Response Inhibition: Neural Correlates and the Impact of Ageing

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Statement of Sources

I declare that this report is my own original work and that contributions of others have been duly acknowledged.

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Acknowledgments

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List of Abbreviations

ΔRT: Delta RT (measure of proactive inhibition)

ADHD: Attention Deficit Hyperactivity Disorder

BH: Benjamini-Hochberg procedure

cTBS: continual Theta Burst Stimulation

DASS21: Short-form Depression, Anxiety and Stress Scale

DLPFC: Dorsolateral Pre-frontal Cortex

ECoG: Electrocortiography

EEG: Electroencephalogram

FDR: False-Discovery Rate

fMRI: functional Magnetic Resonance Imaging

fNIRS: functional Near Infrared Spectroscopy

HbO: Oxyhaemoglobin

HHb: Deoxyhaemoglobin

IFC: Inferior Frontal Cortex

IFG: Inferior Frontal Gyrus

IFJ: Inferior Frontal Junction

M1: Primary Motor Area

PFC: Pre-Frontal Cortex

ROI: Region of Interest

RT: Reaction Time

SMA: Supplementary Motor Area

sMMSE: Standardised Mini Mental State Examination

SSD: Stop-signal Delay

SSRT: Stop-signal Reaction Time

STAC: Scaffolding Theory of Ageing and Cognition

STN: Subthalamic Nucleus

tDCs: transcranial Direct Current Stimulation

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9209 Words

Abstract

The ability to stop a movement based on changing environmental stimuli is a crucial skill for functioning in the world. Two mechanisms are thought to be involved in stopping; top-down or *proactive* expectation of stopping, and bottom-up or *reactive* stopping to stimuli. A group of younger (n = 27) and older adults (n = 12) participated in a Stop-Signal Task to measure stopping ability while functional Near Infrared Spectroscopy (fNIRs) recorded haemodynamic changes in regions of interest of the Pre-Frontal Cortex (PFC). It was hypothesised that neural activity in dorsolateral PFC (DLPFC) would correlate with proactive stopping behaviour, and this was supported by the data. It was also hypothesised that the right inferior frontal cortex (IFC) and supplementary motor area (SMA) would correlate with stopping behaviour, but this was not shown in the data. Older people used more proactive slowing to maintain stopping ability comparable to younger adults. Older adults also exhibited bilateral hyperactivity in the DLPFC during stopping compared to younger adults. Together, these findings demonstrate that older adults engage different stopping strategies to younger adults. This work has implications for older adults in understanding falls and injuries, and demonstrates fNIRs can measure neural correlates of response inhibition.

The ability to stop quickly and adapt a movement in response to new sensory input is a critical skill for everyday life. Response inhibition is the ability to stop a volitional movement once it has been initiated (Aron, 2011). Impairments to response inhibition are implicated in the development of impulse control disorders such as attention deficit hyperactivity disorder (ADHD) (Morein-Zamir et al., 2008; Nigg, 2001), substance addiction (de Wit, 2009) and anxiety (Ansari & Derakshan, 2011; Basten et al., 2011). There is also evidence that the ability to stop a movement quickly reduces with age (Bloemendaal et al., 2016; Coxon et al., 2012; Van Gerven et al., 2016). Poor response inhibition has been identified as a potential risk factor of falls and serious accidents for older adults (Schoene et al., 2017), events which place extended strain on health-care sectors (Vos et al., 2007).

Previous research suggests that the pre-frontal cortex (PFC) plays a prominent role in response inhibition (Aron et al., 2007; Chikzoe et al., 2009; Stuphorn & Emeric, 2012; Zanderbelt & Vink, 2010; Zhang & Iwaki, 2019). The act of motor stopping is thought to be a 'dual-mechanisms' process involving both 'top-down' expectations and 'bottom-up' stimulus-driven responses (Braver, 2012; Meyer & Bucci, 2016). However, the neural correlates relevant to these two mechanisms are not well understood. It also remains unclear whether aged-related deficits in stopping behaviour are associated with changes in neural activation.

Proactive and Reactive Inhibition: Dual-Mechanisms of Control

The ability to stop a movement requires processing the stop cue from the environment, but the movement itself may be impacted by the level of expectation that a stop might be required. For example, driving a car involves both expectations about the likelihood of stopping (e.g. when driving towards a set of green traffic lights you may slow down if you expect the lights will change) and reactions to the stop cue (e.g. the lights do turn red).

The expected or 'top-down' processing of the likelihood of stopping is referred to as *proactive inhibition* (Aron, 2011; Manard et al., 2017). Whereas *reactive inhibition* refers to the unprepared, cue-elicited stopping response (Aron, 2011; Meyer & Bucci, 2016). The 'dual-mechanisms' model of stopping can be observed in an experimental context. These observations can be achieved both behaviourally with reaction time (RT) responses to precisely timed stimuli and in PFC regions of interest (ROIs) using neuroimaging techniques (Braver, 2012; Chikazoe et al., 2009).

The Stop Signal Task

Measuring proactive and reactive inhibition in a laboratory setting can achieved by participants performing the *Stop-Signal Task* (Chikazoe et al., 2009; Logan & Cowen, 1984; Logan et al., 1984). This paradigm is based on the assumptions of the 'independent horse-race model' of stopping (Logan & Cowen, 1984; Logan et al., 1984). The model describes a race between the independent 'go horse' (or Go-process) and 'stop horse' (or Stop-process). If the 'stop horse' wins the race the stop is successful (and the movement stops); however, if the 'go horse' wins then stopping isn't possible (and the movement is executed).

In the stop-signal task, participants respond as quickly as possible to a *Go* signal presented commonly as a choice between a left or right directional cue corresponding to either a left or right finger response (Logan & Cowan, 1984). On a small portion of these trials a *Stop* signal is presented indicating that participants are to withhold their response (Aron et al., 2011; Logan & Cowan, 1984; Matzke et al., 2018). The length of the delay between the presentation of the Go stimuli and the Stop signal is adjusted depending on the success or failure of prior stopping to estimate the stop signal delay (SSD) time that results in 50% stopping success. Longer SSDs elicit greater difficulty in stopping, as the go process is further along in the motor execution (Matzke et al., 2018; Verbruggen et al., 2019). This method is able to estimate the latent stopping ability. To achieve this estimate, the

independent horse-race model mathematically relates the overall probability of stopping, along with the mean SSD to estimate the Stop Signal Reaction Time (SSRT). The stop-signal paradigm can also yield measures of proactive inhibition via measurable differences in go-process RTs when stopping is or isn't expected (Verbruggen et al., 2019).

The Role of the PFC in Response Inhibition

The PFC contains regions thought to be crucial to response inhibition. Lateralisation of response inhibition to the right PFC has been found, with more right PFC blood oxygenation evident in tasks with stops than without (Boeker et al., 2007). Specific sub-regions of the PFC are thought to be involved to different degrees in proactive and reactive stopping according to theories of neural connectivity between cortical and subcortical networks.

Response inhibition in the IFC

Previous research with lesion studies (Aron et al., 2003 & 2004), functional MRI (Chikazoe et al., 2009) and Transcranial Direct Current Stimulation (tDCs) (van Belle et al., 2014) has further localised functions related to response inhibition to the inferior frontal cortex (IFC) of the PFC. Lesion and transcranial magnetic stimulation (TMS) studies have demonstrated that response inhibition is consistently dependent on an intact right IFC (Aron et al., 2003; Verbruggen et al., 2010). Indeed, individuals with left frontal cortex damage yield significantly faster SSRTs than those with right side lesions (Aron et al., 2003)

However, whether the right IFC is crucial for expecting to stop is not well understood (Chikazoe et al., 2009; Swann et al., 2013). Functional magnetic resonance imaging (fMRI) when coupled with a stop-signal task reveals that the right inferior frontal gyrus (IFG), a region within the right IFC, was engaged during reactive inhibition but not during stopping preparation (Chikazoe et al., 2009). It is also remains unclear whether the right IFC is a neural correlate of response inhibition behaviour, or more associated with task-relevant

attentional cues. For example, selective disruption using transcranial magnetic stimulation (TMS) to the inferior frontal junction (IFJ) (the dorsal region of the IFC) revealed alterations to attentional direction to stimuli (Verbruggen et al., 2010).

Inhibitory Connections Between the IFC and SMA

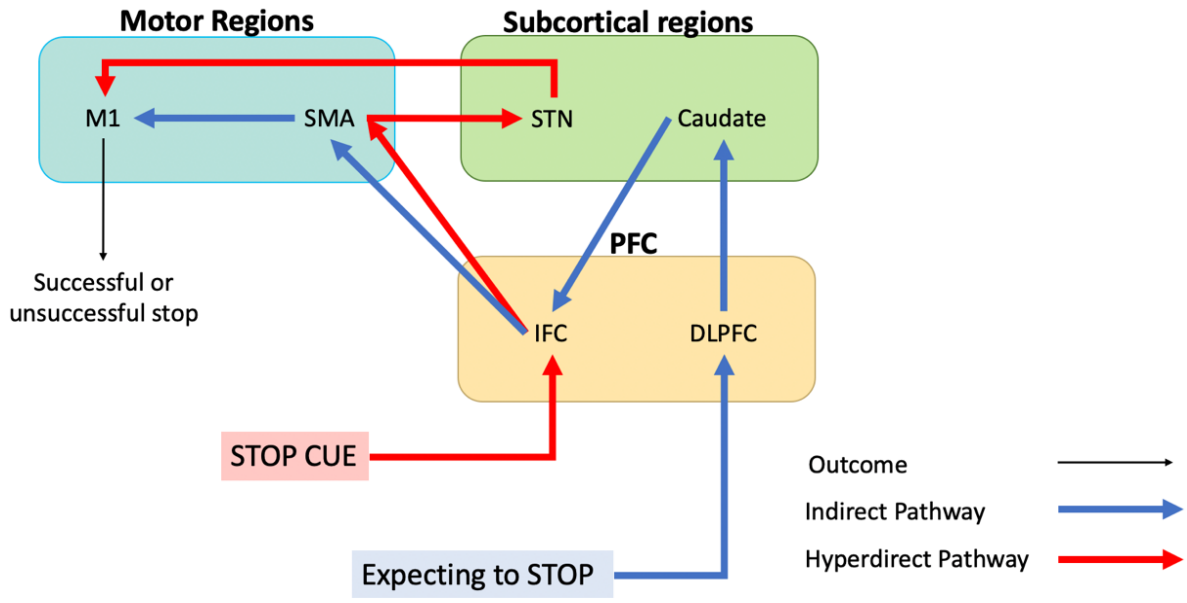
The supplementary motor area (SMA) and pre-SMA are located within the dorsal-medial cortex. The SMA is classically described as a 'negative motor area', whereby activation enacts arrest of behaviour (Aron, 2011; see Fried et al., 1991). The functional role of the SMA is thought to act as a signal relay between the PFC and subcortical regions to engage reactive inhibition (Obseso et al., 2016; Tabu et al., 2011; Zhang & Iwaki, 2019). Indeed, recent work from Obseso and colleagues (2016) using continual theta burst stimulation (cTBS) observed this functional network. By applying localised cTBS to the SMA shorter SSRTs were elicited as compared to placebo conditions (Obseso et al., 2016).

Connectivity and electrophysiology studies have supported this idea of a structural inhibitory network between the SMA and IFC (Swann et al., 2012; Aron et al., 2007). Diffusion imaging has indicated that white matter tracts connect the right IFC to the subthalamic nucleus (STN) via the SMA and terminating in the primary motor area (M1) (Aron et al., 2007; Johansen-Berg et al., 2004). Investigation of this network, referred to as the 'hyperdirect pathway' (Figure 1) occurred in a recent study employing fMRI and a stop-signal task (Zhang & Iwaki, 2019). Through Bayesian modelling it was revealed that during reactive inhibition, frontal-striatal connections from the IFG-SMA-STN-M1 were engaged (Zhang & Iwaki, 2019). In contrast, proactive inhibition engaged a longer 'indirect pathway' from DLPFC-caudate-IFC-SMA-M1 (Figure 1) (Zhang & Iwaki, 2019). This finding is consistent with evidence of the connectivity between the IFC and the SMA being involved in

both proactive and reactive inhibition (Chikazoe et al., 2009; Swann et al., 2013; Zhang & Iwaki, 2019).

Figure 1

Hyperdirect and Indirect Pathways



Note. Red arrows show the *hyperdirect* pathway, initiated during reactive inhibition in response to a surprising stimulus; IFC-SMA-STN-M1. The *indirect* pathway (blue arrows) follows a neural pathway theoretically engaged when stopping to a cue is anticipated; DLPFC-caudate-IFC-SMA-STN-M1. The sum of both neural pathways terminates in M1 as a successful or unsuccessful stop (black arrow).

Expectations to Stop in the DLPFC

Previous studies and reviews have demonstrated the DLPFC plays a crucial role in the maintenance of goals, planning and intentionally directing attention to environmental cues (Badre, 2008; Watanbe, 1990). These preparatory and 'top-down' functions are crucial to principles of proactive motor inhibition. The findings from Zhang & Iwaki (2019) support an

'indirect' network in which the DLPFC is involved when we stop to an anticipated cue. The distinct functions between the regions crucial to purely reactive inhibition and the DLPFC were also demonstrated previously using electrocortiography (ECoG) in a stop-signal paradigm (Swann et al., 2012). In conditions where there was a chance a stop cue may occur, the right DLPFC was active across all trials (demonstrating proactive stopping), whereas the ventrolateral prefrontal cortex (a region encompassing the IFC) activated only for the actual presentation of stop cues (reactive stopping) (Swann et al., 2012). A follow up ECoG and stop-signal study, revealed that increased activity was observed in the IFC during both expecting to stop and at the time of reactive stopping (Swann et al., 2013). Thus, the neural circuitry involved in stopping requires further study in order to form a consensus on whether separate reactive and proactive pathways are involved (Figure 1).

Age-related Modulations to Proactive and Reactive Inhibition

The ability to stop an initiated movement can be reduced in both normal ageing and contribute to increased risk of falls and injuries for older adults (Verghese et al., 2017). It may also be impaired in age-related disorders, such as mild-cognitive impairment and dementias (Wylie et al., 2007). How age affects stopping ability has been previously investigated, but prior work disagrees on whether age affects reactive and proactive stopping in the same way. Indeed, older adults exhibit slower RTs to go cues than that of young adults (Bedard et al., 2002; Bloemendaal et al.., 2016; Van Gerven et al., 2016), but this may reflect overall slower reaction time. In a large community sample, SSRT (reflecting stopping ability) deteriorates with age, whereas proactive inhibition did not change (Smittenaar et al., 2015).

