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Gait variability has been studied in various diseases and in aging, however variability is observed even in young, healthy adults. Variability in stride time can be characterized in terms of short-term, or step-by-step variability, and long-term variability. It is plausible that these temporal parameters in gait have similar neural origins to the dual modes of cognitive control since both require goal-oriented, higher-order processing. A handful of frontoparietal areas have been widely observed to be important for the dynamic nature of these abilities. The purpose of this study is to test the hypothesis that the adaptability of this frontoparietal network, as defined by the variability of the blood oxygen level-dependent (BOLD) signal, underlies a relationship between cognitive control strategies and stride time variability. We recruited twenty healthy young adults between 18 and 35 years old (10 females; average age = 23.6 ± 3.9 years old) to measure performance on a stepping-in-place task, cognitive control, and BOLD signal variability using resting-state functional MRI. A Pearson correlation wase used to determine the association between proactive and reactive cognitive control strategies and long and short-term gait variability, and a partial least squares correlation was used to determine if there is a pattern of BOLD signal variability in a set of frontoparietal regions that jointly explains these cognitive-gait relationships. There was no relationship between cognitive control strategy and long- or short-term variability, however there was a pattern of BOLD variability, primarily in control and salience/ventral attention network regions, that was associated with both short-term gait variability, and to a lesser extent, long-term gait variability (Permutation $p = 0.0323$). These findings provide evidence of gait variability as a marker of brain variability in healthy, young adults and may open the door to understanding its role as a biomarker of brain health.

GAIT VARIABILITY, COGNITVE CONTROL, AND BRAIN BOLD SIGNAL VARIABILITY IN HEALTHY, YOUNG ADULTS

by

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CHAPTER I: INTRODUCTION

Human movement, as with many physiological signals, demonstrates variability. One temporal parameter of gait that has been of interest to researchers is stride time variability. As opposed to the traditional view, which regards this variability as noise, recent theories have proposed that this variability represents the optimization and adaptability of a system. Nonlinear metrics, such as the Lyapunov exponent (LyE), quantify the correlation structure in these signals and has provided great utility in characterizing the short-term and long-term components of variability (Raffalt et al., 2019). Importantly, there is a growing amount of literature that relates cognitive abilities to gait variability in a range of populations (Beauchet et al., 2012; IJmker & Lamoth, 2012; Yogev-Seligmann et al., 2008). The neural correlates of these relationships are poorly understood.

The neural mechanisms that underly stride variability and cognitive control, defined as the ability to coordinate and sequence goal-related thoughts and behaviors (E. K. Miller & Cohen, 2001), have been thoroughly explored, albeit separately. Despite an established motor-cognitive relationship, there is a limited amount of research that captures all these components (i.e., cognition, stride variability, and the intrinsic organization of the brain), and even these studies only indirectly assess these relationships (Beauchet et al., 2015). Preliminary evidence from the ongoing Dual Mechanisms of Cognitive Control (DMCC) Project (Braver et al., 2021), which parallels prior work with a cognitive control network, may provide a useful framework to explore these motor-cognitive relationships. Preliminary evidence from a dual-task paradigm monitored using electroencephalography suggests that reduced gait variability was associated with a shift toward neural correlates of a proactive control strategy (Richardson et al., 2022). However, these designs make it difficult to resolve confounding motor-cognition interactions and

those authors note that individual 'baseline' differences may be important. Such differences are increasingly studied in a task-free or 'resting' state using fMRI.

The variability of the blood oxygen level-dependent (BOLD) signal, assessed using functional magnetic resonance imaging (MRI), has been previously related to motor control (Holtzer et al., 2020) and is thought to represent neural flexibility and support cognitive control (Good et al., 2020; Nomi et al., 2017). Though it has not been tested, the BOLD variability of this network of frontoparietal regions likely gives rise to important stride variability-cognitive control relationships. Therefore, the purpose of this study was to (1) determine the association between cognitive control strategies and long- and short-term stride time variability in healthy, young adults, and (2) to analyze the BOLD signal variability in a set of frontoparietal regions that may jointly explain individual differences in these patterns. Based upon previous literature, the following hypotheses were made:

- Hypothesis 1: Greater utilization of a proactive control strategy is associated with greater long-term variability in stride time (LyEL) and greater utilization of a reactive control strategy is associated with greater short-term variability in stride time, (LyES).
- Hypothesis 2: A pattern of greater BOLD signal variability in a set of frontoparietal regions is associated with cognitive control strategies and gait variability, with regions in the dorsolateral prefrontal cortex (DLPFC) and anterior cingulate cortex/pre-supplementary motor area (ACC/pSMA) predicted as being most important for this relationship.

CHAPTER II: REVIEW OF THE LITERATURE

Gait Variability

Human gait is the forward propulsion made during locomotion and is defined by the repetitive movement pattern of the limbs (Murray, 1967). This requires the proper functioning of balance, which describes the dynamics of posture, or the orientation of a body relative to gravity, in order prevent falling (Winter, 1995). Maintaining movement patterns within a stable range requires coordination and integration of both sensory ('bottom-up') and neuromotor ('top-down') information (Van Emmerik et al., 2005). As with most physiological signals, human gait has intrinsic variability; each stride varies from the next, despite consistent environmental conditions (Van Emmerik et al., 2005). Repeated movements, even well-practiced patterns, like walking or stepping, are practically never identical across cycles. Numerous kinematic and temporal metrics of gait variability have been proposed.

One metric that has been of interest to researchers relates to the temporal nature of gait variability or the variations in time taken for each forward step, referred to as stride time. On average, this variability is relatively small, with the coefficient of variation of stride time being approximately 2-3% percent in healthy young adults (Gabell & Nayak, 1984; Hausdorff et al., 1997). Traditionally, this variability has been considered to be noise (van Beers et al., 2004), with various experiments using goal-directed movement patterns to try to determine the contribution of planning noise versus execution noise. With the traditional approach that considers variability as simply noise, the biological signal represents the planned gait pattern and the variability represents random noise imposed upon this signal (Newell & Corcos, 1993). However, more recently, researchers have acknowledged that variability may be an emergent property of a healthy, functional state that represents the optimization of a biological system.

This has shifted the focus to characterizing the intrinsic variability observed in human gait that is necessary for the maintenance of successful navigation.

One prevailing theory that attempts to explain this variability in human movement is the dynamical systems theory (DST) (Stergiou & Decker, 2011). This theory states that a biological system self-organizes to obtain the most stable solution for a certain movement, with environmental and biomechanical conditions as constraining factors (Kamm et al., 1990). In this framework, greater variability is generally considered to indicate less stable movement patterns, and when environmental conditions cause variability to increase, the system responds adaptively by reducing variability and optimizing stability. Thus, DST is commonly used to describe transitions between movement patterns to explain variability in human gait across varied environments and conditions (Thelen, 1995).

However, variability is observed even in highly repetitive movements under stable conditions, like a baseball pitcher's mechanics across a game (Chaisanguanthum et al., 2014) or during a simple stepping-in-place task (Rhea et al., 2017, 2018). Using nonlinear analyses, this variability can be parsed into its short- and long-term components, using metrics such as the largest Lyapunov exponent (LyE) computed over 0-1 strides (LyES) and 4-10 strides (LyEL), respectively (Dingwell et al., 2001; Raffalt et al., 2019). LyES is thought to represent a system's ability to attenuate small perturbations over a single stride, while LyEL represents this ability over the timescale of several strides. Computing the LyE involves algorithmically determining the rate of exponential convergence or divergences of nearby points for a timeseries that has been transformed into state space. Though not previously tested, these metrics pose great potential in characterizing independent anticipatory processes that are proposed to drive synchronization behaviors: Local, or 'weak anticipation', produces moment- or trial-wise error-

corrections based on internal predictive models, whereas global, or 'strong anticipation', contributes to long-range correlations in biological systems (Dubois, 2003; Stepp & Turvey, 2010).

