Variability in cortical haemodynamic response during executive function tasks in older adults using functional near infrared spectroscopy

by

Drew Halliday
B.A., University of Victoria, 2011

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of the Requirements for the Degree of

MASTER OF SCIENCE

in the Department of Psychology

Supervisory Committee

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Abstract

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Variability in neural activity has historically been treated as noise, in favour of deriving estimates based on central tendency (e.g., mean). Recently, researchers have shown that variability and mean confer different sources of information and that increased variability in neural activity is associated with superior behavioural performance and that it decreases during late-life. Although mounting evidence suggests that neural variability is beneficial, it is less clear whether these findings are driven by within- or between-person factors and whether they are apparent during higher-order cognitive tasks. Further, variability can be derived in several different ways, drawing into question its congruence across operationalizations. The present investigation sought to separate within- and between-person sources of variance in order to ascertain what was driving any observable effects in three operationalizations of cerebral oxygenation, computed based on central tendency (mean), variability (standard deviation) and signal complexity (multivariate multiscale entropy). 25 older adults (71-81 years of age) completed two tasks of executive functions while undergoing assessment using functional near infrared spectroscopy. Time-varying covariation models were employed to estimate the effects of cerebral oxygenation on behavioural performance, as well as the moderating effects of age and fall status. Findings suggest that mean and variability are differentially associated with behavioural performance and are increased in older adults at greater fall risk. Whereas mean based computations were positively associated with more accurate and faster responding, variability based computations were primarily associated with faster responding only and occurred in non-overlapping regions of prefrontal cortex. Future studies of neural variability may consider examining within-

and between-person factors and operationalizing signal complexity in cerebral oxygenation over longer time periods to examine its effects over multiple time scales.

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Acknowledgments

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Introduction

The field of Neuropsychology has evolved remarkably over the past century in its approach to understanding brain-behaviour relationships – from early lesion studies, which formed a strong foundation for the field, through to neuroimaging and epigenetic methodologies, which continue to improve the precision with which we measure the nervous system and identify mechanisms underlying how pathology is manifest and expressed in behaviour. Statistical models have also become more sophisticated, and have allowed researchers to analyze an increasingly rich array of information obtained from these advanced methods. Combined, these methods facilitate exciting opportunities to study novel parameters of the human nervous system, and to advance our collective understanding as to how various insults to it may impair an individual's quality of life. Perhaps most excitingly, these advancements stand to lay the foundation for improved intervention techniques, to restore quality of life in individuals for whom it has been impeded.

Measures of central tendency (i.e., mean, median and mode) are a common metric of functioning at the behavioural (e.g., response time – RT), physiological (e.g., blood pressure – BP) and neuronal (e.g., blood oxygenated level-dependent – BOLD) level, and have typified research in the cognitive behavioural and lifespan sciences (MacDonald, Nyberg & Bäckman, 2006). Although useful, indexing these functions through central tendency has arguably excluded a wealth of information that is contained in variability at the within-person level, which is typically discarded as noise in favour of computing central tendency (e.g, MacDonald et al., 2006; Gamaldo, Weatherbee & Allaire, 2008;

Garrett, Samanez-Larkin, MacDonald, Lindenberger, McIntosh & Grady, 2013). Over the past few decades, researchers have examined within-person variability in multiple domains of functioning, and have uncovered a wealth of information pertaining to the nature of the nervous system and how it functions. Whether increased variability at the within-person level connotes adaptive or maladaptive functioning depends on numerous factors, such as chronological age (e.g., children relative to older adults), cognitive status (e.g., healthy relative to impaired), domain (e.g., behavioural relative to physiological), time metric (e.g., moment-to-moment relative to week-to-week) and level of task difficulty (e.g., easy relative to difficult). Further, most of the literature on within-person variability has focused on behavioural, physical and physiological measures, while variability in neural activity remains relatively understudied (Garrett et al., 2013). This investigation focuses on neurophysiological variability in older adults and discusses the relevance of understanding neural variability through the modulating effects of fall risk and cognitive load in higher order cognitive tasks.

Domains of Variability

Variability may be defined in a number of distinct ways. Cattell (1966) conceptualized variability based on number of persons, measurement occasions, and tasks to derive three primary indices (see Nesselroade 1992 for a review). Between-person variability refers to the distribution of scores that is derived from a number of individuals completing a given task at a given point in time (i.e., single measurement occasion). Dispersion refers to variability within a given person across a number of different measures (e.g., dispersion across a battery of neuropsychological tests). Intraindividual variability (IIV) refers to variability within a given individual, within a given task, across

multiple time-points (e.g., trial-to-trial, or across multiple assessment occasions using the same task). A considerable number of cognitive aging studies have examined IIV across trial-to-trial RT performance, which has contributed greatly to our understanding of the adaptive and maladaptive significance of variability (e.g., Hultsch, MacDonald, Hunter, Levy-Bencheton & Strauss, 2000).

At the cognitive behavioural level, IIV in RT during cognitive tasks (e.g., cognitive interference) is generally viewed as maladaptive, and has been linked to increasing age (Nesselroade & Salthouse, 2004) and impaired cognitive status in older adults (Dixon, Garrett, Lentz, MacDonald, Strauss, & Hultsch, 2007; Hultsch et al., 2000), as well as to schizophrenia (Vinogradov, Poole, Willis-Shore, Ober, & Shenaut, 1998) and ADHD (Klein, Wendling, Huettner, Ruder & Peper, 2006). Accordingly, increased behavioural variability has been suggested as a proxy for central nervous system (CNS) integrity (MacDonald, Li & Bäckman, 2009), which in older adults especially, may result from age-related changes in neuromodulation and white matter demyelination (MacDonald & Stawski, 2015). We recently demonstrated the sensitivity of intraindividual variability in finger tapping speed to cognitive status in a group of individuals with and without Mild Cognitive Impairment (MCI). Across 4 years and up to 17 measurement occasions, individuals with stable MCI demonstrated significant time-varying covariation (or "coupling") with performance on a spatial working memory task, such that on occasions when variability was above their personal mean (in variability), mean spatial working memory performance tended to be slower (Halliday, Stawski & MacDonald, under review). This effect was observed only for MCI individuals however, suggesting that relatively subtle degradation of the CNS may increase behavioural

variability. Notably, IIV in behavioural performance may additionally stem from cognitive (e.g., attentional lapses), affective (e.g., daily levels of stress) as well as physiological (e.g., fluctuations in BP) mechanisms (MacDonald & Stawski, 2015), which are important caveats to consider in designing a study to investigate the functional relevance of IIV. IIV also varies according to level of task difficulty, and may be indicative of strategy search or learning effects in more complex cognitive tasks, relative to simpler tasks that are relatively devoid of strategy (e.g., perceptual-motor tasks). As such, IIV in tasks that provide little opportunity for strategy search or practice-related gains are typically associated with maladaptive outcomes (Hultsch & MacDonald, 2004; Hultsch et al., 2008). Importantly, increases in IIV appear to precede mean level changes in cognition – Lövdén, Li, Shing and Lindenberger (2007) demonstrated that variability in perceptual speed was associated with greater decline in category fluency across a span of 6-years. In contrast, mean levels of category fluency were not reliably associated with subsequent change in perceptual speed variability.

Variability in physiological processes has also been linked to neurocognitive outcomes, and may confer adaptive or maladaptive benefits, depending on the domain and time metric under investigation. Variability in gait parameters is associated with CNS integrity – in older adults, increased step length variability has been linked with a greater degree of brain infarcts, independent of age, cognitive function, gender and cardiovascular disease (Rosano, Brach, Studenski, Longstreth & Newman, 2007). Gait variability is also a strong predictor of fall risk in older adults, with increased variability associated with a greater likelihood of falling (Verghese, Holtzer, Lipton & Wang, 2009). Variability in blood pressure (BP) shares associations with cognitive function as well –

Gamaldo and colleagues (2009) examined the time-varying covariation of within-person BP variability in older adults and found that on occasions when individuals with high-average BP were above their personal averages, they tended to perform worse on a measure of inductive reasoning. In contrast, increased moment-to-moment variability in heart rate shares positive associations to executive functions (Thayer, Hansen, Saus-Rose & Johnsen, 2009) and may be viewed as a marker of healthy vascular functioning. Decreased heart rate variability may be a marker of arterial stiffness, which itself can impede brain perfusion in older adults (Davenport, Hogan, Eskes, Longman & Poulin, 2012). As with cognitive-behavioural variability, the examination of variability in physiological functions such as gait, BP and heart rate has afforded useful insights beyond information obtained through central tendency indices in isolation.

Neural Variability

In contrast to the number of studies examining cognitive-behavioural (e.g., RT) and physiological (e.g., gait) variability in older adults, the study of variability in neural activity is relatively novel. Similar to cognitive-behavioural variability, neural variability is thought to exhibit a U-shaped pattern across the lifespan (see figure 1), however patterns of neural variability are characterized as *inverted* (i.e., increasing through early-life and declining through late-life) with higher levels generally considered adaptive (see Grady, 2012 and Garrett et al., 2013 for reviews). Evidence for this stems from studies of infant and child development, which suggest that neural variability may be associated with the development of more complex neural circuitry (e.g., increased integration of neural circuits and formation of novel neural networks). Multiscale entropy (MSE) is one measure of variability that evaluates the occurrence of repetitive patterns within a

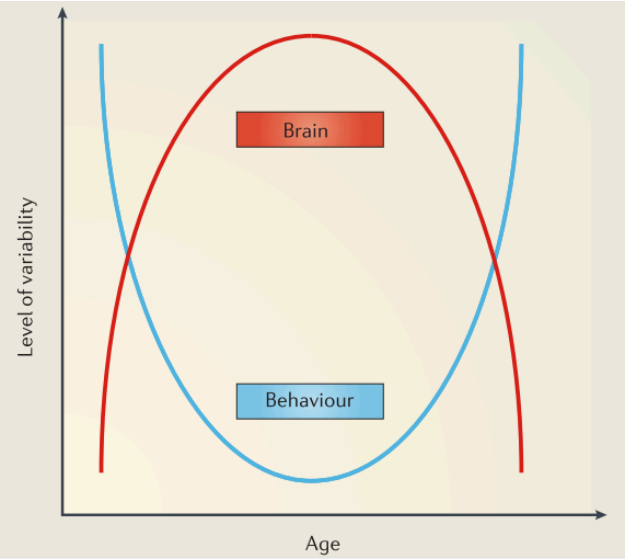

Figure 1. Hypothetical relationship between variability in brain activity and behavioural performance across the lifespan (Grady, 2012).

biological signal, with low values corresponding to more predictable and deterministic time series, and therefore with less signal complexity (Costa, Goldberger, & Peng, 2002). Lippé, Kovacevic and McIntosh (2009) examined MSE in post-synaptic potentials using electroencephalogram (EEG) in infants 1 to 66-months of age, exposed to basic visual and auditory stimuli. They found that, when measured on a continuous scale, age was reliably associated with increased MSE (Lippé et al., 2009), suggesting that neurological maturation may be characterized by increased signal complexity and therefore greater variability. Greater MSE in EEG recordings has also been linked to superior behavioural performance during a face recognition paradigm and to increasing age from childhood through to young adulthood (McIntosh, Kovacevic, & Itier, 2008). The results of this study were extended to examine functional connectivity, with development marked by a decrease in local entropy and an increase in distributed entropy (Vakorin, Lippé, & McIntosh, 2011). These authors have further demonstrated that MSE in task-relevant

regions (fusiform gyrus) is greater for upright relative to inverted faces, suggesting that variability in neural activity is up-regulated during tasks that require a variety of integrative neural computations (Mišić, Mills, Taylor & McIntosh, 2010). EEG functional connectivity during resting state was also examined in a sample of 10-year olds to investigate the functional implications of MSE. Nodes that showed the greatest signal complexity (indexed using MSE) were ones (i) which made the most connections (degree), (ii) were reached more easily by other nodes in the network (efficiency), and (iii) which tended to occupy a position that was the shortest distance between other nodes within the network (betweeness) (Mišić, Valkorin, Paus & McIntosh, 2011). Most recently, the functional implications of MSE have been examined in fNIRS, using a working memory paradigm with a sample of 6 young adults (Angsuwatanakul, Iramina & Kaewkamnerdpong, 2015). Here, the authors found greater MSE in premotor areas for information that was successfully remembered relative to information that was forgotten. Combined, these studies imply that brain maturation in early-life is characterized by increasing signal complexity, itself a proxy for variability, and that this increase in complexity is functionally significant.

In late-life, decreased variability in functional brain activation is associated with increasing age and diminished behavioural performance. Garrett, Kovacevic, McIntosh and Grady (2010) computed blood oxygen level-dependent (BOLD) variability (SD_{BOLD}) as well as mean concentration values ($mean_{BOLD}$) and compared their zero-order and partial correlations with chronological age in a sample of younger (m = 25.8) and older (m = 66.5) adults. They found that greater SD_{BOLD} was associated with younger age, particularly in cortical regions, and that the predictive association to chronological age

was more than 5 times greater for SD_{BOLD} relative to $mean_{BOLD}$. Perhaps most strikingly, the brain regions associated with age were virtually orthogonal between the two indices (i.e., SD_{BOLD} and $mean_{BOLD}$), further supporting the assertion that variability is a robust and independent phenomenon from central tendency. In a follow up study, these authors examined the associations between SD_{BOLD} and behavioural performance (Garrett, Kovacevic, McIntosh & Grady, 2011). They found that younger, faster and more consistent performers (i.e., those who were less variable in RT) showed greater BOLD variability (SD_{BOLD}) across a battery of cognitive tasks (perceptual matching, attentional cueing and delayed match-to-sample), suggesting that variability in BOLD is functionally significant in adulthood. Age and performance were not only associated with greater SD_{BOLD}, but with greater regional differentiation as well. Lastly, these authors examined changes in SD_{BOLD} from rest to experimental condition and found that SD_{BOLD} increased more broadly in younger and faster performing adults (Garrett, Kovacevic, McIntosh & Grady, 2013). Taken together, these studies demonstrate that decreased variability in functional brain activity is associated with advancing age and with poorer cognitive performance.

