**Preregistration Document**

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* **Very short abstract/summary of the aim of the study**

While past literature has investigated aspects of multitasking training via fMRI measures, tDCS, and rTMS (Dux, 2009; Hsu, 2015; Ljubisavljevic, 2019; Nelson 2019; Takeuchi, 2014; Garner, 2015; Thoma, 2008), few studies have directly explored the relationship between multitasking practice and underlying white matter networks via DTI. While fMRI methods are excellent for investigating neuroanatomical correlates and the functional neuroanatomy of executive functions (Schubert, 2003), and electrical stimulation methods are able to establish causal relationships between localised regions and psychological constructs (Filmer, 2014), DTI measures have the capabilities to extend these findings to structural connectivity, allowing for a more in-depth exploration of important features at a microstructural level such as myelination, axonal diameter and fibral density (Alexander, 2007). The present study aims to extend prior literature by investigating the structural connectivity of white matter tracts’ associated with multitasking training and visual search training outcomes. Specifically, we will assess the structural connectivity of the dorsolateral prefrontal cortex to the striatum (cortico-striatal) to examine if there is a relationship between fractional anisotropy values (FA) and the participants’ improvements in multitasking and rate of change, in order to detect whether this tract is associated with performance improvements from multitasking training. Additionally, we will examine the medial superior longitudinal fasciculus and the basal forebrain to superior occipital cortex tract to determine if there is a relationship between FA and improvements in visual search performance and rate of change.

* **The behaviour being observed**

The first observed behaviour is multitasking, an “executive control function” represented by subprocesses including planning, adherence to task rules and time constraints, and attention switching to efficiently coordinate several tasks simultaneously (Thoma et al., 2008). Whether undertaking simple dual-tasks or performing two or more complex tasks in rapid succession, the human brain experiences multitasking costs regardless of task modality, which has prompted several related theories. The “central bottleneck theory”, originally proposed by Welford (1952), suggests that dual-task costs arise from a structural processing bottleneck that leads to disruption of components in parallel. This is reflected in Psychological Refractory Period (PRP) tasks, wherein reaction times are recorded for two stimuli presented (separated by a stimulus onset asynchrony (SOA)). As the SOA shortens (time between stimulus one and stimulus two), the reaction time at stimulus two progressively increases while response times at stimulus one remain relatively unchanged (Pashler, 1994). The delays produced in stimulus two (but not stimulus one) suggest that the brain only contains one “device” capable of executing a given process, indicating that responses are processed serially given task two cannot occur until task one is complete. Han and Marois (2013) further corroborate serial processing theory in their study of performance optimisation in a dual-task situation, finding that participants overwhelmingly fail to show flexibility in processing the tasks and instead serially postpone responses despite the favourable parallel processing conditions. Had participants engaged with parallel processing, they would have displayed shorter response times during task one as well as task two, which was not the case. Ruthruff et al. (2001) also addressed the debate regarding whether the central bottleneck is a structural limitation or a strategic postponement by proposing a novel dual-task paradigm which eliminated noncentral sources of interference and investigating whether dual-task slowing still occurred. In effect, they found that large amounts of dual-task slowing remained despite these efforts, demonstrating that interference is not attributable to voluntary postponement, preparation effects, or conflicts in response production.

Despite robust evidence demonstrating the effects of the PRP paradigm on task two processing, there are also some accounts of the same effect on task one processing. For instance, there have been some accounts of “backward crosstalk”, a phenomenon wherein response to task one is dependent on the response required for task two, an example of this being Miller’s (2006) study of task two response types on response to the first task. In experiments one and two, Miller (2006) sought to understand whether reaction times associated with task one were slowed when task two contained a go/no-go task, finding that responses to task one were consistently slower when a no-go response was required. These findings extend backward crosstalk theory by demonstrating that it can occur even when two tasks are unrelated, however the experiment is potentially limited by the unusual finding that the tasks appeared to induce large SOA effects on task one and smaller effects on task two (which is entirely unexpected given the standard bottleneck model). This is further corroborated by Logan and Schulkind’s (2000) study of parallel retrieval between tasks, finding that within a PRP experiment, reaction times to stimulus one were quicker if they required the same response as stimulus two. This interaction between the two stimuli is potentially interpretable as indicative of backward crosstalk, although namely supporting the parallel retrieval hypothesis wherein retrieval from task two influenced task one processing.