LyE has also been used extensively to study kinematics during non-cued behaviors. For example, in a study observing gait stability during treadmill, older adults exhibited a higher LyES in stride time compared to young adults, indicating greater short-term variability and reduced ability to attenuate small perturbations in gait (Bruijn et al., 2014). A different study in young healthy adults aimed to assess the effect of walking on a treadmill on gait parameters as compared to overground walking, and observed that treadmill walking significantly reduced LyES – i.e., decreased local dynamic variability (Terrier & Dériaz, 2011). Notably, despite the relatively simple nature of these movement patterns, there was a high degree of interindividual variability.

Cognitive Control

A substantial body of evidence demonstrates a relationship between cognitive and motor functions (Allali et al., 2008; Beauchet et al., 2012; Herman et al., 2010; IJmker & Lamoth, 2012; Mirelman et al., 2012; Yogev-Seligmann et al., 2008). In healthy adults, dual-task paradigms have been used extensively to study cognitive-motor interactions (Bishnoi & Hernandez, 2021; Spedden et al., 2017; Springer et al., 2006). Within a dual-task context, stride variability generally decreases when cognitive resources are directed away from the motor task to the cognitive task, but only if the competing cognitive demand is minimally taxing (Hausdorff, 2005; Richardson et al., 2022). However, if the demands of the cognitive task are too great, then stride variability tends to increase and motor performance generally suffers (Lövdén et al., 2008).

Therefore, the ontology of that task can in-turn reveal the degree to which certain cognitive processes are important for motor control.

Dual Mechanisms of Cognitive Control Framework

Cognition is often defined by tests to capture various aspects of executive function and cognitive control, defined as "the ability to regulate, coordinate, and sequence thoughts and actions in accordance with internally maintained goals" (E. K. Miller & Cohen, 2001). Historically, theories to explain these abilities characterize them as relatively static traits that change over long durations, as with aging or in different disease states (Braver & Barch, 2002; Dhanjal & Wise, 2014; Walton et al., 2015; West, 1996). On the other hand, the Dual Mechanisms of Control (DMC) framework was developed to define moment-to-moment variability in cognitive control that occurs in everyday living (Braver, 2012). In this framework, the focus is shifted towards characterizing the temporal dynamics that may explain the intrinsic variability as a key component of cognitive processes.

According to the DMC framework, there are two semi-independent control modes or strategies. Reactive control strategies only recruit attentional resources on an 'as-needed' basis, as a corrective mechanism when errors or conflicts are detected between observation and expectation. On the other hand, proactive control is anticipatory in nature and pre-allocates those same resources in preparation for future goal-relevant information. Proactive and reactive control strategies allow for both anticipatory and adaptive responses in gait to changes in the environment (Potocanac et al., 2015; Richardson et al., 2022; Wagner et al., 2019). Thus, the DMC model provides a useful framework in relating stride variability to the temporal dynamics of cognitive control strategies — i.e., moment-to-moment reconfiguration of these strategies— to optimize performance.

There are notable theoretical and mathematical parallels between Braver's dual modes of cognitive control and DuBois' anticipatory processes (Amon et al., 2018). Although these relationships have not been formally tested, the DMC framework lends a strong neuroanatomical basis through which they may be plausibly biologically linked. Specifically, proactive control requires sustained, anticipatory lateral prefrontal cortex (PFC) activity to bias attentional resources to future goal-specific cues. Such environmental monitoring probably requires phasic dopaminergic input from the basal ganglia, whereas reactive control requires transient recruitment of the lateral PFC in unison with a more diffuse error detection network (Braver et al., 2021). The DMC framework has been used extensively to study schizophrenia, a disease characterized by behavioral variability and lateral PFC dysfunction (Barch & Ceaser, 2012). For example, associations between high response-time variability have been attributed to poor proactive control and a greater reliance on reactive strategies in schizophrenic patients (Chidharom et al., 2021). However, it may be difficult to extend results from cognitive tasks (e.g. 'Go/NoGo') to complex, whole-body movements.

One EEG-based study of 22 healthy younger adults demonstrated that compared to sitting, walking amplified the neural correlates of proactive control and diminished the neural correlates of reactive control (Richardson, 2022). These findings were largely consistent with observations from the aging literature: That the ability to perform context maintenance and rely on proactive strategies appears to decline in healthy aging (Haarmann et al., 2005), but those with mild cognitive impairment exhibit the most pronounced performance decrements during dual-task walking (Bishnoi & Hernandez, 2021). Richardson and colleagues noted in their study that the neural responses induced during walking increased as the task became more difficult.

They interpreted their findings to mean that a fronto-executive network might come 'online' during walking, but at the cost of a conflict-monitoring network.

General support for this interpretation is offered by a study of prefrontal cortex oxygenation in older adults that reported increased oxygenation variability—a purported measure of neural efficiency—in response to a dual-task-walking paradigm compared to walking alone, an effect that was amplified among those with cognitive impairment (Holtzer et al., 2020). However, given the inter-individual variability that these studies on the neural correlates of gait observed, both in brain and behavioral measures, it is also possible that individual differences in the intrinsic properties of these networks might themselves be important for understanding movement variability. Indeed, recent empirical research distinguishes both intra-individual (relating to state) and inter-individual (relating to trait) as sources of variation in cognitive control strategies (Braver et al., 2007).

Neural Correlates of Gait Variability and Cognitive Control

The question of the source of inter- and intra-individual differences in both stride variability and cognitive control strategies has led researchers to explore the neural mechanisms underlying these phenomena. Numerous studies have observed a relationship between features of the brain captured at rest and gait parameters (Beauchet et al., 2015; Lo et al., 2017, 2017; Verlinden et al., 2016; Wilson et al., 2019) and cognition (Cole et al., 2012; Dosenbach et al., 2007; McIntosh, 2000; Reineberg et al., 2015; Reineberg & Banich, 2016) measured outside of the magnet. For instance, Lo and colleagues (2021) observed in older adults that greater stride variability, defined by the coefficient of variation in stride time, was associated with greater resting-state functional connectivity — correlations in the blood oxygen level-dependent signal

as measured by functional magnetic resonance imaging (fMRI) — among and between intrinsic connectivity networks.

These high-order, complex cognitive processes are not isolated to a single region or circuit, but instead rely on interactions between hub regions across the whole brain. Researchers have defined and characterized regions that support a wide range of behaviors required for cognitive control to identify a robust and diffuse cognitive control network (Cole & Schneider, 2007; Dosenbach et al., 2008; Vincent et al., 2008). The cognitive control network, also referred to as the multiple-demand network (Camilleri et al., 2018), is comprised of various cortical regions, including regions such as the dorsolateral prefrontal cortex (DLPFC), anterior cingulate cortex/pre-supplementary motor area (ACC/pSMA), inferior frontal junction, and posterior parietal cortex (PCC). This network has provided a useful framework for an extensive number of studies that have sought to characterize alterations of cognitive control in aging and a wide variety of clinical populations (Alústiza et al., 2017; Campbell et al., 2012; Ray et al., 2017; Shine et al., 2013).

