Neuroanatomical correlates of intelligence

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ABSTRACT

With the advancement of image acquisition and analysis methods in recent decades, unique opportunities have emerged to study the neuroanatomical correlates of intelligence. Traditional approaches examining global measures have been complemented by insights from more regional analyses based on pre-defined areas. Newer state-of-the-art approaches have further enhanced our ability to localize the presence of correlations between cerebral characteristics and intelligence with high anatomic precision. These *in vivo* assessments have confirmed mainly positive correlations, suggesting that optimally increased brain regions are associated with better cognitive performance. Findings further suggest that the models proposed to explain the anatomical substrates of intelligence should address contributions from not only (pre)frontal regions, but also widely distributed networks throughout the whole brain.

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1. Introduction

The substrate of human intelligence has been a topic of considerable interest to scientists, philosophers, and physicians from the time of the ancient Greeks. The advent of modern brain imaging technologies and the development of advanced analysis methods have since provided unique opportunities to examine the biological essence of human intelligence. The goal of this article is to summarize macro-structural associations with intelligence based on magnetic resonance imaging (MRI) data from healthy individuals. However, rather than providing an exhaustive overview, we aimed to demonstrate a variety of research findings using traditional and modern approaches that allow us to analyze correlations with different degrees of regional specificity. This review encompasses studies investigating relationships between global (e.g., brain volume), regional (e.g., lobar volume), and highly localized (e.g., voxel-level) brain measurements and intelligence. Measures cover diverse brain structures (e.g., whole brain, cerebral cortex, corpus callosum)

and cerebral characteristics (e.g., volume, concentration, thickness). A related goal of this article is to highlight that many questions regarding the biological substrates of intelligence remain unresolved — not only due to partly overlapping results across studies and the sparseness of research findings, but also due to limitations in the spatial resolution of the images and other acquisition parameters. Thus, conclusions with respect to the underlying neural architecture and its possible impact on higher cognitive function remain speculative.

2. Volume of the brain and its subregions

As early as the 5th century B.C.E., the brain was assumed to be the location where human thoughts are elaborated (Crivellato & Ribatti, 2007), but controversy has persisted for many centuries concerning the actual associations between cerebral structure and cognitive function. Some early attempts to establish relationships between brain anatomy and intelligence were based on measuring external head parameters (i.e., perimeter, height, length, width). Results from these studies reported relatively weak although sometimes significant relationships (i.e., significant positive correlations between intelligence and head width) (Gignac, Vernon, & Wickett, 2003). Other studies have measured brain weight or volume using *post mortem* data and also revealed

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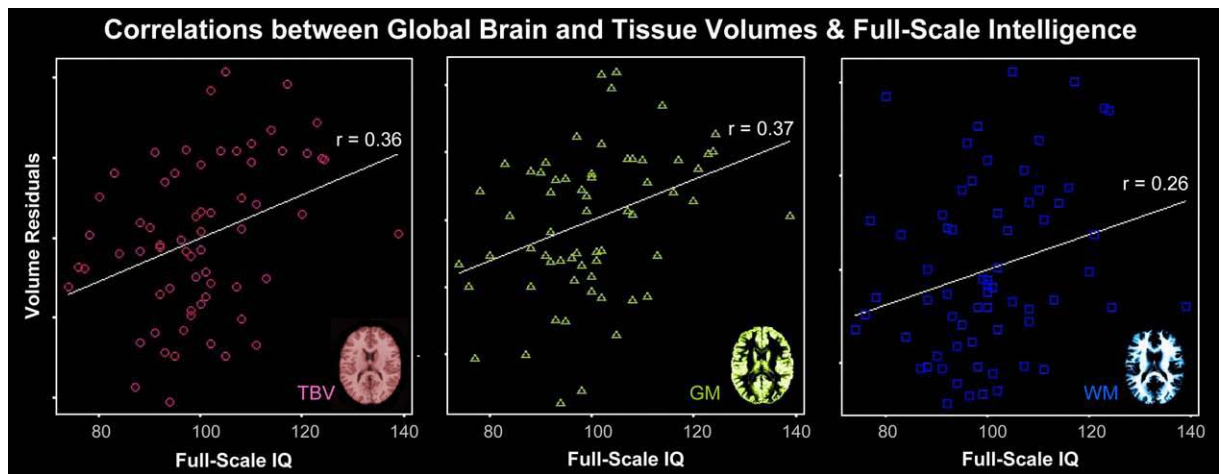*E-mail address:* toga@loni.ucla.edu (A.W. Toga).