Evidence has demonstrated that dual-task costs can be overcome by training, for example, through task processing optimisation, which attributes reduction of dual-task costs and performance improvement to central stage shortening (Ruthruff et al., 2006). Neuroimaging data has further suggested that practice facilitates more efficient dual-task performance due to improved stimulus-response processing activation, as indicated by shorter neural activity and enhanced segregation of individual task representations within the prefrontal cortex (Dux et al., 2009). Another suggestion for the mechanism behind multitasking improvement with practice involves task automatization, wherein demands on the central resources responsible for the bottleneck are eliminated, allowing individuals to “bypass” the bottleneck and perform two central operations simultaneously (Maquestiaux et al., 2010).

Other dual-task interference explanations include “resource theories”, which assume that two response selections can be processed in parallel, however the sharing of the same attentional resources causes multitasking costs (Pashler, 1994). Multiplexing, propagated by Feng (2016), further describes multitasking costs arising because of simultaneous processing of the same resources for different purposes, resulting in decreased performance due to cross-talk. Another theory labelled the “executive control theory of visual attention” (ECTVA) proposes that executive processes control subordinate processes which can be programmed to carry out different tasks by manipulating their parameters, claiming to solve set-switching costs, cross-talk, and concurrence costs (Logan & Gordon, 2001). The theory extends the theory of visual attention (TVA) to dual-task situations, treating TVA as a subordinate process involved in stimulus selection, and exemplar-based random walk (EBRW) theory as a subordinate process involved in response selection, with the addition of one parameter that represents the time required to change a TVA parameter and another that represents the inhibition of random-walk counters. ECTVA demonstrates that the basics of TVA can be generalised to dual-task processing by running TVA twice (once on each stimulus), preferentially in a serial manner.

We will also be observing visual search behaviour, described as the ability to locate an object of interest amongst other elements within a visual environment (Bennett et al., 2012). The localisation of brain regions to this behaviour have classically been based on the attentional processes that guide visual search, wherein top-down guidance of attention (circumstances in which a priori understanding of the features of the target are used to guide target identification) is often associated with the dorsal frontoparietal network including the superior frontal and dorsal parietal regions (Bennett et al., 2016). For instance, Marshall et al. (2015) conducted a study that aimed to predict how the structural connectivity of the medial superior longitudinal fasciculus (SLF) affects top-down control of selective attention via MEG data. In short, they demonstrated an interaction between hemispheric asymmetry and differences in ability to control alpha and gamma oscillations, suggesting that the SLF mediates top-down signals which aid in the control of attention modulations in the visual cortex.

More recently, Schmitz and Duncan (2018) argue that the release of cholinergic neurons within the basal forebrain mimics the effects of directed attention via the firing rate, rate variability, and correlated variability of population neural responses. Within their paper, they point to research that implicates the release of acetylcholine via stimulation of cholinergic neurons in the basal forebrain as a key component of directed attention. Their work points to an alternative structural pathway in the brain that may be important to visual search behaviour, and it is primarily this line of research that will be informing this aspect of our investigation – namely, Schmitz and Duncan’s (2018) question of whether mechanisms exist for routing cholinergic input to aid attentional performance. Additionally, Ricciardi (2013) assessed changes in neural activity after during enhanced cholinergic function during a selective attention task, finding that heightening cholinergic function could improve task performance as delineated by the resulting reduced functional connectivity strength between ventral visual processing areas and task-related occipital, parietal and prefrontal regions, and reduced BOLD signal temporal variability during cholinergic augmentation. They concluded that cholinergic augmentation does enhance neural activity as compared to a control condition, reflected by improvement of selective attention performance, functional connectivity analyses and BOLD variability. Further, Herrero et al. (2008) investigated the cellular mechanisms of attentional influence over neuronal processing in cortical areas by combining iontophoretic pharmacological analysis of cholinergic receptors and single cell recordings in V1 during a top-down attention task. They found that acetylcholine slightly increased the overall firing rates and increased attentional modulation in V1 through muscarinic receptor mechanisms, concluding that the said mechanisms play a central role in mediation of the effects of attention in the primary visual cortex.

