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EXPLORING THE NEURAL SUBSTRATES OF ATTENTIONAL CONTROL AND HUMAN INTELLIGENCE: DIFFUSION TENSOR IMAGING OF PREFRONTAL WHITE MATTER TRACTOGRAPHY IN HEALTHY COGNITION

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Abstract—We combined diffusion tension imaging (DTI) of prefrontal white matter integrity and neuropsychological measures to examine the functional neuroanatomy of human intelligence. Healthy participants completed the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) along with neuropsychological tests of attention and executive control, as measured by Trail Making Test (TMT) and Wisconsin Card Sorting Test (WCST). Stochastic tractography, considered the most effective DTI method, quantified white matter integrity of the medial orbital frontal cortex (mOFC) and rostral anterior cingulate cortex (rACC) circuitry. Based on prior studies, we hypothesized that posterior mOFC–rACC connections may play a key structural role linking attentional control processes and intelligence. Behavioral results provided strong support for this hypothesis, specifically linking attentional control processes, measured by Trails B and WCST perseverative errors, to intelligent quotient (IQ). Hierarchical regression results indicated left posterior mOFC–rACC fractional anisotropy (FA) and Trails B performance time, but not WCST perseverative errors, each contributed significantly to IQ, accounting for approximately 33.95–51.60% of the variance in IQ scores. These findings suggested that left posterior mOFC–rACC white matter connections may play a key role in supporting the relationship of executive functions of attentional control and general intelligence in healthy cognition.

Key words: MRI, diffusion tensor imaging, fractional anisotropy, general intelligence, attention-control capacity.

INTRODUCTION

Attention control is a key function of working memory that is essential for higher-order cognition and intellect. A central component of working memory, attentional control functions as part of an executive system for organizing and planning goal-directed behavior (Smith and Jonides, 2000). The remarkably strong relation of working memory and intelligence is thought to be mediated in large part by processes related to executive attentional control that allow for stimulus representations to be actively maintained on-line in the context of distraction and interference (e.g., Kane and Engle, 2000; Baddeley, 2003). Indeed, so vital is attentional-control capacity for learning that Kane et al. (2005) proposed it as the ''secret ingredient'' that is recruited by working memory tasks and largely explains the relationship of working memory and intelligence (see also Cole et al., 2012). From this perspective, individuals with stronger attention-control capacity have both greater working memory and higher levels of intelligence.

As empirical support for this view, studies have revealed strong correlation with various attentional control measures and working memory tasks (Engle and Kane, 2004; Unsworth and Spillers, 2010; McVay and Kane, 2012). Similarly, findings from structural and functional brain imaging studies have suggested that intelligence as well as attentional control processes of working memory each depend heavily on neural circuitry of the prefrontal lobe (Duncan et al., 2000; Thompson et al., 2001). For intelligence, the prefrontal cortex (PFC) is seen as a key hub in a widely-distributed network of brain areas spanning temporal and parietal sites that supports high-order cognition (Penke et al., 2012). In a similar vein, findings from functional imaging studies have provided evidence that attention-control capacity may be decomposed into regulative and evaluative components, each supported by distinct regions within the PFC. That is, a regulative component, recruited to coordinate the

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Abbreviations: DTI, diffusion tension imaging; EPI, echo planar imaging; FA, fractional anisotropy; IQ, intelligent quotient; mOFC, medial orbital frontal cortex; MRI, magnetic resonance imaging; OFC, orbital frontal cortex; PFC, prefrontal cortex; rACC, rostral anterior cingulate cortex; TMT, Trail Making Test; WAIS-III, Wechsler Adult Intelligence Scale-Third Edition; WCST, Wisconsin Card Sorting Test.

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demands of activation, inhibition, and switching, relies heavily on orbital frontal and lateral prefrontal subdivisions, whereas medial frontal sectors are recruited for monitoring and signaling adjustments in control (Ridderinkhof et al., 2004). Taken together, these findings lead to the hypothesis that attention-control capacity may serve as an intermediate phenotype between the brain, specifically the PFC, and intelligence.

