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The Relationship Between General Intelligence and Cortical Structure 3 in Healthy Individuals 4

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Abstract—Considerable work in recent years has examined the relationship between cortical thickness (CT) and 19 general intelligence (IQ) in healthy individuals. It is not known whether specific IQ variables (i.e., perceptual reasoning [PIQ], verbal comprehension IQ [VIQ], and full-scale IQ [FSIQ]) are associated with multiple cortical measures (i.e., CT, cortical volume (CV), cortical surface area (CSA) and cortical gyrification (CG)) within the same individuals. Here we examined the association between these neuroimaging metrics and IQ in 56 healthy adults. At a cluster-forming threshold (CFT) of p < 0.05, we observed significant positive relationships between CT and all three IQ variables in regions within the posterior frontal and superior parietal lobes. Regions within the temporal and posterior frontal lobes exhibited positive relationships between CV and two IQ variables (PIQ and FSIQ) and regions within the inferior parietal lobe exhibited positive relationships between CV and PIQ. Additionally, CV was positively associated with VIQ in the left insula and with FSIQ within the inferior frontal gyrus. At a more stringent CFT (p < 0.01), the CT–PIQ, CT–VIQ, CT–FSIQ, and CV–PIQ relationships remained significant within the posterior frontal lobe, as did the CV-PIQ relationship within the temporal and inferior parietal lobes. We did not observe statistically significant relationships between IQ and either CSA or CG. Our findings suggest that the neural basis of IQ extends beyond previously observed relationships with fronto-parietal regions. We also conclude that CT and CV may be more useful metrics than CSA or CG in the study of intellectual abilities. © 2018 IBRO. Published by Elsevier Ltd. All rights reserved.

Key words: cortical measures, brain structure-function, intelligence, verbal comprehension, perceptual reasoning, full-scale IQ.

INTRODUCTION

Surface-based structural brain analysis techniques, 12 involving an estimation of morphometric measures such 13 as cortical thickness (CT), cortical volume (CV), cortical 14 surface area (CSA), and cortical gyrification (CG) have 15 expanded our understanding of the impact of various 16 neurodegenerative diseases on brain structure. These 17 measures provide specific indices of several unique 18 aspects of brain structure. These measures also provide 19 insight into the dynamics of brain structure during 20 neurodevelopment (Burgaleta et al., 2014; White et al., 21 2010), the effects of aging on brain structure (Bajaj 22 et al., 2017; Burgaleta et al., 2014; Hogstrom et al., 23 2013), and the relationships between brain structure and 24

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function (Burgaleta et al., 2014; Gregory et al., 2016). 25 Mathematically, many of these structural measures are 26 interrelated. For example, CV is the product of two, genet-27 ically distinct properties: CT and CSA (Winkler et al., 28 2010). CG positively correlates with both total brain vol-29 ume and CSA but negatively with CT (Gautam et al., 30 2015; Hogstrom et al., 2013). Given the complex relation-31 ships between these heterogeneous morphometric prop-32 erties, it is crucial to study the simultaneous relevance 33 of each of these measures to cognition (e.g., their individ-34 ual and joint relationships with measures of human intel-35 lectual ability [IQ)]). For instance, if two structural 36 measures, such as CT and CSA, both have a positive 37 association with cognitive abilities, then CV should also 38 exhibit a positive, and possibly stronger, relationship than 39 either CT or CSA alone. 40

Fundamentally, despite the fact that some cortical 41 measures (CT, CV, CSA and CG) may covary, these 42 measures reflect different facets of brain structure and 43 could each contribute uniquely to cognitive function. 44 Specifically, CT and CSA are considered highly 45 heritable and genetically independent (Eyler et al., 2011; 46

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Abbreviations: CFT, cluster-forming threshold; CG, cortical gyrification; CSA, cortical surface area; CT, cortical thickness; CV, cortical volume; FSIQ, full-scale IQ; IQ, intelligence; PIQ, perceptual reasoning; VIQ, verbal comprehension IQ.

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Kremen et al., 2010; Panizzon et al., 2009). Due to their 47 unique regional variation with the timing of prenatal per-48 turbations, these measures are often understood as sep-49 arate morphometric variables during neurodevelopment, 50 aging, and disease (Eyler et al., 2011; Hogstrom et al., 51 2013; Panizzon et al., 2009). Moreover, CV is considered 52 distinct from, though mathematically related to, CT and 53 CSA (i.e., due to the non-uniform, integrated influence 54 of CT and CSA) (Gerrits et al., 2016). Further, CG repre-55 sents the convolution of brain structure and is influenced 56 by both neuronal density and intra-cranial volume (Toro 57 and Burnod, 2005; Welker, 1990). This folding increases 58 the potential for a greater number of neurons within the 59 60 same space. When coupled with the fact that CSA may facilitate better neuronal signal processing, increased 61 CG and CSA may provide more efficient structural organi-62 zation to facilitate brain connectivity and functional devel-63 opment (Luders et al., 2008; Murre and Sturdy, 1995; 64 Ruppin et al., 1993). This supports the idea that the orga-65 66 nization and gyral structure of the cortex contributes to its function. 67