However, alternate findings suggest proactive inhibition is relied on more with age to a greater extent than reactive inhibition (Manard et al., 2017; Bloemendaal et al., 2016). Older adults exhibit slower RTs to go cues when there is a chance a stop cue may appear (Manard et al., 2016; Williams et al., 1999). Evidence of extended reliance on proactive

inhibition may be due to older adults adopting a more cautious approach and being more focused on the anticipation of stopping in order to rapidly stop when required (Braver et al., 2005). This effect has also been demonstrated when there is an increased cognitive load (Bloemendaal et al., 2016). Investigating the associations between age-related behavioural changes and neural activity may provide clarity on these contradictory findings.

Scaffolding Theory of Ageing and Cognition (STAC)

Investigating the neural correlates of response inhibition may inform theories of neurocognitive ageing. The Scaffolding Theory of Ageing and Cognition (STAC), a prominent theory of neurocognitive ageing, (Park & Reuter-Lorenz, 2009; revised in Reuter-Lorenz & Park, 2014) states that older adults engage additional compensatory neural networks, compared to younger people, in order to maintain cognitive performance. There is evidence from inhibition studies in older people that greater neural activity in broader cortical regions occurs to compensate for stopping deficits due to substantial loss of white matter (Bedard et al., 2002; Coxon et al., 2012; Williams et al., 1999). Interindividual white matter connectivity between the right IFC, STN and SMA is predictive of SSRT in older adults (Coxon et al., 2012). This theory proposes that during response inhibition tasks older adults may show both increased activity and more bilateral activity in ROIs compared to younger adults. If this is the case, increased neural activity would be associated with better response inhibition within older adults. This theory suggests that increased activity compensates for age-related loses in cortical structure and is an adaptive process to maintain response inhibition.

Previous neuroimaging studies have supported the idea of 'compensatory scaffolding' in older adults when engaging response inhibition and motor control (Hsieh & Lin, 2017; Kleerekooper et al., 2016; Fernandaz-Ruiz et al., 2018; St George et al., 2021). Kleerekooper and colleagues (2016) fMRI analysis found hyperactivation in the right IFC in

older adults when expecting to stop (Kleerekooper et al., 2016). However, older adults did not engage in increased proactive inhibition strategies behaviourally (Kleerekooper et al., 2016). This may suggest the compensatory neural activity in the right IFC does not translate to strategic use of proactive stopping in older adults. Further, previous fMRI research has showed hypoactivation in the right IFC, pre-SMA and striatum during reactive inhibition in older individuals (Coxon et al., 2016). This complements a recent fMRI study that found that the right IFC activation decreases with age during a stop-signal task (Sebastian et al., 2013). Finding hypoactivity in the right IFC and SMA in relation to relative deficits in stopping ability in older adults, may instead be representative of less effective neural recruitment in these regions rather than compensation. In support of 'compensatory scaffolding', Coxon and colleagues (2016) found that greater activation was present in the DLPFC during go-trials. Greater activity in the DLPFC may reflect extended reliance on proactive inhibition as a compensatory strategy to maintain stopping in older adults.

Functional Near-Infrared Spectroscopy: Measuring Cortical Activity

Functional Near-Infrared spectroscopy (fNIRs) is a viable method of recording cortical activity during response inhibition and cognitive control tasks (Boecker et al., 2007; Noah et al., 2015). fNIRS is a brain imaging technique that detects changes to hemodynamic activity (Jasdzewski et al., 2003). FNIRs emits a non-invasive infrared light into the cortex via LED sources attached to a wearable cap (Morais et al., 2018). While most human biological tissue (e.g. bone and muscle) is transparent to this infrared light, oxyhemoglobin (HbO) and deoxyhaemoglobin (HHb) in blood are light absorbers within the 700-900nm range (Leon-Carrion & Leon-Dominguez, 2012). Nearby detectors reveal the amount of light absorbed and thus the oxygen consumption of the tissues between sources and detectors is representative of increased neural activity.

Notably, fNIRs is limited in depth of penetration compared to other fMRI which also measures haemodynamic changes. However, by investigating cortical activity in well-established ROIs, fNIRs is a useful tool as it has good spatial resolution compared to other imaging techniques (e.g. electroencephalogram; EEG). This considered, the wearability of fNIRs makes it more applicable for a wider range of inhibitory experimental paradigms (see Noah et al., 2015 for review). FNIRs has been previously applied in a stop signal task (Boecker et al., 2007), and applied in older populations during cognitive tasks (St George et al., 2021). However, applying fNIRs to investigate the neural correlates of proactive and reactive inhibition during a stop-signal task and as a function of age is a novel investigation.

Aims and Hypotheses

Aim 1: To investigate the neural correlates in the PFC of proactive and reactive inhibitory behaviour

The current study aimed to fill gaps in understanding of how proactive and reactive inhibitory behaviours correlate to neural activity in specific ROIs in the PFC. To our knowledge this had not been investigated by using fNIRs to measure neural correlates during a stop-signal task. Specific ROIs were the right IFC, DLPFC and areas of the SMA. Differential patterns of activation in these regions were expected based on evidence of proactive recruitment in parts of the 'indirect pathway' and 'hyperdirect pathway' for reactive control (Zhang & Iwaki, 2019). There is also evidence to show that shared activation of the right IFC and SMA occurs during proactive and reactive control (Chikazoe et al., 2009; Zhang & Iwaki, 2019).

Hypothesis 1a: It was hypothesised that *there would be greater neural activity in the DLPFC when proactive stopping processes were engaged.* That is, DLPFC activity would be higher for Go responses when there was a likelihood of a stop cue appearing (Go trials within

a Mixed block) compared to Go response when there was no likelihood of stopping (Go trials in the Go-only block).

Hypothesis 1b: It was also hypothesised that *increased activity would be observed in the right IFC and SMA for successful stopping trials compared to unsuccessful stopping trials.* These effects were expected across age groups.

Aim 2: To investigate behavioural and neural differences in proactive and reactive inhibition with age

There is conflicting evidence regarding how age affects proactive and reactive inhibition. Indeed, there is reason to expect deficits in behavioural measures of both reactive and proactive inhibition (Bloemendaal et al., 2016; Smittenaar et al., 2015; Van Gerven et al., 2016). There is evidence that older adults rely on more proactive control, in order to maintain stopping ability (Manard et al., 2016).

Hypothesis 2a: It was therefore hypothesised that compared to younger participants, *older participants would have deficits in stopping ability and also greater slowing in reaction times when there is an expectation of stopping (proactive). We expected these effects to be particularly evident for proactive slowing of go responses in anticipation of stopping, suggesting a more cautious strategy in older people.*

The current study also sought to investigate the function of the PFC with age during proactive and reactive control. The STAC (Reuter-Lorenz & Park, 2014) predicts older adults may compensate for age-related deficits in response inhibition with greater bilateral activity and hyperactivation activation in ROIs (Braver et al., 2009; Van Gerven et al., 2016). Coxon and colleagues (2016) observed this effect in the DLPFC. This may be a result of the DLPFC being a distinctive neural correlate of proactive inhibition, and representative of compensatory proactive deficits compared to relative deficits to actual stopping ability in older adults (Van Gerven et al., 2016).

Hypothesis 2b: It was therefore hypothesised that *hyperactivity and/or bilateral activation of the DLPFC would be observed with age and be correlated with behavioural proactive inhibition. This effect of age was expected to produce hypoactivity in the IFC and SMA during stopping, as explained by less effective recruitment of these regions in older adults to stop, rather than a compensatory activity.*

Method

Participants

Two age cohorts of participants were tested at the University of Tasmania Psychology Research Centre. The young group ranged from 19-43 years of age (n = 25, M_{age} = 28.9, SD = 6.9) and were recruited using SONA (a participant recruiting software at the University of Tasmania) and friends of the researchers. The second group of healthy older participants were aged between 60-76 years of age (n = 12, M_{age} = 70.4, SD = 4.8) and recruited via an existing participant database within the Sensorimotor Neuroscience and Ageing Lab.

Participation was entirely voluntary, and participants were free to withdraw at any time. Informed consent was obtained prior to participation. As renumeration, participants entered a draw for one of three $100.00 Coles-Myer Gift Cards. This study was approved by the Tasmanian Health and Medical Human Research Ethics Committee (reference number: H0014865) and was conducted in accordance with the principles stated in the Declaration of Helsinki.

Participants were excluded if they had a diagnosed neurological disorder, experienced pain during standing or walking, had a history of brain injury, metal implants (outside of the mouth), or a history of medical related fainting (Appendix A). General medical information was also noted (Appendix A). Information pertaining to balance and lower body pain were recorded as testing for a related was study was gathered alongside the present study (Healey,

n.d). Participants also had normal or corrected to normal vision. Age and gender were recorded.

Questionnaire Assessment

To screen for dementia, the standardised Mini Mental State Examination (sMMSE) (Molloy & Standish, 1997) was administered to the older group (Appendix B). Given anxiety during the task may have impacted cortical bloodflow (Hasler et al., 2007), participants filled out a brief questionnaire at the completion of the experiment (Appendix C). This questionnaire consisted of seven questions that were adapted from the short-form Depression Anxiety and Stress Scale (DASS21) (Henry & Crawford, 2005), which reliability measures stress and anxiety. The anxiety questionnaire consisted of seven items on a 4-point Likert scale ranging from 0 (Did not apply to me at all) to 3 (Applied to me very much, or most of the time). The score was totalled by multiplying the summed score by two for each question (with Q5 reverse scored), as per the scoring method for the DASS21 (Henry & Crawford, 2005).

Apparatus

FNIRS

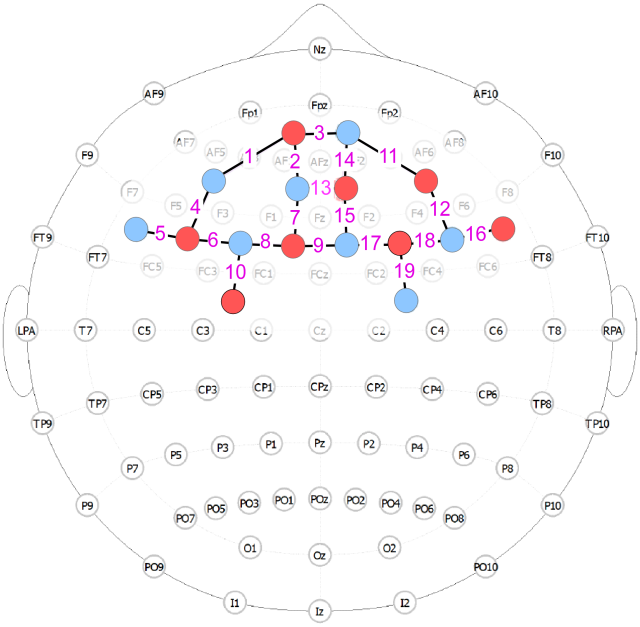
Cortical bloodflow was recorded using a Nirsport device and a custom montage (Figure 2) to record from the ROIs. This custom montage was generated using the Matlab package: fNIRs Optode Location Decider (fOLD) and NirSite software. The brain atlases that informed the placement of the optodes were from Morais and colleagues (2018). The assignment of adjacent sources and detectors was based on a 10-5 EEG system in order to fit ROIs in the PFC (Figure 2). The fNIRs cap is a made of flexible neoprene, in which is embedded the 8 sources of LED light (of two wavelengths 760nm & 850nm) and 8 corresponding detectors. Hemodynamic data was sampled at 7.8125Hz from the bilateral IFC (Juelich atlas), bilateral DLPFC (Brodmann areas 9 and 46) and the bilateral SMA

(Brodmann area 6) (Morais et al., 2018). The distance between the sources and detectors was 3cm. This inter-optode spacing is considered optimal for accurate spatial resolution of the cortex as recording brain tissue at 2cm may produce overly sensitive data, and at 4cm and above sensitivity is decreased (Strangman et al., 2013).

Figure 2

FNIRs Custom Montage

DLPFC left: 1, 2, 6, 7, 8,10
DLPFC right: 11, 14, 15,17, 18,19
IFC left: 4, 5
IFC right: 12, 16
SMA left: 6, 8,10
SMA right: 17,18,19



Note. FNIRs Sources in red, detectors in blue. Inter-optode space (pink) shows corresponding channels used to inform spatial location of ROIs relative to 10-5 EEG layout.

Procedure

Participants were tested individually. The experimental protocol was described to participants via age-relevant information sheets (Appendix D & E). Participants had the opportunity to ask the researcher any questions before informed consent was obtained (Appendix F). The general medical screening questionnaire (Appendix A) was then administered to ensure participants met the inclusion criteria. The group of younger adults

completed the experiment in one session over 2.5 hours. Pilot testing demonstrated that two separate sessions would reduce the effect of fatigue in the older population[1]. The older adult cohort also completed the sMMSE prior to the experimental procedure.

FNIRs Procedure

The experimental setup is depicted in Figure 3. Participants used disinfectant wipes (70% alcohol) on hair and jaw lines. COVID-19 safe guidelines that adhered to the College of Health and Medicine's Risk Assessment Procedures (Appendix G) were followed. As per these guidelines, this included temperature screening of participants and cleaning touch surfaces and equipment between sessions. Participants' nasion to inion (sagittal plane) length and nasion to inion head circumference were recorded. These measurements allowed alignment between the optodes on the fNIRS cap and mean neuroanatomical locations. The fNIRs cap was placed on the participants' head while they were seated and once in the correct alignment, secured in place with the chin strap.

