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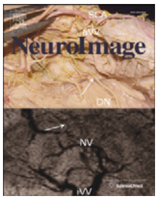

General fluid-type intelligence is related to indices of white matter structure in middle-aged and old adults

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ABSTRACT

General fluid-type intelligence (gF) reflects abstract reasoning and problem solving abilities, and is an important predictor for lifetime trajectories of cognition, and physical and mental health. Structural and functional neuroimaging studies have demonstrated the role of parieto-frontal gray matter, but the white matter (WM) underpinnings of *g*F and the contribution of individual *g*F components to *g*F–WM relationship still need to be explored. The aim of this study was to characterize, in a sample of 100 healthy middle-aged and old subjects (mean = 63.8 years), the relationship between gF and indices of WM structure obtained from diffusion tensor magnetic resonance imaging (DT-MRI) (fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AD)). *g*F was estimated by principal component analysis including measures of episodic memory, reasoning, and processing speed. Tract-based spatial statistics and permutation-based inference statistics were used to test the association between *g*F and WM indices, while controlling for the effect of age and sex. We hypothesized a positive relationship between *g*F and WM structure. Based on previous studies, we further hypothesized that this relationship was heavily influenced by the processing speed component of *g*F.

We found a robust relationship between *g*F and DT-MRI measures of FA, RD and MD in all major WM tracts. Higher *g*F score was related to higher degree of WM integrity, in middle-aged as well as old individuals. Thus, the distributed relationship between *g*F and indices of WM microstructure is consistent with the notion that *g*F reflects efficient signaling between cortical areas. Furthermore, analysis of relationships between WM measures and *g*F components revealed an association with information processing speed and reasoning ability, but not with episodic memory. Thus, although all subcomponents loaded high on *g*F factor, the speed-related components were most strongly associated with DT-MRI-derived measures. These results suggest that DT-MRI can be used to parse gF.

Introduction

An individual's performance across various cognitive tasks tends to be correlated — a high score on one ability test often predicts a high score on another ability test, even when different aspects of cognition are tested (Spearman, 1904). Factor analytic investigations of large samples of ability tests have led to the conceptualization of a hierarchical structure of cognitive function with a psychometric general factor of intelligence (*g*) at the top level (Jensen, 1998; Salthouse et al., 2008; Spearman, 1904). At the next structural level, the concept of *g* has been further separated into crystallized (*g*C) and fluid (*g*F) domains (Cattell, 1963), where *g*C refers to knowledge acquired through education, experience and socialization, and *g*F to more abstract reasoning and problem-solving abilities enabling "intelligent" adaption of acquired knowledge to a changing and complex environment. Importantly, *g*C and *g*F have different lifetime trajectories (Deary, 2001). *g*C is relatively stable in adulthood and normal aging while *g*F has been shown to decline

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linearly from the early 20s. gF therefore captures most of the age-related variance in cognitive decline, and has been shown to be a significant predictor for lifetime trajectories of educational and occupational success, as well as physical and mental health (Deary, 2012; Deary et al., 2010). These findings have motivated research for biomarkers of individual differences in gF (cfr. Deary et al., 2010).

The construction and measures of g/gC/gF have been, and are still, debated (Sternberg and Grigorenko, 2002). Although gF has been measured by a single cognitive test, e.g. Raven's Advanced Progressive Matrices, a more common view is that performance on more than two ability tests is needed to derive a measure of this construct (Nisbett et al., 2012). Accordingly, gF is reflected in ability tests measuring memory and speeded performance (Salthouse et al., 2008). In studies comparing general intelligence across different samples, estimates have been derived from different batteries of ability tests. These estimates have been shown to be highly correlated (Johnson et al., 2004, 2008), suggesting a relative independence of which test measures are included at the first level to generate g. The present study generates a gF from the test-selection used in a recent study by Davies et al. (2011), in which the present sample was included. This selection includes tests of learning and memory function, processing speed and reasoning ability. In Davies et al., gF was shown to be highly polygenic and heritable. In the present study, we investigate the degree to which the same gF estimate is associated with brain white matter (WM) properties as measured with in vivo diffusion tensor magnetic resonance imaging (DT-MRI).

Diffusion tensor magnetic resonance imaging has been extensively used to characterize the brain's structural connectivity in healthy and diseased individuals (Johansen-Berg and Behrens, 2009), and a large body of data suggests that DT-MRI-derived parameters reflect WM health and organization (Beaulieu, 2002, 2011; Le Bihan, 2003). Structural and functional brain imaging studies have demonstrated that gF and g are associated with distributed gray matter regions (Colom et al., 2009, 2010; Gray et al., 2003; Woolgar et al., 2010). In line with this, a relationship between g and WM fiber tracts integrating parieto-frontal cortical areas has been reported (Barbey et al., 2012; Deary et al., 2010; Glascher et al., 2010). Moreover, other DT-MRI studies have linked diffusion indices to measures of intellectual function (Chiang et al., 2008, 2009; Penke et al., 2012; Schmithorst et al., 2005; Tang et al., 2010; Yu et al., 2008). However, the relationship between gF and diffusion measures remains unexplored.

