements in this component concurrent with improvements in Go/Nogo proficiency (for a discussion see Manuel et al., 2010; Schapkin et al., 2007). Our previous work, which considered the effect of decreasing RTDs (Benikos et al., 2013), found that faster Go RTs resulted in incremental increases in Nogo N2 amplitude, interpreted in terms of enhanced response conflict (see also Nieuwenhuis et al., 2003; Smith, 2011). From this perspective, it may be argued that the stable Nogo N2 in the present study reflects a reduction in the relative level of response conflict, given that all three conditions showed declines in Go RT.

Nonetheless, it is interesting to note that the only inhibition training study which reported changes in Nogo N2 amplitude, found this effect after three days of training (Schapkin et al., 2007), while Luu and colleagues (2007) have suggested that changes in the N2 may only be apparent during the later stages of learning. Thus, combined with the fact that participants were presented with fewer Nogo than Go stimuli over the course of the training session (i.e., 30% vs. 70%), the equivalent

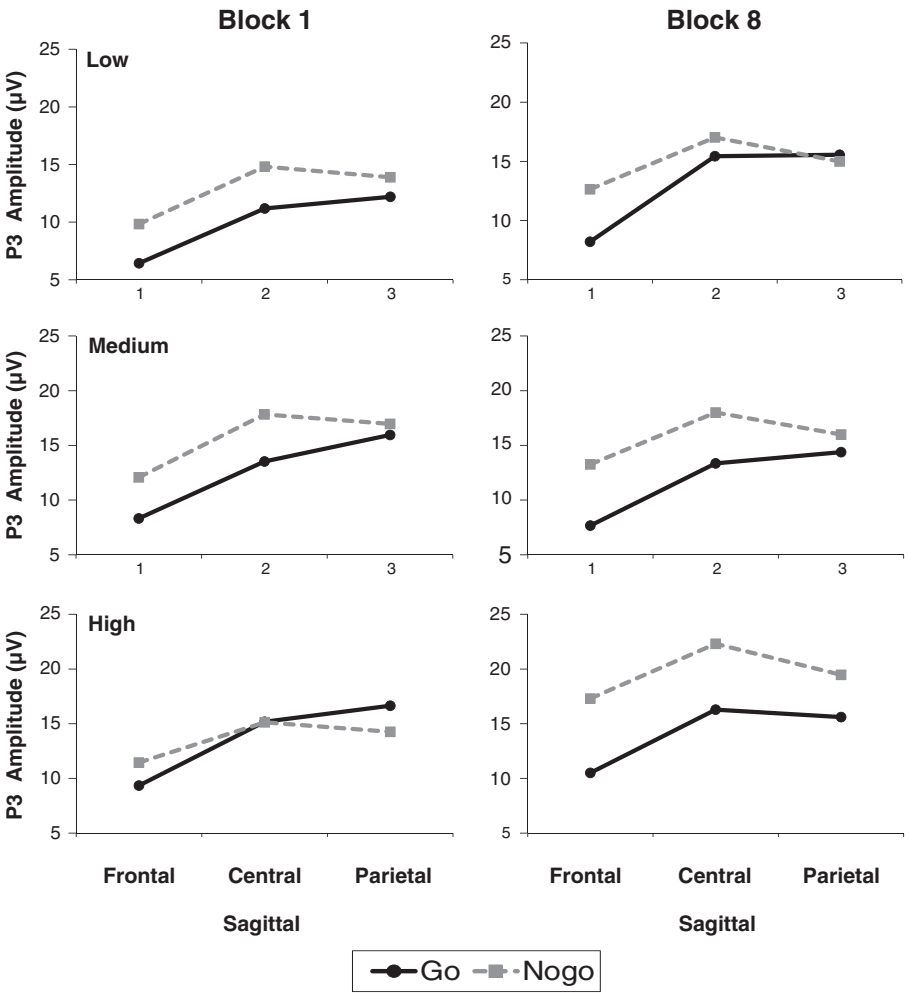

Fig. 6. Time × Stimulus × Sagittal × Condition interaction for P3 amplitude.

Nogo N2 may be due to the slower time course of learning for this component.