Preliminary findings from the ongoing Dual Mechanisms of Cognitive Control Project (Braver et al., 2021) reveals a set of 35 fronto-parietal regions that demonstrate consistent cognitive control demands across a range of tasks designed to modulate proactive and reactive cognitive control strategies. Most of the regions in this set are in areas labeled in the Schaefer atlas as part of the control, salience/ventral attention, or dorsal attention networks. Bilateral regions in the DLPFC, ACC/pSMA, and anterior insular/frontal operculum were the most robustly activated, revealing great parallel with prior work in the cognitive control or multiple-demand network. The modulation of the neural signature of cognitive control under reactive conditions was characterized by a general reduction in activation, although a distinct neural

signature of proactive control has yet to be identified. Braver suggests that this diverse network of frontoparietal regions might serve as a 'core network', consistently adaptive to demands in cognitive control for a wide range of tasks.

Despite an established motor-cognition relationship, and evidence of the neural correlates of both stride variability and cognitive function, there is only a small amount of research that has been conducted to understand the shared neural correlates between stride time variability and cognition. Studies comparing older adults with and without a neurodegenerative disease (Beauchet et al., 2019) or mild cognitive impairment (MCI) (Ali et al., 2022; Beauchet et al., 2015; Sakurai et al., 2021) indirectly test this hypothesis. For instance, Beauchet and colleagues (2015) observed that hippocampal volume was positively associated with a coefficient of variation in stride time, but only in cognitively healthy adults and not in those with MCI. However, this provides limited evidence on the shared neural origins of gait variability and cognitive control given that the association between the observed brain differences were not directly associated with cognitive control.

BOLD Signal Variability

While studies which have assessed brain structure or function, using functional connectivity or graph theoretical metrics, have brought insight into the organization of the brain that is important for these motor-cognitive relationships, these are static measures— and thus likely do not capture the temporal dynamics of the brain's (re)configurations that may underly moment-to-moment behavioral variability (Garrett, Samanez-Larkin, et al., 2013). Just as with gait variability, the variability of the BOLD signal captured with fMRI was once thought to represent noise but has more recently been proposed to represent the facilitation of shifting between states of integration versus segregation (Tognoli & Kelso, 2014). In the context of brain

networks, greater integration is characterized by greater density of connections *between* networks rather than within, and greater segregation is characterized by greater connections *within* a network and less dense connections to other networks, with 'small-world' networks being an economical balance of both models (Bassett & Bullmore, 2006). Thus, a network with high BOLD signal variability or neural flexibility is thought to be capable of adapting or rearranging its configuration or state, illustrative of a greater dynamic repertoire (Fuchs et al., 2007; McIntosh et al., 2008; Nomi et al., 2017).

Extensive research has sought to elucidate the relevance of brain BOLD signal variability for behavior. In general, greater BOLD variability, usually computed as the standard deviation of the BOLD timeseries, is associated with greater accuracy and faster, less variable response times on cognitive tasks ranging from working memory, task-switching, to attention and perception in younger and older adults (Armbruster-Genç et al., 2016; Garrett et al., 2011, 2014; Garrett, Kovacevic, et al., 2013; Grady & Garrett, 2018). Another study in 8 to 33-year-olds using EEG sought to investigate the relationship between neural variability and response accuracy and variability. With increasing age, participants exhibited less variable response times and greater accuracy on a face-recognition task. Though seemingly counterintuitive, this decrease in behavioral variability was associated with greater neural variability, as operationalized by multiscale entropy, demonstrating that these patterns are consistently observed across measurement techniques (EEG and MRI).

Generally, BOLD signal variability appears to increase in adolescence and decrease into adulthood, however these trajectories in BOLD variability appear to be task and region or network-specific (Nomi et al., 2017). This is in line with a recent study comparing performance on a range of cognitive tasks encompassing cognitive control in Alzheimer's disease patients and

healthy controls (Good et al., 2020). Their results revealed that greater BOLD variability in the medial temporal lobe and occipital cortex was related to better cognitive control/speed performance but worse memory scores. While this lends to the growing set of literature linking BOLD signal variability to cognitive abilities, it remains unclear to what degree BOLD variability modulates the dynamic balance between proactive and reactive control strategies and how this pattern is characterized in fronto-parietal regions identified for their robust activations in the DMCC framework (i.e., a 'DMCC' network).

Summary of Literature Review

This review of the literature highlights the research that has been conducting in characterizing gait variability, cognitive control, and the underlying neural correlates that gives rise to these behaviors in humans. While there is evidence of strong and weak anticipation, which has great theoretical overlap with proactive and reactive cognitive control strategies, relating to long- and short-term variability in biological systems, the relation of cognitive control in this framework to gait variability is not well understood. Given that there is a strong and diverse set of literature that has observed a relationship between cognitive abilities and gait, they plausibly have shared neural correlates or biological underpinnings. Preliminary findings from the DMCC Project reports a set of frontoparietal regions, which parallel prior work in a cognitive control network, that are robustly active across a wide range of cognitive tasks that modulate control demand. One metric to characterize the brain assesses the variability of the BOLD signal, which is assessed using fMRI, and has been related to motor control and is thought to represent neural flexibility and support cognitive control. While it has not been formally tested, the dynamics of BOLD variability in this set of frontoparietal regions likely underlies important relationships between cognitive control strategies and gait variability.

CHAPTER III: METHODS

Overview of Research Design

The purpose of this study was to investigate the relationship between short- and long-term stride time variability and utilization of reactive and proactive cognitive control strategies. An additional aim was to determine the underlying neural correlates that explains these motor-cognitive relationships. Cross-sectional data on a stepping-in-place dynamic balance task (AccWalker), performance on the DPX task, and resting-state functional magnetic resonance imaging (fMRI) were collected. Associations between short- and long-term stride time variability and performance on the DPX task (proactive behavioral index) were assessed and, lastly, a multivariate analysis was used to identify a pattern of BOLD signal variability in an underlying brain functional network that jointly explains these motor-cognitive relationships.

Participants

Young adults between the ages of 18-35 years old from the local community were recruited to participate in the study using flyers, email announcements, and social media. Individuals who expressed interest completed an online MRI safety screening form and a general health and demographic survey on REDCap. Eligibility criteria included no known diagnoses of neurological, psychiatric, or gait disorders.

Experimental Design

All participants came to the Joint School of Nanoscience and Nanoengineering (JSNN) for one visit to complete balance and cognitive testing, as well as functional magnetic resonance imaging (fMRI). Participants were instructed to avoid caffeine, alcohol, and exercising 12 hours prior to the study. Upon arrival at JSNN, participants were consented and screened using a questionnaire to ensure they had no contraindications for MRI before carrying out the protocol.

Protocol

Dot Probe Expectancy Task

The AX-Continuous Performance Test (AX-CPT) has become increasingly used to test cognitive control and contextual processing given its simplicity and ease of implementation and has been applied in various populations (Barch et al., 2009; Chatham et al., 2009; Chun et al., 2018). In the current study, participants completed a modified version of the AX-CPT, called the dot-probe expectancy (DPX) task while seated at a computer. Compared to the letters of the traditional AXCPT task, the unfamiliar dot/braille patterns used in the DPX increase the difficulty of the task, an advantage given the recruitment of relatively healthy young adults in the current study. The task requires that participants make a target button push (the letter 'L' key) when a configuration of dots representing the cue is followed by a configuration of dots representing the probe (typically defined as an "AX" trial) and inhibit that button response in all other trials (instead pressing the letter 'A' key). The task consists of 4 blocks of 160 trials each. All sets contained the same proportion of trials (AX = 68.75%, AY = 12.5%, BX = 12.5%, BY = 5%) but the cue-probe delay varies: Two blocks consist of a short (1 sec) or known cue-probe delay (160 trials; ~4 minutes) and two blocks of long (3 ± 0.5 sec) or jittered cue-probe delay (160 trials; ~8 minutes). All blocks were presented in a counter-balanced order (i.e., short blocks were completed before the long for the first participant, and vice-verse for the second participant).