Fig. 1. Correlations between global volumes and full-scale intelligence in a sample of 65 healthy subjects, after removing the partial effects of sex and age (Narr et al., 2007). Illustrated are the intelligence–specific relationships with the residuals of total brain volume (TBV), gray matter volume (GM), and white matter volume (WM).

that greater intellectual abilities are associated with greater cerebral volumes[1], albeit observed correlations "depended on the realm of intelligence studied, as well as the sex and hemispheric functional lateralization of the subject" (Witelson, Beresh, & Kigar, 2006). The most recent approaches (summarized and discussed below) have taken advantage of the improved spatial resolution of MRI and calculated brain volume *in vivo* based on (semi)automatically classifying and quantifying voxels representing brain tissue.

2.1. Global and regional findings of volume-based intelligence correlates

For assessments of relationships between global brain volume and intelligence, results from existing studies have shown predominantly positive correlations ranging from 0 to 0.6, with the majority of MRI studies reporting correlations around 0.3 or 0.4 (McDaniel, 2005; Wickett, Vernon, & Lee, 2000; Witelson et al., 2006). A visual impression of how total brain volume (TBV) relates to intelligence is provided in Fig. 1 (first panel). In order to determine whether all brain regions are equally related to intelligence or whether there are certain structures that are selectively altered in more intelligent individuals, a number of studies have increased their regional specificity by measuring the area or volume of regions of interest (ROIs) following boundaries based on structural or functional anatomy. Again, mainly positive correlations have been reported, where the most significant and frequently detected associations are observed within the frontal, temporal, and parietal lobes, the hippocampus, and the cerebellum (Andreasen et al., 1993; Flashman, Andreasen, Flaum, & Swayze, 1997; MacLullich et al., 2002).

2.2. Possible functional implications

These studies clearly demonstrate a biological basis to intelligence, with larger brains predicting greater intelligence (Gray & Thompson, 2004; Toga & Thompson, 2005). However, complementary findings revealing distinct regional correlations with intelligence suggest that increased global brain volumes observed in more intelligent individuals may be accounted for by selectively enlarged volumes in brain regions especially relevant for higher cognitive function (Andreasen et al., 1993). Intelligence is assumed to reflect various task demands (Andreasen et al., 1993; Flashman et al., 1997), which have been attributed to different brain regions (e.g., verbal task demands to the left inferior frontal and posterior temporal lobe; visuo-spatial demands to the parietal lobe; information encoding and retrieval to the hippocampus; and executive task demands including problem solving, planning, reasoning, etc. to frontal cortices). Notwithstanding, researchers have emphasized the modest nature of regional relationships: "Significant correlations ranged from 0.26 to 0.56, indicating that between 12% and 31% of the variance can be accounted for by the size of the brain or its subregions" (Andreasen et al., 1993). They argue that this relatively small amount of variance suggests that while size may be related to human intelligence, other factors must also play a role. In the sections below we introduce and discuss some other cerebral features that may account for portions of variance when assessing relationships between brain measures and intelligence.

3. Cerebral tissue components

The brain contains different tissue types including gray matter and white matter. Quantifying the amount of gray matter gives an estimate of the density and number of neuronal bodies and dendritic expansions; quantifying white matter helps to approximate the number of axons and their degree of myelination. That is, while the amount of gray matter might reflect the capacity of information processing centers, the amount of white matter might mirror the

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[1] Obviously, intelligence is not driven by global enlargement per se but by some optimal size increase that represents the importance of size x intelligence relationships. For example, macrocephaly (without any identifiable developmental errors) occurs more frequently in autism where intellectual abilities are compromised. The discussed findings in this article are mainly based on healthy samples; thus we will abstain from using the phrase "optimally" increased (which is what we mean) to simplify matters.

efficiency of inter-neuronal communication. Individual intelligence might thus be related to global and/or regional tissue volumes or concentrations.