While little change was seen across the session for the Low condition, the Nogo > Go P3 effect increased as a function of task difficulty particularly over the central regions; showing a greater training-induced augmentation for the High than the Medium condition (Fig. 5). Since previous research has reported no significant change (e.g., Jodo and Inoue, 1990; Johnstone et al., 2010; Schapkin et al., 2007), this result is the first to suggest that increased task difficulty may be required to elicit training-related enhancements in the Nogo P3. Does this effect represent a strengthening of a top-down inhibition mechanism? We have previously shown that increased inhibition difficulty results in reduced Nogo P3 amplitudes (Benikos et al., 2013). An implication here is that P3 amplitude is inversely related to inhibitory load. On this basis, it could be suggested that conditions like practice which tend to reduce task difficulty result in increased Nogo P3 amplitudes (for a similar interpretation regarding memory load see Kok, 1997). Similarly, the training-induced increase in Nogo P3 for the Medium condition accompanied by enhanced Go/Nogo proficiency may be interpreted in this manner. Moreover, despite increased Nogo errors, the greatest Nogo P3 for the High condition may not completely rule-out a practice-based interpretation of this effect; given that Nogo errors plateaued by block 4 for this condition, while the Nogo P3 continued to increase until the conclusion of training. This suggests a continued adaptation to the difficulty of the task and is perhaps unsurprising, considering the brief (42 min) experience participants had with the training and its high difficulty level (for a similar fMRI finding see Kelly et al., 2006b). While it may also be argued that a larger Nogo P3 over the central regions could simply be due to greater monitoring of the inhibition outcome in order to limit the error rate (for a similar argument see Beste et al., 2010), this explanation is unlikely, given the location of this component over the pre-motor cortex and that central increases in the Nogo P3 have been suggested to reflect a motoric inhibition process unrelated to movement related potentials (Smith et al., 2007). Since previous training studies have reported that neural changes can precede behavioural changes (Atienza et al., 2002), and that training in higher-order executive functions can potentially transfer to untrained tasks (Dahlin et al., 2008), an avenue for future research would be to investigate whether training-induced enhancements in the Nogo P3 transfers to unpractised Go/Nogo stimuli. If larger Nogo P3s represent an enhancement in inhibitory control processes, this improvement would be expected to transfer to the untrained stimuli.

Finally, future studies could consider the influence of differences in IQ and potential learning capacity between training conditions. While previous research has generally reported no relationship between IQ and baseline inhibitory performance (Friedman et al., 2006), IQ is a potentially strong predictor of learning ability (Alloway and Alloway, 2010). Thus, it may be helpful for future research to include an index of IQ and potentially other individual differences which may potentially interact with training-related gains in inhibitory performance (e.g., impulsivity; Horn et al., 2003).

4.5. Conclusions

In summary, this study provides novel evidence for the differential effects of task difficulty on the training of inhibitory control. In

particular, the behavioural effects of short-term training appear to be optimised during conditions of moderate rather than low or high inhibitory load. An across-session increase in task-related arousal did not differ between conditions, indicating a generalised increase in demand for mental resources with time-on-task. Moreover, taken together the findings of the present study are of relevance to the theoretical accounts of the effect of training on inhibition-related neural activity. While changes associated with training have typically either been linked to the reinforcement of top-down executive control processes, or to the emergence of automatic bottom-up forms of inhibitory control, our results imply that these effects may be dependent on task demands. Whereas conditions of Low task difficulty may primarily lead to early bottom-up perceptual learning as reflected by enhancements in the centroparietal Nogo P2, top-down changes, particularly in the Nogo P3 appear to be associated with enhanced task difficulty. Although further research is needed in this area, these findings implicate the potentially key role of task difficulty for researchers attempting to design effective inhibition training paradigms to ameliorate inhibitory control deficits as seen in disorders such as ADHD.

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Appendix C – *SPSS Data output*

The data and statistical analyses for studies 1 to 4 are are contained on the attached CD-ROM. The statistical package SPSS was used for all analyses. Each of these folders contain "output" files, which contains the relevant statistical results for (a) the task performance, (b) self-report, (c) skin conductance and (d) ERP amplitudes and latency measures.

Note: CD-ROM not provided by author