AccWalker

Recently, smartphone applications have utilized sensors embedded within the phone as a feasible way to capture spatial and temporal metrics of gait and balance. This is particularly useful since smartphones are relatively cheap, portable, and feasible to use out in the field. Of the

mobile device applications that are available to monitor static or dynamic balance and have been tested, only 38% evaluated its validity and only 23% assessed the reliability of their device (Roeing et al., 2017). The AccWalker application was developed as a portable tool to capture dynamic balance or neuromotor control in the field and currently can be used on Android phones (Kuznetsov et al., 2018). AccWalker was designed to quantify thigh and trunk orientation during a dynamic balance task and was shown to produce reliable and valid spatiotemporal variables when tested against a motion capture system (Kuznetsov et al., 2018).

The standard AccWalker protocol involves two trials of each of three conditions: stepping-in-place with eyes open and gaze fixed at a crosshair, stepping-in-place with eyes closed, and lastly stepping-in-place with gaze fixed at a crosshair while rotating the head back and forth. This study utilized only the eyes open condition to assess baseline, intrinsic variability in gait when visual and vestibular sensory inputs are not disturbed. Normally, each trial is seventy seconds in duration, with an audible metronome (period = 0.575 seconds, or 1.74 Hz) beeping for the first ten seconds. Participants are instructed to synchronize their steps to the metronome and continue stepping at that pace for the remaining sixty seconds. In the current study, trials were extended to 180 seconds (3 minutes) in order to capture enough strides to adequately compute the short- and long-term components of variability using the Lyapunov exponent (Terrier & Dériaz, 2013). Thus, each participant completed one, thirty second practice followed by two three-minute trials of the eyes open condition.

Magnetic Resonance Imaging (MRI)

MRI has been used for more than three decades to image human tissue *in vivo* and is safe given that participants are properly screened for contraindications prior to scanning. Screened participants were be placed in the bore of the 3T Siemens Magnetom scanner with a 16-channel

head coil for structural (sMRI) and functional (fMRI) measurements that took approximately 25 minutes. First, a brief (10 second) localizer scan was used to center subsequent scans. Next, sMRI was performed using a high-resolution, T1-weighted MPRAGE sequence (FoV: 256 x 256; 224 sagittal slices; slice thickness = 1mm; TE = 4.18 ms; Flip Angle = 12 degrees; PEdir = AP) lasting approximately 7 minutes. fMRI was performed using a T2*-weighted sequence (70 oblique slices; slice thickness = 3mm, no gap; TE = 30 ms; TR = 2.6 seconds; Flip Angle = 79 degrees; PEdir = AP; GRAPPA Factor = 2) lasting approximately 12 minutes. Finally, gradient echo and spin-echo fieldmaps were collected (3 minutes) for offline susceptibility distortion correction.

Data Processing

Proactive Behavioral Shift Index (PBI)

Reaction times and accuracies, computed using Python, were imported into Microsoft Excel and the proactive behavioral shift index (PBI) was computed for each participant using AY and BX error rates according to the equation below (Braver et al., 2009), where E_{AY} and E_{BX} represent the error rate for AY and BX trials, respectively. A correction was made for trials which had some errors equal to zero (error +0.5)/(trial type frequency + 1) (Braver et al., 2009). The PBI metric was computed from the error rates of the short known cue-probe delay trials, given its ability to differentiate cognitive control strategies in young adults (Janowich & Cavanagh, 2018). The PBI is a composite measure of the strength of context processing and varies between -1 to +1. Scores closer to +1 indicate greater use of a proactive strategy is, while scores closer to -1 is represent greater utilization of a reactive control strategy.

$$PBI = \frac{E_{AY} - E_{BX}}{E_{AY} + E_{BX}}$$

Lyapunov Exponent (LyE)

Data was imported into Matlab 2022a (Mathworks, Natick MD). A timeseries of acceleration parameters is imported into Matlab and filtered using a 5 Hz low-pass Butterworth filter. Time between minima (milliseconds) in the velocity timeseries were extracted to represent stride times. Following the recommendations of Raffalt and colleagues (2019), each timeseries was standardized to 145 strides and 14,500 data points and reconstructed in state space using delay embedding. Appropriate time delay and dimension for embedding was computed using the average mutual information and false nearest neighbor algorithm (Bruijn et al., 2013; Rosenstein et al., 1993). For this sample, the time delay and embedding dimension were on average 30.3 ± 2.9 and 6.6 ± 0.6 for the anterior-posterior direction. Thus, state space was reconstructed using a time delay of 30 and an embedding dimension of 7 for the anterior-posterior direction. LyE was then calculated with custom Matlab scripts and extracted over 0 -1 strides to represent short-term variability (LyES) and 4-10 strides to represent long-term variability (LyEL). The LyES and LyEL were average for the two trials for each participant, and thus every participant had one value each for LyES and LyEL.

sMRI and fMRI Preprocessing

Data was converted from raw DICOM to NIFTI and organized according to the BIDS standard before being uploaded to *longleaf*, the high-performance cluster hosted by UNC Chapel Hill. sMRI and fMRI data was preprocessed using fMRIPrep (Esteban et al., 2019). fMRI data was truncated to minutes 2-12 to capture only resting-state and remove an initial 2-minute 'breath-hold' procedure that is not associated with the current project. Briefly, the fMRIPrep pipeline involves motion correction, susceptibility distortion correction, normalization, brain extraction, and surface-based registration. This pipeline includes specific and heavily referenced

boilerplate language: Results included in this manuscript come from preprocessing performed using fMRIPrep 22.1.1 (Esteban et al., 2019; RRID:SCR_016216), which is based on Nipype 1.8.5 (Gorgolewski et al., 2011; RRID:SCR_002502).

Preprocessing of B0 inhomogeneity mappings. A total of 2 fieldmaps were found available within the input BIDS structure for this particular subject. A B0 nonuniformity map (or fieldmap) was estimated from the phase-drift map(s) measure with two consecutive GRE (gradient-recalled echo) acquisitions. The corresponding phase-map(s) were phase-unwrapped with prelude (FSL 6.0.5.1:57b01774). A B0-nonuniformity map (or fieldmap) was estimated based on two (or more) echo-planar imaging (EPI) references with topup (Andersson et al., 2003; FSL 6.0.5.1:57b01774).

Anatomical data preprocessing. A total of 1 T1-weighted (T1w) images were found within the input BIDS dataset. The T1-weighted (T1w) image was corrected for intensity non-uniformity (INU) with N4BiasFieldCorrection (Tustison et al., 2010), distributed with ANTs 2.3.3 (Avants et al., 2008; RRID:SCR_004757), and used as T1w-reference throughout the workflow. The T1w-reference was then skull-stripped with a Nipype implementation of the antsBrainExtraction.sh workflow (from ANTs), using OASIS30ANTs as target template. Brain tissue segmentation of cerebrospinal fluid (CSF), white-matter (WM) and gray-matter (GM) was performed on the brain-extracted T1w using fast (FSL 6.0.5.1:57b01774, RRID:SCR_002823, Zhang et al., 2001). Brain surfaces were reconstructed using recon-all (FreeSurfer 7.2.0, RRID:SCR_001847, Dale et al., 1999), and the brain mask estimated previously was refined with a custom variation of the method to reconcile ANTs-derived and FreeSurfer-derived segmentations of the cortical gray-matter of Mindboggle (RRID:SCR_002438, Klein et al., 2017). Volume-based spatial normalization to two standard spaces (MNI152NLin2009cAsym,

MNI152NLin6Asym) was performed through nonlinear registration with antsRegistration (ANTs 2.3.3), using brain-extracted versions of both T1w reference and the T1w template. The following templates were selected for spatial normalization: ICBM 152 Nonlinear Asymmetrical template version 2009c [Fonov et al., 2009, RRID:SCR_008796; TemplateFlow ID: MNI152NLin2009cAsym], FSL's MNI ICBM 152 non-linear 6th Generation Asymmetric Average Brain Stereotaxic Registration Model [Evans et al., 2012, RRID:SCR_002823; TemplateFlow ID: MNI152NLin6Asym].