Mechanisms and Determinants

How neural variability relates to superior cognitive performance and to aging is an area of active exploration. SD_{BOLD} was recently examined in relation to dopamine (DA) binding potential and to disengagement of the default-mode network, as potential mechanisms supporting spatial working memory performance in younger and older adults (Guitart-Masip, Salami, Garrett, Rieckmann, Lindenberger & Bäckman, 2015). Greater variability in subcortical areas was associated with worse performance, increasing age,

and less DA binding potential. In contrast, variability in cortical regions was associated with more accurate performance and younger age, but was not associated with DA binding potential. Cortical variability was, however, associated with decreased activity in the default-mode network, suggesting that disengagement of this network may be a key mechanism through which neural variability enhances cognitive function (Guitart-Masip et al., 2015).

Variability in brain activity is also affected by neurological insults. Raja Beharelle, Kovačević, McIntosh and Levine (2012) used magnetoencephalography (MEG) to compare MSE in participants with moderate to severe traumatic brain injury (TBI) to healthy controls. They used a feature integration task (Stuss, Streth, Hugenholtz, Picton, Pivik, & Richard, 1989) in which participants identified a target from three options based on one or more features of the shape (e.g., shape, colour, line orientation). MSE was computed for non-target trials as a proxy for sustained attention and greater values were associated with decreased behavioural variability in both controls and patients with TBI. This relationship between MSE and behavioural performance was stronger in TBI individuals, suggesting that increased neural variability may be associated with better behavioural recovery following injury. In relation to neurodegenerative conditions, EEG MSE was examined across fine- and course-grained time scales, and compared between patients with presenile Alzheimer's disease (AD) and healthy controls. At fine-grained time scales, MSE values in the AD group were smaller, whereas across course-grained time scales, they were greater in the AD group (Mizuno et al., 2010). These findings indicate that neural variability is affected by neurodegenerative conditions such as AD, but that the significance of MSE values is

dependent on the scale of time metric (i.e., fine- vs. course-grained). Signal complexity appears to confer functional benefits at finer scales, where variation is apparent across shorter concatenations of samples, relative to longer ones (i.e., course-grained). Across longer concatenations of samples, signal complexity may instead be indicative of neurophysiological inconsistency (e.g., due to neurodegenerative processes) as opposed to complexity.

In addition to the empirical evidence supporting the functional relevance (i.e., developmental, cognitive, health) of neural variability, several authors have offered theoretical explanations on the same account. McDonnell and Ward (2011) argue that neural networks are more robust when they are generated in the presence of greater noise (through "stochastic facilitation"), which is further supported by the aforementioned studies of infant and child development. Arduini (1963) and Pinneo (1966) distinguished between tonic (i.e., ongoing neural fluctuations) and phasic neural activity (i.e., stimulus-driven activity), and argued that tonic activity provides the necessary foundation for effective neural functioning. Phasic activity represents a relatively small proportion of total activity, and operates on pre-existing tonic activity. Garrett et al., (2013) suggest that, "without the continual, fluctuating and variable 'hum' of tonic brain activity then, state-to-state transitions may prove more difficult" (p. 611). Tonic activity may be equally as informative as phasic activity, although its functional significance is understudied by comparison. Variability in tonic activity may be functionally significant (i) by facilitating a greater dynamic range, (ii) according to Bayesian optimization and (iii) by enabling itinerant dynamics (Garrett et al., 2013). Variability in functional brain activity facilitates a greater dynamic range by providing a greater range of responses to a

greater range of stimuli. Further, a greater distribution of potential responses facilitates Bayesian optimization, such that a population of neurons will select a response that approaches a theoretical optimum from that distribution of responses. Lastly, the brain avoids determinacy by destroying fixed points and enabling itinerancy to allow for exploration of alternative responses. Collectively, there is strong evidence empirically and theoretically to support the investigation of the functional utility of neural variability.

Operationalizations of Neural Variability

Mean-based computations of neuroimaging data have historically been employed to account for the variability contained within a given signal, in an attempt to derive a robust estimate of neural activity. Procedures for operationalizing variability in neuroimaging data fall roughly into two categories; computation of standard deviation (SD) about a block normalized mean and multiscale entropy (MSE). Concerning the former, Garrett and colleagues championed the approach in their seminal paper, wherein they first normalized like-experimental conditions and then concatenated them together, before computing SD from the overall block normalized mean (Garrett et al., 2010). This approach is most appropriate for fMRI data, which is sampled at a relatively low temporal resolution (e.g., each 20 second fixation block contained only 10 samples), but which affords an analysis of variability across a relatively fine level of spatial resolution. In adopting the SD approach, one could then combine voxels to create multivariate patterns, which create a more robust image of the patterns of activity that can then be contrasted against other patterns (e.g., SD contrasted against mean).

In contrast to the SD approach, MSE computations capitalize on superior temporal resolution and examine a given signal at multiple temporal scales. Costa et al.

(2002) introduced MSE as an entropy metric specific to physiological signals, in recognition that the dynamical complexity of biological signals likely operates across a range of temporal scales. Ahmed and Mandic (2011) have since adapted this approach for multichannel data, in order to account for within- and cross-channel dependencies that may be present in multichannel data (e.g., adjacent regions of interest). Much of the extant MSE neuroimaging literature pertains to EEG studies, as EEG methodology is particularly well suited, given its superior temporal resolution.

Current Investigation

Moment-to-moment variability in neural activity is an emerging area of research and shows promise in shedding novel insights to the human nervous system. Data from infant (e.g., Lippé et al., 2009; McIntosh et al., 2008; Mišić et al., 2011; Vakorin et al., 2011) and older-adult studies (e.g., Garrett et al., 2010; 2011; 2013) suggest that the developmental trajectory of neural variability is U-shaped and that increased variability is associated with superior performance (Angsuwatanakul et al., 2015; Garrett et al., 2011; 2013; McIntosh et al., 2008; Mišić et al., 2010) and better recovery from TBI (Raja Beharelle et al., 2012). The functional significance of neural variability during higher-order cognitive tasks (i.e., whether greater variability enhances behavioural performance) is virtually unexplored in older adults, and has been limited to perceptual and attentional cueing (e.g., Garrett et al., 2011; 2013), basic working memory tasks (e.g., Garrett et al., 2011; 2013; Guitart-Masip et al., 2015) and face recognition tasks (e.g., McIntosh et al., 2008) so far. Thus, examining neural variability across additional cognitive domains (e.g., cognitive interference) represents an important contribution to the field. Additionally, modulation of signal variability due to cognitive load is an important area

of exploration, as divergent findings have been observed in tasks that are less cognitively demanding (e.g., He, 2011; Takahashi et al., 2009). The majority of studies examining neural variability in older adults have used fMRI to index the BOLD signal, however given that the average sampling rate of fMRI methodology is comparatively slow (e.g., Garrett et al., 2010; 2011; 2013 used a TR of 2000 ms), these studies provide a relatively course estimate of BOLD variability. Further investigation of variability in cerebral oxygenation is therefore an important avenue of exploration, and may be better suited to neuroimaging methodologies indexing brain blood flow that use faster sampling rates (e.g., functional Near Infrared Spectroscopy – fNIRS).

This investigation examines several operationalizations of the cortical haemodynamic response in older adults during executive function tasks at the within- and between-person levels. Given that the majority of the extant neural variability literature is based on between-person effects, it was of interest to parse apart these sources of variance. The goal in doing so was to avoid the ecological fallacy (Robinson, 1950), which refers to the phenomenon where results at the individual level may be of a particular magnitude and direction, but when aggregated at the group level, become driven by between-person confounds (e.g., age, cognitive status) that may obscure the effect of interest. It was of additional interest to examine variability during executive function tasks as these (a) represent higher-order cognitive processes for which neural variability remains poorly understood, and (b) allow for an analysis of the modulating effects of cognitive load (i.e., easy relative to difficult conditions). Lastly, it was of interest to examine modulation by fall status, given that falls in older adulthood may serve as a proxy for early cognitive decline (Kearney, Harwood, Gladman, Lincoln &

Masud, 2013). The risk for falling is greater in older adults with MCI than in those without (Delbaere et al., 2012; Liu-Ambrose, Ashe, Graf, Beattie, & Khan, 2008) and falls may serve as clinically salient index events for those presenting in the prodromal stages of dementia, due to neurodegeneration that affects cognitive and postural control.

Key research objectives include understanding the extent to which opposing operationalizations of cortical haemoglobin concentrations are differentially modulated as a function of cognitive domain, cognitive load and fall status (fallers vs. non-fallers). It was hypothesized that the more demanding tasks would result in greater recruitment of neural tissue, but that the patterns would differ across the operationalizations (e.g., by behavioural metric and cortical region). It was also anticipated that these patterns would be further modulated by fall status and chronological age. To the extent that behavioural performance was comparable across the groups, it was expected that fallers and older individuals would recruit additional neural tissue to perform the tasks relative to non-fallers and younger individuals. Lastly, it was anticipated that the variability operationalizations of haemoglobin would show greater utility in predicting fall status than the mean-based computation.

Method

Participants

Data were collected from 25 older adults (13 females, 12 males) 71 – 81-years of age (*m* = 75.88, *SD* = 3.28). Exclusionary criteria included self-report of: (a) physician-diagnosed major medical illness with residual motor or sensory deficits (e.g., Parkinson's disease, stroke, heart disease, dementia, cancer, brain tumour), (b) severe sensory impairment (e.g., difficulty reading newspaper sized print, difficulty hearing a normal spoken conversation, difficulty writing or pressing buttons), (c) drug or alcohol abuse, (d) history of inpatient psychiatric treatment, (e) significant cognitive impairment (i.e., Mini Mental State Examination - MMSE score below 24), or (f) English as a second language.

Participants were also screened and followed for instances of falls, with 14 of the 25 having experienced at least one fall within 12 months of their first study visit (i.e., 12 months before or after intake). Participants underwent a comprehensive multimodal assessment including physical and mobility measures (e.g., gait, balance, proprioception) as well as neuropsychological (e.g., fluid reasoning, processing speed) and computerized cognitive testing.

Measures

The computerized cognitive tests included measures of cognitive interference (multi-source interference task – MSIT) and working memory (number-back – N-Back). The MSIT is a computerized task of cognitive interference, and was designed to activate the cingulo-frontal-parietal (CFP) cognitive attention network in subjects while undergoing functional neuroimaging (Bush, Shin, Holmes, Rosen & Vogt, 2003; Bush & Shin, 2006). The task shares similarities with the Stroop, Eriksen Flanker and Simon

tasks and is suitable for the purposes of this investigation for notable reasons. Previous investigations using the MSIT have elucidated a reliable network of neuroanatomical correlates that are engaged during task performance (e.g., Bush et al., 2003; Bush & Shin, 2006), including several which are accessible by fNIRS methodology using a relatively basic array positioned over the forehead (see Figure 4). The MSIT was designed with neuropsychiatric populations in mind and is regularly employed in studies of cognitive aging, however it has yet to be used to examine variability in functional brain activity. The nature of the MSIT is such that behavioural performance can be readily yoked to neural activity, as the task demands remain relatively constant from trial to trial within a block. Overall, cognitive interference is a suitable construct from which to ascertain patterns of variability and is best indexed through the MSIT for present purposes. Moreover, given the relevance of mitigating interfering information to avoid a fall (e.g., to inhibit a prepotent response and to refocus attention to avoid a fall), as well as the sensitivity of interference tasks during functional neuroimaging, there is reason to explore the utility of interference tasks with regard to differentiating high- from low-risk fallers.

In the MSIT, participants are presented with an array of three numbers (ranging in value from 0 - 3), one of which is a different numerical value than the others. Using a response input device, participants respond to the value of the odd target as quickly as possible while remaining accurate, across a total of 15 trials within a 30-second block. Trial durations are fixed at 2,000msec, allowing behavioural responses to be time-locked to the corresponding samples within a neuroimaging recording. Participants begin with either the control (location and value of the target are congruent) or interference condition (location and value of the target are incongruent), and complete a total of four

blocks for each of the conditions, which alternate (see Figure 2). A measure of interference can be derived by comparing the easier (control) to the more demanding (interference) condition, across several outcomes measures of interest, including accuracy, RT and haemodynamic response.

The N-Back task was originally introduced by Kircher (1958) and is a commonly used measure of working memory that is amenable to functional neuroimaging methodologies (Schreppel et al., 2008; Vermeij, van Beek, Rikkert, Claassen & Kessels, 2012). Meta-analyses have implicated a large network of neuroanatomical correlates that are recruited during N-Back performance involving verbal stimuli (e.g., letters, numbers) (Owen, McMillan, Laird & Bullmore, 2005), including several which are accessible by fNIRS methodology using a relatively basic array positioned over the forehead (see Figure 3). This task is of particular interest as it taps into a higher-order cognitive construct (working memory) with established neuroanatomical correlates that is used increasingly more often with older adults, yet it remains relatively unexplored in terms of neurophysiological variability. During the N-Back task, participants are presented with a sequence of 10 letters and are required to indicate whether each letter is the same or different to the letter that preceded it *n*-trials earlier. In our version of N-Back, participants completed 7 blocks of the 2- and 3-back conditions. Blocks began with an instruction slide to remind participants of the required response (e.g., "Is the current letter the same as the letter 2 slides ago?"), followed by a sequence of 10 letters (1,500msec each) separated by inter-stimulus intervals of 500msec (Figure 3).