With respect to structural measurements and 68 cognition, the relationship between general intelligence 69 (IQ) and structural measures, particularly CT and CSA, 70 71 is likely age-dependent. Notably, Schnack and 72 colleagues reported that among children (~10 years of 73 age), higher standardized IQ scores were associated 74 with thinner cortex within the left hemisphere (Schnack et al., 2015). This pattern differed in young adults, where 75 thicker left hemisphere cortex was associated with higher 76 IQ scores, suggesting that maturation-related structural 77 changes may play an important role in the expression of 78 IQ. Consistent with these findings, Shaw and colleagues 79 reported a shift from a negative correlation between CT 80 and IQ in early childhood (age range 3.8-8.4 years) to a 81 positive correlation in late childhood (age range 8.6-82 83 11.7 years) and into early adulthood (age range 11.8-84 29 years) (Shaw et al., 2006). In other work with healthy children and adolescents, changes in CT, but not CSA, 85 were associated with changes in performance IQ, verbal 86 IQ, and full-scale IQ (Burgaleta et al., 2014). Furthermore, 87 higher CG in middle-aged participants (44-48 years) was 88 associated with better mental flexibility, larger brain vol-89 90 ume, but also thinner cortex (Gautam et al., 2015). There-91 fore, relationships between IQ and the structural characteristics of the cortex appear to exhibit dynamic, 92 age- and developmental stage-dependent changes. 93

A recent meta-analysis suggested that much of the 94 previous literature may over-estimate/over-simplify the 95 association between brain volume and IQ (Pietschnig 96 97 et al., 2015). The association instead appears to be more complex than suggested by simple volumetric measures. 98 Surface-based cortical measures, rather than purely volu-99 metric measures, may therefore provide more useful 100 information about the complex and widespread relation-101 ships between cortical structure and general IQ. 102

Prior work has generally focused on individual structural measures in isolation and their association with IQ. Given that neural structure–function relationships are likely more complex than can be accounted for by simple volumetric measures, it is crucial to examine the parallel associations between 108 multiple brain structure measures (CT, CV, CSA, and 109 CG) and multiple aspects of general IQ (perceptual 110 reasoning (PIQ), verbal comprehension and full-scale 111 IQ) in the same sample of healthy young adults. The 112 primary aim of the current study is therefore to 113 investigate the vertex-wise associations between these 114 structural metrics and these different IQ variables. 115 Based on prior research, we hypothesized that both CT 116 and CV would be positively associated with all domains 117 of IQ. However, due to inconsistent and limited 118 evidence regarding the relationship between CSA or CG 119 and cognitive abilities, we had no specific hypothesis 120 regarding the relationships between these specific 121 metrics and IQ. Thus, these latter analyses were 122 primarily for exploratory purposes. 123

EXPERIMENTAL PROCEDURES

Participants

Fifty-six healthy participants between 18 and 45 years of 126 age (mean age = 30.8 ± 8.1 years, 27 females; 29 127 males) participated in this study. Participants were 128 recruited from the New England area and screened via 129 a comprehensive telephone interview. Individuals with 130 any history of psychiatric, neurological, or significant 131 medical problems, current use of psychotropic 132 medications, or current use of illicit substances were 133 excluded. Participants were all primary native English 134 speakers, with 14.95 years of formal education (SD = 2. 135 18 years). 69.6% of participants were Caucasian, 14.2% 136 were African American, 8.9% were Asian, 3.6% reported 137 polyethnic backgrounds and 3.6% reported other ethnic 138 backgrounds. All participants provided written informed 139 consent prior to enrollment. The study protocol was 140 approved by the Institutional Review Boards of McLean 141 Hospital and Partners Healthcare, and the U.S. Army 142 Human Research Protections Office. Other behavioral 143 data and structural estimates from this sample have 144 been reported elsewhere (Killgore et al., 2013), but the 145 vertex-wise cortical measures and their associations with 146 IQ reported in this study are novel and have not been pre-147 viously reported. 148

Data acquisition

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Neuroanatomical data. We recorded high-resolution 150 T1-weighted magnetic resonance imaging data using a 151 3-Tesla Siemens TIM Trio whole-brain MR scanner 152 located at the McLean Hospital Imaging Center. Before 153 the scan, each participant was instructed to rest, relax 154 and try his/her best to minimize movement during the 155 entire scan. Head movement was further minimized with 156 foam padding placed comfortably about the head. T1-157 weighted data for each participant were acquired using 158 a 3D magnetization-prepared rapid acquisition gradient 159 echo (MPRAGE) sequence, which consisted of 128 160 sagittal slices (slice thickness = 1.33 mm, voxel resolu 161 tion = $1.33 \times 1 \times 1$ mm, field of view (FOV) = 256 mm 162

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