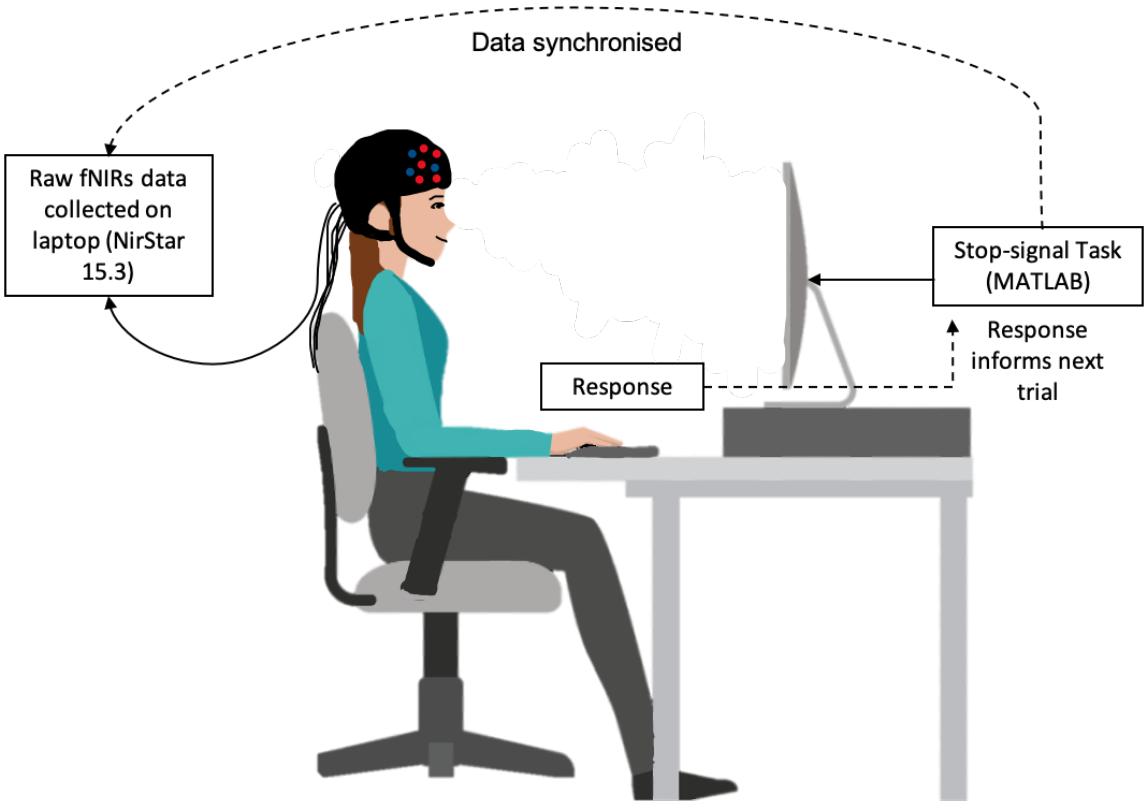
An initial calibration of the optodes was performed using NirStar (15.3) fNIRS recording software, to determine the level of noise on each channel. Occasionally, moving participants' hair using a cue tip was required to improve scalp contact. If further adjustments were required the system was recalibrated. A black shower cap was worn over the fNIRs cap to block ambient light interfering with the infrared recording (Baker et al., 2017). The NIRSport system was connected to a laboratory laptop via a USB cable running NirStar. After the cap was removed optodes were disinfected with the 70% alcohol wipes as per

[1] This project fulfilled a component of broader research at the University of Tasmania from Healey (n.d) applying the same experimental paradigm adapted for the lower body (stepping and foot tap conditions). Due to the longer testing time required for this research, testing for the present study was completed within one session for younger adults (2.5 hrs), and two sessions for older adults (2 X 1.5hrs). Conditions were counterbalanced to limit practice and fatigue effects (Appendix H)

guidelines from NIRx (2017**).**

Figure 3

The Experimental Procedure showing FNIRs recording during The Stop-Signal Task



Note. Success or failure to stop when a stop cue is presented adjusts the stop signal delay in the next stop trial. Trial data is synchronised via a digital trigger from the SST (run in MATLAB) to the fNIRs data collected using NirStar software (15.3).

Stop-Signal Task

Participants sat 60cm from an Intel HD Graphics 4600 monitor (1920 X 1080 res) running the stop-signal task (Figure 4). The stop-signal task was adapted from the STOP-IT2 freely available code written in MATLAB (Verbruggen, 2019). Reponses were recorded via finger-taps on a QWERTY keyboard. Participants were instructed to respond as quickly as they could to the 'Go' cue. A white arrow represented the 'Go' cue, and the arrow's direction indicated whether a left (F Key for left pointing arrow) or right (J Key for right pointing

arrow) button press was required. The 'Stop' cue was when the arrow changed from white to blue. If the arrow changed to blue, participants attempted to cancel the response.

Before each trial 'Get Ready' was displayed on the screen for 3000ms, this was followed by a fixation dot presented in the centre of the screen. The fixation cue varied in duration between 500ms and 1000ms with an exponential distribution to reduce response anticipation. Feedback on the response was presented for 1000 ms at the end of each trial; either 'correct (with the reaction time)', 'incorrect' (if the wrong button was pressed), 'do not respond' (if a response was made on a stop trial), or 'too slow' (if the response to Go trial did not occur within 800ms). RT was recorded for all trials when a response was made. Therefore, the time between the Go cues of each trial were at least 5000 ms, which previous research has shown is sufficient for fNIRS traces to show event-related responses (Schroeter et al., 2004).

The delay between 'Go' and 'Stop' signals was adjusted with a dynamic 'staircase' to approach a 50/50 probability of a successful stop across trials ($P_{respond|stop}$). If a participant's stop was successful, the SSD on the next stop trial increased by 50ms. If a participant failed to stop, the SSD was reduced by 50ms for the next stop trial. The initial SSD was 200ms.

This overall probability of stopping, along with the mean SSD were used to estimate the latent stopping ability (the stop signal reaction time or SSRT) of each participant, using the integration approach (Matzke et al., 2016) according to Equation 1 below:

$$SSRT = nth_{RT} - \overline{SSD} \qquad (1)$$

Where nth_{RT} is calculated as the number of RTs multiplied by $P_{respond|stop}$.

In order to estimate the involvement of proactive stopping, the difference between the mean reaction time to respond to the 'Go' cues when there was no chance of stopping (Go

trials in Go-only block) was subtracted from the mean reaction time to respond to 'Go' cues when there was some expectation of stopping (Go trials in Mixed block) (Equation 2)

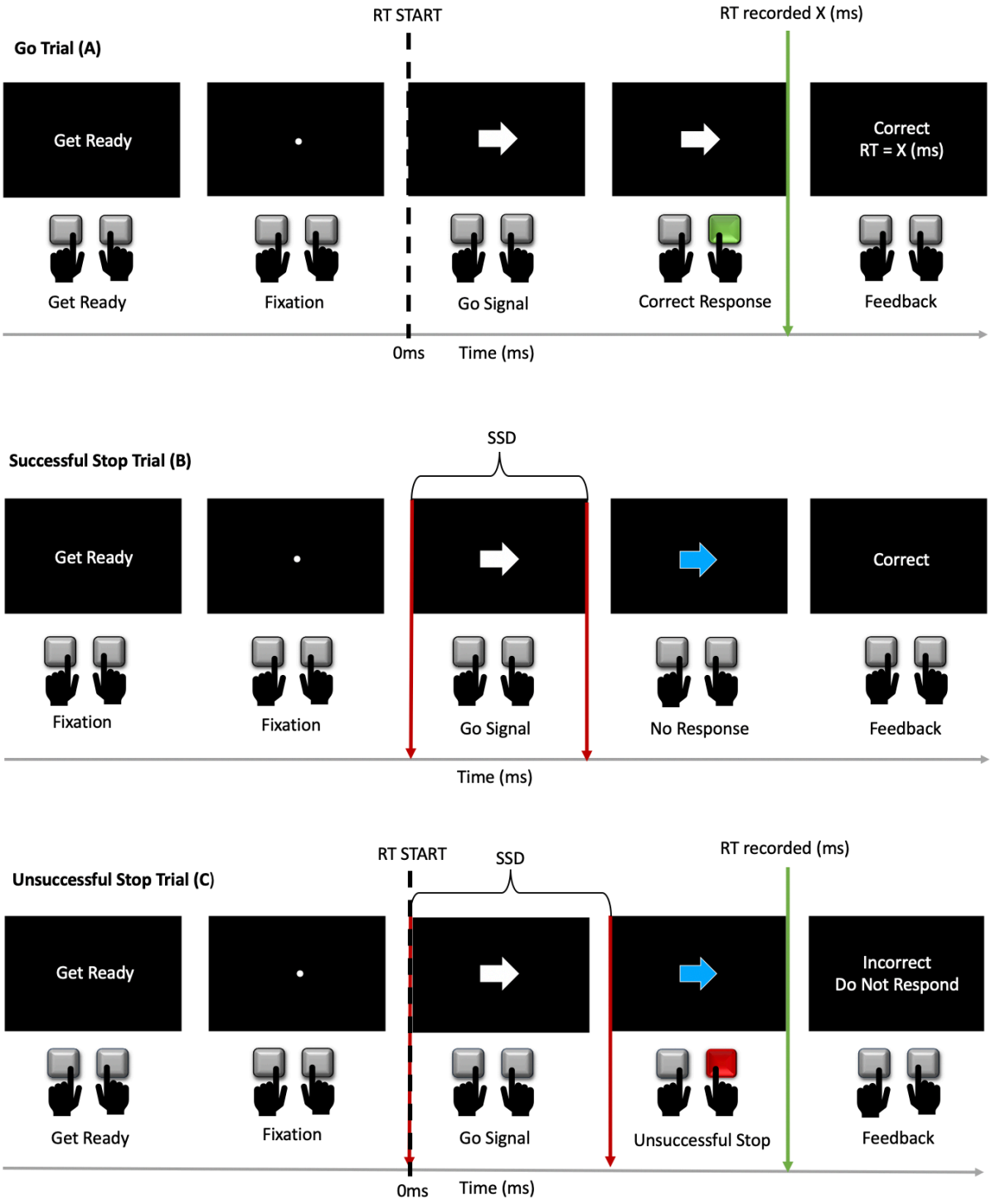
$$\Delta\mathrm{RT} = \frac{1}{n}\sum_{i=1}^{n} x_i - \frac{1}{m}\sum_{j=1}^{m} y_j \qquad (2)$$

Where *n* is the number of go trials in the Mixed block *x* with response *i*, and *m* is the number of trials in the Go-only block *y* with response *j*.

'Go-only' blocks of 30 trials (plus 8 practice trials) were always the first block presented in order to measure responses and fNIRS signals before there was any notion or expectation of having to stop (Verbruggen, et al., 2019). In the 'Mixed' block, a stop cue was presented after the go cue on 25% of trials (20 out of 80 trials). There were 3 'Mixed' blocks for a total of 240 'Mixed' trials, including 60 stop trials which is sufficient for accurate estimate of SSRT (Verbruggen et al., 2019). The total number of all trials was 270 (excluding 8 practice trials given before each new block type). The fNIRs cap was worn during the Go-only block and the first Mixed block as pilot testing revealed wearing the cap for up to an hour induced discomfort which may have impacted behavioural performance and fNIRS responses.

Figure 3

Stop-Signal Task; Response Types and Timeline



Note. (A) Go trial; correct go response. (B) Successful stop trial; withheld response. (C) Unsuccessful stop trial; response on stop trial. Staircased SSD; SSD increases by 50ms on the next stop trial after a successful stop and decreases on the next stop trial after an unsuccessful stop.

Data Acquisition and Processing

FNIRS

Raw fNIRS signals were processed using a specialized fNIRS toolbox in MATLAB (HOMER3) to isolate haemodynamic responses associated with neural activity from other sources (physiological, movement artefacts, electrical noise). The pipeline for artefact detection, removal and filtering and conversion to oxy- and deoxy- haemogloblin changes is presented in Appendix I.

Given the greater signal to noise ration of the HbO to HHb concentration signal, HbO concentration was used in the statistical analysis (St George, 2021). The mean HbO changes for the left and right ROIs were calculated using the channel groupings shown in Figure 2. The change in HbO concentration in the ROIs was calculated between the time point when the 'Go' cue was presented and 3.5 seconds later – to allow for the haemodynamic delay associated with the neural events to be reflected in the HbO concentration.

Design and Statistical Analysis

To investigate Hypothesis 1, correlational analyses were conducted between neural activity (HbO) in the six ROIs and behavioural measures of response inhibition. For Hypothesis 2a, independent samples t-tests compared the effect of Age Group on both SSRT (stopping ability) and ΔRT (proactive expectation of stopping). Hypothesis 2b was addressed with independent t-tests to assess age effects on neural activity during stopping and expecting to stop on bilateral ROIs. All analyses were conducted using Jamovi (Version 1.6).

The two groups had unequal sample sizes and a Levene's test for SSRT between groups indicated unequal variances ($p = .015$), (full test results in Appendix J). The assumption of normality was violated across neural and behavioural measures of response inhibition between age groups. This was revealed with low p-values on Shapiro-Wilk testing (Appendix J) and upon inspection of Q-Q residual plots for behavioural and neural measures

between groups. Based on these data assumption checks, non-parametric analyses were selected with independent group analyses (Welch's *t*) and correlations (Spearman's *r*). Between groups effect sizes were interpreted as per Cohen's *d* cut-offs; *d* = .2, (small) *d* = .5 (moderate), *d* >.8 (large). Correlational effect sizes were interpreted as; *r* = .01 (small), *r* = .3 (moderate), *r* >.5 (large). Means and standard deviations for behavioural RT are reported in milliseconds (ms). Neural activity means and standard deviations as measured by HbO concentration are reported in mircomoles (μmol).

The probability of responding to a stop signal p(respond|signal) (i.e. overall response rate to the stop-cue) for participants ranged between 40% and 66.7% (*N* = 37), with a mean probability of successful stop was 49% (*SD* = 0.06). The accepted p(respond|signal) range for reliable estimation of SSRT is between 25– 75% for an individual participant (Verbruggen et al., 2019). Reliable estimation of SSRT according to the horse-race model also assumes there is independence between the stop and go process, whereby RTs to stop cues (unsuccessful stop) should be shorter than GoRTs in Mixed blocks. This assumption was violated by three participants. It is recommended that participants are removed from the dataset when this assumption is not upheld (Matzke et al., 2016). Statistical analyses were run both with the three participants included and excluded and results pertaining to fNIRs and behavioural data yielded the same statistical outcomes for significance. Excluding the participants from analysis was considered too conservative to answer the correlational hypotheses between behaviour and neural activity.

Multiple Comparisons

Given the multiple dependent variables and multiple analyses, the false discovery rate (FDR)-correction was applied to all t-tests and correlations using the Benjamini-Hochberg procedure (BH) (Benjamini & Hochberg, 1995). This is justified given the highly hypotheses driven nature of the study rather than data driven (i.e. where null hypotheses are frequently

true). Therefore, using conservative Bonferroni or false positive rate corrections would increase the risk of Type II errors and do not accurately reflect the priori selection of specific ROIs. The BH procedure is viewed as an alternative for health studies to limit the consequences of not providing p-value corrections or applying too cautious significance adjustments (see Glickman et al., 2014). The BH critical value for significance was (p <.040) with a chosen FDR of .15, and calculations are provided in Appendix K.