The aim of the present study was threefold. First, we aimed to characterize the relationship between gF and WM structure, as measured by DT-MRI-derived indices. To calculate gF we used principal component analysis (PCA) on measures of episodic memory function, processing speed and reasoning ability in 100 healthy middle aged and elderly individuals. Then, we used Tract Based Spatial Statistics (TBSS) to investigate the relationship between gF and WM structure. From earlier studies we hypothesized that gF would be positively related to fractional anisotropy (FA) and inversely related to mean diffusivity (MD), radial diffusivity (RD) and axial diffusivity (AD) in widespread WM areas. The second aim of the study was to investigate whether the relationship between gF and WM structure changed with age. Thirdly, we examined the relationship between WM structure and each cognitive component of gF and their contribution to the gF–WM association. Since processing speed relates to WM microstructure and is shown to mediate the relationship between global WM properties and g (Penke et al., 2012; Turken et al., 2008), we expected to find that gF–WM relationship is highly overlapping with the relationship found between WM and processing speed.

Materials and methods

Participants

The participants constitute a subsample of the Norwegian Cognitive NeuroGenetics (NCNG sample (Espeseth et al., 2012)). Healthy individuals were invited through advertisement to take part in the first wave of a longitudinal study on cognitive aging. Subjects with a history of substance abuse, present neurologic or psychiatric disorder, or other significant medical conditions, were excluded from the study. All participants were examined according to an extensive neuropsychological test protocol and a MRI protocol including T1-weighted images and DT-MRI. An experienced neuroradiologist evaluated the T1-weighted 3D images of all subjects at inclusion. Presence of brain tumors, cysts, recent infarctions or gross regional or global signal abnormalities was the exclusion criteria. All participants were invited to a follow-up study three–four years after the first examination, and the present study included 100 participants from this second wave of the study (mean age = 63.8 years, range 49–80, 67 females). None of the included participants were diagnosed with dementia, or had symptoms of mild cognitive impairment (MCI) (Petersen, 2004). All subjects obtained a score ≥26 on Mini Mental State Examination (MMSE) (Folstein et al., 1975), and provided their informed consent to participation. The Regional Committee for Medical and Health Research Ethics of Western Norway approved the second wave of the study.

Neuropsychological assessment

All participants completed a battery of neuropsychological tests, including measures of episodic memory function (California Verbal Learning Test, second version (CVLT-II) (Delis et al., 2000)), reasoning ability (the Matrix Reasoning (MR) subtest from Wechsler Abbreviated Scale of Intelligence (WASI), (Wechsler, 1999)), and processing speed. Processing speed was derived from performance on the Color–Word Interference Test (CWIT) (Delis and Kaplan, 2001) and from an experimental visuo-spatial attention task involving letter discrimination with location cues of varying validity (CDT) (Espeseth et al., 2006). Performance on these cognitive tests, identical to the ones included in the study of Davies et al. (2011), was used to calculate gF in the present study.

Episodic memory function was assessed by the Norwegian translation of the CVLT-II. The participants were presented a list of 16 words (List A) five times. Immediately after the fifth trial, the participants were read a new list (List B) and asked to recall it. Then, the participants were asked to recall words from List A, immediately after the recall of List B (short-delayed free recall) and 30 min later (long-delayed free recall), followed by a recognition trial. The present study included the following three CVLT-II measures: the number of hits across the five learning trials (immediate recall (trials 1–5)) and the short and long-delayed conditions.

Four conditions of CWIT from the Delis–Kaplan Executive Function System (D-KEFS) were included to calculate one of the two processing speed measures used in our study. In the first condition, the participants were shown color patches in three different colors (red, blue and green) on a white surface, and the task was to name the colors as fast and accurate as possible. In the second condition they were shown three words (red, blue and green) written in black ink on a white surface, and the task was to read the words as fast and correctly as possible. In the third and more cognitively demanding condition, they were shown the same three words, but now the words were written in incongruent ink color. The task was to name the ink color and by that inhibit the more automatic response of word reading. The fourth condition measured both inhibition and switching. The same three words were written in incongruent colors, but some of the words were written inside a rectangular box. The task was to switch between naming the ink color (inhibit reading the word) and reading the word when the word was inside of a box. The outcome measure used in the present study was the time required to finish each task.

The overall reaction time (RT) measure from CDT (Espeseth et al., 2006) was included as a second measure of processing speed. In the present study, subjects were asked to fixate on a centrally located