The current study aimed to examine what structural properties of local PFC circuitry might be important for attention-control capacity. The principal research question asks to what extent can quantifiable neuroanatomical differences in local PFC circuitry supporting attention-control capacity account for normal variation in intelligence. To address this question, we focus on the structural integrity of white matter connections linking medial orbital frontal cortex (mOFC) and rostral anterior cingulate cortex (rACC). These white matter connections provide local neural circuitry of a wider network of functionally diverse brain regions vital to learning and attention (e.g., Posner and Petersen, 1990; Ridderinkhof et al., 2004; Jung and Haier, 2007). Indeed, mOFC and rACC are important targets of dopaminergic neurons originating in the midbrain ventral tegmental region, transmitting to the nucleus accumbens, with direct connections to not only mOFC and rACC but also to dorsolateral PFC, hippocampus, amygdala, insula, and hypothalamus (Kringelbach, 2005). Coordinated activity within these sites is widely thought to enhance the development of conscious and declarative knowledge (Clark and Squire, 1998).

To examine mOFC–rACC connections, we employ diffusion tensor imaging (DTI). DTI has been used to examine white matter properties, and is sensitive to white matter fiber coherence, density and myelination. This imaging method estimates the fiber tracts that make up white matter by following the direction of maximal water diffusion of white matter voxels (Mori et al., 2005). Among the measures that reflect the white matter properties, fractional anisotropy (FA) is regarded as one of the most reliable measures. Previous studies have used FA to quantify the integrity of specific tracts (e.g., Nestor et al., 2004) and the strength of the connections of two particular regions of interest (Kreher et al., 2008). Nevertheless, few studies have directly examined the FA of local and specific mOFC–rACC circuitry in relationship to both intelligence and attentional control. As such, the current study combines DTI and neuropsychological measures to provide a novel test of the attentional control hypothesis of intelligence.

We previously examined the attentional control hypothesis in a sample of healthy participants who had both neuropsychological testing and 1.5-T magnetic resonance imaging (MRI) gray matter volume studies of the orbital frontal cortex (OFC) parcellated into three regions: gyrus rectus, middle orbital gyrus, lateral orbital gyrus (Nestor et al., 2015). The results showed that increased gray matter OFC volume was strongly associated with both better Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) (Wechsler, 1997) intelligent quotient (IQ) scores and greater attentional control, as measured by Trails B of the Trail Making Test (TMT) and perseverative errors on the Wisconsin Card Sorting Test (Nestor et al., 2015). As such, these data may be interpreted as providing neuropsychological and neuroanatomical support for the attentional control hypothesis of intelligence.

We now aim to extend our previous findings in a new sample of healthy participants who completed neuropsychological measures of intelligence and executive attention, and who had available 3-T MRI-DTI studies of mOFC and rACC white matter, as indexed by FA. We focus specifically on left posterior mOFC–rACC pathways based on our previous findings linking white matter integrity of these structural connections to higher IQ scores (Ohtani et al., 2014). Accordingly, we hypothesize that attentional control may be a key contributor underlying the significant relationship of left posterior mOFC–rACC white matter integrity and IQ.

EXPERIMENTAL PROCEDURES

Twenty-six male subjects (age range: 19–55; mean age: 38.62 ± 10.61) were recruited through advertisements in newspapers (the detail of the demographic information is described in Table 1). All participants were right-handed, native speakers of English, without histories of ECT, neurological illness, and without alcohol or drug abuse in the past 5 years. They met Structured Clinical Interview for DSM-IV Axis I Disorders-Non-patient Edition (SCID-I/NP) (First et al., 2002) and Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II) (First et al., 1997) criteria of no past or current Axis I and/or Axis II disorder. This

Table 1. Demographic information and neuropsychological test scores

Demographic information	Mean ± standard deviation
Age (years old)	38.62 ± 10.61
Education (years)	15.04 ± 1.89
Social economic status	1.96 ± 0.68
Parental socio economic status	2.29 ± 1.20
Neuropsychological tests	**Mean ± standard deviation**
Trail making test	
Trails A	
Time spent (second)	27.01 ± 5.49
Number of errors	0.12 ± 0.33
Trails B	
Time spent (second)	63.75 ± 27.63
Number of errors	0.20 ± 0.50
Wisconsin card sorting test	
Number of category achieved	5.52 ± 1.34
Number of correct responses	70.48 ± 12.63
Number of perseverative errors	11.48 ± 9.84
Number of non-perseverative errors	10.39 ± 10.39
Wechsler Adult Intelligence Scale-3rd Edition	
Full-scale IQ	112.56 ± 15.16

Abbreviation: IQ, intelligent quotient.