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Sex differences in the IQ-white matter microstructure relationship: A DTI study

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ABSTRACT

Sex differences in the relationship between general intelligence and brain structure are a topic of increasing research interest. Early studies focused mainly on gray and white matter differences using voxel-based morphometry, while more recent studies investigated neural fiber tracts using diffusion tensor imaging (DTI) to analyze the white matter microstructure. In this study we used tract-based spatial statistics (TBSS) on DTI to test how intelligence is associated with brain diffusion indices and to see whether this relationship differs between men and women. 63 Men and women divided into groups of lower and higher intelligence were selected. Whole-brain DTI scans were analyzed using TBSS calculating maps of fractional anisotropy (FA), radial diffusivity (RD), and axial diffusivity (AD). The results reveal that the white matter microstructure differs between individuals as a function of intelligence and sex. In men, higher intelligence was related to higher FA and lower RD in the corpus callosum. In women, in contrast, intelligence was not related to the white matter microstructure. The higher values of FA and lower values of RD suggest that intelligence is associated with higher myelination and/or a higher number of axons particularly in men. This microstructural difference in the corpus callosum may increase cognitive functioning by reducing inter-hemispheric transfer time and thus account for more efficient brain functioning in men.

1. Introduction

The investigation of how intelligence and sex differences are manifested in the brain's structure has become an exciting research question in the differential psychological approach in the last decade. Although there are no sex differences in general intelligence, sex differences in the relationship between general intelligence and brain structure have been observed. One of the earliest reports goes back to Haier, Jung, Yeo, Head, and Alkire (2005). In an MRI study using voxel-based morphometry (VBM), they demonstrated that, in women, intelligence is positively related to white matter volume in the frontal lobe, whereas men show positive intelligence-gray matter correlations in frontal and parietal lobes. Thus, although the sexes do not differ in general intelligence, the neuroanatomical structures of intelligence are different for women and men. Burgaleta et al. (2012) tested the relationship between general intelligence and global brain features, like total and tissue-specific volumes, related to sex differences. Interestingly, their findings are not in line with Haier's results. Women showed a positive intelligence-gray matter volume relationship but no significant intelligence-white matter volume correlation was found. For men, no significant correlations between general intelligence and total volumetric measures were observed. The discrepant findings could in part be the result from different analysis methods. While Haier et al. (2005) explored the relationship on a regional level, Burgaleta's study analyzed total volumetric measures. These studies provide first evidence that the correlation between intelligence and the brain structure is moderated by sex.

While the focus of earlier studies lies mainly on volumetric differences using VBM, more recent studies investigated neural fiber tracts using diffusion tensor imaging (DTI) to analyze the white matter microstructure. Specifically, fractional anisotropy (FA), radial diffusivity (RD), and axial diffusivity (AD) provide estimates of the integrity and density of fibers and the degree of myelination.

Even though there exists no sex difference in general intelligence on a behavioral level, it becomes apparent from the literature reviewed above that the relationship between intelligence and brain structure varies between the sexes. Thus, the current study aims at testing whether the correlation between intelligence

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and the white matter microstructure using DTI differs between men and women.

1.1. Intelligence correlates of white matter microstructure

By now, few studies have employed DTI to characterize structural connectivity differences in the brain between lower and higher intelligent individuals. There is evidence that general intelligence is related to higher integrity of WM fiber tracts connecting parieto-frontal cortical areas (Barbey, Colom, Paul, & Grafman, 2013; Gläscher et al., 2010). This result is in line with the parieto-frontal integration theory, assuming that general intelligence is particularly associated with effective parieto-frontal information processing (Jung & Haier, 2007). Another study testing the relationship between intelligence and the white matter microstructure found positive correlations with FA in bilateral frontal and occipito-parietal regions (Schmithorst, Wilke, Dardzinski, & Holland, 2005), indicating higher white-matter fiber integrity of those regions in higher intelligent individuals. Clayden et al. (2012) demonstrated that FA in the splenium and left-side inferior longitudinal and arcuate fasciculi positively predicts intelligence. This tract connects regions within hemispheres, which is crucial for the integration of information between frontal (including Broca's area) and temporo-parietal regions (including Wernicke's area). Interhemispheric white matter microstructure differences between lower and higher intelligent individuals were found by Navas-Sánchez et al. (2014). They reported a positive correlation of intelligence with FA in the corpus callosum.