Results

Descriptive Statistics

Demographic information was collected from all participants and shown in Table 1. Total *N* participants and group *n* are shown in Table 1. The older adult group completed the sMMSE questionnaire and total scores were recorded. The mean total score on the sMMSE was 29.5 (*SD* = 0.67). This questionnaire was not considered a covariate due to it being applied as an exclusion criterion to the older group rather than as a predictor for neural measures. All participants completed the experiment, although fNIRS measurements could not be obtained from one participant in the older group due to cap misfit.

Table 1

Means, Standard Deviations, Age Range and Gender of Young and Old Groups Demographic Scores

		Gender		Age (years)		Age Range	
Group	*n*	*Female*	*Male*	*M*	*SD*	*Min*	*Max*
Young	25	12	13	28.9	6.9	19	43
Old	12	6	6	70.4	4.8	60	76
Total	37	18	19	42.4	20.6	19	76

Hypothesis 1a & b: Neural Correlates of Inhibitory Behaviour

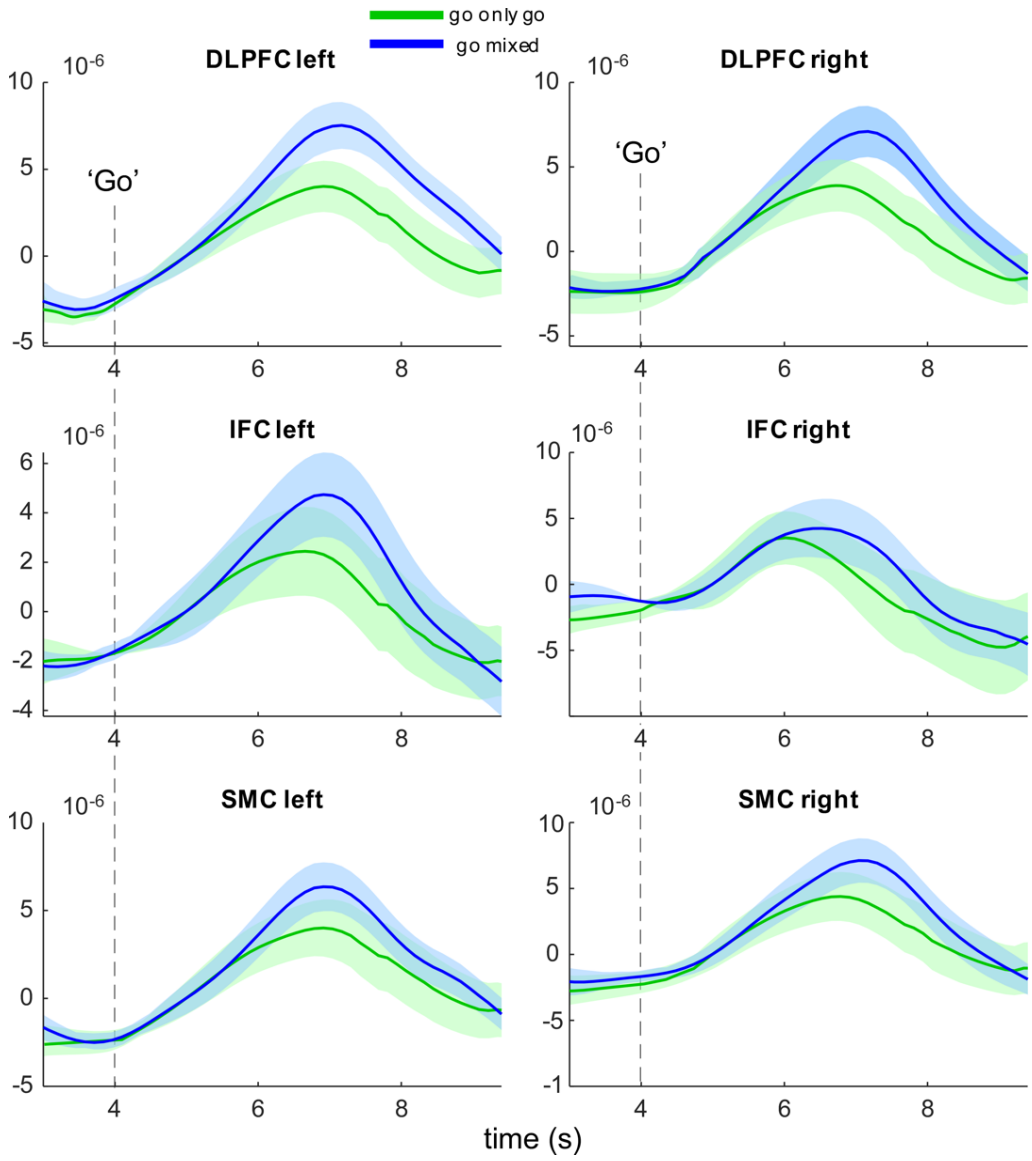
Timeseries concentration changes in HbO across the six ROIs for go responses in the Go-only and Go-Mixed are presented in Figure 5. The difference between these neural responses reflects proactive inhibition. It is observed in Figure 5 that neural activity appears higher in both the left and right DLPFC for Go-Mixed than Go-only blocks following a 3-4 second delay from the go cue. This 3-4 second time scale reflects the haemodynamic delay of neural events happening shortly after the go cue. Figure 6 shows the mean HbO concentration changes in the six ROIs when there was a stop cue. As can be observed in the figure, activity in the right IFC tended to be higher when participants were able to successfully inhibit the response compared to when there was a failure to inhibit the response.

Mean differences in neural activity for successful versus unsuccessful stopping in each of the regions of interest are presented in Table 2. Also presented are the mean differences in neural activity for going when there was an expectation that a stop might be required versus going when a stop was not expected (Proactive Inhibition). Across age groups the total SSRT value was 227.0ms, (*SD* = 30.7), and for ΔRT the total mean was 80.07ms, (*SD* = 84.9). Means and standard deviations for each region of interest, separated by group are also shown in Table 2.

Correlational analyses were conducted between neural activity and behavioural measures of response inhibition (SSRT and ΔRT) (Table 3). A small positive correlation was identified between activity in the right DLPFC and proactive inhibition behaviour (ΔRT) with statistical significance (p = .027), (Table 3). Activity in the right IFC was not significantly associated with successful versus unsuccessful stopping (p = .405) (Table 3). No other significant relationships between any other ROI and stopping behaviours were identified. The correlational analysis did identify a moderate negative relationship (Table 3) between ΔRT and SSRT, which was statistically significant (p = .006) (depicted in Figure 7).

Figure 5

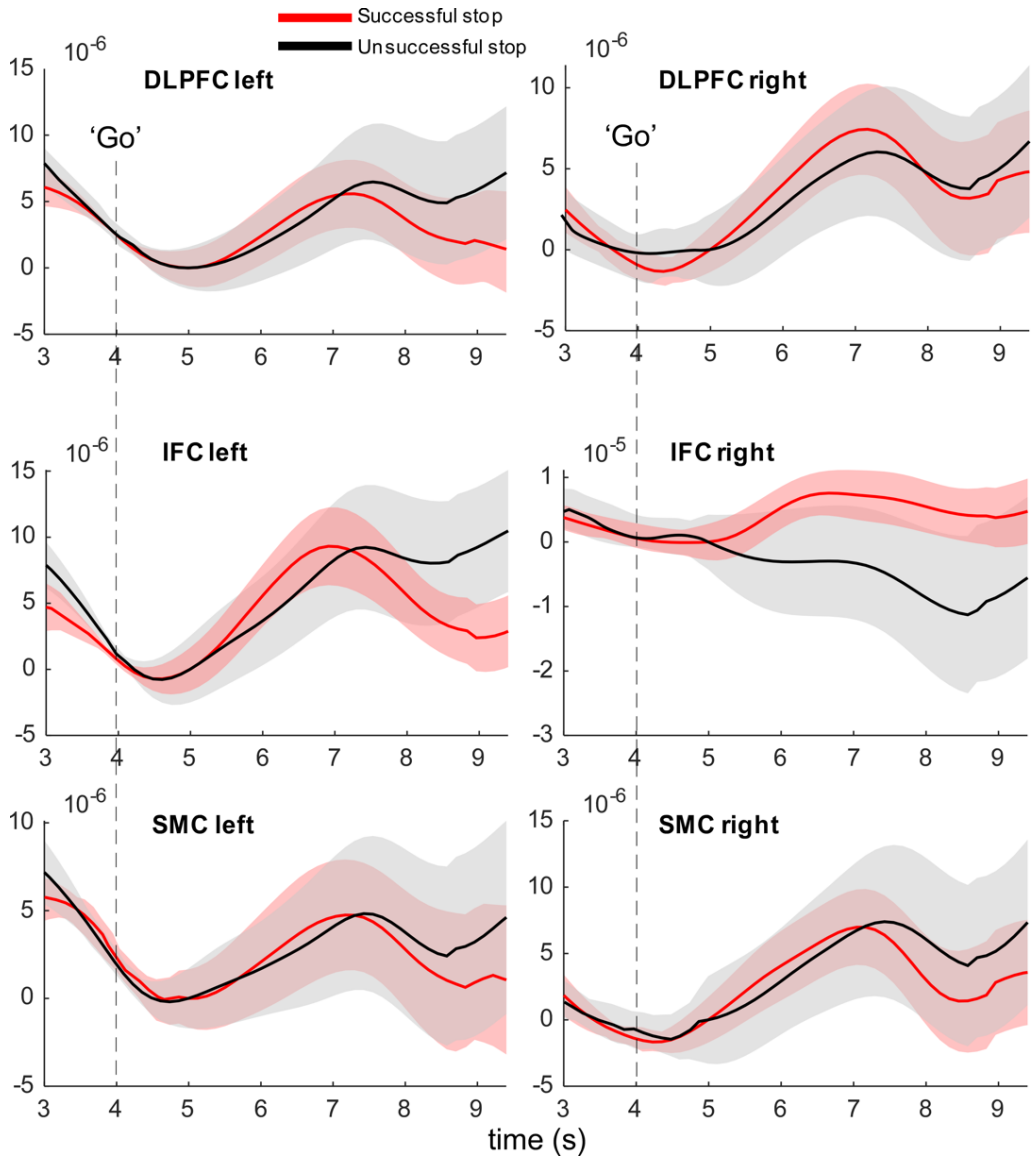
Mean Concentration Changes in HbO in ROIs for Go Responses in the Go-Only and Go-Mixed Trials



Note. Event-related HbO concentration changes across all participants in the ROIs. The green trace shows the mean response when responding to the 'Go' cue in the Go-only block, whereas the blue trace is the mean response when responding to a 'Go' cue in the Mixed block. Shaded regions show the standard error of the mean.

Figure 6

Mean Concentrations Changes in HbO in ROIs during Successful compared to Unsuccessful Stopping



Note. Event-related HbO concentration changes across all participants in the ROIs. The red trace shows the mean response when the response to the 'Go' cue is successfully inhibited when a stop cue appears (~200ms after the 'Go' cue). The black trace is the mean response when a response in unsuccessfully inhibited. Shaded regions show the standard error of the mean.

Table 2

Neural Activity Difference for Successful versus Unsuccessful Stops & Proactive Slowing With, versus Without, an Expectation of Stopping

Group	Young Adults $n = 25$		Older Adults $n = 11$		Total $N = 36$	
Successful-Unsuccessful Stop	*M*	*SD*	*M*	*SD*	*M*	*SD*
DLPFC Left	-6.92	24.98	15.06	17.30	-0.20	24.88
DLPFC Right	-4.08	20.95	14.09	21.36	1.47	22.44
IFC Left[a]	-4.73	18.63	10.57	23.52	0.22	21.26
IFC Right	8.32	41.89	16.40	26.09	10.79	37.58
SMA Left	-5.26	28.06	12.78	18.73	0.25	26.67
SMA Right	-4.50	22.90	9.95	19.44	-0.09	22.66
Proactive Inhibition	*M*	*SD*	*M*	*SD*	*M*	*SD*
DLPFC Left	2.13	9.80	7.24	11.61	3.69	10.49
DLPFC Right	2.48	8.42	6.60	12.48	3.74	9.84
IFC Left[a]	0.52	10.50	7.23	15.56	2.69	12.53
IFC Right[b]	1.68	13.01	5.35	14.58	2.84	13.41
SMA Left	0.76	11.76	6.05	11.70	2.37	11.84
SMA Right	2.36	8.98	5.10	10.55	3.20	9.42

Note. Neural activity measured in μmol of HbO

[a] n = 23 for regions, individual channels lost during analysis

[b] n = 24 for region, individual channels lost during analysis

Table 3

Correlation Matrix Behavioural Measures of Stopping and Neural Activity

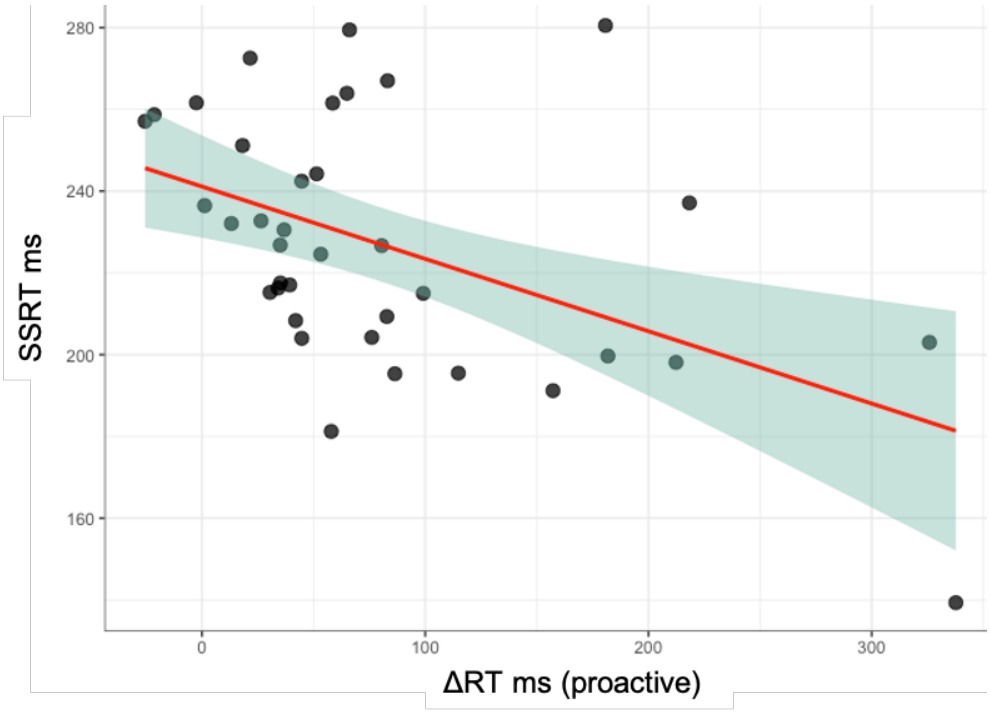
Variable			SSRT	ΔRT
		N [a]	*r*	*r*
	SSRT	37	-	
	ΔRT	37	-.44**	-
Successful-Unsuccessful Stop				
	DLPFC Left	36	.03	.08
	DLPFC Right	36	.04	.05
	IFC Left	34	.07	-.07
	IFC Right	36	-.14	.20
	SMA Left	36	.02	.07
	SMA Right	36	.02	.07
Proactive				
	DLPFC Left	36	-.05	.21
	DLPFC Right	36	-.08	.37*
	IFC Left	34	-.12	.22
	IFC Right	35	-.10	.25
	SMA Left	36	-.14	.28
	SMA Right	36	-.05	.32

Note. Test statistic; Spearman's *r* correlation.* p <. 04 (BH critical value correction), **p <.01,

[a]*N* varies due to fNIRs channel loss in analysis.