3.1. Global and regional findings of tissue-based intelligence correlates

In studies assessing associations with overall tissue volumes, the majority of data suggests that higher intelligence and/or cognitive performance scores are associated with increased gray matter volumes (Andreasen et al., 1993; Colom, Jung, & Haier, 2006; Frangou, Chitins, & Williams, 2004; Gignac et al., 2003; Gur et al., 1999; Narr et al., 2007; Posthuma et al., 2002; Reiss, Abrams, Singer, Ross, & Denckla, 1996; Wilke, Sohn, Byars, & Holland, 2003). Similarly, positive correlations between intelligence and white matter volumes have been reported (Gignac et al., 2003; Gur et al., 1999; Narr et al., 2007; Posthuma et al., 2002; Schoenemann, Budinger, Sarich, & Wang, 2000). Global gray and white matter correlations are suggested to be roughly equally distributed (Gignac et al., 2003) but findings also appear to indicate that associations are stronger for gray matter in general, as demonstrated in Fig. 1 (second and third panel).

To examine the correlations between intelligence and tissue volumes for cerebral subregions, prior studies have divided the brain into smaller-sized and possibly more functionally meaningful compartments. One study was based on a somewhat unusual approach that projected planes through the brain revealing different sections in each hemisphere (Reiss et al., 1996). This study detected significant positive correlations between intelligence and prefrontal gray matter volume; although arguably such an anatomical partitioning approach does not "conform well to the extensive individual differences among subjects in brain size and morphology" (Haier, Jung, Yeo, Head, & Alkire, 2004). Another study (Thompson et al., 2001) was based on manually outlining ROIs (i.e., following structure-specific boundaries and dividing the brain surface into its different lobes). In agreement with Reiss et al. (1996), this approach revealed a highly significant positive association between intellectual function and gray matter volume in the frontal cortex. Still, this method only provides gray matter correlations at the lobar level, suggesting that more spatially detailed measurements may offer greater anatomical precision.

3.2. Local findings of tissue-based intelligence correlates

In contrast to whole-brain or ROI-based methods, a fully-automated voxel-by-voxel analysis technique allows the examination of intelligence–specific relationships across the entire brain. For example, voxel-based morphometry (VBM; Ashburner & Friston, 2000) provides the means to calculate a voxel-wise correlation between tissue amounts and individual intelligence measures. Several studies have utilized this VBM approach, where the most frequently replicated positive correlations[2] appear localized in the lateral and medial frontal

cortex (Colom et al., 2006; Frangou et al., 2004; Gong et al., 2005; Haier et al., 2004; Haier, Jung, Yeo, Head, & Alkire, 2005) and in the (anterior) cingulate (Frangou et al., 2004; Haier et al., 2004; Wilke et al., 2003). However, less significant positive correlations also seem to exist in other medial and lateral temporal, parietal, and occipital sections, as well as subcortically and in the cerebellum. Voxel-wise positive correlations between intelligence and white matter are less common, but have been found mainly in frontal and temporal regions (Haier et al., 2004, 2005).

3.3. Possible functional implications

The MRI signal reflects the cellular characteristics of the brain to some degree: For example, increased gray matter might indicate more or increased density of neurons or glial cells which could allow more efficient information processing. This may lead to improved cognitive function and account for the observed positive correlations between gray matter and intelligence. However, Haier and colleagues (1988, 1992) demonstrated that intelligence measures and glucose consumption are negatively correlated, supporting the assumption that more intelligent individuals use their neurons more efficiently, and fewer neurons may not necessarily be associated with reduced cognitive performance. Thus, positive correlations between gray matter and intelligence might more closely reflect other micro-topographic features, such as the formation and usage-dependent selective elimination of synapses which help to create and sculpt neural circuitry (Shaw et al., 2006).