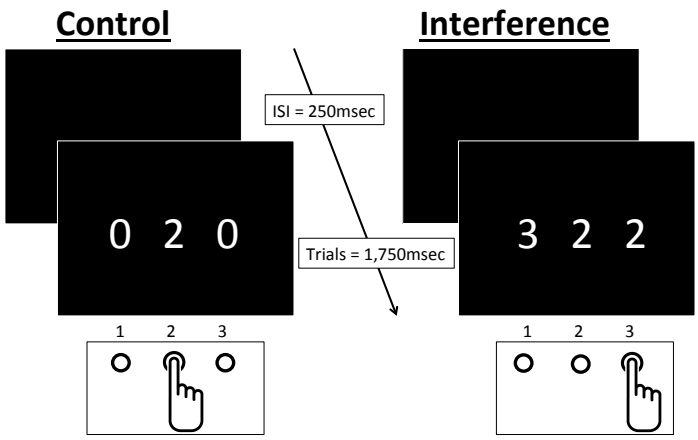

Figure 2. The Multi-Source Interference Task (MSIT). Participants are presented with three numbers and indicate the value of the number that is different. The value and location are congruent during control, and incongruent during the interference.

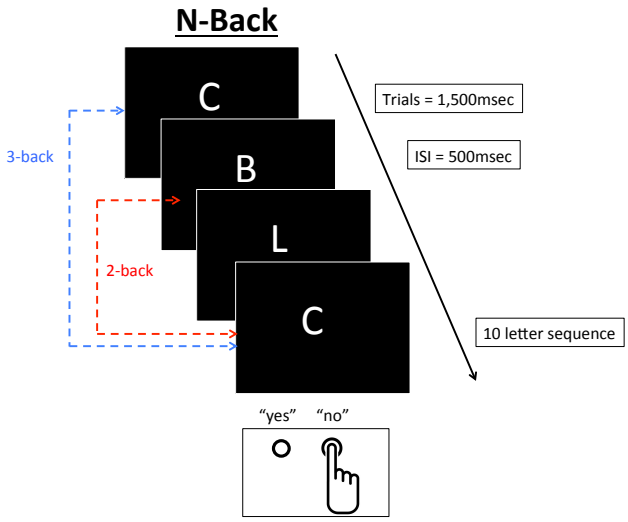

Figure 3. The Number Back (N-Back) test. Participants are presented with a series of 10 letters and indicate whether each letter is identical to the one that preceded it *n* trials ago, where *n* is 2 or 3, depending on the condition. Participants complete a total of 7 blocks for the 2- and 3-back conditions.

Functional Near Infrared Spectroscopy Recording

Functional Near Infrared Spectroscopy (fNIRS) is a non-invasive neuroimaging technique that determines cortical haemoglobin concentrations by measuring changes in light absorption. Changes in oxy- (HbO) and deoxyhaemoglobin (HbR) occur in response to neural activity, and can be measured continuously using fNIRS. By continuously measuring these changes during experimental conditions, an image of the brain can be reconstructed to determine how different regions of interest respond due to different cognitive demands. The magnitude of the haemodynamic response function (HRF) is then typically compared within individuals and between groups. The TechEn CW6 system (TechEn Inc., Milford, MA) samples at 50Hz (corresponding to TR = 20 ms), resulting in an image capture rate of one per .02 seconds. The output is therefore amenable to computing entropy metrics (e.g., MSE) to examine signal complexity at fine and course-grained time scales. Similarly, the computation of temporal variability using the SD computation approach is relatively robust in comparison to fMRI.

During computerized testing, participants were registered to the continuous-wave fNIRS system, which recorded cortical haemodynamic responses that were time-locked to events within the tasks. Participants wore custom-built fNIRS headgear consisting of an array positioned over prefrontal cortex (PFC) (Figure 4) containing 10 channels (8 at 3cm separation, 2 at 1.5cm separation), and were tested using a TechEn CW6 system (TechEn Inc., Milford, MA), using wavelengths of 690nm and 830nm to index deoxyhaemoglobin (HbR) and oxyhaemoglobin (HbO), respectively. The array was designed to maximize coverage of PFC, given the relevance of PFC areas during

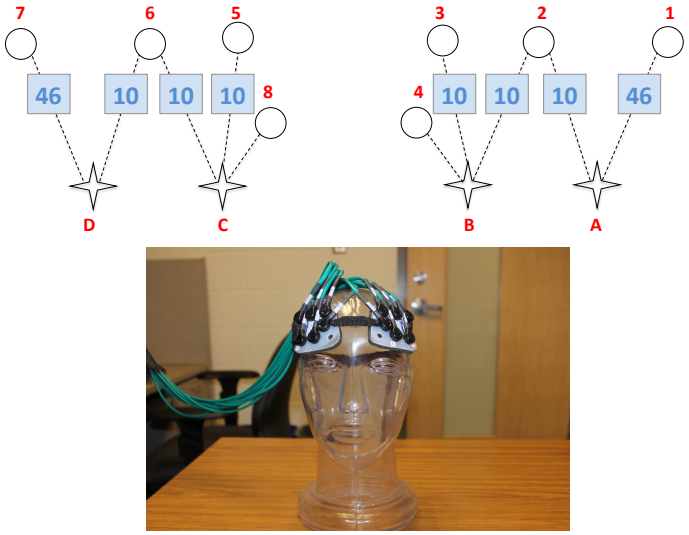

Figure 4. Top panel: The array design showing the location of the sources (star), detectors (circle), channels (dashed line) and Brodmann's areas (squares). Bottom panel: Frontal array positioned relative to 10-20 landmarks (Fpz, Fz, F7 and F8)

performance on the MSIT and N-Back tasks. The optical array was positioned relative to several 10-20 landmarks (Fpz, Fz, F7 and F8), and then 3D coordinates of scalp reference as well as optode locations were obtained using a Polhemus Fastrak digitizer system (Polhemus, Colchester, VT), in order to perform probabilistic spatial registration (Singh, Okamoto, Dan, Jurcak & Dan, 2005; Tsuzuki & Dan, 2014). Following this procedure, Montreal Neurological Institute (MNI) coordinates were generated for the mid-point of each source-detector pair (i.e., channel) for each participant, as well as average and composite standard deviation values across the group. Last, we converted the MNI coordinates to Brodmann's areas (BA) to ascertain macroanaotmical labels using Talairach Client software (Lancaster et al., 2000). The lateral most channels in both hemispheres recorded over Brodmann's area 46, with all remaining channels recording

over Brodmann's area 10 (Figure 4). The short-separation channels were not of interest for the present investigation, given the inability of these channels to capture information at the cortical surface. Therefore, they were dropped from subsequent analyses. Left-hemisphere channels covered inferior frontal gyrus (A1) and middle frontal gyrus (A2, B2 and B3) and right- hemisphere channels covered superior frontal gyrus (C5 and C6) and middle frontal gyrus (D6 and D7). To further ascertain whether the array facilitated adequate coverage from PFC regions of interest, the probabilistic path of the light photons using the Monte Carlo forward model (10^6 photons) was simulated, in order to derive a sensitivity matrix (Aasted et al., 2015) (Figure 5). This model was based on the Colin27 atlas, which specifies the absorption properties of scalp, skull, cerebral spinal fluid, gray matter and white matter. As is evident, the array captured information that is uniformly distributed across PFC.

The methods undertaken as part of this study were well situated to investigate age and cognitive load modulation of neural variability. Although fNIRS is limited in its spatial resolution to cortical regions, the greatest age-related group differences in BOLD variability (between young and old) have emerged in relation to cortical regions (Garrett et al., 2010; Guitart-Masip, 2015). Further, the PFC in particular is linked with greater inconsistency in behavioural performance (Stuss, Murphy, Binns & Alexander, 2003) and are heavily implicated in executive functions (e.g., cognitive interference, working memory). Although our array is limited to coverage of PFC, we are nevertheless recording from an area that is highly relevant to the phenomenon of interest.

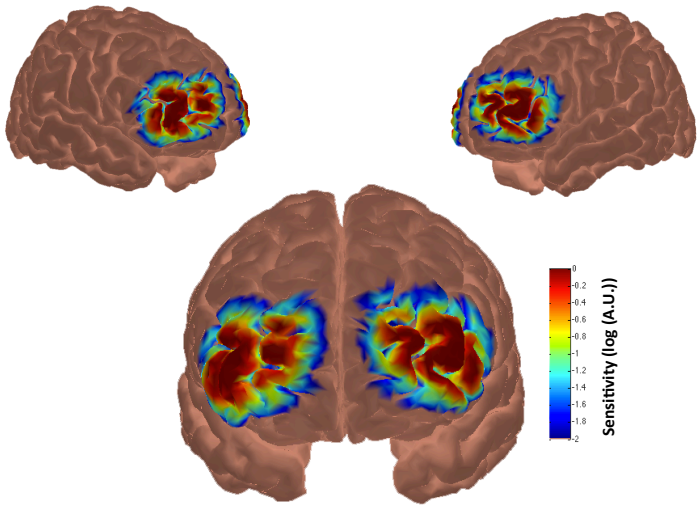

Figure 5. Sensitivity Profile based on the Monte Carlo forward model (10^6 photons) for the fNIRS array.

Preprocessing

Preprocessing of the fNIRS data was performed using Homer 2 software (Huppert, Solomon, Franceschini, & Boas, 2009). After converting the raw wavelengths to optical density values, we corrected for motion using a wavelet transformation algorithm (Molavi & Dumont, 2012) using an interquartile range of 0.1 (Brigadoi et al., 2014; Cooper et al., 2012). Next, we applied bandpass filtering to correct for physiological noise using a high-pass filter value of 0.01Hz and a low-pass filter value of 0.1Hz. We then converted from optical density to haemoglobin concentrations by applying the Modified Beer-Lambert Law, and then exported for subsequent operationalizations.

Operationalizations of Oxyhaemoglobin

Three operationalizations of HbO were derived for the purposes of this study; mean, SD and multivariate multiscale entropy (MMSE). Outliers were identified as

values greater than 3 SD from the sample mean and were deleted pairwise, with subsequent modelling based on full information maximum likelihood.

Mean estimates of HbO were estimated by aggregating across all samples contained within a given experimental condition. Given the nature of the haemodynamic response function, which typically unfolds over the course of 15-25 seconds, we derived single estimates of HbO within a given block. This equated to 8 segments for the MSIT task (4 control, 4 interference) and 14 segments for the N-Back task (7 2-back, 7 3-back). Block normalized SD was used to estimate signal variance, based on in-house software following the approach used by Garrett and colleagues (2010; 2011; 2013). As with the mean estimates, we derived a single SD estimate per block to maximize stability of the estimates, while enabling us to employ time-varying covariation models.

MMSE was used to estimate entropy in multivariate regions at different time scales, based on in-house software derived from Ahmed and Mandic (2011). Four regions of interest (ROI) were specified; left lateral (A1 and A2), left medial (B2 and B3), right medial (C5 and C6) and right lateral (D6 and D7). Based on the Ahmed and Mandic review (2011), we set the threshold parameter to $r = 0.5$, which dictates how similar adjacent vectors must be. Entropy was computed across 2-300 scales, resulting in time scales of .04-6 seconds. For subsequent analyses, MMSE estimates were aggregated across all scales to derive a single estimate. Although previous studies of MSE in neural activity examine fine- and course-grained estimates (e.g., Mizuno et al,. 2010; Angsuwatanakul et al., 2015), the paradigms utilized in the present study did not afford segment lengths long enough to generate reliable course-grained estimates. Further, the

models employed subsequently, maximize information that is contained across shorter estimates of the haemoglobin time course.

Results

Behavioural Data

MSIT scores were first screened for blocks with accuracy performance less than 50%. Given the nature of the task and potential EF difficulties experienced by the participants, there were several blocks of interference results in which participants appeared to have reversed the criteria, responding to the location of the target instead of its value. These blocks were removed from both behavioural and fNIRS analyses, yielding a total of 19 cases (9 fallers, 10 non-fallers) with one or more valid blocks of interference responding. Independent samples t-tests were conducted to examine the effect of group status on MSIT accuracy and response latency (based on attempted trials only) for both the control (fallers, $n = 14$; non-fallers, $n = 11$) and interference (fallers, $n = 9$; non-fallers, $n = 10$) conditions. No significant differences were observed as a function of fall status (all ps > .05; see Table 1).

N-Back behavioural performance was examined in terms of accuracy and response latency (based on attempted trials only) and subsequently compared between fallers and non-fallers. No significant differences were observed as a function of fall status (all ps > .05; see Table 1).

Time-Varying Covariation Models

HLM 6.08 software was used to fit linear mixed models to examine the time-varying covariation between each operationalization of haemoglobin (i.e., mean, SD and MMSE) and behavioural performance (i.e., accuracy and response time). Models were run separately for each paradigm (i.e., MSIT and N-Back). For the mean and SD

Table 1. Group differences on computerized tasks. Data for MSIT control and interference are based on blocks with at least 50% accuracy. RT values are based on attempted trials only for MSIT and N-Back.

	Non-Fallers	Fallers	*t* value	*p* value
Control Accuracy	98.64 (2.56)	97.38 (4.70)	0.795	0.435
Control RT	620.13 (87.99)	614.57 (142.08)	0.114	0.911
Interference Accuracy	84.00 (14.62)	80.06 (12.65)	0.624	0.541
Interference RT	993.68 (83.84)	942.97 (114.52)	1.109	0.283
2-Back Accuracy	58.00 (18.45)	62.35 (9.44)	0.426	0.674
2-Back RT	901.67 (124.02)	923.99 (128.30)	0.758	0.456
3-Back Accuracy	45.14 (18.41)	51.63 (7.96)	0.685	0.501
3-Back RT	872.10 (108.76)	770.66 (213.88)	1.181	0.250

based computations, separate models were run for each fNIRS channel (i.e., A1, A2, B2, B3,C5, C6, D6, D7), whereas for MMSE, separate models were run for each ROI (i.e., As, Bs, Cs, Ds). Outliers were discarded as values greater than 3 SD from an individual's mean. In order to derive distinct between- and within-person estimates of cortical haemoglobin on behavioural performance, we person-mean centered each operationalization of haemoglobin, before entering it into the model (see Hoffman & Stawski, 2009). The following equations outline the analyses conducted to examine the block-to-block covariation between haemoglobin and behavioural performance (i.e., accuracy and response latency):

$$Behaviour_{ij} = \pi_{0i} + \pi_{1i}(block_{ij}) + {}_{+}\pi_{2i}(haemoglobin_{ij}) {}_{+} e_{ij} \quad \text{(level-1)}$$

$$\beta_{0i} = \gamma_{00} + \gamma_{01}\,(haemoglobin) + u_{0i} \quad \text{(level-2)}$$

$$\beta_{1i} = \gamma_{10} + u_{1i}$$

$$\beta_{2i} = \gamma_{20} + u_{2i}$$

where behaviour represents the outcome measures of accuracy or response latency for either MSIT or N-Back for person i and block j. Within-person variance is reflected in the

level-1 residuals Var(e_{ij}), associated with within-person variability block-to-block. Between-person variance is reflected in the level-2 residuals, Var(U_{0j}) and indicates the amount of variability in a given HbO operationalization that exists between-persons. Given several a priori hypotheses regarding expected directional effects, one-tailed tests were employed for specific, planned comparisons.