Functional data preprocessing. For each of the 1 BOLD runs found per subject (across all tasks and sessions), the following preprocessing was performed. First, a reference volume and its skull-stripped version were generated using a custom methodology of fMRIPrep. Head-motion parameters with respect to the BOLD reference (transformation matrices, and six corresponding rotation and translation parameters) are estimated before any spatiotemporal filtering using mcflirt (FSL 6.0.5.1:57b01774, Jenkinson et al., 2002). The estimated fieldmap was then aligned with rigid-registration to the target EPI (echo-planar imaging) reference run. The field coefficients were mapped on to the reference EPI using the transform. BOLD runs were slice-time corrected to 1.29s (0.5 of slice acquisition range 0s-2.57s) using 3dTshift from AFNI (Cox & Hyde, 1997, RRID:SCR_005927). The BOLD reference was then co-registered to the T1w reference using bbregister (FreeSurfer) which implements boundary-based registration (Greve & Fischl, 2009).

Co-registration was configured with six degrees of freedom. Several confounding time-series were calculated based on the preprocessed BOLD: framewise displacement (FD), DVARS and three region-wise global signals. FD was computed using two formulations following Power (absolute sum of relative motions, Power et al., 2014) and Jenkinson (relative root mean square

displacement between affines, Jenkinson et al., 2002). FD and DVARS are calculated for each functional run, both using their implementations in Nipype (following the definitions by Power et al., 2014). The three global signals are extracted within the CSF, the WM, and the whole-brain masks. Additionally, a set of physiological regressors were extracted to allow for component-based noise correction (CompCor, Behzadi et al., 2007). Principal components are estimated after high-pass filtering the preprocessed BOLD time-series (using a discrete cosine filter with 128s cut-off) for the two CompCor variants: temporal (tCompCor) and anatomical (aCompCor). tCompCor components are then calculated from the top 2% variable voxels within the brain mask. For aCompCor, three probabilistic masks (CSF, WM and combined CSF+WM) are generated in anatomical space.

The implementation differs from that of Behzadi et al., 2007 in that instead of eroding the masks by 2 pixels on BOLD space, a mask of pixels that likely contain a volume fraction of GM is subtracted from the aCompCor masks. This mask is obtained by dilating a GM mask extracted from the FreeSurfer's aseg segmentation, and it ensures components are not extracted from voxels containing a minimal fraction of GM. Finally, these masks are resampled into BOLD space and binarized by thresholding at 0.99 (as in the original implementation). Components are also calculated separately within the WM and CSF masks. For each CompCor decomposition, the k components with the largest singular values are retained, such that the retained components' time series are sufficient to explain 50 percent of variance across the nuisance mask (CSF, WM, combined, or temporal). The remaining components are dropped from consideration.

The head-motion estimates calculated in the correction step were also placed within the corresponding confounds file. The confound time series derived from head motion estimates and global signals were expanded with the inclusion of temporal derivatives and quadratic terms for

each (Satterthwaite et al., 2013). Frames that exceeded a threshold of 0.5 mm FD or 1.5 standardized DVARS were annotated as motion outliers. Additional nuisance timeseries are calculated by means of principal components analysis of the signal found within a thin band (crown) of voxels around the edge of the brain, as proposed by (Patriat et al., 2017). The BOLD time-series were resampled onto the following surfaces (FreeSurfer reconstruction nomenclature): fsaverage. Grayordinates files (Glasser et al., 2013) containing 91k samples were also generated using the highest-resolution fsaverage as intermediate standardized surface space. All resamplings can be performed with a single interpolation step by composing all the pertinent transformations (i.e. head-motion transform matrices, susceptibility distortion correction when available, and co-registrations to anatomical and output spaces). Gridded (volumetric) resamplings were performed using antsApplyTransforms (ANTs), configured with Lanczos interpolation to minimize the smoothing effects of other kernels(Lanczos, 1964). Non-gridded (surface) resamplings were performed using mri_vol2surf (FreeSurfer).

Many internal operations of fMRIPrep use Nilearn 0.9.1 (Abraham et al., 2014, RRID:SCR_001362), mostly within the functional processing workflow. For more details of the pipeline, see the section corresponding to workflows in fMRIPrep's documentation (https://fmriprep.readthedocs.io/en/latest/workflows.html). The above boilerplate text was automatically generated by fMRIPrep and is released under the CC0 license.

The primary output from this pipeline is a pre-processed surface-mapped dense BOLD timeseries (91k greyordinates). The pipeline also outputs nuisance regressors representing physiological noise that was used in a subsequent step to 'clean' the dense timeseries using the *ciftify* toolbox (Dickie et al., 2019). Specifically, high-pass filtering, to remove scanner drift at and below .0008 Hz, was performed using a discrete cosine transform basis set. Components

from the cerebrospinal fluid and white matter that each explained 50% of the variance in the BOLD signal were removed and head motion was corrected by regression in 24 parameters and using framewise displacement and the derivative of its variance (DVARS) as additional regressors (Parkes et al., 2018; Power et al., 2014).

BOLD signal variability

The cleaned, surface-mapped BOLD data (91k greyordinates) was imported into Matlab and BOLD variability was computed as the root mean square of successive differences (RMSSD) in the BOLD signal timeseries. In the equation for RMSSD below, z*TS* is the z-scored value of the BOLD signal (TS) at time *t*. The BOLD variability for each parcel was then averaged to comprise a total of 400 areas according to the standardized Schaefer atlas (Marcus et al., 2011; Schaefer et al., 2018). The BOLD variability from our 35 regions of interest (ROI) in putative dorsal attention, salience/ventral attention, and control networks were extracted such that each participant is represented by a vector of 35 BOLD variability values (see Appendix 1 for a list of the 35 ROIs).