Similarly, positive white matter correlations may exist if increased white matter volume reflects a higher degree of myelination and thus an enhanced facilitation of neural transmission. For example, fractional anisotropy, a diffusion data-derived measure of white matter integrity, is known to correlate with full-scale IQ (Chiang et al., 2008). Still, other variables (e.g., biochemical) may also account for the observed correlation given that white matter-specific pH levels have been shown to correlate positively with intelligence (Rae et al., 1996), possibly via modulating nerve action amplitude and conduction time.

To date, the underlying biological processes accounting for tissue-specific correlations in particular brain regions and/or across the whole brain remain uncertain. Also, it remains to be established whether white matter-specific correlations are a secondary consequence of gray matter-specific correlations (or vice versa) or whether there is no general rule but, instead, region-specific mechanisms apply. Notwithstanding, the detected significant positive correlations between gray/white matter and intelligence underscore that the structural integrity of particular brain regions is important to support higher cognitive functions.

4. Cortical thickness

The cerebral cortex holds two thirds of the brain's neurons and thus appears to be a promising candidate for determining the primary neuroanatomical correlates of intelligence. Measures of cortical thickness range between 1.5 and 4.5 mm, and although linked with other measures of gray matter (Narr et al., 2005), they might be more closely related

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[2] To our knowledge, only one VBM study analyzing the relationship between brain tissue and intelligence has reported significant *negative* correlations that were observed for gray matter density in the caudate nucleus (Frangou et al., 2004).

to intellectual abilities than volumetric or intensity-based gray matter concentration measures (Narr et al., 2007).

4.1. Global and regional findings of thickness-based intelligence correlates

There is a lack of findings concerning global or ROI-specific correlations between intelligence and cortical thickness. The cerebral cortex consists of layers of cells organized into columns that vary in depth as dependent on number and thickness of layers, the types of neurons and glial cells, and their size and density. Given that these underlying cytoarchitectural characteristics defining cortical thickness vary within different cortical regions (von Economo, 1929), possible structure–function relationships can be overlooked when correlating individual intelligence scores with averaged measures of cortical thickness (i.e., mean thickness across the entire cortex or within pre-defined regions).

4.2. Local findings of thickness-based intelligence correlates

By increasing the spatial resolution of the thickness measurement (i.e., analyzing the thickness of the cortex across thousands of surface locations) it becomes more likely that region-specific associations with individual intelligence can be detected. Although such detailed thickness measurements are now available (Fischl & Dale, 2000; Jones, Buchbinder, & Aharon, 2000; Kabani, Le, MacDonald, & Evans, 2001; Lerch & Evans, 2005; Memoli, Sapiro, & Thompson, 2004; Thompson et al., 2004), to date, there are only two published reports of correlations between intelligence and local variations in cortical thickness. Using a longitudinal design, the first study (Shaw et al., 2006) revealed a developmental shift from a predominantly negative correlation in early childhood to a positive correlation in late childhood and beyond. However, when analyzing all age groups combined, the authors detected modest and non-significant positive correlations throughout most of the frontal, parietal and occipital cortex, and similarly non-significant negative correlations in the anterior temporal cortex. The authors thus concluded that "the trajectory of change in the thickness of the cerebral cortex, rather than cortical thickness itself, is most closely related to level of intelligence." In contrast, prominent correlations between full-scale intelligence and cortical thickness were revealed in a number of regions in a recently published study in adults (Narr et al., 2007). The authors reported significant positive correlations between intelligence and cortical thickness across the lateral surface (i.e., prefrontal cortex and inferior temporal gyrus) and medial surface (i.e., fusiform gyrus and hippocampal cortex) (Fig. 2). The findings of positive correlations in prefrontal and temporal cortical regions in adult subjects are consistent with the cross-sectional thickness results of Shaw and colleagues (2006) within the late-adolescent and early-adulthood age groups and with gray matter-specific correlations in frontal regions, as analyzed with VBM (Frangou et al., 2004; Haier et al., 2004, 2005).