Finally, Sarter’s (2005) review demonstrated that the cortical cholinergic input system contributes to the optimisation of processing of signals in attentionally demanding contexts, suggesting that acetylcholine amplifies thalamic input processing. They also cite evidence supporting the notion that cortical cholinergic inputs play a critical role in mediating attentional functions.

* **DTI tract/s of interest.**

We will be examining four tracts of interest, both contralaterally and ipsilaterally. Firstly, we will be observing a cortico-striatal tract from the caudate nucleus to the dorsolateral prefrontal cortex (DLPFC)(BA8 -10 & 46), reflective of a dorsolateral prefrontal circuit (Alexander, 1986).

**DLPFC-Cn:** Multitasking training is suggested to be associated with resting functional connectivity within the DLPFC (Takeuchi, 2014). Hsu et al. (2015) conducted a study of the involvement of the DLPFC during multitasking with tDCS, which aimed to modulate neural activity over the DLPFC with anodal stimulation. The results found aided in demonstrating a causal role of the DLPFC in multitasking performance, showing a 20% reduction in multitasking costs in the second session compared to first, and linking the left DLPFC to higher-order cognitive controls that are assumed to be required during multitasking. Ljubisavljevic et al. (2019) also conducted a study examining the effects of unilateral and bilateral tDCS stimulation targeting the DLPFC on improving dual-task performance, specifically instructing participants to refrain from prioritising either task over the other. They found that bilateral, anodal stimulation on the left DLPFC was successful in significantly improving cognitive dual-task costs, which they suggested is potentially due to augmentation of the networks involved in multitasking rather than causing reallocation of resources between tasks. The DLPFC has further been found to be a mediator of multitasking performance across several paradigms (Verghese, 2016), and has been implicated in several studies examining the effects of DLPFC activity on directing attentional resources (Braver, 2003; Koechlin, 1999; Wagner, 2005; Watanabe, 2014).

The caudate nucleus plays a critical role in planning and executing behaviour required to complete complex goals (Grahn, 2008), and is implicated in tasks which require goal-directed action such as anticipation of a reward. For instance, Tricomi (2004) found that the caudate nucleus was only reliably activated when the participants tested believed that their actions would determine a rewarded outcome during dual-task performance. Brovelli et al. (2011) conducted a study which aimed to identify global monitoring signals that support goal-directed and habitual processes during learning of instrumental behaviours with fMRI analyses and reaction times on a visuomotor learning task. Ultimately, they found that the caudate nucleus contains two clusters involved in performance monitoring and integration of such with cognitive control, wherein the anterior caudate integrates information about performance and cognitive control demands during learning. They suggest that the caudate and putamen interact to produce acquisition and early consolidation of learning, and are therefore tightly linked to goal-directed and habitual behaviours. This is further evidenced by Gerrarty’s (2018) study of network dynamics in reinforcement learning, who found that the striatum’s ability to alter connectivity with the sensory and value-processing regions provided a mechanism for information integration during decision-making. Specifically, Gerrarty (2018) found that rate of learning negatively correlated with network flexibility (brain’s tendency to communicate with different networks) in the caudate, and that participants who relied more on the learned value overall showed more dynamic connectivity within this region. Further, Monchi’s (2006) study found that the caudate nucleus is activated by the cognitive decision to shift behavioural strategy. Finally, the striatum appears necessary for normal multitasking performance, as evidenced by the depletion of performance on a divided attention task in basal ganglia-lesioned patients (Thoma, 2008).

