Brain grey and white matter predictors of verbal ability traits in older age: The Lothian Birth Cohort 1936

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ABSTRACT

Cerebral grey and white matter MRI parameters are related to general intelligence and some specific cognitive abilities. Less is known about how structural brain measures relate specifically to verbal processing abilities. We used multi-modal structural MRI to investigate the grey matter (GM) and white matter (WM) correlates of verbal ability in 556 healthy older adults (mean age = 72.68 years, s.d. = .72 years). Structural equation modelling was used to decompose verbal performance into two latent factors: a storage factor that indexed participants' ability to store representations of verbal knowledge and an executive factor that measured their ability to regulate their access to this information in a flexible and task-appropriate manner. GM volumes and WM fractional anisotropy (FA) for components of the language/semantic network were used as predictors of these verbal ability factors. Volume of the ventral temporal cortices predicted participants' storage scores (β = .12, FDR-adjusted p = .04), consistent with the theory that this region acts as a key substrate of semantic knowledge. This effect was mediated by childhood IQ, suggesting a lifelong association between ventral temporal volume and verbal knowledge, rather than an effect of cognitive decline in later life. Executive ability was predicted by FA fractional anisotropy of the arcuate fasciculus (β = .19, FDR-adjusted p = .001), a major language-related tract implicated in speech production. This result suggests that this tract plays a role in the controlled retrieval of word knowledge during speech. At a more general level, these data highlight a basic distinction between information representation, which relies on the accumulation of tissue in specialised GM regions, and executive control, which depends on long-range WM pathways for efficient communication across distributed cortical networks.

Introduction

In humans, the characteristics of both grey and white matter brain structures are informative predictors of the level and age-related change in cognitive abilities (e.g., Deary et al., 2010b; Ritchie et al., 2015). Higher general intelligence has been associated with greater brain volume and cortical thickness in a wide network of grey matter (GM) regions, principally in frontal and parietal cortices (Deary et al., 2010b; Jung and Haier, 2007). The structure of white matter (WM) tracts also makes a contribution to cognitive abilities (Ziegler et al., 2010). In older adults general fluid-type intelligence was associated moderately with a global measure of fractional anisotropy (FA) in WM tracts across the brain (Penke et al., 2012). This association was mediated entirely by a latent trait of information processing speed, suggesting that the efficiency of long-range neural connections contributes to ensuring efficient communication between brain regions, which in turn benefits complex cognitive functions.

Much of research linking brain structural indices with cognitive functions has focused on fluid-type cognitive abilities (Horn and Cattell, 1967), such as reasoning, working memory, executive function, and processing speed. Less is known about the aspects of brain structure that predict performance on verbal tasks that probe knowledge of words and their meanings. Such tasks are typically thought to depend heavily on crystallised-type abilities – i.e., stored knowledge. Colom et al. (2009) found that a measure of crystallised intelligence, based on tests of vocabulary, and verbal and numerical reasoning, was associated with greater GM volumes in many of the frontal and parietal sites linked to fluid abilities. In addition, however, crystallised ability
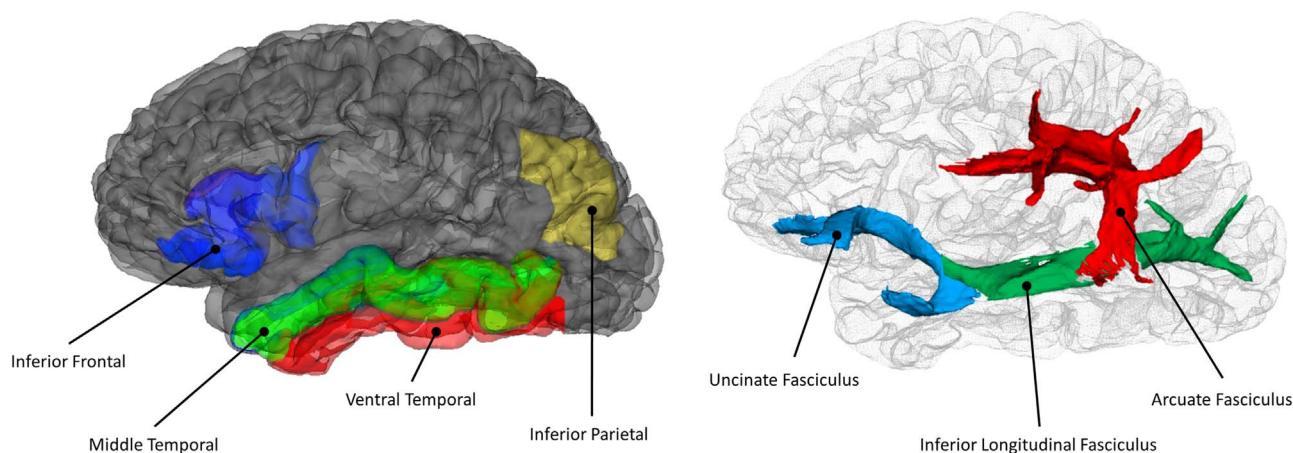

Fig. 1. A schematic illustration of regions and tracts implicated in verbal-semantic processing. Cortical regions of interest are displayed on the cerebral mantle (left), and white matter tracts of interest are shown through a glass brain (right).

was uniquely linked with greater volume in the anterior temporal cortex. This finding has been replicated by others (Choi et al., 2008), and is congruent with the suggestion that anterior temporal regions play a key role in representing semantic knowledge (Binder and Desai, 2011; Hoffman et al., 2014; Patterson et al., 2007). Semantic knowledge refers to our store of word and object concepts and thus is involved in most verbal tasks.