Figure 7

Correlation between Stopping Ability (SSRT) and Proactive Inhibition (ΔRT)



Note. Dots show individual participant means. Red line represents correlation between SSRT and ΔRT (see Table 3; *Correlation Matrix*). Green shading represents strength of correlation.

Hypothesis 2a: Age Effects on Stopping Ability

Older adults used more proactive inhibition (ΔRT) (M = 129.8ms, SD = 84.1) than younger participants (M = 56.2ms, SD = 75.8), which was significant and at a large effect, $t(16.57) = -2.57$, $p = .018$, $d = -0.92$. The older age group had slower mean SSRTs (M = 230.3ms, SD =38.9) than the younger age group (M = 225.3ms, SD = 27.1). However, there was no significant difference in SSRT with age, $t(16.57) = -0.41$, $p = .687$, $d = 0.15$.

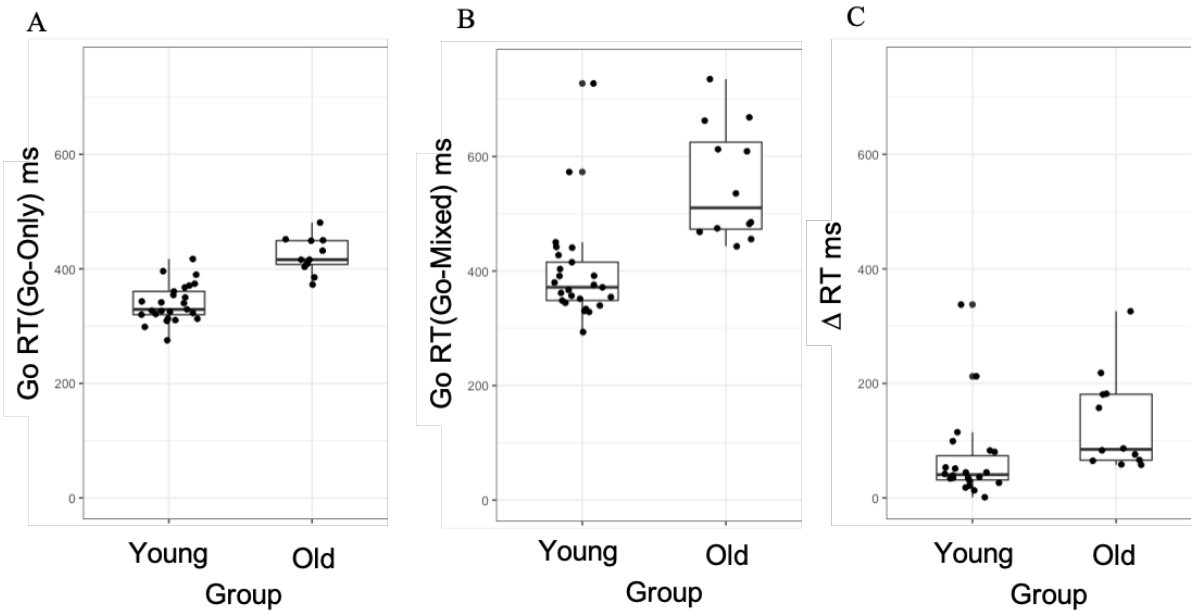
Figure 8 shows individual participant means, and medians for young and old groups for GoRTs on Go-Only trials, and on Mixed trials (trials where there was some expectation of stopping). By group, older adults had slower GoRTs on Go-Only trials and Mixed trials

(Figure 8A & B). Figure 8C shows individual participant means, and age group medians for ΔRT as calculated by mean GoRT on Go-Only Trials subtracted by mean GoRT on Mixed Trials (Equation 2)

Figure 9 shows individual participant means, and medians for young and old groups for SSD and SSRT. By group, older adults had longer SSDs than the younger group (Figure 9A). Mean SSDs informed calculations (Equation 1) of stopping ability as measured by SSRT (Figure 9B).

Figure 8

Boxplots of Individual Means and Group Medians for GoRT (Go-Only), GoRT (Go-Mixed) and ΔRT between Young and Old Groups

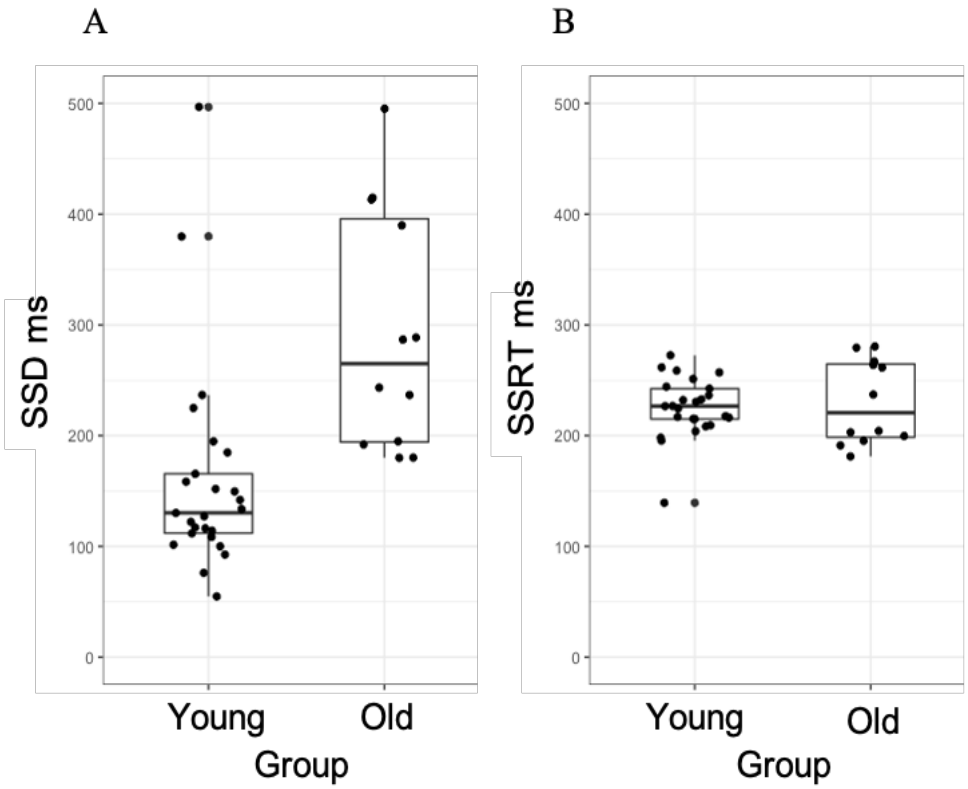


Note. Measures of stopping expectation; (A) Mean GoRTs on Go-Only Trials for individuals in Young and Old groups; (B) Mean GoRT on Mixed Trials for individuals in Young and Old groups; (C) Mean ΔRT for individuals in Young and Old groups as a measure of proactive inhibition calculated by mean GoRT on Go-Only Trials subtracted by mean GoRT on Mixed Trials.

Dots represent individual participant means. The ends of each box represent the first (lower, Q1) and third (upper, Q3) quartiles. The median is represented by the dividing line within the interquartile range (IQR). The whisker lines range between Q3+1.5xIQR to Q1-1.5xIQR. Dots outside of whisker lines are potential outliers.

Figure 9

Boxplots of Individual Means and Group Medians for SSD and SSRT between Young and Old Groups



Note. Measures used to estimate stopping ability (A) Mean SSDs (delay between Go and Stop cue) for individuals in Young and Old groups; (B) Mean SSRTs as an estimate of latent stopping ability for individuals in Young and Old Groups. The ends of each box represent the first (lower, Q1) and third (upper, Q3) quartiles. The median is represented by the dividing line within the interquartile range (IQR). The whisker lines range between Q3+1.5xIQR to Q1-1.5xIQR. Dots outside of whisker lines are potential outliers.

Hypothesis 2b: Age effects on Neural Correlates of Inhibition

Older adults had greater mean HbO (μmol) in all ROIs during both successful compared to unsuccessful stopping (SSRT) than younger adults (Table 2). Independent

samples t-tests were conducted to assess whether these differences were significant between age groups for each ROI. The t-tests indicated that increased HbO activity in the older group between successful and unsuccessful stopping was not significant in the left IFC, $t(16.24) = -0.70$, $p = .076$, $d = -0.72$, nor the right IFC, $t(29.66) = -0.70$, $p = .488$, $d = -0.23$. The analyses also revealed that older adults had significantly more HbO activity during successful compared to unsuccessful stopping than younger adults in the left DLPFC, $t(27.22) = -3.04$, $p = .005$, $d = -1.02$, and in the right DLPFC, $t(18.85) = -2.37$, $p = .029$, $d = -0.86$ at large effect sizes. Compared to younger adults, older adults had significantly more HbO activity when comparing successful stopping to unsuccessful stops in the left SMA with a moderate effect, $t(28.09) = -2.27$, $p = .031$, $d = -0.76$. This effect was not significant in the right SMA, $t(22.46) = -1.94$, $p = .065$, $d = -0.68$.

The older adult group also showed increased mean HbO activity in all ROIs in engaging proactive inhibition (ΔRT) compared to the young adult group (Table 2). This effect was not significant in any bilateral ROIs: left DLPFC; $t(16.57) = -1.27$, $p = .220$, $d = -.48$, right DLPFC; $t(14.17) = -1.00$, $p = .335$, $d = -0.39$, left IFC; $t(14.52) = -1.30$, $p = .215$, $d = -0.51$, right IFC; $t(17.60) = -0.71$, $p = .484$, $d = -0.27$), left SMA; $t(19.28) = -1.25$, $p = .227$, $d = -0.45$, and right SMA; $t(16.69) = -0.75$, $p = .463$, $d = -0.28$.

Covariates

Level of anxiety has been previously identified as a covariate in PFC activity (Hasler et al., 2007). The anxiety questionnaire was completed by 36 of the total 37 participants. The mean anxiety score was 5.5, ($SD = 5.27$) out of a total score of 42, which is within the normal range according to DASS21 severity cut-offs (Henry & Crawford, 2005). The scores ranged between 0 (normal) to 26 (extremely severe). Total anxiety score was positively associated with increased proactive inhibition HbO activity in the left DLPFC ($r = .37$, $p = .027$) at a small effect. Small positive associations were also found between total anxiety score in the

right DLPFC (r = .34, p =.045) and left SMA (r = .35, p = .041), however, did not remain significant after BH corrections at a p <.04 threshold. Total anxiety score was not significantly associated with proactive inhibitory HbO activity in the left IFC, (r = .29, p = .107), right IFC (r = .26, p = .078) nor right SMA, (r = .30, p = .078).

Total anxiety was not significantly correlated with any ROI during stopping: left DLPFC; (r = -.02, p = .843), right DLPFC; (r = -.03, p = .843), left IFC; (r = -.08, p = .673), right IFC; (r = -.03, p = .882) left SMA; (r = -.06, p = .743), and right SMA; (r = .07, p = .685).

Discussion

The aim of the current study was twofold; to investigate the neural correlates of proactive and reactive inhibition behaviour, and to determine whether older adults exhibit neural and behavioural differences in these processes. Hypothesis 1a, that DLPFC activity would be higher for go responses when there was a likelihood of a stop cue appearing was supported by the data. The significant correlation indicated that the right DLPFC was engaged at a heightened level during the Mixed block, when there was some expectation of needing to stop than during the Go-only block, when there was no chance of needing to stop. This observation was specific to the DLPFC, with none of the other ROIs showing a difference between activity in Go responses between blocks. This finding contributes clarity to the right DLPFC as a neural correlate of proactive inhibition via the indirect pathway, consistent with findings from Zhang and Iwaki (2019). The data showed this effect was only found in the right DLPFC which supports the lateralisation of response inhibition to right PFC regions (Boeker et al., 2007). This finding is the first using the fNIRS technique to identify the right DLPFC as a crucial neural correlate of proactive inhibition.

Hypothesis 1b, which predicted activity in the right IFC and SMA would be higher in successful stopping trials compared to unsuccessful stopping trials was not supported by the

data. Although the effect was in the predicted direction, it did not reach statistical significance. This is in contrast to previous findings in the right IFC and SMA during stopping (Aron et al., 2003; Chikazoe et al., 2009). This finding may reflect high variability in low participant numbers, or that the right IFC and SMA may be more associated with directing attention to task-relevant cues rather than response inhibition, which has been suggested in prior work (Verbruggen et al., 2010). It is possible that participants were engaging attention directing to the stop cue rather than activation associated with inhibiting the motor command. This finding suggests that the right IFC and SMA may not be uniquely engaged during response inhibition.

Hypothesis 2a, which predicated that worse stopping ability and greater proactive slowing would be observed with age, was partially supported. The between group analyses suggested there were no differences in older adults stopping ability compared to younger adults. However, as hypothesised older adults did show greater reliance on proactive inhibition than younger adults. Older adults slowed their go responses more than younger adults when there was a likelihood of needing of stopping. It may be that older adults engaged in a more cautious strategy of slowing go responses in order to maintain outright stopping ability when required.

This is supported by the negative correlation between SSRT and ΔRT regardless of age (i.e. as proactive slowing increases SSRT is faster), which has also been found in previous research (Castro-Meneses et al., 2016; Chikazoe et al., 2009). This aligns with previous research that suggests older adults use more proactive mechanisms to stop rather than cue-dependent stopping (Bloemendaal et al., 2016; Manard et al., 2017). However, the finding is in contrast with lifespan research and in large community samples in which SSRT is slower in older adults (Smittenaar et al., 2015; Van Gerven et al., 2016). This considered, it is possible that proactive slowing is a strategy engaged on an interindividual basis for older

adults rather than as a concrete function of ageing. Our small sample size of particularly healthy and active older adults may reflect proactive strategies in this cohort; however, older or more frail adults may have different stopping abilities.