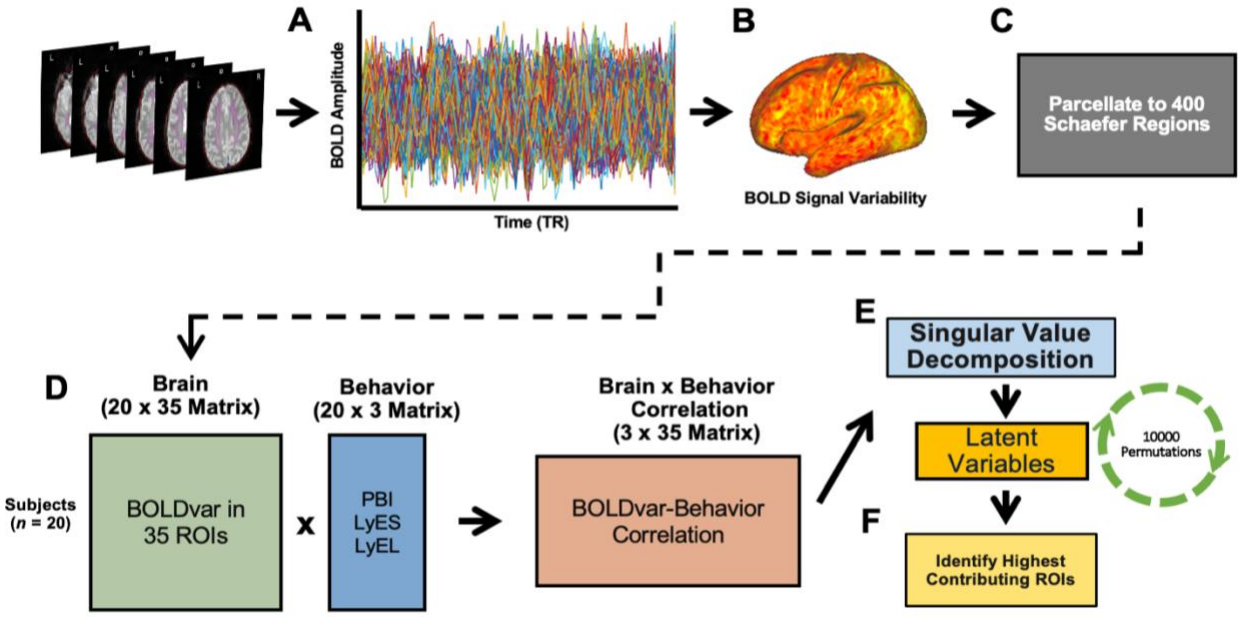
$$RMSSD = \sqrt{\frac{\sum(zTS_{t+1} - zTS_t)^2}{length(TS) - 1}}$$

Statistical Analyses

Statistical analyses were performed using Matlab 2020a. A Pearson correlation was conducted to determine the association between PBI and short-term variability (LyES) and, separately, PBI and long-term variability (LyEL). A partial least squares correlation (McIntosh & Lobaugh, 2004) was then run to determine if there was a pattern of brain BOLD signal variability in the 35 ROIs that was associated with proactive and reactive cognitive control, and LyES and LyEL (short- and long-term gait variability). Briefly, this involves decomposing a

'brain' matrix (20 rows x 35 columns) and a 'behavior' matrix (20 rows x 3 columns), where each row represents a participant and each column is their score for PBI, LyES, and LyEL. The brain-behavior correlation matrix was parsed into a vector of singular values and saliences, resulting in three latent variables that represent the optimal covariance between some pattern of BOLD signal variability and a behavior. After 10,000 permutations, latent variables with less than 500 permutations yielding greater singular values than observed were kept as significant. Boot strap resampling (1000x) revealed ROIs that contributed most to this observed salience. See Figure 1 for a schematic of the brain data processing and statistical methods.

Figure 1. MRI Data Processing Schematic



Note. The root means square of successive differences (RMSSD) was computed for each clean times series (A) to represent BOLD variability (B) and was parcellated using a standardized atlas (C). A resulting brain matrix (D), where each row represents the BOLD variability in the 35 ROIs for one subject, was multiplied by a behavior matrix, where each row represents a subject's proactive behavioral shift index (PBI), short Lyapunov exponent (LyES), and long Lyapunov exponent (LyEL). The resultant correlation matrix then underwent singular value decomposition (E), revealing 3 latent variables for which p-values are generated through 10,000 permutations of the original data. Boot strap resampling revealed brain regions that contributed most to this relationship (>2 standard deviations).

CHAPTER IV: RESULTS

Data was collected on 20 participants, which were between the ages of 19 – 33 years old (average = 23.6 ± 3.9 years). See Table 1 for a summary of demographic information. Two of the twenty participants were on medication (subject 1: anorectic medication and subject 2: glucocorticoid, SSRI, and benzodiazepine). All participants were free of neurological, psychiatric, or gait-related disorders, however, one patient reported having a concussion approximately 1.5 weeks prior to the study (no loss of consciousness).

Table 1. Demographic Information

Biological Sex	10 Male /10 Female	
Age (years)	23.6 ± 3.9	
Race and Ethnicity	60% White 10% Asian 10% Hispanic 5% Black or African American 15% Other (listed 2)	
Average height (inches)	66.4 ± 2.8	
Average weight (lbs)	162.1 ± 35.22	
BMI (kg/m^2)	26.0 ± 6.1	
Dominant Hand (% Right)	90	
Dominant Leg (% Right)	95	
Mean Proactive Behavioral Shift Index (PBI)	0.252 ± 0.40	
Mean Lyapunov Exponent	LyES = 0.63 ± 0.06	LyEL= 0.06 ± 0.01

There was no significant correlation between PBI and LyES ($r(19) = 0.235$, $p = 0.318$; Figure 2A) or PBI and LyEL ($r(19) = 0.223$, $p = 0.346$; Figure 2B). A partial least squares (PLS) correlation analysis revealed one significant latent variable (Permutation $p = 0.0323$) explaining 87% of the cross-block covariance in the brain-behavior model. This latent variable represented a weighted sum of brain BOLD variability in the 35 ROIs (so-called 'brainscore') that was positively correlated to both LyES and LyEL and was not correlated with PBI (Figure 3A). All regions with boot strap ratios (BSR) in the 95% confidence interval are highlighted in Figure 3B. Brain regions that contributed most strongly to this relationship were the PCFl_5 ROI (Parcel 139) in the control network (BSR = 4.84) and the FrOperIns_9 (Parcel 5) and FrOperIns_7 (Parcel 103) in the salience/ventral attention network (BSR = 3.74 and 3.64, respectively). A post-hoc regression analysis revealed different slopes between brainscore (predictor) and exponent (outcome) based on 'type' (long vs. short; moderator) ($t(36) = -2.372$, $p = 0.023$; Figure 3C).