4.3. Possible functional implications

An analysis by Kruggel, Bruckner, Arendt, Wiggins, and von Cramon (2003) revealed a high correspondence between MRI-based intensity profiles and cytometry-based descriptions of the local layer structure and cytoarchitectonic fields, but the exact underlying architecture of increased cortical thickness and how it contributes towards higher intelligence still remains to be established (see discussion with respect to gray matter). Although the observed correlations in prefrontal
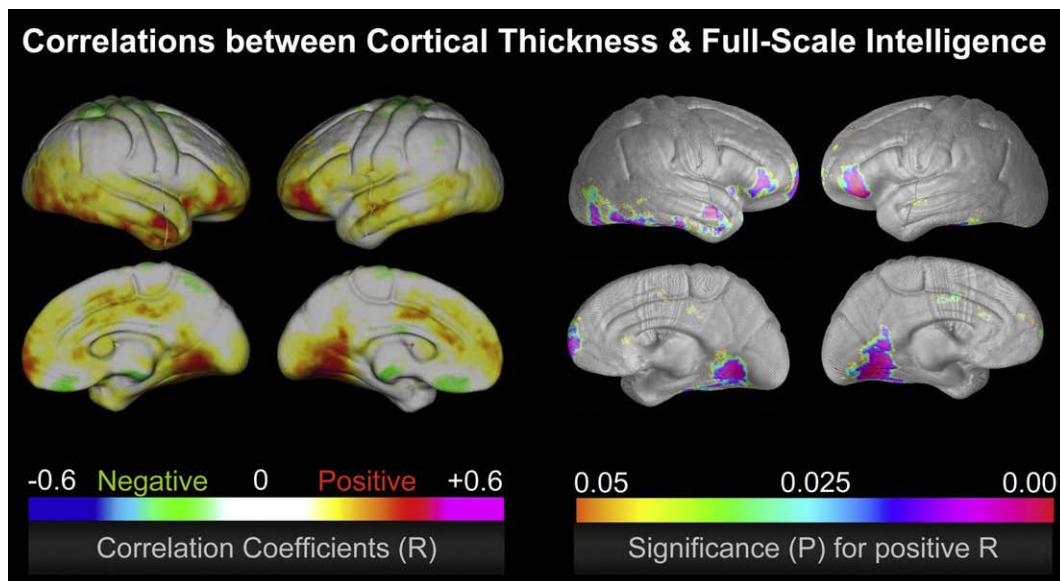

Fig. 2. Correlations between cortical thickness and full-scale intelligence in a sample of 65 healthy subjects, after removing the partial effects of sex and age (Narr et al., 2007). The left color bar encodes the *r*-values that depict the magnitude and direction of correlations; the right color bar encodes the significance (*p*) associated with the positive correlations, where significance was confirmed by permutation testing (*p* < 0.01) in frontal and temporal regions. Significant negative correlations were completely absent.

areas support the idea of a frontal-lobe network consistently recruited for problem solving, planning, sequencing, reasoning, and judgment (Duncan & Owen, 2000; Duncan et al., 2000), other brain regions are shown to contribute to individual intellectual abilities as well. For example, Narr and colleagues (2007) argue with respect to their significant thickness-based correlations observed in the temporal cortex that "cortical association area 37 [...] participates in the analysis of visual form, motion, and the representation of objects". Observations of specific links between cortical thickness and intelligence in this region (and within proximal visual association area 36) suggest that variations in cortical thickness influence visual analysis abilities, which are integral to cognitive processing.

5. Cortical convolution

Over the course of evolution, the cerebral cortex has grown considerably in surface area, which seems to be not only the result of a larger brain but, perhaps more importantly, of an increased folding of the brain's surface. It has been suggested that the high degree of cortical gyrification in humans may be a morphological substrate that supports some of our species' most distinctive cognitive abilities. Consequently, individual intelligence within the human species might be modulated by the degree of cortical convolution.

5.1. Global and regional findings of convolution-based intelligence correlates

To our knowledge, there is no information on relationships between intelligence and global whole-brain or regional measures of cortical convolution. Traditional two-dimensional methods (e.g., Zilles, Armstrong, Schleicher, & Kretschmann, 1988) can estimate a gyrification index (i.e. the ratio between deep and superficial cortex in coronal sections) and even more sophisticated mesh-based techniques (e.g., Magnotta et al., 1999; Thompson, Schwartz, Lin, Khan, & Toga, 1996; Thompson, Schwartz, & Toga, 1996) make it possible to investigate three-dimensional cortical and surface complexity in particular ROIs. Even so, these methods may lack the spatial resolution necessary to reveal significant relationships.