The above findings are considered in relation to neural differences between young and older adults with age. Hypothesis 2b, which predicted that hyperactivation and/or bilateral activation in the DLPFC would vary as a function of older age, was supported. However, unlike what was hypothesised, greater activation in the DLPFC was only significant when older adults were responding to stop cues, not when responding to the go cues stopping. This effect was significant in both the left and right DLPFC, suggesting bilateral activation during the stop for older adults. The findings in the DLPFC suggests that both hyperactivation and bilateral activity occurred for older adults during stopping.

This pattern of activity in the DLPFC with age measured with fNIRS agrees with findings from Coxon and colleagues (2016), where hyperactivation measured via fMRI was found during Go-trials for older adults. The DLPFC hyperactivation from the Coxon study was explained by working memory related to the cue rather than inhibition (Aron et al., 2014). While the DLPFC may be important to working memory, our findings instead suggest the DLPFC is engaged to a greater extent during successful compared to unsuccessful stopping in older adults.

As the right DLPFC was significantly correlated with the behavioural measure of stopping expectation (proactive inhibition), and not stopping ability (SSRT), it strongly suggests older adults are relying more on proactive neural processes to achieve stopping compared to the younger adults. This notion of age-related difference in neural activity to achieve similar performance aligns with the Scaffolding Theory of Ageing and Cognition (Reuter-Lorenz & Park, 2014), which states that older adults engage compensatory neural networks to maintain cognition.

The neural activity found in the SMA with age was in contrast to what Hypothesis 2b predicted. We hypothesised that the SMA would show hypoactivation with age during unsuccessful compared to successful stopping, due to compensatory activity occurring in the DLPFC with proactive strategies. In contrast to the hypothesis, we found a significant effect of hyperactivation in the right SMA during stopping for older adults compared to young. The presence of hyperactivity during unsuccessful compared to successful stopping may be reflective of the SMA as a 'negative motor area', in which the region inhibits behaviour with activation. However, we hypothesised that hypoactivtity would occur in this region due to compensatory hyperactivation occurring in the DLPFC with proactive slowing as found in previous work (Coxon et al., 2016). When considered in conjunction with the age-related increases in neural activity found in the DLPFC during stopping, it proposes that the SMA may also be compensating with greater activation to maintain stopping ability. Indeed, older adults had no significant difference in behavioural stopping ability to their younger counterparts. Therefore, in line with the STAC (Reuter-Lorenz & Park, 2014), hyperactivity in the SMA may be evidence of flexibility of neural pathways to maintain successful stopping.

We did not find a significant effect of age on neural activity bilaterally in the IFC. Hypothesis 2b predicted that the right IFC would demonstrate hypoactivation with age. Contrary to what was hypothesised and previous fMRI research (Sebastian et al., 2013) the right IFC showed a trend towards greater activity in both left and right regions for older adults. However, between groups analysis revealed that this effect was not significant during stopping expectation and stopping ability.

It is possible that lack of age effects in the IFC are due to compensatory activity occurring in the DLPFC and SMA, which therefore maintains the IFC at a level not significantly different from older adults. However, this is discordant with previous fMRI

research which has demonstrated hyperactivation of the right IFC in older adults, without proactive response slowing, and irrespective of cue context (i.e. go or stop cue) (Kleerekooper et al., 2016). Kleerekooper and colleagues (2016) explained their finding as overall compensatory activity in the right IFC. However, our findings demonstrate compensatory bilateral and hyperactivity in the DLPFC not in the IFC, during the stop. Our findings suggest that hyperactivity in the IFC may not occur with age due to the compensatory activity occurring in both the DLPFC and SMA.

Similarly, hyperactivity in the right SMA during stopping may be compensating for lack of age effects on activity in the IFC. This is would be consistent with the explanation that brain structure is related to function and hence informs behaviour. Indeed, the previously researched white matter connections between the IFC and SMA (Coxon et al, 2012), and fMRI evidence of SMA and IFC neural circuitry with the hyperdirect and indirect pathways, align with this explanation (Zhang & Iwaki, 2019). Previous research demonstrated that white matter tracts connecting the IFC and the pre-SMA via the STN (the hyperdirect pathway) were associated with stronger activation of the pre-SMA in older adults regardless of the stop or go cue (Coxon et al., 2016). We demonstrated that while the IFC was not associated with increased activity during expecting to stop or stopping with age, it is likely that the connections between these regions facilitated hyperactivation in the SMA. Within region associations were outside the scope of this thesis.

There was a significant positive correlation between higher subjective levels of anxiety and the change in blood oxygenation levels in the DLPFC between the Go-only block and Go-only trials in the Mixed block (proactive inhibitory behaviour). Previous research has demonstrated that the left DLPFC is involved in anxiety, as repeated TMS to the left DLPFC of highly anxious individuals improved memory retrieval (Balconi & Ferrari, 2013). This aligns with previous research that has shown that highly anxious individuals have increased

blood oxygenation when expecting to stop in the DLPFC (Basten et al., 2011). Notably, the left DLPFC activity was not significantly different when comparing successful to unsuccessful stopping, indicating that anxiety was related to the general expectation of having to stop in the Mixed block rather than stopping ability. Therefore, the findings suggest that individuals that have anxiety during a stop-signal task have increased activity associated with proactive inhibition in the left DLPFC.

Clinical Implications

It is apparent from the results that older adults tend to rely on more proactive inhibition rather than reactive inhibition to stop motor actions. These results have important clinical applications. Strategic proactive slowing has been demonstrated to be less effective at high information loads (Bloemendaal et al., 2016). This suggests that compensatory activity and proactive strategies may be possible when the task is relatively easy (i.e. stop signal task in finger button presses) but could be more difficult to maintain in a real-world context - where older adults may have to stop one action in the context of competing demands. Indeed, previous studies have demonstrated that higher PFC activity during walking is predictive of falls in older populations (Verghese et al., 2017). Furthermore, when an environmental cue to stop is completely surprising (i.e. no prior expectation) then older adults will be completely reliant on reactive stopping networks, which are likely to be less efficient than a younger counterpart, and injuries may occur.

Recent research that applied anodal transcranial direct current stimulation (tDCS) localised to the pre-SMA and rIFG found that upregulating these regions improved stopping ability and decision making for older adults (Fujiyama et al., 2021). Further, while the older sample of adults in the current study had the same ability to react to stop cues as younger adults, many previous studies have found poorer stopping ability with age (Smittenaar et al., 2015; Van Gerven et al., 2016). It is possible that due to older adults upregulating the DLPFC

to perform the stop task, other functions that utilise the region may be impaired, such as working memory and decision making. Neurocognitive training has been found to increase cognitive load capacity required for dual- and multi-tasking and improve the efficiency of neural activity (Lustig et al., 2009). Improving motor response inhibition via training in dual physical-cognitive tasks in the upper and lower limbs may also enhance stopping ability and balance (Falbo et al., 2016). Longitudinal studies are currently investigating whether applying dual-task training reduces the incidence of falls and injuries for older adults (Sturnieks et al., 2019).

The study demonstrates that fNIRS can be used to investigate the neural correlates of response inhibition. This highlights the potential of fNIRS to be applied in clinical settings. For example, Monden and colleagues (2011) found that prior to drug-treatment, children with ADHD, had no significant activation in the lateral PFC during response inhibition as measured by fNIRs. However, after an intervention of ADHD psychostimulants cognitive performance on a go/no-go task was associated with measurable increases in blood oxygen activity in the lateral PFC (Monden et al., 2011). The significant correlation found in the current study between activity in the left DLPFC and levels of anxiety during expected stopping proposes similar clinical applications. The relationship between heightened anxiety and increased neural activity in the left DLPFC during proactive inhibition may direct repeated TMS research to this area of interest.

Limitations

In fNIRs research a notable limitation is the temporal resolution of hemodynamic activity. Unlike EEG, which records the electrical activity of neural firing, fNIRS records the haemodynamic response, thus similar to the BOLD response in fMRI there is a 3-4 second delay between the neural signal and the peak response. Although not as temporally specific as EEG, fNIRS is far less prone to motion artifact, has better spatial resolution, and is faster to

set up. Synchronising EEG and fNIRs signals could allow for better temporal specificity in further response inhibition studies (Ahn & Jun, 2017).

Another limitation of fNIRs studies is that the signal derived from the analysis contains physiological and movement artefacts from cardiac rhythm, blood pressure and respiration rate. The signal processing pipeline (Appendix I) enabled isolation of neural activity from physiological and movement artefacts and averaging over many repeated trials also reduces artifacts. However, it is possible that the oxyhaemoglobin activity related to behavioural correlates contain other events not addressed in filtering. For example, during the experiment, participants may have vocalised (e.g. speaking or sighing) during the task in response to unsuccessfully or successfully stopping. However, if this occurred participants were reminded to remain silent during fNIRs recording to limit this interference.

Three participants did not meet the race test assumption of independence between the stop and go processes, whereby RTs to stop cues (unsuccessful stop) should be shorter than GoRTs in Mixed blocks to accurately estimation SSRT. Recommendations for these assumption violations suggest removal of the participants from analysis (Maztake et al., 2016). Statistical analyses were run both with, and without the three participants included and results pertaining to fNIRs and behavioural data yielded the same statistical outcomes for significance. As the hypothesised questions were related to within-subject correlational analysis between fNIRs and behaviour, removing participants was considered too conservative.

Slowing of go responses in the Mixed block in some cases may reflect a ‘waiting strategy’ rather than proactive inhibition. When using a waiting strategy participants consciously decide to wait for the stop cue to appear for a period of time before deciding whether to engage the go response (Rieger & Gauggel, 2002). If waiting occurs, the SSRT calculation no longer estimates stopping ability. Consensus recommendations for minimizing

the chance of a waiting strategy were used in the current experiment; i) the use of RT feedback after each trial, and mean RT after each block encouraged participants to maintain speeded responses; ii) allowing a maximum time window of 800ms to respond, with "Too Slow" feedback presented if responses were beyond this window; iii) specific instruction at the beginning of the experiment and before each block to respond "as quickly and as accurately as you can" both in the text instruction and with verbal reminders from the researcher.

Unequal group sizes were also a limitation in our study design. Group sizes of $n = 25$ would have provided sufficient statistical power, based on previous fNIRs research and response inhibition tasks within older populations (Lague-Beauvais et al., 2013; St George et al., 2021). While this was achieved in the younger cohort, this was not the case for the older cohort. Increased societal hesitancy for older adults to participate in research due to the COVID-19 pandemic may have been a contributing factor. It is also possible that older adults were harder to recruit for two sessions, compared to one session required for younger adults. However, not having dual sessions for older adults would not be feasible given the risk of fatigue or strain in an older population. Unequal samples sizes were adequately accounted for with non-parametric statistical analysis. Further, older adult participants were a fit and healthy sample, and stopping abilities and neural activity may therefore be different in frailer or cognitively impaired older groups.

Conclusion

The current study was a novel investigation of the effects of age on proactive and reactive inhibition applying fNIRs with a stop-signal task. The investigation of neural correlates of response inhibition identified the right DLPFC as a crucial region of proactive inhibition regardless of age. As hypothesised, older adults used more proactive inhibition, but were just as capable to stop when required as younger adults. Older adults also showed

hyperactivity in the left and right DLPFC and right SMA, but not bilateral regions of the IFC during unsuccessful compared to successful stopping. Age-related differences in neural activity were likely compensatory mechanisms used to maintain stopping ability in the older adults.

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Appendices

Appendix A

Medical Screening Questionnaire

ID:_____

Screening and General Medical Questionnaire

Please answer the following questions. The purpose of these questions is to make sure that there are no medical contraindications to your participation in the study. The information you provide will be treated as strictly confidential and will be held in secure conditions.

Screening Questions

Do you suffer pain with standing or walking?	Y / N
Do you have a neurological disorder? E.g. Parkinson's Disease, Multiple Sclerosis, stoke history, traumatic brain injury, Dementia.	Y / N
Do you have any metal in your head (outside the mouth) such as shrapnel, surgical clips, cochlear implants, or fragments from metalwork?	Y / N
Have you ever fainted during a medical procedure?	Y / N
Have you eaten yet today?	Y / N
Did you have more than 5 hours of sleep last night?	Y / N

General Medical and Demographic Questions

Do you have a heart condition?	Y / N
Do you have a mental health disorder?	Y / N
Are you currently taking any psychiatric or neuroactive medications (e.g. antidepressants, sedatives)?	Y / N
Have you ever had a brain injury (e.g. neurosurgery or a serious head injury/illness requiring hospitalization)?	Y / N
Have you ever been told that your blood pressure is high or low?	Y / N
Do you have diabetes?	Y / N
Do you or have you ever suffered from dizziness?	Y / N
In the last 12 hours, have you consumed more than 3 units of alcohol?	Y / N
In the last 12 hours, have you consumed any recreational drugs?	Y / N
In the last two hours, have you consumed more than 2 caffeinated drinks?	Y / N
Do you have any concerns about your balance?	Y / N
How many times have you fallen in the past year?	
How many languages do you speak?	

Appendix B

Standardised Mini Mental State Examination sMMSE

Name of patient:		DOB:	/ /	Name of examiner:		Date of test:	/ /

Standardised Mini-Mental State Examination (SMMSE)

Please see accompanying guidelines for administration and scoring instructions

Say: *I am going to ask you some questions and give you some problems to solve. Please try to answer as best you can.*

1. Allow ten seconds for each reply. **Say:**

   a) *What year is this?* (accept exact answer only) /1
   b) *What season is this?* (during the last week of the old season or first week of a new season, accept either) /1
   c) *What month is this?* (on the first day of a new month or the last day of the previous month, accept either) /1
   d) *What is today's date?* (accept previous or next date) /1
   e) *What day of the week is this?* (accept exact answer only) /1

2. Allow ten seconds for each reply. **Say:**

   a) *What country are we in?* (accept exact answer only) /1
   b) *What state are we in?* (accept exact answer only) /1
   c) *What city/town are we in?* (accept exact answer only) /1
   d) <At home> *What is the street address of this house?* (accept street name and house number or equivalent in rural areas) /1
      <In facility> *What is the name of this building?* (accept exact name of institution only) /1
   e) <At home> *What room are we in?* (accept exact answer only) /1
      <In facility> *What floor of the building are we on?* (accept exact answer only) /1

3. **Say:** *I am going to name three objects. When I am finished, I want you to repeat them. Remember what they are because I am going to ask you to name them again in a few minutes* (say slowly at approximately one-second intervals).