Figure 2. Proactive Behavioral Shift Index – Lyapunov Exponent Correlations

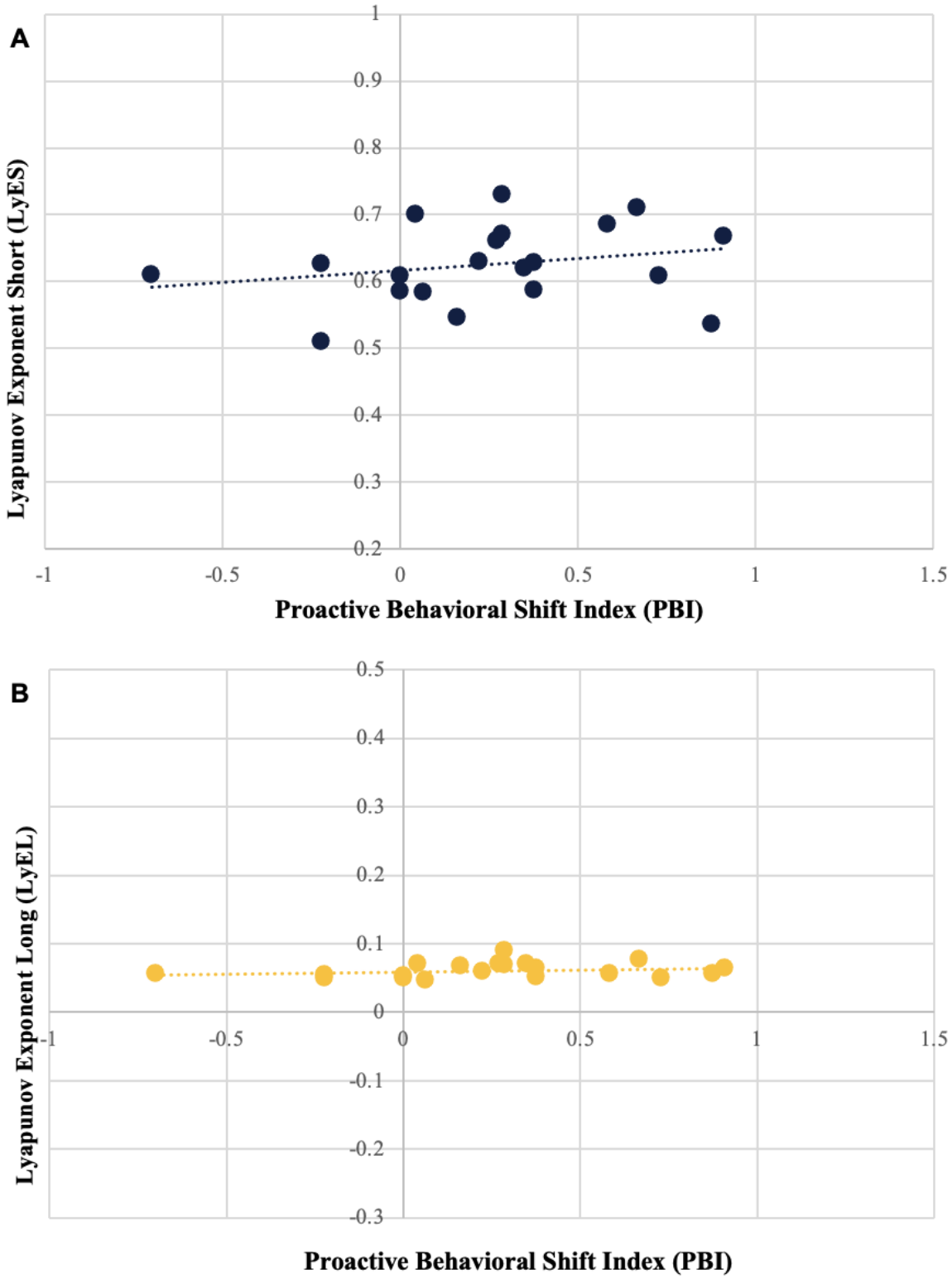
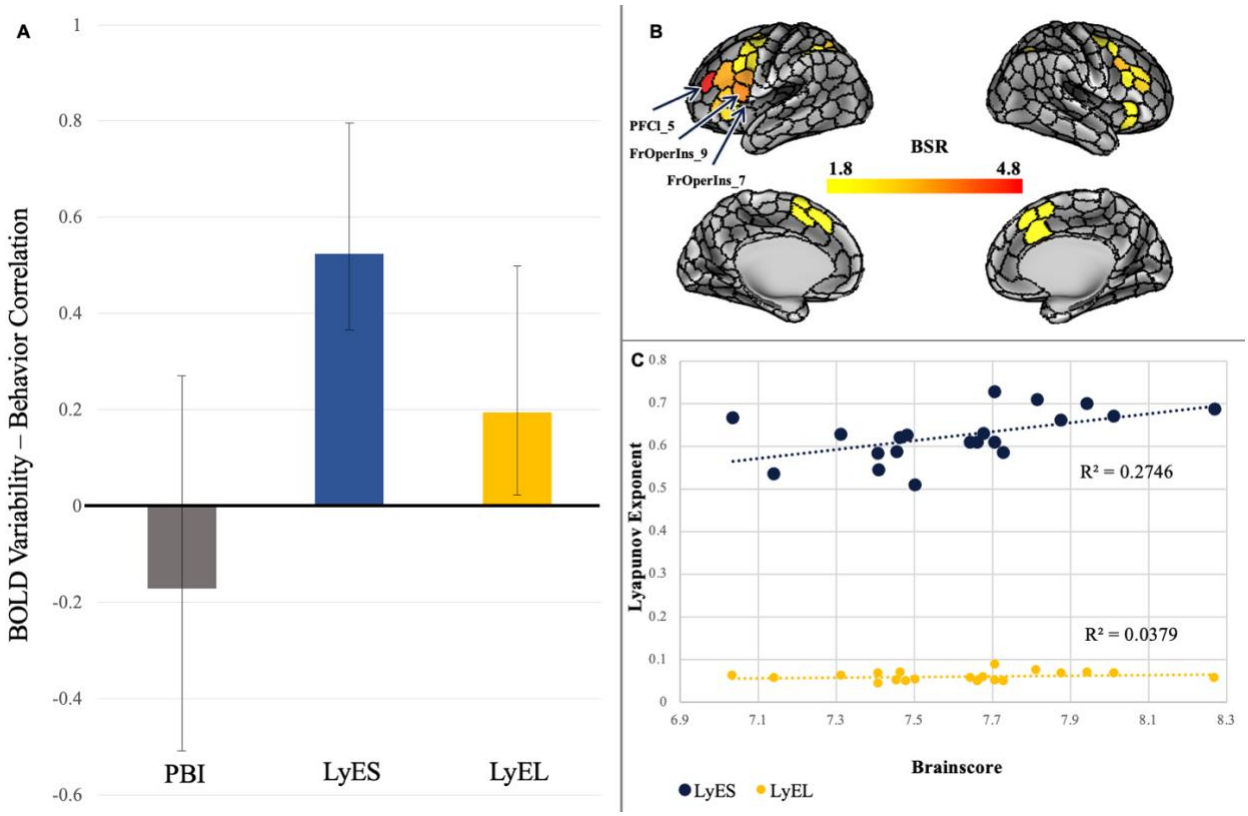


Figure 3. Partial Least Squares Analysis



Note. A) Bar plot depicting the results of the partial least squares correlation (PLS), representing the correlation between a pattern of BOLD variability in the 35 ROIs and the proactive behavioral shift index (PBI), and the short and long Lyapunov exponents (LyES and LyEL) ($p = 0.0323$), B) Brain model highlighting the boot strap ratios of the ROIs that significantly contributed to the observed salience, such that as the color shifts from yellow to red, the regions extend beyond 2-3 standard deviations and contribute more strongly to the behavior salience. C) A scatter plot of the LyE (short and long) versus participant's 'brainscore', or the degree to which they represented the pattern in (A).

CHAPTER V: DISCUSSION

The purpose of this study was to test the hypothesis that individual differences in cognitive control and motor control are related through functional variability of brain areas previously implicated in cognitive control. Previous research supports a relationship between gait variability and cognitive abilities (Allali et al., 2008; Beauchet et al., 2012; Herman et al., 2010; IJmker & Lamoth, 2012; Mirelman et al., 2012; Yogev-Seligmann et al., 2008) and that task-driven neural variability is associated with both cognition (Braver et al., 2009) and motor performance (Haar et al., 2017; Holtzer et al., 2020). However, intrinsic brain functional properties have proven clinically relevant in populations that cannot perform cognitive or motor tasks (Fox & Greicius, 2010). Indeed, one of the earliest findings from resting-state fMRI findings was an overlap between resting-connectivity and task-activation in the motor cortex (Biswal et al., 1995). In partial support of our second hypothesis, our primary and novel finding was a pattern of brain BOLD signal variability in 35 areas defining a putative cognitive control network that was related to stride time variability.