HbO mean. The within- and between-person associations of HbO mean on variation in behavioural performance were tested separately for each paradigm, behavioural metric and fNIRS channel. Table 2 summarizes the effects.

For MSIT, significant between-person effects were observed for accuracy in both the control (A1: β=-0.022, p<.05; A2: β=-0.018, p<.05) and interference conditions (A1: β=-0.104, p<.05; D6: β=-0.060, p<.05), such that greater recruitment of HbO was associated with less accurate performance. This suggests that at the between-person level, greater recruitment of HbO may be a harbinger of unsuccessful behavioural compensation.

For N-Back, significant between-person effects were observed for RT in both the 2- (C5: β=-43.86, p<.05, one tailed; C6: β=-55.33, p<.05; D7: β=-61.32, p<.05) and 3-back conditions (D7: β=-53.10, p<.05, one tailed), such that greater recruitment of HbO in right hemisphere was associated with faster performance. At the within-person level, significant effects were observed for accuracy in both the 2- (C6: β=0.023, p<.05, one tailed; D7: β=0.022, p<.05, one tailed) and 3-back conditions (D7: β=0.019, p<.05, one tailed) in right hemisphere channels, indicating that on blocks when more HbO was recruited relative to a person's own mean, accuracy was greater. At both the between- and within-person levels, greater recruitment of HbO appears to have facilitated

Table 2. Two-Level Multilevel Models of Coupling Between mean HbO and Behavioural Performance (mean and RT) for MSIT and N-Back.

Task	Outcome	Channel	Intercept (γ_{00})	PM (γ_{01})	Slope Segment (γ_{10})	Slope PMC (γ_{20})
Control	Accuracy	A1	0.964**	**-0.022***	0.010	0.005
		A2	0.967**	**-0.018***	0.008	-0.002
		B2	0.961**	-0.006	0.012*	-0.024
		B3	0.965**	-0.007	0.009	-0.008
		C5	0.966**	-0.005	0.009	-0.002
		C6	0.967**	-0.002	0.008	-0.003
		D6	0.967**	-0.008	0.008	-0.002
		D7	0.968**	-0.007	0.007	-0.004
Interference	Accuracy	A1	0.773**	**-0.104***	0.046*	0.016
		A2	0.764**	-0.024	0.047*	-0.008
		B2	0.764**	-0.003	0.046*	-0.016
		B3	0.767**	-0.025	0.046*	-0.015
		C5	0.751**	0.040	0.052*	-0.020
		C6	0.764**	0.021	0.046*	-0.022
		D6	0.764**	**-0.060***	0.049*	0.044
		D7	0.753**	0.014	0.053*	**-0.060**$^{\#}$
Control	RT	A1	640.69**	-22.19	-15.78*	-4.44
		A2	643.21**	-10.54	-18.13*	-1.15
		B2	639.59**	-19.70	-15.05$^{\#}$	-2.54
		B3	638.21**	-3.66	-14.13$^{\#}$	-5.57
		C5	644.33**	-20.77	-18.21*	-10.65
		C6	645.48**	3.32	-18.98*	-9.26
		D6	646.67**	-15.97	-19.77*	**-23.09***
		D7	643.39**	-25.79	-17.58*	-9.06
Interference	RT	A1	977.24**	-17.92	11.40	-3.47
		A2	985.00**	-3.66	6.48	-13.28
		B2	989.78**	14.16	3.11	-10.48
		B3	987.30**	2.60	4.55	-15.31
		C5	992.31**	8.26	1.03	29.75
		C6	991.37**	16.47	1.69	13.02
		D6	972.96**	7.83	14.00	6.54
		D7	973.60**	9.72	13.93	4.48

**$p < .001$, *$p < .05$, $^{\#}p < .05$, one tailed

Task	Outcome	Channel	Intercept (γ_{00})	PM (γ_{01})	Slope Segment (γ_{10})	Slope PMC (γ_{20})
2-back	Accuracy	A1	0.537**	0.003	0.023*	0.014
		A2	0.539**	-0.004	0.022*	0.006
		B2	0.536**	0.025	0.023*	0.004
		B3	0.541**	0.025	0.021*	0.010
		C5	0.536**	-0.010	0.023*	0.009
		C6	0.539**	0.027	0.022*	**0.023**$^{\#}$
		D6	0.537**	0.037	0.023*	0.013
		D7	0.539**	0.013	0.022*	**0.022**$^{\#}$
3-back	Accuracy	A1	0.440**	-0.006	0.016*	0.007
		A2	0.439**	-0.002	0.017*	-0.001
		B2	0.437**	0.015	0.018*	0.004
		B3	0.438**	0.022	0.017*	-0.002
		C5	0.436**	-0.006	0.018*	0.003
		C6	0.437**	0.014	0.017*	0.009
		D6	0.443**	**0.048***	0.015*	0.003
		D7	0.443**	0.016	0.015*	**0.019**$^{\#}$
2-back	RT	A1	967.11**	-2.52	-17.47*	9.57
		A2	968.84**	2.69	-18.05*	9.43
		B2	965.44**	-16.85	-16.92*	13.49
		B3	966.74**	-6.79	-17.35*	**25.26***
		C5	962.44**	**-43.86**$^{\#}$	-15.91*	5.28
		C6	966.85**	**-55.33***	-17.38*	12.88
		D6	964.06**	-29.49	-16.46*	-1.74
		D7	967.62**	**-61.32***	-17.64*	16.99
3-back	RT	A1	995.38**	31.25	-15.54*	9.57
		A2	995.37**	24.27	-15.44*	-0.97
		B2	992.08**	16.10	-14.33*	-8.49
		B3	995.21**	-8.84	-15.37*	-4.56
		C5	995.62**	-7.48	-15.53*	-10.53
		C6	993.92**	-35.91	-14.98*	-14.02
		D6	992.66**	-6.21	-14.53*	-9.28
		D7	994.07**	**-53.10**$^{\#}$	-14.98*	-5.83

**$p < .001$, *$p < .05$, $^{\#}p < .05$, one tailed

successful compensation; that is, greater cerebral oxygenation appears to have enhanced performance during N-Back, but not MSIT.

HbO SD. The within- and between-person associations of HbO SD on variation in behavioural performance were tested separately for each paradigm, behavioural metric and fNIRS channel. Table 3 summarizes the effects.

For MSIT, significant between-person effects were observed for RT in the control condition in two lateral left hemisphere channels (A1: β=0.60, p<.05, one tailed; A2: β=0.41, p<.05, one tailed), such that greater variability in HbO was associated with slower performance. At the between-person level for RT in the interference condition, the effects for each left hemisphere channel were in the negative direction. Although not statistically significant, these trends suggest that greater variability may be associated with faster performance in the more cognitively demanding condition (interference), relative to the less demanding condition (control).

For N-Back, significant between-person effects were observed for accuracy in the 2-back condition in the lateral-most left hemisphere channel (A1: β=-0.001, p<.05), such that greater variability in HbO was associated with less accurate performance. Conversely, significant between-person effects were observed for RT in the 3-back condition in a lateral left hemisphere channel (A2: β=-0.41, p<.05), such that greater variability in HbO was associated with faster performance. Overall, these effects were sparse and somewhat disparate

HbO MMSE. The within- and between-person associations of HbO MMSE on variation in behavioural performance were tested separately for each paradigm, behavioural metric and ROI. Table 4 summarizes the effects.

Table 3. Two-Level Multilevel Models of Coupling Between SD HbO and Behavioural Performance (mean and RT) for MSIT and N-Back.

Task	Outcome	Channel	Intercept (γ_{00})	PM (γ_{01})	Slope Segment (γ_{10})	Slope PMC (γ_{20})
Control	Accuracy	A1	0.953**	0.000	0.009	-0.000
		A2	0.956**	0.000	0.009	0.000
		B2	0.955**	0.000	0.012	0.000
		B3	0.971**	-0.000	0.008	0.000
		C5	0.965**	0.000	0.009	0.000
		C6	0.971**	-0.000	0.009	0.000
		D6	0.965**	0.000	0.009	0.000
		D7	0.961**	0.000	0.008	0.000
Interference	Accuracy	A1	0.720**	0.000	0.051*	-0.000
		A2	0.768**	-0.000	0.047*	-0.000
		B2	0.745**	0.000	0.046*	-0.000
		B3	0.739**	0.000	0.053**	0.000
		C5	0.797**	-0.001	0.055**	-0.000
		C6	0.788**	-0.000	0.051*	0.000
		D6	0.750**	0.000	0.051*	**0.000**$^{\#}$
		D7	0.834**	-0.001	0.051*	-0.000
Control	RT	A1	584.62**	**0.60**$^{\#}$	-16.55*	0.07
		A2	589.03**	**0.41**$^{\#}$	-17.33*	-0.07
		B2	654.76**	-0.13	-14.90$^{\#}$	0.05
		B3	615.57**	0.22	-18.15*	-0.06
		C5	637.57**	0.03	-15.46$^{\#}$	-0.04
		C6	648.46**	-0.08	-15.01$^{\#}$	0.04
		D6	633.97**	0.11	-17.26*	0.05
		D7	625.97**	0.14	-14.64$^{\#}$	0.11
Interference	RT	A1	961.20**	0.15	8.24	-0.04
		A2	962.13**	0.09	12.41	-0.09
		B2	968.11**	0.13	9.99	-0.30
		B3	973.77**	0.00	15.17	-0.15
		C5	979.52**	-0.16	16.34	-0.13
		C6	990.15**	-0.14	13.01	0.10
		D6	979.22**	-0.13	16.58	0.17
		D7	991.55**	-0.22	13.78	-0.02

**$p < .001$, *$p < .05$, $^{\#}p < .05$, one tailed

Task	Outcome	Channel	Intercept (γ_{00})	PM (γ_{01})	Slope Segment (γ_{10})	Slope PMC (γ_{20})
2-back	Accuracy	A1	0.616**	**-0.001***	0.022*	-0.000
		A2	0.554**	-0.000	0.03*	-0.000
		B2	0.508**	0.000	0.022*	-0.000
		B3	0.496**	0.001	0.021*	-0.000
		C5	0.521**	0.000	0.023*	0.000
		C6	0.546**	-0.000	0.024*	-0.000
		D6	0.506**	0.000	0.022*	-0.000
		D7	0.579**	-0.000	0.022*	-0.000
3-back	Accuracy	A1	0.453**	-0.000	0.018*	-0.000
		A2	0.423**	0.000	0.017*	-0.000
		B2	0.394**	0.000	0.017*	-0.000
		B3	0.444**	-0.000	0.018*	-0.000
		C5	0.480**	-0.000	0.016*	-0.000
		C6	0.460**	-0.000	0.016*	-0.000
		D6	0.431**	0.000	0.017*	0.000
		D7	0.444**	-0.000	0.018*	0.000
2-back	RT	A1	953.40**	0.09	-16.41*	0.04
		A2	967.62**	-0.02	-17.45*	0.13
		B2	930.99**	0.36	-16.27*	0.00
		B3	962.23**	-0.03	-15.81*	-0.04
		C5	953.09**	0.00	-13.31$^{\#}$	0.16
		C6	959.52**	0.04	-16.36*	0.10
		D6	963.68**	0.01	-16.74*	-0.05
		D7	938.64**	0.32	-17.08*	**0.14**$^{\#}$
3-back	RT	A1	991.54**	0.01	-14.87*	0.01
		A2	1046.45**	**-0.41***	-14.18*	0.01
		B2	996.91**	-0.03	-15.23*	0.01
		B3	975.27**	0.14	-13.84*	-0.04
		C5	986.02**	0.06	-14.76*	0.12
		C6	950.95**	0.34	-13.18*	0.02
		D6	992.24**	0.05	-15.89*	0.15
		D7	969.69**	0.24	-14.51*	0.04

**$p < .001$, *$p < .05$, $^{\#}p < .05$, one tailed

Table 4. Two-Level Multilevel Models of Coupling Between MMSE HbO and Behavioural Performance (mean and RT) for MSIT and N-Back.