Two studies which demonstrated anatomical organisation between the frontal cortex and the striatum via DTI investigation include Penttinen (2016) and Leh et al. (2007). Penttinen’s (2016) study tracked connections between the striatum, the frontal areas and the motor areas using DTI, finding further evidence of cortico-striatal circuits including robust connections between the DLPFC and caudate nucleus. Leh et al.’s (2007) study sought to reconstruct the connections between the striatum and frontal cortex, ultimately identifying DLPFC to caudate nucleus connections. These findings are consistent with prior fMRI studies proposing the existence of a “dorsolateral prefrontal loop” as suggested by Alexander (1986), and Jarbo’s (2015) finding that structural connections to the caudate nucleus convergence zone overlap with clusters of positive functional connectivity in the DLPFC. Further, Gerrarty’s (2018) investigation of network dynamics underlying reinforcement learning demonstrated that learning may involve dynamic coordination of distributed brain regions that could represent the formation of efficient circuits for integrating decision variables (also see Postuma, 2006). Filmer et al. (2013) also demonstrated the ability of cathodal tDCS stimulation of the pLPFC in selectively improving dual-task performance relative to sham and anodal stimulation, wherein performance was significantly reduced in participants undertaking the dual-task paradigm versus single-task immediately after cathodal stimulation. In addition, it has been suggested that multitasking performance costs are related to prefrontal activity via a fronto-striatal system, which functions to differentiate the fronto-striatal response between trained tasks to expand the capacity for concurrent task processing (Garner & Dux, 2015; Thoma, 2008). As indicated by Dux (2009) and Garner and Dux (2015), multitasking costs could be overcome (or at least reduced) either via central stage shortening associated with the DLPFC-Cn tract moderating the rate of information exchange, or via task automatization leading to elimination of capacity limitations. Strobach (2016) suggested that practice-related optimisations of multitasking are substantially supported by evidence of the task processing optimisation principle, which associates dual-task improvement with shortening of the response selection stage (and no perceptual stage shortening), and the automatization theory that automatic tasks should not require cognitive control and therefore should be processed in parallel with concurrent tasks, reducing costs (also related to Yin, 2006; Brovelli, 2011; Maquestiaux, 2010).

**DLPFC-Putamen:** We will also be observing a second cortico-striatal tract between the putamen and the DLPFC. The purpose of analysing the putamen in this context lies within its relation to habit formation. While goal-directed actions facilitate caudate activation implicated in the rate of learning, well-learned sequences appear to activate the putamen, reflected by its correlation to the learning curve itself, as indicated by Williams and Eskandar’s (2006) study of the firing rates of monkey single-unit neural activity (Yin, 2006). This account of habit-formation processes relates to the task processing optimisation principle mechanism of reducing dual-task costs discussed previously, wherein training dual-task behaviours could shift activity from the caudate nucleus to the putamen as the behaviours become more automatic (Strobach, 2016). Furthering this, the putamen is suggested to track the likelihood of correct response to a stimulus, and consequently form stimulus-response habits that remain active until the demand of cognitive control increases once again (Brovelli, 2011). It is suggested that the interaction between cortico-striatal networks is critical for transforming actions into habits, and is essential for optimal performance in divided attention tasks (Thoma, 2008). This fits with research into task optimisation and automaticity that is suggested in studies wherein participants successfully “bypass” the central bottleneck of processing (Maquestiaux, 2010).

**Basal Forebrain-Occipital Cortex:** Based primarily on work by Schmitz and Duncan (2018), we intend to examine a basal forebrain to superior occipital cortex pathway to incorporate a visual search control tract. It has been suggested that cortical cholinergic modulation from the basal forebrain mimics the effects of directed attention on population neural activity (Schmitz & Duncan, 2018). Further, acetylcholine has a role in regulating visual attention and refining visual cortex pathways, particularly within the primary visual cortex (Herrero, 2008; Ricciardi, 2013), wherein any basal forebrain region with visual projections can modulate visual processing (Huppe-Gourgues, 2018). The basal forebrain has been shown to be modulated by caudate-putamen input (Gielow, 2017). Finally, Botly (2012) demonstrated that Ach and nucleus basalis magnocellularis lesioned rats took significantly longer to locate a target stimulus within a conjunctive search, suggesting that the cholinergic contributions to visuospatial attention are important for efficient visual search.

**Medial Superior Longitudinal Fasciculus (mSLF):** We will be testing the mSLF in association with the visual search and multitasking paradigm. It has been shown that the integrity of white matter tracts connecting the dorsal frontoparietal network (the SLF) contribute to visual search performance (Bennett, 2012). Further, frontoparietal regions are activated during covert shifts of attention and overt eye movements, suggesting that attentional and oculomotor processes are linked at the neural level (Corbetta, 1998).