   Ball Car Man

   For repeated use: Bell, jar, fan; bill, tar, can; bull, bar, pan

   Say: *Please repeat the three items for me* (score one point for each correct reply on the first attempt) /3

   Allow 20 seconds for reply; if the person did not repeat all three, repeat until they are learned or up to a maximum of five times (but only score first attempt)

4. **Say:** *Spell the word WORLD* (you may help the person to spell the word correctly). **Say:** *Now spell it backwards please* (allow 30 seconds; if the person cannot spell world even with assistance, score zero). Refer to accompanying guide for scoring instructions (score on reverse of this sheet) /5

5. **Say:** *Now what were the three objects I asked you to remember?* /3

   (score one point for each correct answer regardless of order; allow ten seconds)

6. Show wristwatch. **Ask:** *What is this called?* /1

   (score one point for correct response; accept 'wristwatch' or 'watch'; do not accept 'clock' or 'time', etc.; allow ten seconds)

7. **Show pencil. Ask:** *What is this called?* /1

   (score one point for correct response; accept 'pencil' only; score zero for pen; allow ten seconds for reply)

8. **Say:** *I would like you to repeat a phrase after me: No ifs, ands, or buts* /1

   (allow ten seconds for response. Score one point for a correct repetition. Must be exact, e.g. no ifs or buts, score zero)

9. **Say:** *Read the words on this page and then do what it says* /1

   Then, **hand** the person the sheet with CLOSE YOUR EYES (score on reverse of this sheet) on it. If the subject just reads and does not close eyes, you may repeat: *Read the words on this page and then do what it says*, a maximum of three times. See point number three in Directions for Administration section of accompanying guidelines. Allow ten seconds; score one point only if the person closes their eyes. The person does not have to read aloud.

10. **Hand** the person a pencil and paper. **Say:** *Write any complete sentence on that piece of paper* (allow 30 seconds. Score one point. The sentence must make sense. Ignore spelling errors). /1

11. **Place** design (see page 3), pencil, eraser and paper in front of the person. **Say:** *Copy this design please.* Allow multiple tries. /1

    Wait until the person is finished and hands it back. Score one point for a correctly copied diagram. The person must have drawn a four-sided figure between two five-sided figures. Maximum time: one minute.

12. **Ask** the person if he is right or left handed. **Take** a piece of paper, hold it up in front of the person and **say** the following: *Take this paper in your right/left hand* (whichever is non-dominant), *fold the paper in half once with both hands and put the paper down on the floor.*

Takes paper in correct hand_____ /1

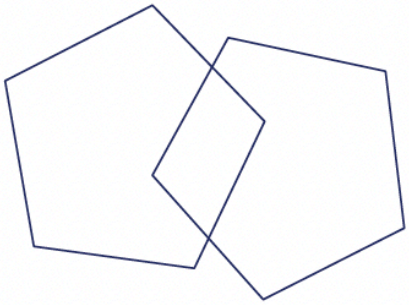
Folds it in half_____ /1

Puts it on the floor_____ /1

TOTAL TEST SCORE: /30

ADJUSTED SCORE: /

Molloy DW, Alemayehu E, Roberts R. Reliability of a standardized Mini-Mental State Examination compared with the traditional Mini-Mental state Examination. *American Journal of Psychiatry*, Vol. 14, 1991a, pp.102-105.



Time:

D	L	R	O	W

=

CLOSE YOUR EYES

Appendix C

Anxiety Questionnaire

Post-experiment Reflection Questionnaire Participant ID:

Please read the following statements and circle *either* 0, 1, 2 or 3 to indicate how much each statement applied to you ***during the task***. There are no right or wrong responses. Please answer as accurately as possible. Do not spend too long on each statement.

Please rate the scale as follows:

0 Did not apply to me at all
1 Applied to me to some degree, or some of the time
2 Applied to me to a considerable degree, or a good part of time
3 Applied to me very much, or most of the time

During the task:	
1. I felt I had a lot of nervous energy	0 1 2 3
2. I found it difficult to work up the energy to focus on the task	0 1 2 3
3. I found myself getting agitated	0 1 2 3
4. I found myself intolerant of any distractions	0 1 2 3
5. I felt relaxed and at ease during the task	0 1 2 3
6. I was worried I might fall or lose balance during the experiment	0 1 2 3
7. I felt anxious about my performance on this task	0 1 2 3

Appendix D

Older Participant Information Sheet

OLDER PARTICIPANT INFORMATION SHEET

(Version 8 04.05.21)

Age-related changes in the cerebral cortex for human balance

You are invited to participate in a study investigating age-related change in cortical activity and response times when people are initiating movements: either stepping with the lower limb or moving the fingers.
The study is being conducted by:

- Dr Rebecca St George, School of Medicine, University of Tasmania
  Email: Rebecca.StGeorge@utas.edu.au
  Phone: 03 6226 2558
- Dr Mark Hinder, School of Medicine, University of Tasmania.
  Email: Mark.Hinder@utas.edu.au
- Dr Michele Callisaya, Menzies Menzies Institute for Medical Research, University of Tasmania. Email: Michele.callisaya@utas.edu.au; phone: 0418 295 933
- Prof. Jeff Summers, School of Medicine, University of Tasmania
  Email: Jeff.Summers@utas.edu.au
- Rebecca Healey, School of Medicine, University of Tasmania.
  Email: rhealey0@utas.edu.au

The study will be conducted at either:

1. The Cognitive and Motor Aging Laboratory, Psychology Research Centre, Sandy Bay Campus, University of Tasmania, (03) 6226 2887.
2. The Menzies Research Institute, MS2 building, Hobart.

You will be notified prior to your experiment the location of the study.

You may be asked to participate in multiple sessions. If this is the case the investigator will inform you before you begin of the number of sessions involved. A single session will last up to two hours and multiple sessions will be separated by at least 24 hours. Every effort will be made to schedule multiple sessions at mutually convenient times.

'What is the purpose of this study?'
The aims of the project are firstly to investigate how the cortex is involved in the control of balance and stepping, and secondly to understand how the cortical contributions to stepping change with age. This study will increase our understanding of how people initiate and stop movements in older age.

'Why have I been invited to participate in this study?'
You are invited to participate if you are over the age of 60 and have no known neuromuscular or neurological disorders, or joint or muscle pain when standing.

Cortical Activity will be recorded with Functional Near Infrared Spectroscopy (fNIRS). fNIRS carries no risk to any participant although people with metal implants in the head will be excluded as this may alter the quality of the recording.

Certain medications (for example some types of anti-depressant medications) can influence how the brain responds to sensory stimulation and voluntary movements. *Therefore, we ask that you inform the researcher if you are taking any psychoactive medication prior to participating in the study*.

'What if I don't want to take part in this study, or if I want to withdraw later?'
Participation in the study is completely voluntary. If you agree to participate, you are free to withdraw from the study at any time without prejudice. You can decide to terminate your participation at any point without giving a reason. If you decide not to participate, it will not affect your relationship with the University of Tasmania in anyway. If you withdraw from the study, any data that you have supplied can be identified through the alpha-numeric coding system and withdrawn from the study if you wish.

'What does this study involve?'
You will be asked to attend at least two sessions lasting up to 2 hours each. Every effort will be made to schedule the session at a mutually convenient time. Parking will be provided. At the beginning of the session you will meet the researchers and they will explain the procedure to you and you will have the opportunity to ask any questions you may have.

This study will involve:

- Being asked questions regarding your physical health, to ensure that you will not be exposed to any avoidable risks as part of participation in this study.
- Signing a Participant Consent Form
- Performing a brief (10 minute) cognitive screening test (Montreal cognitive assessment). The results of this test will be made available for you.
- Sitting and stepping movement tasks will be performed while brain activity is measured with Functional Near Infrared Spectroscopy.

Sitting and stepping movement tasks: You will be asked to perform the following sitting and standing tasks:

- You will be asked to sit in front of a computer screen and respond to visual stimuli with your left or right index finger to a cue presented on the screen.
- You will be asked to stand or sit still and then step to a visual target. Stepping may be with your left or right foot.
- On some of these sitting or stepping trials, you will need to stop or amended the trajectory of a movement that you have already initiated when a 'STOP' cue is presented.

The experimenter will provide you with the specific details prior to the start of each condition. To ensure safety, a researcher will be standing close by to offer stability if required and in the standing trials you will be in a secure harness to prevent falling. To minimize fatigue from prolonged standing you will take seated rest breaks every 10 minutes or more frequently if you feel fatigued.

fNIRS. You will wear a light-weight headband that transmits information about your brain activity. fNIRS measures changes in the oxygenation level of the blood flow at the cortex which reflects the neuronal activity. This is a safe, passive technique that measures the tissue interaction properties of light within the near infrared range. There is no radiation, and no discomfort.

'How is this study being paid for?'

This research is funded by a grant from the National Health and Medical Research Council (NHMRC: APP1036234) and a PhD Scholarship funded by the University of Tasmania College of Health and Medicine.

'Will taking part in this study cost me anything, and will I be paid?

Participation in this study will not cost you anything. You will go in a draw to win $100 Coles/Myer vouchers.

'Are there risks to me in taking part in this study?'

You may experience some fatigue due to standing. If you become uncomfortable please inform the researcher and more rest breaks can be given or the procedures can immediately be stopped. There may also be risks associated with this study that are presently unknown or unforeseeable.

'What happens if I suffer injury or complications as a result of the study?'

In the unlikely event that you suffer any injuries or complications as a result of this study, you should contact Dr St George (Rebecca.stgeorge@utas.edu.au) as soon as possible on 03 6226 2887, who will assist you in arranging appropriate medical treatment.

'Will I benefit from the study?'

It is unlikely that you will benefit personally from participating in this research project, but the results will help our understanding of some basic functions of the healthy human brain. Indeed, we hope that the results of this study will eventually help us to understand how mobility may be maintained in older adults.

'How will my confidentiality be protected?'

Your individual experimental data will be coded alpha-numerically and stored on a secure computer server that will be available only to the investigators via a password system. All future use of your data will be by the alpha-numeric code only to ensure anonymity. Your data will be retained securely at the University of Tasmania for at least five years. When it is no longer required by law, your data will be destroyed by the deletion of electronic files and shredding of documents.
You will be asked to sign an informed consent form to evidence your consent to participate in the study. Consent forms will be locked in a filing cabinet in the Cognitive and Motor Aging Laboratory at the University of Tasmania and kept separately from your data.

'What happens with the results?'
All data will be presented anonymously in any publications arising from this study. If you wish to be notified on the results of this study, please feel free to contact us.

'What should I do if I want to discuss this study further before I decide?'
If you have any queries, concerns or issues with this study at any time, please feel free to contact us:

Dr Rebecca St George (03 6226 2887 or Rebecca.StGeorge@utas.edu.au)
Dr Mark Hinder (03 6226 2945 or Mark.Hinder@utas.edu.au)
Dr Michele Callisaya (+61418295933 or Michele.Callisaya@utas.edu.au)
Rebecca Healey (rhealey0@utas.edu.au)

'Who should I contact if I have concerns about the conduct of this study?'
This study has been approved by the Tasmanian Health & Medical Human Research Ethics Committee. If you have concerns of complaints about the conduct of this study you should contact the Executive Officer of the HREC (Tasmania) Network on (03) 6226 6254 or email human.ethics@utas.edu.au. The Executive Officer is the person nominate to receive complaints from research participants. You will need to quote ethics reference number **H0014865**.

You will be provided with a copy of this information sheet and a statement of informed consent to keep. When finalized, results of the study will be posted on the University of Tasmania website, . It can be expected that results of individual studies will be available within a year of data collection.

Thank you for taking the time to consider this study.
If you wish to take part in it, please sign the attached consent form.
This information sheet is for you to keep.

Appendix E

Younger Participant Information Sheet

YOUNG PARTICIPANT INFORMATION SHEET

(Version 8 04.05.21)

Age-related changes in the cerebral cortex for human balance

You are invited to participate in a study investigating age-related change in cortical activity and response times when people are initiating movements: either stepping with the lower limb or moving the fingers.

The study is being conducted by:

- Dr Rebecca St George, School of Medicine, University of Tasmania
  Email: Rebecca.StGeorge@utas.edu.au
  Phone: 03 6226 2558
- Dr Mark Hinder, School of Medicine, University of Tasmania.
  Email: Mark.Hinder@utas.edu.au
- Dr Michele Callisaya, Menzies Menzies Institute for Medical Research, University of Tasmania. Email: Michele.callisaya@utas.edu.au; phone: 04.. ... ...
- Prof. Jeff Summers, School of Medicine, University of Tasmania
  Email: Jeff.Summers@utas.edu.au
- Rebecca Healey, School of Medicine, University of Tasmania.
  Email: rhealey0@utas.edu.au

The study will be conducted at either:

1. The Cognitive and Motor Aging Laboratory, Psychology Research Centre, Sandy Bay Campus, University of Tasmania, (03) 6226 2887.
2. The Menzies Research Institute, MS2 building, Hobart.

You will be notified prior to your experiment the location of the study.

You may be asked to participate in multiple sessions. If this is the case the investigator will inform you before you begin of the number of sessions involved. A single session will last up to two hours and multiple sessions will be separated by at

least 24 hours. Every effort will be made to schedule multiple sessions at mutually convenient times.

'What is the purpose of this study?'
The aims of the project are firstly to investigate how the cortex is involved in the control of balance and stepping, and secondly to understand how the cortical contributions to stepping change with age. This study will increase our understanding of how people initiate and stop movements in older age.

'Why have I been invited to participate in this study?'
Individuals (male and female) between 18 and 35 years of age are invited to participate in this research. Interested volunteers should have no known neuromuscular or neurological disorders, or recent pain or discomfort associated with standing.

Cortical Activity will be recorded with Functional Near Infrared Spectroscopy (fNIRS). fNIRS carries no risk to any participant although people with metal implants in the head will be excluded as this may alter the quality of the recording.

Certain medications (for example some types of anti-depressant medications) can influence how the brain responds to sensory stimulation and voluntary movements. *Therefore, we ask that you inform the researcher if you are taking any psychoactive medication prior to participating in the study*.

'What if I don't want to take part in this study, or if I want to withdraw later?'
Participation in the study is completely voluntary. If you agree to participate, you are free to withdraw from the study at any time without prejudice. You can decide to terminate your participation at any point without giving a reason. If you decide not to participate, it will not affect your relationship with the University of Tasmania in anyway. If you withdraw from the study, any data that you have supplied can be identified through the alpha-numeric coding system and withdrawn from the study if you wish.