Task	Outcome	Variables	Intercept (γ_{00})	PM (γ_{01})	Slope Segment (γ_{10})	Slope PMC (γ_{20})
Control	Accuracy	ROI A	0.940**	0.041	0.009	-0.051
		ROI B	0.955**	0.002	0.016#	-0.091
		ROI C	0.971**	-0.006	0.008	-0.097
		ROI D	0.952**	0.025	0.008	0.008
Interference	Accuracy	ROI A	0.673**	0.138	0.044*	-0.124
		ROI B	0.799**	-0.067	0.041*	**-0.285***
		ROI C	0.500*	**0.367***	0.058**	-0.096
		ROI D	0.612*	0.205	0.051*	0.119
Control	RT	ROI A	532.41**	172.80	-15.36*	-5.39
		ROI B	572.78**	120.92	-15.50#	-5.77
		ROI C	693.86**	-83.07	-18.85*	-97.97
		ROI D	605.74**	55.59	-15.62#	-65.57
Interference	RT	ROI A	1069.45**	-140.87	5.83	-154.29
		ROI B	1036.68**	-108.01	8.49	**-237.10#**
		ROI C	982.47**	-13.91	9.57	-133.63
		ROI D	945.44**	30.82	15.51	157.55

**$p < .001$, *$p < .05$, #$p < .05$, one tailed

Task	Outcome	Variables	Intercept (γ_{00})	PM (γ_{01})	Slope Segment (γ_{10})	Slope PMC (γ_{20})
2-Back	Accuracy	ROI A	0.840*	-0.444	0.023*	0.072
		ROI B	0.552*	-0.023	-0.023*	0.064
		ROI C	0.383	0.231	0.023*	-0.045
		ROI D	0.477#	0.085	0.024*	-0.047
3-Back	Accuracy	ROI A	0.924**	**-0.723***	0.016*	**0.104#**
		ROI B	0.700*	-0.298	0.017*	0.085
		ROI C	0.718*	-0.425	0.017*	-0.056
		ROI D	0.621*	-0.273	0.018*	-0.085
2-Back	RT	ROI A	713.40*	368.82	-16.88*	1.47
		ROI B	905.18**	81.37	-15.11*	138.91
		ROI C	1315.89**	-536.49	-15.53*	**166.45***
		ROI D	1173.87**	-313.76	-17.86*	48.39
3-Back	RT	ROI A	999.37**	-8.37	-14.91*	12.21
		ROI B	9543.69**	57.08	-14.43*	79.58
		ROI C	901.79*	143.14	-15.70*	40.22
		ROI D	1288.76**	-429.63	-15.25*	19.06

For MSIT, significant between-person effects were observed for accuracy in the interference condition (ROI C: β=0.367, p<.05), such that greater signal complexity in HbO in medial right hemisphere was associated with more accurate performance. At the within-person level, significant effects were observed for accuracy (ROI B: β=-0.285, p<.05), and RT (ROI B: β=-237.10, p<.05, one tailed), in the interference condition, indicating that on blocks when HbO signal complexity in medial left hemisphere was greater relative to a individual's mean, performance was faster but less accurate.

For N-Back, significant between-person effects were observed for accuracy in the 3-back condition (ROI A: β=-0.723, p<.05), such that greater signal complexity in HbO in lateral left hemisphere was associated with less accurate performance. Although non-significant, the between-person effects for accuracy in the 3-back condition for all other ROIs were in the negative direction, suggesting that greater signal complexity in HbO for the 3-back condition was not associated with enhanced behavioural performance, possibly due to the level of task demand.

Moderation of Coupling by Age and Fall Status

Having demonstrated significant between- and within-person effects across each operationalization of HbO in multiple conditions and ROIs, the moderating effects of age and fall status were examined subsequently. Fall status was not significantly associated with chronological age, $F(1,23)=1.54$, p=.89, and thus the two between-person predictors were entered into the model simultaneously. The following equations outline the analyses conducted to examine the block-to-block covariation between HbO and behavioural performance, as well as the moderating variables of interest:

$$Behaviour_{ij} = \pi_{0i} + \pi_{1i}(block_{ij}) + {}_{+}\pi_{2i}(haemoglobin_{ij}) {}_{+} e_{ij} \quad \text{(level-1)}$$

$$\beta_{0i} = \gamma_{00} + \gamma_{01}(fall\ status) + \gamma_{02}(age) + \gamma_{03}(haemoglobin) + u_{0i} \quad \text{(level-2)}$$

$$\beta_{1i} = \gamma_{10} + u_{1i}$$

$$\beta_{2i} = \gamma_{20} + \gamma_{21}(fall\ status) + \gamma_{22}(age) + u_{2i}$$

where behaviour represents the outcome measures of accuracy or response latency for either MSIT or N-Back for person i and block j. Within-person variance is reflected in both the level-1, Var(e_{ij}) residuals, associated with within-person variability block-to-block. Between-person variance is reflected in the level-2 residuals, Var(U_{0i}), Var(U_{1i}) and Var(U_{2i}) and indicates the amount of variability in a given HbO operationalization that exists between-persons. The effects of fall status (γ_{01}) and age (γ_{02}) on the between-person intercept, as well as on the magnitude of the coupling association (fall status (γ_{21}) and age (γ_{22})) were examined by their respective parameters. Given the relatively narrow age cohort, age was entered primarily as a covariate. A full summary of the moderated effects can be found in Appendix A.

HbO mean. The within- and between-person associations of HbO mean on variation in behavioural performance were tested separately for each paradigm, behavioural metric and fNIRS channel.

Fall status modulated several effects for interference RT, in right hemisphere channels. At the between-person level, where greater recruitment of HbO was associated with slower performance during the interference condition (C6: Υ_{03}=41.27, p<.05, one tailed; D7: Υ_{03}=36.33, p>.05), the effect was greater in fallers relative to non-fallers (C6: Υ_{01}=-59.00, p<.05, one tailed; D7: Υ_{01}=-63.84, p<.05, one tailed), such that greater HbO recruitment was associated with slower performance in fallers and faster performance in

non-fallers. With the inclusion of age and fall status in the model, the within-person effect of mean HbO on control RT emerged as significant in several right hemisphere channels (C5: Υ_{20}=-36.60, p<.05, one tailed; C6: Υ_{20}=-45.73, p<.05, D6: Υ_{20}=-40.97, p<.05), suggesting that on blocks where individuals recruited more HbO relative to their personal averages, they tended to perform faster. This effect was modulated by age in a lateral right hemisphere channel (D6: Υ_{22}=3.94, p<.05, one tailed), such that the magnitude of the coupling association was significantly smaller with each additional year of age. Taken together, these results suggest that greater recruitment of HbO may have facilitated successful compensation in the non-fallers relative to fallers and in younger relative to older adults.

Fall status modulated two between-person effects for 3-back accuracy in right hemisphere channels. Where greater recruitment of HbO was associated with more accurate performance (D6: Υ_{03}=0.050, p<.05; C6: Υ_{20}=0.032, p>.05), the effect was greater in fallers relative to non-fallers (D6: Υ_{01}=0.090, p<.05, one tailed; C6: Υ_{01}=0.093, p<.05, one tailed). Taken together, these findings tentatively suggest that greater recruitment of HbO during the 3-back condition may have enhanced behavioural performance in fallers more so than non-fallers.

HbO SD. The within- and between-person associations of HbO SD on variation in behavioural performance were tested separately for each paradigm, behavioural metric and fNIRS channel.

Fall status modulated the effects of HbO SD on interference RT at both the between- and within-person levels. At the between-person level, where greater variability in HbO was associated with faster performance during the interference

condition (D7: Υ_{03}=-0.30, p>.05), the effect was greater in non-fallers relative to fallers (D6: Υ_{01}=-61.55, p<.05, one tailed). At the within-person level, fall status modulated the coupling association, where greater variability relative to an individual's mean was associated with faster performance in the interference condition in the lateral-most channels (corresponding with DLPFC), bilaterally (A1: Υ_{20}=-0.23, p>.05; D7: Υ_{20}=-1.74, p>.05). Here, the effects were greater in non-fallers relative to fallers (A1: Υ_{21}=0.42, p<.05, one tailed; D7: Υ_{21}=2.37, p<.05), suggesting that increased variability relative to an individual's mean may be a harbinger of successful performance in low-risk individuals only in regions that have been previously associated with cognitive interference (i.e., dorsolateral prefrontal cortex - DLPFC; Bush et al., 2003; 2006).

Age and fall status emerged as significant across several computations of N-Back, however the patterns were generally inconsistent. At the within-person level, age modulated the effects of HbO on SD accuracy in both the 2- (C6: Υ_{22}=0.000, p<.05; D6: Υ_{22}=-0.000, p<.05) and 3-back conditions (B2: Υ_{22}=-0.000, p<.05; D7: Υ_{20}=-0.000, p<.05). Fall status modulated the within-person coupling association between greater HbO variability and slower RT in the 3-back condition (B3: Υ_{20}=0.23, p>.05; C5: Υ_{20}=0.36, p>.05), such that the effect was greater in fallers relative to non-fallers (B3: Υ_{22}=-0.43, p<.05; C5: Υ_{22}=-0.71, p<.05). Tentatively, these patterns might suggest that greater variability during more demanding cognitive tasks (3-back) does not facilitate superior behavioural performance and that this is especially the case for high-risk individuals.

HbO MMSE. The within- and between-person associations of HbO SD on variation in behavioural performance were tested separately for each paradigm, behavioural metric and fNIRS channel.

Fall status modulated the effects of HbO MMSE on interference RT at the between-person level in medial right hemisphere (ROI C: Υ_{03}=10.35, p>.05), such that greater signal complexity was associated with faster performance in the non-fallers relative to the fallers (ROI C: Υ_{01}=-58.64, p<.05). This suggests that increased signal complexity may be a harbinger of successful performance in low-risk individuals only. No within-person associations emerged as significant.

Fall status modulated the effects of HbO MMSE on 2-back RT at the within-person level in lateral right hemisphere (ROI D: Υ_{20}=-0.073, p>.05), such that on occasions when signal complexity in HbO was greater relative to their personal means, fallers were less accurate (ROI D: Υ_{21}=-0.443, p<.05). No between-person associations emerged as significant.

Discussion

This investigation sought to examine opposing operationalizations of the cortical haemodynamic response during executive function tasks in older adults. Neuroimaging data have historically been examined through central tendency computations, in order to derive what has been perceived as a more stable estimate of neural activity. Recent work has revisited previous assertions that neural variability is not merely noise (Arduini, 1961; Pinneo, 1966), and has shown that the variability inherent in neural activity conveys functional significance, including associations with brain maturation (McIntosh et al., 2008; Lippé et al., 2009; Vakorin et al., 2011), brain senescence (Garrett et al., 2010; 2011; 2013) and recovery from TBI (Raja Beharelle et al., 2012). Research also shows that variability in neural activity is associated with enhanced behavioural performance, however these studies have been limited to perceptual and attentional cueing (e.g., Garrett et al., 2011; 2013) and basic working memory tasks (Garrett et al., 2011; 2013; Guitart-Masip et al., 2015). The impetus for the present investigation was therefore to examine neural variability during higher-order cognitive tasks of executive function and to explore the moderation of this variability by cognitive load as well as fall risk. Further, the variability literature on cerebral oxygenation has been restricted to fMRI methodology, which is limited by temporal sampling resolution. Thus, more densely sampled profiles of variability for cerebral oxygenation remain virtually unexplored. Notably, although evidence continues to mount in favour of the functional significance of neural variability, it is less clear whether these effects are driven by within- or between-person factors. Given the potential for effects at each level to differ

due to unaccounted for between-person variables (e.g., age, practice effects), it is both conceptually and statistically feasible that as a predictor, neural variability may account for variance at the between- but not the within-person level (i.e., that it may be associated with superior behavioural performance, but be driven by between-person factors). Higher-order cognitive tasks may be more likely to exhibit practice effects relative to other cognitive constructs of interest, further underscoring the importance of separating within- and between-person sources of variance. Therefore, the present investigation also sought to separate these two sources of variance in order to ascertain what was driving any observable effects by computing a more stringent within-person test. Using fNIRS, three operationalizations of HbO were derived, based on central tendency (mean), variability (SD) and signal complexity (MMSE). Time-varying covariation models were employed to estimate the within- and between-person effects of HbO on behavioural performance, as well as the moderating effects of age and fall status in a sample of otherwise healthy older adults. Using person-mean centering, individuals effectively served as their own baselines (Hoffman & Stawski, 2009), such that deviations from their personal averages were not conflated by unaccounted for variables (e.g., differences in practice effects).

The effects observed within the MSIT task (a hybrid executive function task of cognitive interference) are relatively consistent and suggest that the recruitment of additional neural tissue enhanced behavioural performance overall, but that this occurred for non-fallers relative to fallers and for younger relative to older adults. To the extent that fall status and older age are associated with degradation of neural tissue (e.g., cortical atrophy), these findings suggest that such additional recruitment was beneficial for

individuals at low risk only. With the accrual of additional age-related neural degradation, additional recruitment of neural tissue from PFC may no longer be beneficial in enhancing behavioural performance. These patterns are in keeping with the compensation-related utilization of neural circuits hypothesis (CRUNCH) (Reuter-Lorenz & Cappell, 2008; Grady, 2012), which suggests that at greater levels of task demand, additional recruitment of neural tissue in older adults may no longer facilitate behavioural compensation. Across operationalizations, greater mean concentrations of HbO were associated with greater accuracy and faster performance, whereas greater variability (SD) and signal complexity (MMSE) were associated primarily with faster performance. Using the MMSE operationalization, the observed patterns suggest that signal complexity in medial left hemisphere may correspond to a speed-accuracy trade-off, wherein responding faster is prioritized above responding more accurately.

On mass, these findings are in keeping with assertions that mean and variability confer orthogonal sources of information (e.g., Garrett et al., 2010). Whereas greater mean was primarily associated with one behavioural outcome (accuracy), variability was primarily associated with another (RT). These effects were observed at both between- and within-person levels. Notably, the congruency between channels and ROIs that showed significant activation across operationalizations was also inconsistent. Although the coverage of cortical regions is limited by both the methodology (fNIRS) and design (array covering regions of PFC only), these findings are consistent with previous results demonstrating that mean and variability are spatially distinct and are orthogonal in nature (e.g., Garrett at al., 2010) (see Figure 6).