Our results revealed that greater BOLD variability in 35 frontoparietal regions was associated with greater movement variability as defined by the Lyapunov exponent over a window of 0-1 strides (LyES) and, to a lesser extent, over a window of 4-10 strides (LyEL). The difference in strength of the correlation may in part be due to the wider spread of LyES values compared to LyEL, which is consistent with reports from prior literature (Mehdizadeh, 2018). This demonstrates notable parallels with prior studies that relate behavioral/kinematic variability and task-driven neural variability. For example, greater variability in oxygenated hemoglobin measured over the prefrontal cortex using functional near-infrared spectroscopy (fNIRS) was associated with greater stride variability as task difficulty increased among older adults (Holtzer

et al., 2020). A different study of young adults reported greater inter-trial variability in the BOLD signal during an out-and-back reaching task in the scanner that was associated with greater arm movement variability (Haar et al., 2017). Overall, there appears a positive correlation between neural variability and movement variability across the lifespan. However, it is not known whether these patterns represent individual differences in muscle recruitment, effort, or motor control strategies. The findings of the current study replicate and extend these patterns and represent the first to demonstrate a relationship between variability in resting brain BOLD signal and gait variability.

These brain areas were selected based on prior work by Braver et al. (2021) demonstrating their role in performing a similar cognitive control task. In support of Hypothesis 2, a region in the left dorsolateral prefrontal cortex had the highest predictive value (PFCl_5, BSR = 4.84) in its association with the Lyapunov exponent, such that individuals exhibiting the greatest BOLD variability in this region also exhibited the greatest stride time variability during the stepping-in-place task. Interestingly, this pattern of BOLD variability was predominantly left-lateralized. Dorsolateral prefrontal cortical interactions are thought to play a central role in attentional control and integration of sensory information important for directing goal-relevant behavior (Jiang et al., 2015; B. T. Miller & D'Esposito, 2005; E. K. Miller & Cohen, 2001), and further research has explored its role in inhibitory responses in motor control (Krämer et al., 2013). Recently, Thompson et al. (2021) reported that increases in BOLD variability in an 'inhibition network', which had high connectivity to the lateral PFC, related to better inhibitory performance in young adults. It is possible to speculate that greater variability in this network may represent a high capacity to flexibly modulate its activity in coordination with other brain networks and be important for the maintenance of optimal gait during a guided task (Jiang et al.,

2015). Future research to extend and replicate these findings in older adult samples, who exhibit altered patterns of BOLD variability (Good et al., 2020; Rieck et al., 2022), may open the door to an improved understanding of movement variability during a stepping-in-place task as a biomarker of brain health.

It was surprising that this same pattern of BOLD variability did not also relate to PBI, given that the areas were specifically selected for their putative role in cognitive control. The incongruency in results may arise from uncertainties in localizing task-activations to cortical areas using a volume-based approach, as Braver et al. (2021) did. Volume-based registration, as compared to the surface-based approach used here, result in a greater degree of uncertainty, particularly for cortical areas that are characterized by deep grooves and display high inter-individual morphological variability (Coalson et al., 2018). Thus, it is possible that the ROIs selected here are not identical to those frontoparietal regions identified by Braver et al. (2021) even though they were developed using the same parcellation approach (Schaefer et al., 2018).

On the other hand, the hypothesized univariate relationships between PBI and LyE were also not supported. While proactive cognitive control relies on strong anticipation in a neuroanatomical framework proposed by Braver, this may not reflect the theoretical model of anticipation defined by Dubois (2003), designed to characterize independent anticipatory capabilities during synchronization behaviors. While the stepping-in-place task (AccWalker) begins with an audible metronome to guide the participant's stepping pace, there is no cue during the cycles used to compute LyE, and thus may not lend toward coupling or synchronization as observed in signals of anticipatory biological systems (Stephen et al., 2008; Stepp & Turvey, 2010). Furthermore, given the wide distribution of PBI scores in the current sample (0.252 ±

0.40), it is equally possible that the heterogeneity observed in the current sample may not be representative of a young adult population (Janowich & Cavanagh, 2018).

Limitations

Despite the novel findings reported here, this study is not without limitations. Given our sample size (n = 20), a Pearson correlation would only be sensitive to detect the effects of r = 0.58 with 80% power, (two-tailed, alpha = 0.05; Faul et al., 2007). However, it is important to consider that most studies observing motor-cognitive relationships typically report only small to moderate effect sizes (Demnitz et al., 2016). Another potential limitation was an audible noise from the MRI equipment (cooling pump) in the scanning suite where the behavioral data, including the stepping-in-place task, was collected. It is possible that participants gradually adjusted their pace over the 3-minute stepping trial to match the frequency of the MRI pump, approximately 2.3 Hz (which is faster than the prescribed stepping-rate of 1.7 Hz for AccWalker), and thus may have confounded the measures of gait variability. Finally, future studies should consider including the analysis of task-negative brain functional networks, such as the default mode network, given extensive evidence of its relation to individual differences in motor behaviors (Crockett et al., 2017; Lo et al., 2017, 2021) and cognitive control (Leech et al., 2011; Rieck et al., 2022), as well as it sensitivity to aging and disease (Bai et al., 2008; Greicius et al., 2004; Hafkemeijer et al., 2012).

Conclusions

To the author's knowledge this is the first report of a pattern of resting brain BOLD signal variability that relates to gait variability. The lack of a relationship observed here between cognitive control strategies and either movement variability or intrinsic properties of a cognitive control brain network reinforces the complex nature of motor-cognition relationships and calls

for future research to further explore these dynamics in other populations and brain networks. These findings provide evidence of gait variability as a marker of brain variability in healthy, young adult and may open the door to understanding its role as a biomarker of brain health.

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APPENDIX A: 35 FRONTOPARIETAL REGIONS OF INTEREST

Parcel Number	Hemisphere	Network	ROI	x	y	z
77	Left	Dorsal attention	Post_9	−33	−46	41
78	Left	Dorsal attention	Post_10	−29	−58	50
86	Left	Dorsal attention	FEF_1	−40	−3	51
87	Left	Dorsal attention	FEF_2	−25	−1	55
88	Left	Dorsal attention	FEF_3	−30	−8	52
90	Left	Dorsal attention	PrCv_1	−49	6	26
91	Left	Dorsal attention	PrCv_2	−50	3	38
99	Left	Salience/ventral attention	FrOperIns_3	−33	25	−1
101	Left	Salience/ventral attention	FrOperIns_5	−33	19	8
103	Left	Salience/ventral attention	FrOperIns_7	−43	12	2
105	Left	Salience/ventral attention	FrOperIns_9	−52	9	13
110	Left	Salience/ventral attention	Med_4	−5	9	48
127	Left	Control	Par_1	−29	−74	42
130	Left	Control	Par_4	−35	−62	48
132	Left	Control	Par_6	−45	−41	47
139	Left	Control	PFCl_5	−42	38	22
140	Left	Control	PFCl_6	−45	20	27
141	Left	Control	PFCl_7	−39	7	34
148	Left	Control	PFCmp_1	−4	28	47
172	Left	Default	PFC_7	−48	28	0
175	Left	Default	PFC_10	−53	19	11
185	Left	Default	PFC_20	−42	7	48
189	Left	Default	PFC_24	−6	10	65
290	Right	Dorsal attention	FEF_1	39	−3	53
306	Right	Salience/ventral attention	FrOperIns_5	37	23	5
311	Right	Salience/ventral attention	Med_1	7	19	35
314	Right	Salience/ventral attention	Med_4	6	11	58
337	Right	Control	Par_6	41	−55	48
340	Right	Control	PFCv_1	34	21	−8
346	Right	Control	PFCl_6	50	30	18
347	Right	Control	PFCl_7	48	18	23
349	Right	Control	PFCl_9	47	29	28
350	Right	Control	PFCl_10	39	11	34
353	Right	Control	PFCl_13	43	7	51
361	Right	Control	PFCmp_2	5	28	48

Note. Listed in this appendix are the 35 parcels with a modulatory effect of cognitive control demand identified by Braver et. al., 2021.