'What does this study involve?'
You will be asked to attend at least two sessions lasting up to 2 hours each. Every effort will be made to schedule the session at a mutually convenient time. Parking will be provided. At the beginning of the session you will meet the researchers and they will explain the procedure to you and you will have the opportunity to ask any questions you may have.

This study will involve:

- Being asked questions regarding your physical health, to ensure that you will not be exposed to any avoidable risks as part of participation in this study.
- Signing a Participant Consent Form
- Performing a brief (10 minute) cognitive screening test (Montreal cognitive assessment). The results of this test will be made available for you.
- Sitting and stepping movement tasks will be performed while brain activity is measured with Functional Near Infrared Spectroscopy.

Sitting and stepping movement tasks: You will be asked to perform the following sitting and standing tasks:

- You will be asked to sit in front of a computer screen and respond to visual stimuli with your left or right index finger to a cue presented on the screen.
- You will be asked to stand or sit still and then step to a visual target. Stepping may be with your left or right foot.
- On some of these sitting or stepping trials, you will need to stop a movement that you have already initiated when a 'STOP' cue is presented.

The experimenter will provide you with the specific details prior to the start of each condition. To ensure safety, a researcher will be standing close by to offer stability if required and in the standing trials you will be in a secure harness to prevent falling. To minimize fatigue from prolonged standing you will take seated rest breaks every 10 minutes or more frequently if you feel fatigued. The testing time, including breaks is approximately one hour.

fNIRS. You will wear a light-weight headband that transmits information about your brain activity. fNIRS measures changes in the oxygenation level of the blood flow at the cortex which reflects the neuronal activity. This is a safe, passive technique that measures the tissue interaction properties of light within the near infrared range. There is no radiation, and no discomfort.

'How is this study being paid for?'

This research is funded by a grant from the National Health and Medical Research Council (NHMRC: APP1036234) and a PhD Scholarship funded by the University of Tasmania College of Health and Medicine.

'Will taking part in this study cost me anything, and will I be paid?

Participation in this study will not cost you anything. You will go in a draw to win $100 Coles/Myer vouchers, or you will be granted course credit.

'Are there risks to me in taking part in this study?'

You may experience some fatigue due to standing. If you become uncomfortable please inform the researcher and more rest breaks can be given or the procedures can immediately be stopped.
There may also be risks associated with this study that are presently unknown or unforeseeable.

'What happens if I suffer injury or complications as a result of the study?'

In the unlikely event that you suffer any injuries or complications as a result of this study, you should contact Dr St George (Rebecca.stgeorge@utas.edu.au) as soon as possible on 03 6226 2887, who will assist you in arranging appropriate medical treatment.

'Will I benefit from the study?'

It is unlikely that you will benefit personally from participating in this research project, but the results will help our understanding of some basic functions of the healthy human brain. Indeed, we hope that the results of this study will eventually help us to understand how mobility may be maintained in older adults.

'How will my confidentiality be protected?'
Your individual experimental data will be coded alpha-numerically and stored on a secure computer server that will be available only to the investigators via a password system. All future use of your data will be by the alpha-numeric code only to ensure anonymity. Your data will be retained securely at the University of Tasmania for at least five years. When it is no longer required by law, your data will be destroyed by the deletion of electronic files and shredding of documents.
You will be asked to sign an informed consent form to evidence your consent to participate in the study. Consent forms will be locked in a filing cabinet in the Cognitive and Motor Aging Laboratory at the University of Tasmania and kept separately from your data.

'What happens with the results?'
All data will be presented anonymously in any publications arising from this study. If you wish to be notified on the results of this study, please feel free to contact us.

'What should I do if I want to discuss this study further before I decide?'
If you have any queries, concerns or issues with this study at any time, please feel free to contact us:

Dr Rebecca St George (03 6226 2887 or Rebecca.StGeorge@utas.edu.au)
Dr Mark Hinder (03 6226 2945 or Mark.Hinder@utas.edu.au)
Dr Michele Callisaya (+614..... or Michele.Callisaya@utas.edu.au)
Rebecca Healey (rhealey0@utas.edu.au)

'Who should I contact if I have concerns about the conduct of this study?'
This study has been approved by the Tasmanian Health & Medical Human Research Ethics Committee. If you have concerns of complaints about the conduct of this study you should contact the Executive Officer of the HREC (Tasmania) Network on (03) 6226 6254 or email human.ethics@utas.edu.au. The Executive Officer is the person nominate to receive complaints from research participants. You will need to quote ethics reference number **H0014865**.

You will be provided with a copy of this information sheet and a statement of informed consent to keep. When finalized, results of the study will be posted on the University of Tasmania website, . It can be expected that results of individual studies will be available within a year of data collection.

Thank you for taking the time to consider this study.
If you wish to take part in it, please sign the attached consent form.
This information sheet is for you to keep.

Appendix F

Consent form

CONSENT FORM

Age-related changes in the cerebral cortex for human standing

(Version 5, May 20, 2021)

Principle Investigators: Dr Rebecca St George, A/Prof Mark Hinder, A/Prof Michele Callisaya, Ms Rebecca Healey & Prof Jeff Summers

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1. I have read the participant information sheet.
2. I have been informed of and understand the purposes of the study
3. I have been given an opportunity to ask questions
4. I understand I can withdraw at any time without prejudice
5. Any information which might potentially identify me will not be used in published material.
6. I agree to participate in the study as outlined to me.

Name of participant _____

Signature of participant _____ Date _____

I have explained this project and the implications of participation in it to this volunteer and I believe that the consent is informed and that he/she understands the implications of participation.

Name of investigator _____

Signature of investigator _____ Date _____

Appendix G:

College of Health and Medicine Risk Assessment Procedures

UNIVERSITY of TASMANIA

RISK ASSESSMENT

A Risk Assessment is a simple tool to look at an activity such as a task, project or event to identify health and safety risks that are likely to pose a threat to a person's safety or impact operations of the University and to establish appropriate risk controls to minimise harm.

KEY STEPS SUMMARISED:

1. Provide summary of activity.
2. Break the activity down into a series of steps (from start to finish).
3. Identify potential hazards for each step. Use the *Hazard Identification Checklists* for help.
4. Assess the inherent risk (*before* control measures) for each hazard identified by:
    a. Evaluating the possible consequence of the hazard using the Consequence Scale.
    b. Evaluate the likelihood of that consequence using the Likelihood Scale.
    c. Determine risk rating of each hazard using the University Risk Matrix.
5. Develop appropriate risk control measures to eliminate or reduce the risks.
6. Assess the residual risk (i.e. *after* control measures) once again by:
    a. Evaluating the possible consequences of the hazard using the Consequence Scale.
    b. Evaluate the likelihood of that consequence using the Likelihood Scale.
    c. Determine risk rating of each hazard using the University Risk Matrix.
7. Identify persons responsible for implementing and monitoring relevant steps. Ensure they have appropriate licenses and qualifications.
8. Determine highest remaining residual risk.
9. Determine if a Safe Work Procedure (SWP) is to be developed from the Risk Assessment.
10. Seek delegation sign off in accordance with the University Schedule of Risk Delegations.
11. Ensure all persons involved in the activity have read, understand and sign the risk assessment before work starts.

The following Risk Assessment template has been provided in a word format to enable you to type in information and to electronically transmit and save the document. Refer to the *Project / Task Risk Assessment Procedure* for instructions and guidance on how to use this *Risk Assessment Template*. If you require assistance with reviewing your assessment, first speak with your colleagues, line supervisor or elected Health and Safety Representative. If further assistance is required, please contact the University Work Health and Safety Unit via health.safety@utas.edu.au.

Appendix H

Counterbalancing Procedure for Healey (n.d) Study

Key:

A; Finger Tap Condition

B; Foot Tap Condition

C; Stepping Condition

ID	GO ONLY (fNIRs)			MIXED (fNIRs)			MIXED (no fNIRs)				
1	A	B	C	A	B	C	C	C	A	A	B	B
2	C	B	A	A	B	C	C	C	B	B	A	A
3	B	C	A	A	C	B	B	B	A	A	C	C
4	C	A	B	A	C	B	B	B	C	C	A	A
5	A	C	B	C	A	B	B	B	C	C	A	A
6	A	B	C	C	A	B	B	B	A	A	C	C
7	B	C	A	C	B	A	A	A	C	C	B	B
8	B	A	C	C	B	A	A	A	B	B	C	C
9	C	B	A	B	C	A	A	A	B	B	C	C
10	C	A	B	B	C	A	A	A	C	C	B	B
11	C	A	B	B	A	C	C	C	B	B	A	A
12	C	A	B	B	A	C	C	C	A	A	B	B
13	A	B	C	A	B	C	C	C	A	A	B	B
14	C	A	B	A	B	C	C	C	B	B	A	A
15	C	B	A	A	C	B	B	B	A	A	C	C
16	C	A	B	A	C	B	B	B	C	C	A	A
17	B	A	C	C	A	B	B	B	C	C	A	A
18	B	A	C	C	A	B	B	B	A	A	C	C
19	A	B	C	C	B	A	A	A	C	C	B	B
20	C	B	A	C	B	A	A	A	B	B	C	C
21	C	B	A	B	C	A	A	A	B	B	C	C
22	A	B	C	B	C	A	A	A	C	C	B	B
23	C	A	B	B	A	C	C	C	B	B	A	A
24	B	C	A	B	A	C	C	C	A	A	B	B
25	C	A	B	A	B	C	C	C	A	A	B	B
26	C	A	B	A	B	C	C	C	B	B	A	A
27	C	A	B	A	C	B	B	B	A	A	C	C
28	A	C	B	A	C	B	B	B	C	C	A	A
29	B	A	C	C	A	B	B	B	C	C	A	A
30	B	A	C	C	A	B	B	B	A	A	C	C
31	A	C	B	C	B	A	A	A	C	C	B	B

32	B	C	A	C	B	A	A	A	B	B	C	C
33	C	B	A	B	C	A	A	A	B	B	C	C
34	C	B	A	B	C	A	A	A	C	C	B	B
35	C	B	A	B	A	C	C	C	B	B	A	A
36	B	C	A	B	A	C	C	C	A	A	B	B
37	A	C	B	A	B	C	C	C	A	A	B	B
38	B	A	C	A	B	C	C	C	B	B	A	A
39	C	A	B	A	C	B	B	B	A	A	C	C
40	C	B	A	A	C	B	B	B	C	C	A	A
41	C	B	A	C	A	B	B	B	C	C	A	A
42	B	C	A	C	A	B	B	B	A	A	C	C
43	A	C	B	C	B	A	A	A	C	C	B	B
44	A	C	B	C	B	A	A	A	B	B	C	C
45	A	C	B	B	C	A	A	A	B	B	C	C
46	B	A	C	B	C	A	A	A	C	C	B	B
47	C	B	A	B	A	C	C	C	B	B	A	A
48	C	B	A	B	A	C	C	C	A	A	B	B

Appendix I

Signal Processing Pipeline

Function	
PreprocessIntensity_NaN: spline interpolation of missing data points	
PruneChannels: prunes channels if their signal is too weak, too strong or their standard deviation is too great	dRange: 0.01:3 SNRthresh: 2 SDrange: 0.0: 45.0
Intensity2OD: Converts intensity data to optical density	
MotionCorrectPCArecurse: Identifies motion artefacts, if there is a signal change greater than STDEVthresh or AMPthresh then a segment of data around that datapoint is marked as a motion artefact. Principle components are identified and, if nSV=0.97 then the filter removes the first n components of the data that removes a fraction of the variance up to nSV (Yucel et al). maxIter is the maximum number of iterations.	tMotion:0.5 tMask:1.0 STDEVthresh: 20.0 AMPthresh: 5.00 nSW: 0.97 maxIter: 5
BandpassFilt:Bandpass_filter_OpticalDensity: Performs a bandpass filter between hpf and lpf	hpf:0 lpf:0.5
OD2Conc: The Beer-Lambert Law that converts optical density to concentration	ppf:1.0 1.0

Appendix J

Assumption Testing: Homogeneity of Variances (Levene's test) and Normality Test (Shapiro-Wilk)

Appendix. J.1

Homogeneity of Variances Test (Levene's)

	F	df	df2	p
Pro_DLPFC_L	0.19	1	34	0.668
Pro_DLPFC_R	0.19	1	34	0.663
Pro_IFC_L	1.27	1	32	0.268
Pro_IFC_R	0.13	1	33	0.718
Pro_SMC_L	0.01	1	34	0.904
Pro_SMC_R	0.04	1	34	0.852
Rea_DLPFC_L	1.75	1	34	0.194
Rea_DLPFC_R	0.11	1	34	0.744
Rea_IFC_L	0.79	1	32	0.379
Rea_IFC_R	0.03	1	34	0.875
Rea_SMC_L	1.75	1	34	0.195
Rea_SMC_R	0.01	1	34	0.923
Delta_Go	1.34	1	35	0.255
SSRT	6.59	1	35	0.015

Note. A low p-value suggests a violation of the assumption of equal variances

Appendix J.2

Normality Test (Shapiro-Wilk)

	W	p
Pro_DLPFC_L	0.92	0.015
Pro_DLPFC_R	0.90	0.004
Pro_IFC_L	0.95	0.145
Pro_IFC_R	0.92	0.012
Pro_SMC_L	0.95	0.101
Pro_SMC_R	0.95	0.139
Rea_DLPFC_L	0.95	0.109
Rea_DLPFC_R	0.98	0.744

Normality Test (Shapiro-Wilk)

	W	p
Rea_IFC_L	0.99	0.960
Rea_IFC_R	0.69	< .001
Rea_SMC_L	0.95	0.113
Rea_SMC_R	0.92	0.013
Delta_Go	0.80	< .001
SSRT	0.97	0.388

Note. A low p-value suggests a violation of the assumption of normality

Appendix K

False-Discover Rate Calculations: Benjamini-Hochberg procedure

Equation 3: $BH\ critical\ value\ =\ P\ <\ (i/m)Q$

where i = ranked p-value, m = total number of tests, Q = chosen FDR

	P	Rank	BH value
Rea_DLPFC_L	0.005	1	0.01
Delta_Go	0.018	2	0.02
Rea_DLPFC_R	0.029	3	0.03
Rea_SMC_L	0.031	4	0.04
Rea_SMC_R	0.065	5	0.05
Rea_IFC_L	0.076	6	0.06
Pro_IFC_L	0.215	7	0.08
Pro_DLPFC_L	0.22	8	0.09
Pro_SMC_L	0.227	9	0.10
Pro_DLPFC_R	0.335	10	0.11
Pro_SMC_R	0.463	11	0.12
Pro_IFC_R	0.484	12	0.13
Rea_IFC_R	0.488	13	0.14
SSRT	0.687	14	0.15