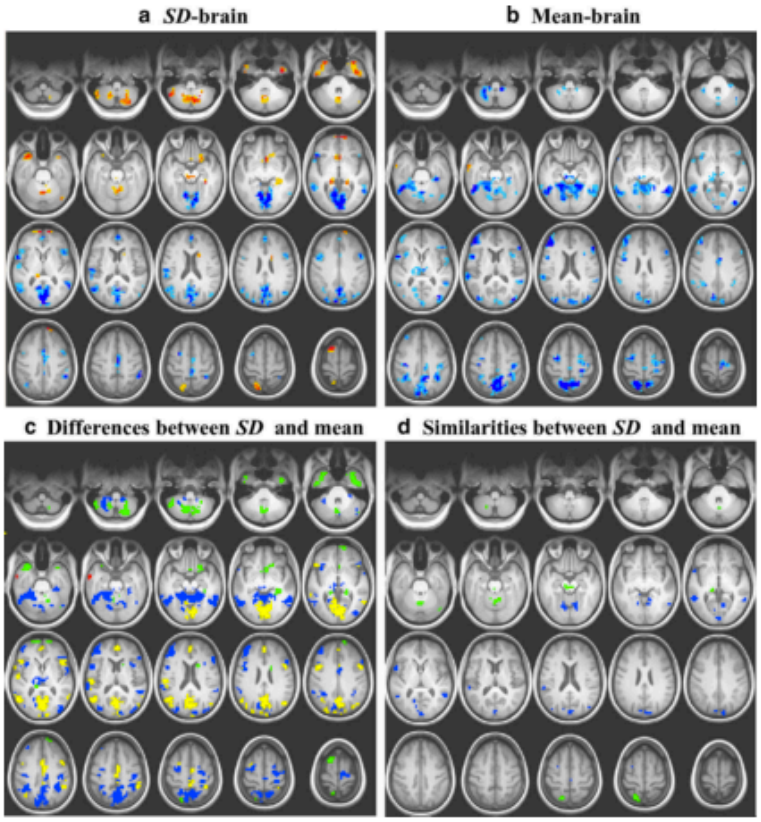

Figure 6. From Garrett, Kovacevic, McIntosh & Grady (2010) where blue regions depict age-related decreases and yellow/ red depict age-related increases in (a) BOLD SDs and (b) BOLD means. Panel (c) shows the overlay of differences between age-based SD- and mean-brain spatial patterns. Red shows mean increase, no SD effect; blue, mean decrease, no SD effect; green, SD increase, no mean effect; yellow, SD decrease, no mean effect. Panel (d) shows the overlay of similarities between age-based SD- and mean-brain spatial patterns. Blue shows mean and SD decreases with age; green, mean decrease, SD increase.

To the extent that falls represent an early marker of risk for cognitive decline in older adulthood (Kearney et al., 2013; Delbaere, et al., 2012), the fact that additional neural recruitment across operationalizations appears to have enhanced behavioural performance in the group of non-fallers relative to the group of fallers suggests that the fallers may have recruited additional brain regions outside of those recorded by the fNIRS methodology (e.g., premotor cortex, temporal gyri). Further, fallers appear not to have recruited sufficient resources from PFC regions that are heavily implicated during

cognitive interference (Bush et al., 2003; 2006) and updating working memory (Owen et al., 2005) tasks. Given the lack of observed differences in behavioural performance between the groups (i.e., no significant differences in accuracy or RT), it is possible that fallers engaged additional components of the cingulo-frontal-parietal cognitive attention network to perform the task. A pattern such as this is in keeping with the notion of dedifferentiation; that brain senescence is associated with a loss of selectivity, such that neural activity that is typically localized becomes more distributed with age (Grady, 2012).

The effects observed within the N-Back task (a measure of updating working memory) were primarily limited to the mean-based operationalization of HbO. At the within- and between-person levels, additional recruitment of HbO facilitated more accurate as well as faster responding, primarily in the less demanding 2-back condition. In the 3-back condition, additional recruitment of HbO appears to have facilitated more accurate responding for the group of fallers more so than the group of non-fallers, however this occurred at the between-person level only. This suggests that there may be additional unaccounted for between-person variables of relevance that were driving the effect. The lack of observed effects for the variability (SD) and signal complexity (MMSE) operationalizations is not entirely unsurprising, given the nature of the N-Back task. In contrast to the MSIT task, which is consistent from trial to trial within a block, the N-Back task necessitates that participants keep on task for the entire block. Indeed, losing set in the N-Back task may result in participants disengaging from the task until the next block, such that the variability contained within the corresponding neural

dynamics (HbO) is a harbinger of task disengagement more than it is facilitative of task-relevant neural firing.

Limitations and Future Directions

The observed effects that have been reported in this study are underpowered due to sample size constraints and are also limited by design. To ascertain fully the extent to which each operationalization of HbO is driven by within- or between-person effects, a greater sample size is required; ideally, one in which the incidence of a potential cognitive impairment is apparent (e.g., recurrent falls as a proxy of prodromal MCI). As previous results have shown patterns of mean- and SD-based computations of neural activity that are spatially and inferentially distinct (e.g., Garrett et al., 2010), the discrepancies reported here between associations of each operationalization of HbO with behavioural performance are likely to become more clear with greater statistical power. Increasing the sample size of both the low- (e.g., non-fallers) and high-risk groups (e.g., fallers) as well as the number of blocks within each experiment is likely to increase the statistical power substantially.

MMSE computations of fNIRS recordings have to date been examined in only one other study (Angsuwatanakul et al., 2015) and thus drawing comparisons to established findings was not possible here. Further, MMSE computations are typically computed across a longer and more densely sampled time course, such that contrasting fine- and course-grained estimates was not possible, given the upper-bound of the scaling factor employing during the MMSE computation. Given the block designs employed for the current measures (i.e., MSIT and N-Back), it was not possible to examine MMSE values at courser-grained estimates. Future investigations may seek to examine resting-

state fNIRS data across longer recordings in order to compare MMSE estimates across a larger scale range. In a review of MMSE computations across different complex signals, Ahmed and colleagues (2011) suggest an upper-bound of 20,000 samples, which would correspond to roughly 6.5 minutes of fNIRS recording at 50Hz. Given that coverage was limited to regions of PFC as well as the comparatively short upper-bound of the MMSE scale computation, the present investigation was not able to examine the extent to which fine- relative to course-grained MMSE estimates reflect long-range interactions across distributed neural populations (e.g., within the cingulo-frontal-partietal cognitive attention network), which is an area of active investigation (McDonough & Nashiro, 2014).

The block normalized SD computation was conducted for each channel, yielding a total of 8 estimates. This approach differs from that which has been employed in fMRI studies to date. In these studies, a whole-brain estimate across all voxels and regions is derived, which is used subsequently during inferential statistical comparisons (e.g., between young and old adults). Future investigations may seek to examine whole-brain SD from fNIRS recordings in order to derive a more robust estimate of variability in cerebral oxygenation.

Acquisition of the fNIRS data was complicated by an as yet unexplained technical issue, wherein some recordings appear to have been down-sampled to 25Hz. This issue occurred at random, and was apparent in both the MSIT and N-Back recordings. In spite of this issue, there remained an abundance of information for each operationalization of HbO. For example, in deriving the MMSE estimates, we selectively down-sampled several 50Hz cases in order to compare the results when derived at both the intended (i.e.,

50Hz) as well as the lower (i.e., 25Hz) sampling frequencies. On aggregate, sampling frequency appeared to have no bearing on the corresponding values.

Conclusion

In summary, the present findings suggest that distinct patterns of neural activity exist between opposing operationalizations derived from higher-order cognitive tasks. The utility of applying variability and entropy metrics to measures of cerebral oxygenation in furthering our understanding of neural activity remains a promising avenue of exploration. As with other neuroimaging modalities (e.g., fMRI, EEG, MEG), researchers employing fNIRS may consider exploiting the comparatively high sampling frequency of the technique to index profiles of variability, rather than simply averaging the signal in favour of central tendency. To further demonstrate brain-behaviour relationships across opposing operationalizations of neural activity, researchers may also consider parsing variance at the within- and between-person levels to account for potential confounds. Doing so will yield purer estimates of these relationships, as our understanding of neural variability continues to unfold.

Bibliography

Aasted, C. M., Yücel, M. A., Cooper, R. J., Dubb, J., Tsuzuki, D., Becerra, L. et al., (2015). Anatomical guidance for functional near-infrared spectroscopy: AtlasViewer tutorial. *Neurophotonics, 2,* 020801.

Ahmed, M. U., & Mandic, D. P. (2011). Multivariate multiscale entropy: A tool for complexity analysis of multichannel data. *Physical Review, 84,* 061918.

Angsuwatanakul, T., Iramina, K. & Kaewkamnerdpong, B. (2015). Brain complexity analysis of functional near infrared spectroscopy for working memory study. *BMEiCON,* 1-5. doi: 10.1109/BMEiCON.2015.7399531.

Arduini, A., 1963. The tonic discharge of the retina and its central effects. In: Moruzzi, G., Fessard, A., Jasper, H.H. (Eds.), Progress in Brain Research. Elsevier, New York, pp. 184–206.

Brigadoi, S., Ceccherini, L., Cutini, S., Scarpa, F., Scatturin, P., Selb, J., Gagnon, L.,Boas, D. & Cooper, R. J. (2014). Motion artifacts in functional near-infrared spectroscopy: A comparison of motion correction techniques applied to real cognitive data. *NeuroImage*, *85*, 181–191.

Bush, G., & Shin, L. M. (2006). The Multi-Source Interference Task: An fMRI task that reliably activates the cingulo-frontal-parietal cognitive/attention network. *Nature Protocols*, *1*(1), 308–13. doi:10.1038/nprot.2006.48

Bush, G., Shin, L. M., Holmes, J., Rosen, B. R., & Vogt, B. A. (2003). The Multi-Source Interference Task: Validation study with fMRI in individual subjects. *Molecular Psychiatry*, *8*(1), 60–70. doi:10.1038/sj.mp.4001217

Cattell, R. B. (1966). Patterns of change: Measurement in relation to state-dimension, trait change, lability, and process concepts. In R. B. Cattell (Ed.), *Handbook of multivariate experimental psychology* (pp. 355–402). Chicago, IL: Rand McNally.

Cooper, R. J., Selb, J., Gagnon, L., Phillip, D., Schytz, H. W., Iversen, H. K., Messoud, A., & Boas, D. A. (2012). A systematic comparison of motion artifact correction techniques for functional near-infrared spectroscopy. *Frontiers in Neuroscience*, *6*, 147. doi:10.3389/fnins.2012.00147

Costa, M., Goldberger, A.L., Peng, C.K., 2002. Multiscale entropy analysis of complex physiologic time series. Physical Review Letters 89, 068102.

Davenport, M. H., Hogan, D. B., Eskes, G. A., Longman, S., & Poulin, M. J. (2012). Cerebrovascular reserve: The link between fitness and cognitive function? *Exercise and Sport Science Reviews, 40,* 153-8.

Delbaere, K., Kochan, N. a, Close, J. C. T., Menant, J. C., Sturnieks, D. L., Brodaty, H., … Lord, S. R. (2012). Mild cognitive impairment as a predictor of falls in community-dwelling older people. *The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry*, *20*(10), 845–53. http://doi.org/10.1097/JGP.0b013e31824afbc4

Dixon, R. A., Garrett, D. D., Lentz, T. L., MacDonald, S. W. S., Strauss, E., & Hultsch, D. F. (2007). Neurocognitive resources in cognitive impairment: Exploring markers of speed and inconsistency. *Neuropsychology, 21,* 381–399.

Gamaldo, A. A., Weatherbee, S. R. & Allaire, J. C. (2008). Exploring the within-person coupling of blood pressure and cognitive in elders. *Journal of Gerontology, 63B,* 386-9.

Garrett, D.D., Kovacevic, N., McIntosh, A.R., Grady, C.L., 2010. Blood oxygen level-dependent signal variability is more than just noise. *Journal of Neuroscience 30*, 4914–4921.

Garrett, D.D., Kovacevic, N., McIntosh, A.R., Grady, C.L., 2011b. The importance of being variable. *Journal of Neuroscience 31*, 4496–4503.

Garrett, D.D., Kovacevic, N., McIntosh, A.R., Grady, C.L., 2013. The modulation of BOLD variability between cognitive states varies by age and processing *speed. Cerebral Cortex 23*, 684–693.

Garrett, D. D., Samanez-Larkin, G. R., MacDonald, S. W. S., Lindenberger, U., McIntosh, A. R. & Grady, C. L. (2013). Moment-to-moment brain signal variability: A next frontier in human brain mapping? *Neuroscience and Biobehavioral Reviews, 37,* 610-24.

Grady, C. (2012). The cognitive neuroscience of ageing. *Nature Reviews Neuroscience, 13,* 491-505.

Halliday, D.W.R., Stawski, R., & MacDonald, S.W.S. (under review). Mild Cognitive Impairment moderates the time-varying association between finger tapping inconsistency and executive performance. *Journal of International Neuropsychological Society.*

He, B.J. (2011). Scale-free properties of the functional magnetic resonance imaging signal during rest and task. *Journal of Neuroscience 31*, 13786–13795

Hultsch, D. F., MacDonald, S. W. S., Hunter, M. A., Levy-Bencheton, J. & Strauss, E. (2000). Intraindividual variability in cognitive performance in older adults: Comparison of adults with mild dementia, adults with arthritis, and healthy adults. *Neuropsychology, 14,* 588-98.

Hultsch, D. F., & MacDonald, S. W. S. (2004). Intraindividual variability in performance as a theoretical window onto cognitive aging. In R. A. Dixon, L. Bäckman, & L.-G. Nilsson (Eds.), *New frontiers in cognitive aging* (pp. 65–88). Oxford, UK: Oxford University Press.

Hultsch, D. F., Strauss, E., Hunter, M. A., & MacDonald, S. W. S. (2008). Intraindividual variability, cognition, and aging. In F. I. M. Craik & T. A. Salthouse (Eds.), *The handbook of aging and cogni- tion* (3rd ed., pp. 491–556). New York, NY: Psychology Press.

Huppert, T. J., Diamond, S. G., Franceschini, M. A., & Boas, D. A. (2009). HomerER: A review of time-series analysis methods for near-infrared spectroscopy of the brain. *Appl. Pot. 48,* D280-D298.

Kearney, F. C., Harwood, R. H., Gladman, J. R. F., Lincoln, N. & Masud, T. (2013). The relationship bewteen executive function and falls and gait abnormalities in older adults: A systematic review. *Dementia and Geriatric Cognitive Disorders, 36,* 20-35.

Kirchner, W. K. (1958). Age differences in short-term retention of rapidly changing information. *Journal of Experimental Psychology, 55(4),* 352-358.

Klein, C., Wendling, K., Huettner, P., Ruder, H., & Peper, H. (2006). Intra-subject variability in attention-deficit hyperactivity disorder. *Biological Psychiatry, 60,* 1088-97.