1.2. Sex differences in the white matter microstructure

Turning to sex differences in the white matter microstructure, Szeszko et al. (2003) reported that women have higher FA in the left frontal lobe as compared to men. Schmithorst, Holland, and Dardzinski (2008) found that females (average age of 12 years) show higher FA in the splenium of the corpus callosum, while males have higher FA in associative white matter regions (including the frontal lobes). Higher FA and lower RD in men as compared to women were reported by Menzler et al. (2011) in the corpus callosum, the cingulum, and the thalamus. While sex differences in the corpus callosum and cingulum have been previously observed (Westerhausen et al., 2003), the finding that men show higher thalamic FA accompanied by lower RD than women has not been described before. Instead, higher local efficiency in cortical anatomical networks was found in women, especially those with smaller brains, specifically in the precuneus, the precentral gyrus, and the lingual gyrus (Yan et al., 2011). Although these studies provide some evidence for sex differences in white matter structure, research on the intelligence-WM relationship has rarely considered sex a potential moderator variable.

1.3. Sex differences in the IQ-white matter microstructure relationship

Studies focusing on intelligence (Clayden et al., 2012; Schmithorst et al., 2005) typically apply statistical techniques to control for morphological differences associated with age and sex. According to Tang et al. (2010), sex differences in brain structure and function make it necessary to explore the relationship between intelligence and brain parameters separately for both sexes (even when there are no general ability differences in intelligence). Tang et al. (2010) analyzed intelligence differences separately for the two sexes and found that higher intelligent males show lower FA in the forceps major, while in females, FA in parts of the forceps major (extension of the splenium) is positively correlated with general intelligence. The negative FA correlation in men was interpreted as an indicator of interference from contralateral sides of the brain who rely mostly on the right side of the brain. The positive FA correlation in women was associated with the observation that the splenium may be larger in females.

A developmental study by Wang et al. (2012) used TBSS to study sex differences in the association between intelligence and white matter microstructure in the adolescent brain. Considering the whole sample, full-scale IQ was positively related to FA in the frontal part of the right inferior fronto-occipital fasciculus, which suggests that region specific increases in FA are associated with optimal cognitive performance. Moreover, in females, significant correlations between verbal IQ and FA could be found in two clusters including the left corticospinal tract and superior longitudinal fasciculus (a region associated with language). Considering full-scale IQ, however, no correlations with FA could be found neither in females nor males.

1.4. Research question

The literature usually reports no sex differences in general intelligence. From the above reviewed literature, however, it becomes evident that the relationship between intelligence and brain structure may vary between the sexes. Thus, the current study aims at testing whether sex moderates the correlation between intelligence and the white matter microstructure applying TBSS. Most of the research on white matter microstructure is based on region of interest (ROI) analyses or fiber tracking analyses. A novel method is to use tract-based spatial statistics (TBSS; Smith et al., 2006) to perform automated analysis of white matter integrity. TBSS uses a carefully tuned nonlinear registration method followed by a projection onto a mean FA skeleton. This skeleton represents the centers of all tracts common to the group and the resulting data fed into voxel-wise cross-subject statistics. Thus, TBSS combines the strength of both voxel-based and tractographic analyses to overcome the limitations of conventional methods including standard registration algorithms and spatial smoothing. TBSS is assumed to improve the sensitivity, objectivity, and interpretability of multi-subject diffusion imaging studies (Smith et al., 2006).

In addition to analyses of FA, we also investigate RD and AD, which allows for a clearer interpretation of potential FA differences in terms of myelination and axonal integrity. The FA measure represents the relative degree of anisotropy or directionality at each voxel and is an unspecific indicator of alterations in white matter microstructure (Peled, Gudbjartsson, Westin, Kikinis, & Jolesz, 1998). As FA is a summary measure of microstructural changes, it should be further characterized by RD and AD (Alexander, Lee, Lazar, & Field, 2007; Alexander et al., 2011). RD indicates the diffusivity along directions which are orthogonal to the primary diffusion direction and is an indirect indicator of myelination (Song et al., 2005; Wu et al., 2011). In contrast, AD represents the diffusivity along the primary diffusion direction and is assumed to characterize the integrity of axons (Gao et al., 2009; Glenn et al., 2003; Sun et al., 2006). This study investigates sex differences in the relationship of intelligence and WM microstructure (FA, RD, AD) in an adult sample using TBSS.

2. Method

2.1. Participants

Participants were recruited via a local newspaper as well as the university's mailing lists, to obtain a heterogeneous and not solely student sample. Participants had to be between 18 and 50 years old, speak German (mother tongue), and had to be without any neurological and/or mental disorders and medication. 16% of the participants had at least nine years of schooling, 60% had at least