* **A brief summary of the data, where it has come from (Garner & Dux, 2015), etc.**

Garner and Dux (2015) utilised interindividual variability in the blood oxygen level-dependent signal to reveal underlying aspects of brain function which predict multitasking improvements, and applied multivoxel pattern analysis to assess the task representations in brain regions. 100 participants underwent six experimental sessions (familiarisation session, two MRI sessions (pre- and post-training scans) and three behavioural training sessions). All participants completed the multitasking paradigm (single-task or multi-task condition) in the pre- and post-training scan sessions. During the three-day training period, participants either trained on the multitasking paradigm (training group; shape single-task, sound single-task and multitask trials) or a visual search paradigm (control group; varied among set sizes of 7, 11 or 15). They were pseudorandomly allocated to the training or control group, which were matched for age (training M = 24.3 y; control M = 24.6 y), years of education (training M = 16.3 y; control M = 16.8 y), sex (training = 15 males; control = 11 males), and handedness (training = 3 left handers; control = 4 left handers). Participants were asked to decrease their reaction times whilst maintaining high accuracy, completing a total of 3024 training trials overall. T1-weighted anatomic images and functional T2\*-weighted images were collected with whole-brain coverage, and diffusion tensor imaging data (DTI).

* **Hypotheses**

DVs: (1) multitasking paradigm (varies upon single vs multitask) - performance improvement as described by a power/exponential practice function, plus rate of change as described by the first derivative; (2) visual search paradigm (varies upon set sizes) performance improvement as described by a power/exponential practice function, plus rate of change as described by the first derivative

We will be investigating how the fractional anisotropy values from the pre-training sessions of each participant are associated with how much participants improved on the multitasking and visual search paradigms, and how quickly the participants improved on the multitasking and visual search paradigms. We expect that the FA will be able to predict both the participants’ improvement on the paradigms and their rate of change.

* We expect that multitasking improvement will be associated more strongly with the FA values reflected within the cortico-striatal tracts (Cn-DLPFC & Put-DLPFC), whereas visual search improvement will be associated more strongly with the basal-forebrain to visual cortex tract (BF-V1) FA values
* **Very general data analysis plan**

The basis of the analysis is a multiple linear regression of the FA values of the Cn-DLPFC tract onto the two DVs (performance improvement and rate of change) for each condition (multitasking paradigm and visual search paradigm); the Put-DLPFC tract onto the DVs, the BF-V1 tract onto the DVs and the mSLF tract onto the DVs. Prior to analysis, we will fit an exponential practice function and a power practice function to the data so as to generate our performance improvement measures for each condition and for each participant, and take the first derivative of the function for each condition and each participant to generate our rate of change measure.

1. Initial data exploration and cleaning:
   1. Analysis of variables and descriptive statistics – initial visualisations of data such as boxplot and qqplot to identify outliers and determine normality, check for nonlinearity and heteroscedasticity, and multicollinearity, etc.
   2. Decision to exclude any outliers, based on the magnitude of the effect the outliers have on the included data points
   3. Decision to transform any of the data given the spread of the distributions, etc.
   4. Reliability analysis – perform correlation analysis for each tract for those who have session 1 and session 2 data
   5. Raincloud plot of final distribution
2. Run EFA of behavioural practice data for multitask and visual search paradigms, taken from the practice sessions of the Garner and Dux (2015) data to reduce 16 proposed tracts (4 pathways per tract, ipsi- and contralateral possibilities)
   1. Look at correlations between data
   2. Kaiser's criterion: eigenvalues
   3. Principal Axis Factoring: acknowledges shared variance and unique variance, allows correlation
   4. Oblique rotation: allows correlation
   5. Assess the factor loadings/solutions and decide which is the most beneficial to retain
3. Run power and exponential practice functions on each participant and each factor
   1. Simple model comparison
   2. Run both on each participant for each condition in the behavioural paradigm (performance improvement variable)
   3. Take the first derivative of the function for each participant and corresponding pathway (rate of change variable)
   4. DVs: MT performance improvement and rate of change; VS performance improvement and rate of change
4. Multiple Regression Analysis: estimate the model, fit the regression line to the data to model the relationship between participant scores on the underlying factors as defined by the EFA, and performance improvement/rate of change
5. Evaluate the validity and usefulness of the model, check degree of fit of our model to our data using , *F-*test and *t*-test for significance
   1. Also utilise Bayes variants to the significance tests, though the resulting conclusions will be primarily based off of the NHST tests

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