Liu-Ambrose, T. Y., Ashe, M. C., Graf, P., Beattie, B. L., & Khan, K. M. (2008).Increased risk of falling in older community-dwelling women with mild cognitive impairment. *Physical Therapy*, *88*(12), 1482–91. http://doi.org/10.2522/ptj.20080117

Lancaster, J. L., Woldorff, M. G., Parsons, L. M., Liotti, M., Freitas, C. S., Rainey, L., Kochunov, P. V., Nicerson, D., Mikiten, S. A., Fox, P. T. (2000). Automated Talairach atlas labels for functional brain mapping. *Brain Mapp. 10,* 120-131.

Lippé, S., Kovacevic, N., McIntosh, A.R., 2009. Differential maturation of brain signal complexity in the human auditory and visual system. Frontiers in Human Neuroscience 3, 48

Lövdén, M., Li, S.-C., Shing, Y. L., & Lindenberger, U. (2007). Within-person trial-by-trial variability precedes and predicts cognitive decline in old and very old age: Longitudinal data from the Berlin Aging Study. *Neuropsychologia, 45,* 2827–2838. doi: 10.1016/j.neuropsychologia.2007.05.005

McDonnell, M.D., Ward, L.M., 2011. The benefits of noise in neural systems: Bridging theory and experiment. *Nature Reviews Neuroscience 12,* 415–426.

MacDonald, S. W., Nyberg, L. & Bäckman, L. (2006). Intra-individual variability in behavior:links to brain structure, neurotransmission and neuronal activity. *Trends in Neuroscience, 29,* 474-80.

MacDonald, S. W. S., Li, S-C. & Bäckman, L. (2009). Neural underpinnings of within-person variability in cognition functioning. *Psychology and Aging, 24,* 792-808.

MacDonald S. W. S. & Stawski, R. S. (2014). Intraindividual variability – An indicator

of vulnerability or resilience in adult development and aging? In Diehl, M., Hooker, K., & Sliwinski, M. J. (Eds.) *Handbook of Intraindividual Variability Across the Life Span* (pp. 231-57). New York, NY: Taylor & Francis.

McDonough, I. A., & Nashiro, K. (2014). Network complexity as a measure of information processing across resting-state networks: Evidence from the Human Connectome Project. *Frontiers in Human Neuroscience, 8,* 1-15.

McIntosh, A.R., Kovacevic, N., Itier, R.J., 2008. Increased brain signal variability accompanies lower behavioral variability in development. *PLoS Computational Biology 4*, e1000106.

McIntosh, A.R., Kovacevic, N., Lippe, S., Garrett, D., Grady, C., Jirsa, V., 2010. The development of a noisy brain. *Archives Italiennes de Biologie 148*, 323– 337.

Mišić, B., Mills, T., Taylor, M. J., & McIntosh, A. R. (2010). Brian noise is task dependent and region specific. *Journal of Neurophysiology, 104,* 2667-2676.

Mišić, B., Vakorin, V.A., Paus, T., McIntosh, A.R., 2011a. Functional embedding predicts the variability of neural activity. *Frontiers in Systems Neuroscience 5, 90.*

Mizuno, T., Takahashi, T., Cho, R. Y., Kikuchi, M., Murata, T., Takahashi, K. & Wada, Y. (2010). Assessment of EEG dynamic complexity in Alzheimer's disease using multiscale entropy. *Clinical Neurophysiology, 121,* 1438-46.

Molavi, B., & Dumont, G. A. (2012). Wavelet-based motion artifact removal for functional near-infrared spectroscopy. *Physiological Measurement*, *33*(2), 259–70. doi:10.1088/0967-3334/33/2/259

Nesselroade, J. R. (1992). Adult personality development: Issues in assessing constancy and change. In A. I. Rabin, R. A. Zucker, R. A. Emmons, & S. Franks (Eds.), *Studying persons and lives* (pp. 41–85). New York, NY: Springer.

Nesselroade, J. R., & Salthouse, T.A. (2004). Methodological and theoretical implications of intraindividual variability in perceptual motor performance. *Journals of Gerontology: Series B. Psychological Sciences and Social Sciences, 59B,* P49–P55. doi: 10.1093/geronb/59.2.P49

Owen, A.M., McMillan, K.M., Laird, A.R., & Bullmore, E. (2005). N-Back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. *Human Brain Mapping, 25,* 46-59.

Pinneo, L.R., 1966. On noise in the nervous system. *Psychological Review 73*, 242–247

Raja Beharelle, A., Kovacevic, N., McIntosh, A.R., Levine, B., 2012. Brain signal variability relates to stability of behavior after recovery from diffuse brain injury. *NeuroImage 60,* 1528–1537.

Reuter-Lorenz, P. A. & Cappell, K. A. (2008). Neurocognitive aging and the compensation hypothesis. *Current Direction in Psychological Science, 17,* 177-182.

Robinson, W. S. (1950). Ecological correlations and the behaviour of individuals. *Sociological Review, 15,* 351-357.

Rosano, C., Brach, J., Studenski, S, Longstreth Jr., W. T., & Newman, A. B. (2007). Gait variability is associated with subclinical brain vascular abnormalities in high-functioning older adults. *Neuroepidemiology, 29,* 193-200.

Schreppel, T., Egetemeir, J., Schecklmann, M., Plichta, M. M., Pauli, P., Ellgring, H., Fallgatter, A. J., & Hermann, M. J. (2008). Activation of the prefrontal cortex in working memory and interference resolution processes assessed with near-infrared spectroscopy. *Neuropsychobiology, 57,* 188-93.

Singh, A. K., Okamoto, M., Dan, H., Jurcak, V., & Dan, I. (2005). Spatial registration of multi-channel multi-subject fNIRS data to MNI space without MRI. *NeuroImage, 27,* 842-51.

Stuss, D.T., Steth, L.L., Hugenholtz, H., Picton, T., Pivik, J., & Richard, M.T. (1989). Reaction time after head injury: Fatigue, divided and focused attention, and consistency of performance. *J. Neurol. Neurosurg. Psychiatry 52*, 742–748.

Stuss, D. T., Murphy, K. J., Binns, M. A., Alexander, M. P. (2003). Staying on the job: The frontal lobes control individual performance variability. *Brain, 126,* 2363-80.

Takahashi, T., Cho, R.Y., Murata, T., Mizuno, T., Kikuchi, M., Mizukami, K., Kosaka, H., Takahashi, K., Wada, Y., 2009. Age-related variation in EEG complexity to photic stimulation: A multiscale entropy analysis. *Clinical Neurophysiology 120*, 476–483.

Thayer, J. F., Hansen, A. L., Saus-Rose, E., Johnsen, B. H. (2009). Heart rate variability, prefrontal neural function, and cognitive performance: The neurovisceral integration perspective on self-regulation, adaptation, and health. *Annals of Behavioral Medicine, 37,* 141-153.

Tsuzuki, D., & Dan, I. (2014). Spatial registration for functional near infrared spectroscopy: From channel position on the scalp to cortical location in individual and group analyses. *NeuroImage, 85,* 92-103.

Vakorin, V.A., Lippe, S., McIntosh, A.R., 2011. Variability of brain signals processed locally transforms into higher connectivity with brain development. *Journal of Neuroscience 31*, 6405–6413.

Verghese, J., Holtzer, R., Lipton, R. B., & Wang, C. (2009). Quantitative gait markers and incident fall risk in older adults. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, *64*(8), 896–901. doi:10.1093/gerona/glp033

Vermeij, A., van Beek, A. H. E. A., Olde Rikkert, M. G. M., Claassen, J. A. H. R., & Kessels, R. P. C. (2012). Effects of aging on cerebral oxygenation during working-memory performance: A functional near-infrared spectrocopy study. *PloS One, 7,* e46210.

Vinogradov, S., Poole, J. H., Willis-Shore, J., Ober, B. A., Shenaut, G. K. (1998). Slower and more variable reaction times in schizophrenia: What do they signify? *Schizophrenia Research, 32,* 183-90.

Appendix A

Multilevel Model Summaries with Fall Status and Age

Two-Level Multilevel Models of Coupling Between mean HbO and Behavioural Performance for MSIT and N-Back (mean and RT), with age and fall status moderating factors.

Task	Outcome	Variables	Intercept (γ00)	Falls (γ01)	Age (γ02)	PM (γ03)	Slope Segment (γ10)	Slope PMC (γ20)	Falls (γ21)	Age (γ22)
Control	Accuracy	ROI A1	0.957**	-0.013	0.003	-0.024*	0.010	0.010	-0.006	-0.000
		ROI A2	0.964**	-0.015	0.002	-0.020*	0.009	-0.021	-0.003	0.004
		ROI B2	0.958**	0.002	0.000	-0.006	0.013#	-0.046	0.005	0.004
		ROI B3	0.955**	0.002	0.001	-0.008	0.011#	-0.040#	0.011	0.006#
		ROI C5	0.962**	-0.009	0.002	-0.007	0.009	-0.024	0.015	0.002
		ROI C6	0.962**	-0.008	0.002	-0.003	0.008	-0.028	0.022	0.001
		ROI D6	0.961**	-0.006	0.002	-0.008	0.008	-0.018	0.012	0.001
		ROI D7	0.964**	-0.007	0.002	-0.007	0.007	-0.009	-0.002	0.001
Interference	Accuracy	ROI A1	0.783**	0.001	-0.004	-0.071	0.046*	0.045	-0.041	-0.002
		ROI A2	0.810**	-0.008	-0.010	-0.032	0.047*	0.031	-0.041	-0.002
		ROI B2	0.825**	-0.007	-0.011	-0.058	0.041*	0.054	-0.111#	-0.001
		ROI B3	0.820**	0.010	-0.012	-0.092#	0.044*	0.035	-0.054	-0.003
		ROI C5	0.815**	-0.013	-0.011	0.028	0.048*	-0.002	-0.027	-0.003
		ROI C6	0.837**	-0.017	-0.010	0.010	0.034*	-0.015	-0.084	0.008
		ROI D6	0.800**	-0.008	-0.010	-0.024	0.053*	0.123	-0.095	-0.009
		ROI D7	0.809**	-0.013	-0.011	0.012	0.053*	0.020	-0.047	-0.012
Control	RT	ROI A1	675.58**	-15.18	-5.52	-20.39	-15.42#	-21.00	8.74	3.04
		ROI A2	685.72**	-25.52	-6.16	-9.97	-16.87#	-18.61	1.43	3.26
		ROI B2	689.70**	-25.83	-7.19	-21.36	-15.41#	-20.07	-1.35	3.16
		ROI B3	680.59**	-9.63	-7.69	-5.36	-13.76	-20.08	-4.25	3.58
		ROI C5	693.83**	-19.49	-7.79	-19.02	-18.60*	-36.60#	14.69	2.53
		ROI C6	691.08**	-13.36	-7.50	8.08	-20.01*	-45.73*	31.70	1.84
		ROI D6	679.00**	-8.38	-5.87	-12.07	-19.10*	-40.97*	3.68	3.94#
		ROI D7	676.05**	-5.92	-5.78	-25.21	-18.34*	-26.99	2.47	4.52
Interference	RT	ROI A1	1024.17**	-39.38	-7.05	7.95	11.29	34.11	-8.42	-14.86
		ROI A2	1030.82**	-38.06	-6.55	6.87	5.36	15.56	-60.57	-0.38
		ROI B2	1036.02**	-41.65	-6.05	18.41	1.29	25.51	-95.26	5.56
		ROI B3	1033.18**	-44.46	-6.09	16.08	4.03	21.66	-74.93	-0.96
		ROI C5	1047.11**	-48.60	-7.13	24.14	-1.31	43.39	-57.55	4.84
		ROI C6	1058.81**	-59.00#	-9.20	41.27#	0.02	38.85	-56.32	1.13
		ROI D6	1028.68**	-55.69	-8.54	30.67	16.67	88.80	-82.44	-8.37
		ROI D7	1056.87**	-63.84#	-10.10	36.33	5.24	-19.26	18.12	4.87

**$p < .001$, *$p < .05$, #$p < .05$, one tailed

Task	Outcome	Variables	Intercept (γ00)	Falls (γ01)	Age (γ02)	PM (γ03)	Slope Segment (γ10)	Slope PMC (γ20)	Falls (γ21)	Age (γ22)
2-back	Accuracy	ROI A1	0.547**	0.042	-0.008	0.009	0.024*	0.004	0.039	-0.002
		ROI A2	0.543**	0.047	-0.007	-0.009	0.023*	0.008	0.017	-0.002
		ROI B2	0.562**	0.020	-0.008	0.024	0.023*	0.022	0.033	-0.008*
		ROI B3	0.550**	0.047	-0.008	-0.003	0.021*	0.020	0.008	-0.004
		ROI C5	0.552**	0.026	-0.007	-0.007	0.024*	-0.016	0.051#	-0.004*
		ROI C6	0.551**	0.055	-0.010	0.028	0.023*	0.011	0.056	-0.006
		ROI D6	0.545**	0.052	-0.009	0.043	0.023*	-0.014	0.038	0.002
		ROI D7	-0.544**	0.046	-0.007	0.011	0.023*	-0.036	0.052	0.003
3-back	Accuracy	ROI A1	0.423**	0.075	-0.006	0.005	0.016*	0.003	0.003	0.001
		ROI A2	0.421**	0.072	-0.005	-0.008	0.017*	-0.011	0.006	0.002
		ROI B2	0.420**	0.068	-0.005	0.008	0.018*	-0.014	0.008	0.004
		ROI B3	0.416**	0.069	-0.004	0.006	0.018*	-0.018	0.009	0.004
		ROI C5	0.412**	0.084	-0.005	0.012	0.017*	-0.017	-0.001	0.005
		ROI C6	0.422**	0.093#	-0.008	0.032	0.017*	-0.009	-0.019	0.002
		ROI D6	0.424**	0.090#	-0.007	0.050*	0.015*	-0.025	0.042	0.001
		ROI D7	0.428**	0.073	-0.005	0.013	0.015*	-0.024	0.018	0.011*
2-back	RT	ROI A1	930.09**	17.96	5.43	-2.69	-17.15*	16.91	6.59	-2.11
		ROI A2	934.88**	17.41	4.48	-0.18	-17.15*	5.73	16.65	-1.69
		ROI B2	923.62**	26.67	5.28	-22.48	-16.45*	6.83	27.48	-2.15
		ROI B3	945.36**	14.99	2.90	-5.64	-17.68*	37.09	-15.21	-0.27
		ROI C5	936.07**	-18.40	7.69	-48.19#	-15.62	0.28	19.76	-2.06
		ROI C6	911.63**	-15.08	13.50#	-69.05*	-17.24*	2.37	16.34	-0.01
		ROI D6	917.39**	15.82	7.72	-33.83	-16.09*	-9.52	20.56	-0.92
		ROI D7	914.29**	33.08	7.17	-65.45*	-17.56*	16.65	2.22	-0.60
3-back	RT	ROI A1	960.91**	-27.29	9.77	20.88	-14.19*	-31.55	21.51	6.56
		ROI A2	957.59**	-38.74	12.05	33.90	-14.20*	-33.30	25.90	4.44
		ROI B2	961.01**	-41.49	11.19	19.46	-13.46*	-32.93	-0.86	6.30
		ROI B3	976.81**	-48.76	10.09	3.24	-15.60*	-8.77	-16.02	3.49
		ROI C5	988.06**	-69.57	9.94	-25.90	-15.04*	-30.58	8.81	3.64
		ROI C6	974.75**	-82.97	12.87	-61.86*	-12.66#	-13.27	23.78	-1.71
		ROI D6	978.11*	-49.29	9.54	-8.60	-15.04*	1.30	-13.00	-0.46
		ROI D7	962.49**	-36.96	11.12	-53.21*	-14.70*	-35.22	16.81	5.30

**$p < .001$, *$p < .05$, #$p < .05$, one tailed

Two-Level Multilevel Models of Coupling Between SD HbO and Behavioural Performance for MSIT and N-Back (mean and RT), with age and fall status moderating factors.