5.2. Local findings of convolution-based intelligence correlates

A recently introduced approach (Luders, Thompson et al., 2006) has allowed for a point-specific estimation of cortical convolution and was based on the calculation of *mean curvature* (Do Carmo, 1976) at 65,536 vertex points across the lateral and medial cortical surface. When assessing relationships between cortical convolution and full-scale intelligence, statistically significant positive correlations were detected within the left temporo–occipital lobe, particularly in the outermost section of the posterior cingulate gyrus (retrosplenial areas) (Luders et al., 2008) (Fig. 3). Although comparable data with respect to local convolution do not exist, this observation supports previous *in vivo* and *post mortem* findings of predominantly positive associations between intelligence and brain morphology in general. Moreover, it agrees with findings based on phylogenetic research, where brains of larger primates (who, presumably, are more intelligent) are more highly folded than smaller primate brains (Rilling & Insel, 1999; Zilles, Armstrong, Moser, Schleicher, & Stephan, 1989). In addition, cortical convolution was reported to increase more rapidly with brain size among later evolved (and likely more intelligent) primates compared with earlier evolved primates
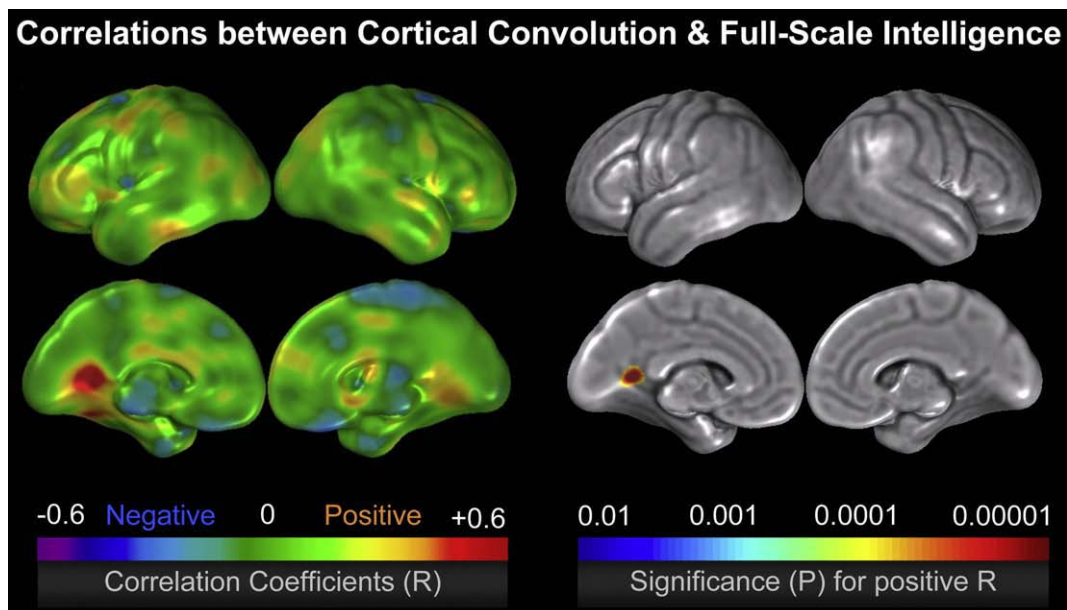

Fig. 3. Correlations between cortical convolution and full-scale intelligence in a sample of 65 healthy subjects, after removing the partial effects of age (Luders et al., 2008). The left color bar encodes the *r*-values that depict the magnitude and direction of correlations; the right color bar encodes the significance (*p*) associated with the positive correlations (*p*<0.05, corrected, using the false discovery rate method). Significant negative correlations were completely absent.

(Zilles et al., 1988, 1989). Finally, the regional specificity of these observed convolution-based correlations are in agreement with findings of thickness-based correlations in similar temporo–occipital regions across the medial cortical surface (Narr et al., 2007).