Few studies have focused specifically on the structural neural correlates of semantic knowledge in healthy individuals. de Zubicaray et al. (2011) found that semantic ability in older adults, measured by extracting the first principal component from a range of verbal and non-verbal semantic tasks, was correlated with GM volumes in the anterior temporal cortex. In this study, better performance was associated with *reduced* GM volume. In the same study, higher semantic scores were linked to greater FA in the uncinate fasciculus and inferior fronto-occipital fasciculus, two tracts which link temporal regions with prefrontal cortex. Another study failed to find any GM or WM regions that were linked specifically with performance on verbal semantic tasks (Ziegler et al., 2010). In both of these studies, however, sample size was relatively modest (N=55 in de Zubicary et al.; N=38 in Ziegler et al.). The number of participants in the present study (N=556) is an order of magnitude greater than these previous investigations.

Although few studies have investigated how the structure of the healthy brain is associated with semantic abilities, a rich neuropsychological literature has linked impairments in semantic processing with distinct areas of brain damage. The syndrome of semantic dementia (also known as the semantic variant of primary progressive aphasia) is characterised by a selective and often profound deterioration in semantic knowledge, accompanied by atrophy to anterior temporal regions (Hodges and Patterson, 2007). In this condition, the amount of cortical atrophy in the anterior fusiform gyri is strongly predictive of the severity of patients' semantic impairment, suggesting a major role for this region in representation of semantic knowledge (Butler et al., 2009; Mion et al., 2010). Semantic dementia is also associated with damage to WM tracts connecting the temporal cortex to other sites, including the uncinate, arcuate and inferior longitudinal fasciculi (Acosta-Cabronero et al., 2011; Agosta et al., 2010). It is not clear at present, however, how WM damage contributes to the loss of semantic knowledge in this condition.

Impairments in semantic processing also occur as a consequence of damage to prefrontal and posterior temporoparietal cortex in stroke (Berthier, 2001; Noonan et al., 2010). However, whereas semantic dementia patients suffer from degradation of semantic representations, patients with prefrontal and temporoparietal damage have intact knowledge representations but fail to access and use these appropri-

ately (Jefferies, 2013; Jefferies and Lambon Ralph, 2006). This neuropsychological dissociation is consistent with current theories which hold that semantic abilities are underpinned by two interacting but distinct systems: a store of semantic knowledge and an executive system that regulates flexible and goal-directed access to that information (Hoffman et al., 2015; Rogers, Patterson et al., 2015). The executive element of semantic processing is critical because we hold a wide range of information about particular words/concepts and situations often require us to select specific aspects of this information while inhibiting others (e.g., selecting the contextually appropriate interpretation of words with multiple meanings; Hoffman et al., 2011; Rodd et al., 2005). Functional neuroimaging studies have implicated left inferior prefrontal, posterior middle temporal, and inferior parietal regions in these executive processes (Noonan et al., 2013). Less is known about potential WM contributions to executive semantic processing, though it has been suggested that the uncinate fasciculus may play an important role (Harvey et al., 2013). This tract connects temporal and frontal cortices.

These findings in clinical populations suggest that verbal ability is underpinned by a store of verbal-semantic representations and by executive processes involved in accessing them. They also suggest that these two elements have distinct neural correlates. Despite this, no studies have investigated whether individual differences in these abilities in healthy individuals can be predicted by brain structure. In the present study, we investigated GM and WM associations with verbal abilities in the Lothian Birth Cohort 1936 (LBC1936; Deary et al., 2012; Deary et al., 2007), a longitudinal study of cognitive ageing that includes structural neuroimaging data for over 700 healthy older adults. We used structural equation modelling to isolate a factor of verbal ability associated with storage of verbal knowledge and one indexing executive processes that govern access to that knowledge. We then used multi-modal MRI to assess associations of key GM and WM structures with both of these components. Four GM regions and three WM tracts were identified as being of potential importance, based on existing theories of verbal processing (shown in Fig. 1). Their volumes/FA were used as predictors of verbal abilities. The Method section contains more details of the regions and tracts and why they were chosen *a priori* as predictors. We hypothesised that storage of verbal knowledge would be predicted by volume in GM regions implicated in semantic processing, particularly regions of the ventral temporal lobes associated with representation of semantic information. We expected WM tract FA to be associated with the executive component of verbal ability, since regulating access to information requires the co-ordination of activity across distributed cortical sites.