Task	Outcome	Variables	Intercept (γ00)	Falls (γ01)	Age (γ02)	PM (γ03)	Slope Segment (γ10)	Slope PMC (γ20)	Falls (γ21)	Age (γ22)
Control		ROI A1	0.952**	-0.007	0.002	0.000	0.007	0.000	-0.000	-0.000
		ROI A2	0.953**	-0.010	0.002	0.000	0.009	0.000	-0.000	0.000
		ROI B2	0.951**	-0.002	0.001	0.000	0.012	0.000	-0.000	-0.000
		ROI B3	0.970**	-0.010	0.002	-0.000	0.008	0.000	-0.000	-0.000
		ROI C5	0.964**	-0.010	0.002	-0.000	0.009	0.000	0.000	0.000
		ROI C6	0.975**	-0.015	0.002	-0.000	0.008	0.000	-0.000	0.000
		ROI D6	0.964**	-0.010	0.002	-0.000	0.009	0.000	-0.000	-0.000
		ROI D7	0.958**	-0.009	0.002	0.000	0.008	0.000	0.000	-0.000
Interference	Accuracy	ROI A1	0.759**	0.014	-0.009	0.000	0.051*	0.000	0.000	-0.000
		ROI A2	0.844**	-0.022	-0.011	-0.000	0.046*	0.000	0.000	-0.000
		ROI B2	0.781**	0.014	-0.011	0.000	0.043*	0.000	0.000	-0.000
		ROI B3	0.775**	0.010	-0.010	0.000	0.053*	-0.000	-0.000	0.000
		ROI C5	0.853**	-0.040	-0.006	-0.001	0.052*	-0.000	-0.001	0.000
		ROI C6	0.861**	-0.025	-0.011	-0.000	0.049*	0.000	-0.000	-0.000
		ROI D6	0.797**	-0.001	-0.011	0.000	0.051*	0.000	0.000	0.000
		ROI D7	0.911**	-0.034	-0.009	-0.001	0.046*	-0.000	0.000	0.000
Control	RT	ROI A1	624.86**	-6.26	-6.16	0.53	-16.80	0.14	-0.22	0.00
		ROI A2	633.40**	-22.08	-6.45	0.40#	-17.07*	-0.11	-0.06	0.02
		ROI B2	705.27**	-13.31	8.95	-0.15	-13.19	-0.31	0.36	0.05
		ROI B3	662.67**	-20.60	-7.25	0.22	-18.15*	-0.07	-0.01	0.00
		ROI C5	694.11**	-25.12	-7.46	-0.01	-16.29*	-0.22	-0.33	0.06
		ROI C6	702.75**	-32.74	-6.64	-0.12	-14.35#	-0.22	-0.02	0.05
		ROI D6	693.31**	-24.87	-7.69	0.04	-18.12*	0.11	-0.14	0.01
		ROI D7	671.94**	-20.67	-7.59	0.15	-13.92	-0.05	0.09	0.02
Interference	RT	ROI A1	1009.37**	-38.75	-7.12	0.12	9.61	-0.23	0.42#	0.02
		ROI A2	1022.65**	-42.51	-7.34	0.02	11.96	0.04	-0.15	-0.03
		ROI B2	1026.90**	-44.67	-6.04	0.04	5.58	-0.09	0.32	0.10
		ROI B3	1022.02**	-38.25	-6.45	-0.03	14.42	-0.14	-0.08	-0.02
		ROI C5	1053.55**	-60.98	-6.26	-0.38	14.74	-0.39	-0.36	0.08
		ROI C6	1055.21**	-51.30	-7.44	-0.25	14.88	-0.14	-0.21	0.09
		ROI D6	1046.53**	-53.64	-6.84	-0.20	11.03	-0.49	1.08	0.12
		ROI D7	1075.53**	-61.55#	-8.07	-0.30	4.01	-1.74	2.37*	0.24

**$p < .001$, *$p < .05$, $^{\#}p < .05$, one tailed

Task	Outcome	Variables	Intercept (γ00)	Falls (γ01)	Age (γ02)	PM (γ03)	Slope Segment (γ10)	Slope PMC (γ20)	Falls (γ21)	Age (γ22)
2-back	Accuracy	ROI A1	0.612**	0.030	-0.005	-0.001#	0.023*	-0.000	-0.000#	0.000
		ROI A2	0.567**	0.051	-0.008	-0.000	0.026*	-0.000	-0.000	0.000
		ROI B2	0.524**	0.047	-0.006	0.000	0.022*	-0.000#	0.000	0.000
		ROI B3	0.455**	0.078	-0.008	0.001	0.021*	-0.000	0.000	-0.000
		ROI C5	0.536**	0.041	-0.007	0.00	0.023*	0.000	0.000	0.000
		ROI C6	0.605**	0.035	-0.010	-0.000	0.022*	-0.000	-0.000	0.000*
		ROI D6	0.518**	0.048	-0.006	0.000	0.021*	-0.000	-0.000	0.000*
		ROI D7	0.622**	0.047	-0.011	-0.000#	0.022*	-0.000	-0.000	0.000
3-back	Accuracy	ROI A1	0.408**	0.074	-0.005	0.000	0.019*	0.000	0.000#	-0.000
		ROI A2	0.422**	0.070	-0.006	-0.000	0.018*	0.000	0.000	-0.000
		ROI B2	0.352**	0.081	-0.003	0.000	0.018*	0.000	0.000	-0.000*
		ROI B3	0.392**	0.085	-0.006	0.000	0.018*	-0.000	-0.000	0.000
		ROI C5	0.463**	0.067	-0.004	-0.000	0.015*	-0.000	0.000#	-0.000
		ROI C6	0.460**	0.078	-0.006	-0000	0.016*	0.000	0.000	-0.000
		ROI D6	0.425**	0.079	-0.005	0.000	0.016*	-0.000	0.000#	-0.000
		ROI D7	0.442**	0.070	-0.008	-0.000	0.017*	0.000*	-0.000	-0.000*
2-back	RT	ROI A1	923.70**	17.07	4.34	0.08	-16.14*	0.14	0.08	-0.02
		ROI A2	929.64**	22.28	5.93	-0.06	-17.15*	0.17	-0.17	0.02
		ROI B2	872.12**	15.99	7.82	0.49	-15.98*	-0.16	-0.08	0.06
		ROI B3	922.20**	18.78	5.41	0.01	-15.71*	0.02	-0.03	-0.01
		ROI C5	898.90**	28.10	6.52	0.13	-14.27*	-0.61	0.83	0.08
		ROI C6	896.19**	22.54	6.77	0.20	-15.52*	-0.06	-0.14	0.06
		ROI D6	928.94**	18.24	5.46	0.02	-17.66*	-0.21	0.21	0.01
		ROI D7	857.13**	25.33	11.09	0.50	-17.41	0.22	-0.04	-0.02
3-back	RT	ROI A1	988.84**	-56.02	10.79	-0.11	-14.39*	0.07	-0.02	-0.01
		ROI A2	988.61**	-8.95	12.08	-0.43#	-14.22*	0.05	-0.06	0.00
		ROI B2	973.37**	-47.43	9.59	0.02	-14.69*	0.20	-0.14	-0.03
		ROI B3	963.43**	-37.04	11.36	-0.01	-15.50*	0.23	-0.43*	-0.03
		ROI C5	951.90**	-47.03	10.85	0.18	-14.88*	0.36	-0.71*	0.04
		ROI C6	891.08**	-51.99	15.04#	0.54	-13.55*	0.09	0.02	-0.02
		ROI D6	972.83**	-54.32	8.75	0.15	-16.27*	0.04	0.13	0.00
		ROI D7	861.04**	-20.63	19.98*	0.53#	-15.07*	0.09	0.09	-0.05

**$p < .001$, *$p < .05$, $^{\#}p < .05$, one tailed

Two-Level Multilevel Models of Coupling Between MMSE HbO and Behavioural Performance for MSIT and N-Back (mean and RT), with age and fall status moderating factors.

Task	Outcome	Variables	Intercept (γ00)	Falls (γ01)	Age (γ02)	PM (γ03)	Slope Segment (γ10)	Slope PMC (γ20)	Falls (γ21)	Age (γ22)
Control	Accuracy	ROI A	0.938**	-0.009	0.002	0.041	0.009	-0.053	-0.053	0.007
		ROI B	0.966**	-0.011	0.000	-0.008	0.015*	-0.083	-0.184	0.016
		ROI C	0.972**	-0.008	0.001	-0.008	0.008	-0.115	-0.155	0.022
		ROI D	0.954**	-0.007	0.002	0.012	0.008	0.088	-0.060	-0.010
Interference	Accuracy	ROI A	0.758**	-0.047	-0.015	0.147	0.042*	0.183	-0.068	-0.062
		ROI B	0.868**	-0.043	-0.014	-0.033	0.039*	-0.118	-0.221	-0.015
		ROI C	0.547*	0.009	-0.015	0.387	0.058**	-0.291	-0.009	0.045
		ROI D	0.633**	0.028	-0.015	0.259	0.050*	0.122	-0.152	0.018
Control	RT	ROI A	577.32**	-12.89	-7.48	166.87	-13.70#	-144.82	140.08	13.83
		ROI B	628.78**	-16.80	-8.11	111.14	-16.52*	-65.28	-88.22	18.71
		ROI C	786.79**	-31.26	-8.61	-141.38	-18.37*	17.84	-283.14	9.79
		ROI D	676.24**	-21.07	-7.66	21.43	-15.59*	-71.88	22.72	-1.00
Interference	RT	ROI A	1107.67**	-51.08	-7.49	-113.43	4.88	-50.69	81.41	-36.07
		ROI B	1123.36**	-59.33	-7.28	-144.83	2.23	-178.33	-356.16	21.28
		ROI C	1026.90**	-58.64#	-8.32	10.35	10.28	-176.51	-200.09	51.39
		ROI D	1021.48**	-53.79	-8.37	12.71	11.75	40.77	-39.54	31.35

**$p < .001$, *$p < .05$, #$p < .05$, one tailed

Task	Outcome	Variables	Intercept (γ00)	Falls (γ01)	Age (γ02)	PM (γ03)	Slope Segment (γ10)	Slope PMC (γ20)	Falls (γ21)	Age (γ22)
2-Back	Accuracy	ROI A	0.845*	0.051	-0.006	-0.452	0.023*	-0.232	0.164	0.044
		ROI B	0.497#	0.040	-0.008	0.078	0.023*	0.126	-0.071	-0.004
		ROI C	0.344	0.048	-0.008	0.302	0.023*	-0.325	0.056	0.055#
		ROI D	0.515#	0.040	-0.007	0.044	0.025*	-0.073	-0.443*	0.062*
3-Back	Accuracy	ROI A	0.839*	0.048	-0.002	-0.619#	0.015*	0.046	0.004	0.012
		ROI B	0.569*	0.053	-0.003	-0.229	0.017*	0.092	-0.010	-0.001
		ROI C	0.601*	0.064	-0.004	-0.270	0.017*	-0.000	-0.147	0.008
		ROI D	0.572*	0.072	-0.005	-0.229	0.018*	-0.000	-0.077	-0.010
2-Back	RT	ROI A	700.13*	12.91	3.48	353.98	-17.04*	178.56	347.556#	3.34
		ROI B	877.70*	21.43	1.88	90.93	-15.21*	-27.12	54.01	27.64
		ROI C	1298.40**	4.28	1.97	-528.32	-15.43*	128.60	-110.41	18.62
		ROI D	1143.20**	8.69	2.79	-293.26	-18.19*	-226.28	-274.80	99.32*
3-Back	RT	ROI A	1081.86**	-57.47	9.45	-148.21	-14.98*	-113.54	177.58	5.56
		ROI B	1204.14**	-76.87	13.77	-353.68	-13.90*	268.28	-126.84	-25.79
		ROI C	1051.43*	-53.51	9.60	-105.74	-15.54*	353.25#	-119.66	-49.66#
		ROI D	1314.68**	-66.96	8.98	-475.47	-14.46*	-213.40	-11.34	48.66#

**$p < .001$, *$p < .05$, #$p < .05$, one tailed