5.3. Possible functional implications

The regional degree and pattern of the convolution of the cortex has been suggested to reflect regional interconnectivity or neuronal circuitry (Caviness, 1975; Goldman-Rakic, 1981; Rakic, 1988; Rademacher, Caviness, Steinmetz, & Galaburda, 1993; Roland & Zilles, 1994; Van Essen, 1997; Watson et al., 1993). Thus, certain architectonic constellations in the retrosplenial area – their precise nature remains to be established – might benefit intellectual abilities. In support of this hypothesis, the temporo–occipital region of the medial cortex was suggested recently to be fundamental in determining individual differences in intelligence "by serving as a brain site in which higher-order language-based concepts converge with the incoming visual information stream" (Haier, White, & Alkire, 2003). In addition, this region might be an important contributor towards individual intelligence via modulating pathways to (pre)frontal regions. These assumptions corroborate a recently proposed theory — The Parieto-Frontal Integration Theory (P-FIT) of intelligence (Jung & Haier, 2007) highlighting the integration of anterior and posterior brain regions in most intelligence research.

6. The corpus callosum

The corpus callosum (CC) is a white matter structure and the largest commissure in the human brain, connecting the two hemispheres through more than 200 million fibers. The midsagittal callosal area is an indicator of the total number of small diameter fibers within the CC (Aboitiz, Scheibel, Fisher, & Zaidel, 1992). Since small diameter fibers are particularly involved in transferring higher-order cognitive information (Aboitiz, 1992), callosal morphology may reflect the capacity for inter-hemispheric processes that modulate intellectual abilities.

6.1. Global and segment-specific findings of callosal intelligence correlates

There is a large pool of studies where associations between cognitive abilities and callosal characteristics were examined in samples with neurological conditions, developmental disabilities and disorders, or diseases. The majority of these studies report positive correlations, with larger callosal area measurements being associated with better cognitive performance (Atkinson, bou-Khalil, Charles, & Welch, 1996; Fletcher et al., 1992; Strauss, Wada, & Hunter, 1994; Spencer et al., 2005; Schatz & Buzan, 2006). Although most of these studies examined correlations with total callosal size (measured as callosal area across the whole midsagittal section), a few conducted more specific analyses by subdividing the midsagittal section of the CC into macroscopic subregions according to parcellation schemes (e.g., Witelson, 1989). Here, the CC is arbitrarily divided into several sections suggested to correspond to a certain topographic organization and func-

tional boundaries. Measuring segmental subunits (in contrast to evaluating the CC as a whole) allows more precise conclusions with respect to the relevance of callosal sections and interconnected homotopic cortical regions for higher cognitive functions. However, traditional parcellation schemes have recently generated some controversy with respect to the assumed topography of callosal fibers, where for example callosal motor fiber bundles were found to cross the CC in a much more posterior location than previously indicated (Hofer & Frahm, 2006).

6.2. Local findings of callosal intelligence correlates

Some newer studies try to circumvent the pitfalls associated with callosal segmentation; they can map relationships between callosal characteristics and intelligence with high spatial resolution without relying on pre-defined areas. As described above, VBM provides voxel-wise estimators of local tissue concentration throughout the whole brain but existing VBM studies did not detect white matter correlates of intelligence in the region of the CC (Haier et al., 2004, 2005). A different high-resolution approach – based on anatomical mesh-based geometrical modeling (Thompson, Schwartz, & Lin et al., 1996; Thompson et al., 1996, 1997) – provides point-wise distance measures and was applied to correlate intelligence and callosal thickness at 100 points across the whole callosal surface (Luders, Narr et al., 2006). This approach revealed significant positive correlations between callosal thickness and full-scale IQ in several callosal regions (Luders et al., 2007). Correlations were most significant at the border between posterior body and isthmus but extended farther anterior (covering almost the entire posterior midbody) and also farther posterior (covering the remainder of the isthmus and anterior sections of the splenium). In addition, another smaller region at the border between anterior third and anterior midbody was detected to exhibit positive correlations (Fig. 4). These findings are in agreement with previous global or segment-specific results indicating positive correlations between callosal area size and cognitive measurements in non-normative samples (Atkinson et al., 1996; Fletcher et al., 1992; Strauss et al., 1994; Spencer et al., 2005; Schatz and Buzan, 2006).

6.3. Possible functional implications

Positive correlations between callosal thickness and full-scale IQ may indicate that additional or better-myelinated callosal pathways facilitate a more efficient inter-hemispheric information transfer, which is likely to benefit the integration and processing of information and positively affect intellectual performance (Luders et al., 2007). At the same time, local variations in callosal thickness (and their correlations with intelligence) might also partly reflect the relevance of topographically connected cortical regions for processing higher-order cognitive information (e.g., the posterior association cortex). Although precise anatomical boundaries of higher-order networks are vaguely defined and proposed maps of callosal connectivity lack consistency (Hofer and Frahm, 2006; Witelson, 1989; Zarei et al., 2006), these findings suggest that inter-hemispheric communication mediated by the CC in posterior parietal as well as occipital
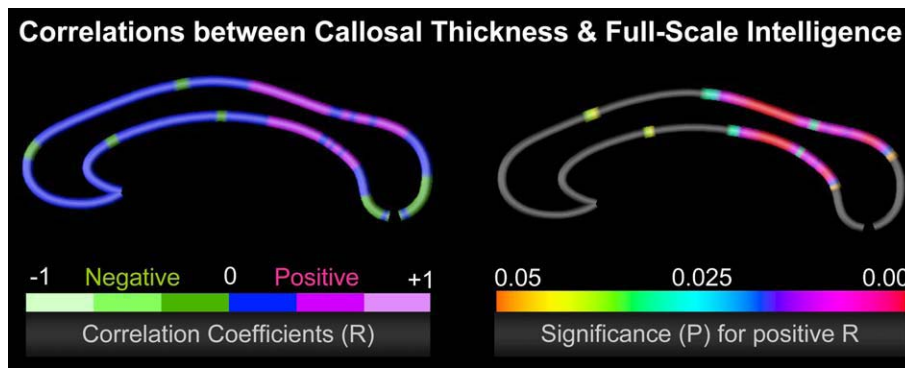
Fig. 4. Correlations between callosal thickness and full-scale intelligence in a sample of 62 healthy subjects, after removing the partial effects of brain volume (Luders, Narr et al., 2006). The left color bar encodes the *r*-values that depict the magnitude and direction of correlations; the right color bar encodes the significance (*p*) associated with the positive correlations, where significance was confirmed by permutation testing ($p < 0.05$). Significant negative correlations were completely absent.

association regions appears to be fundamental in determining individual differences in intelligence. Further support for the involvement of not only anterior but also posterior brain regions comes from a functional study designed to examine the neural bases for intellectual giftedness (superior-g) in adolescents (Lee et al., 2006). Here the authors concluded that superior-g may be achieved due to facilitation of the fronto-parietal network particularly driven by the posterior parietal activation. This claim is also in agreement with the above mentioned theory by Jung and Haier (2007) as well as with findings discussed throughout this article suggesting that variations in a widely distributed network throughout the brain predict individual differences in intelligence.

7. Future developments

Modern neuroimaging methods have contributed considerably to our understanding of the neurobiology of intelligence. In addition to structural MRI (which constituted the main focus of this article) other imaging techniques will further contribute to elucidating the physical correlates of human intelligence and have the potential to resolve how structural, physiological, histological, or neuro–chemical characteristics of the brain are interrelated. Systematically combining structural MRI with functional MRI (fMRI) or with positron emission tomography (PET) could add information regarding whether more or less tissue in a particular region is associated with more or less activation during a given cognitive task. Moreover, applying magnetic resonance spectroscopy (MRS) in combination with structural MRI or with diffusion tensor imaging (DTI) could help to clarify how regional concentrations of particular neurometabolites are related to other white matter measurements (e.g., fractional anisotropy; concentration; volume). Last but not least, imaging genomics could provide unprecedented opportunities to establish common biological determinants for both brain structure and higher cognitive function. The development of such methods allowing cross-correlation of region-specific measurements will be a valuable step in the still-emerging field linking brain anatomy with intelligence.

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