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Diffusion-tensor imaging of major white matter tracts and their role in language processing in aphasia

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ABSTRACT

A growing literature is pointing towards the importance of white matter tracts in understanding the neural mechanisms of language processing, and determining the nature of language deficits and recovery patterns in aphasia. Measurements extracted from diffusion-weighted (DW) images provide comprehensive *in vivo* measures of local microstructural properties of fiber pathways. In the current study, we compared microstructural properties of major white matter tracts implicated in language processing in each hemisphere (these included arcuate fasciculus (AF), superior longitudinal fasciculus (SLF), inferior longitudinal fasciculus (ILF), inferior frontal-occipital fasciculus (IFOF), uncinate fasciculus (UF), and corpus callosum (CC), and corticospinal tract (CST) for control purposes) between individuals with aphasia and healthy controls and investigated the relationship between these neural indices and language deficits.

Thirty-seven individuals with aphasia due to left hemisphere stroke and eleven age-matched controls were scanned using DW imaging sequences. Fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD), axial diffusivity (AD) values for each major white matter tract were extracted from DW images using tract masks chosen from standardized atlases. Individuals with aphasia were also assessed with a standardized language test in Russian targeting comprehension and production at the word and sentence level.

Abbreviations: DTI, diffusion tensor imaging; DF, diffusion-weighted; FA, fractional anisotropy; MD, mean diffusivity; AD, axial diffusivity; RD, radial diffusivity; AF, arcuate fasciculus; SLF, superior longitudinal fasciculus; ILF, inferior longitudinal fasciculus; IFOF, inferior frontal-occipital fasciculus; UF, uncinate fasciculus; MdLF, middle longitudinal fasciculus; CST, corticospinal tract; CC, corpus callosum; MNI, Montreal Neurological Institute.

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Individuals with aphasia had significantly lower FA values for left hemisphere tracts and significantly higher values of MD, RD and AD for both left and right hemisphere tracts compared to controls, all indicating profound impairment in tract integrity. Language comprehension was predominantly related to integrity of the left IFOF and left ILF, while language production was mainly related to integrity of the left AF. In addition, individual segments of these three tracts were differentially associated with language production and comprehension in aphasia. Our findings highlight the importance of fiber pathways in supporting different language functions and point to the importance of temporal tracts in language processing, in particular, comprehension.

1. Introduction

Aphasia is an acquired neurogenic communication disorder leading to deficits in oral and written language comprehension and production (Hallowell & Chapey, 2008). Aphasia in most instances occurs after damage due to stroke or traumatic-brain injury to perisylvian areas in the dominant hemisphere. As early as the 19th century, it was acknowledged that damage to both cortical areas and subcortical fiber pathways (white matter tracts) could lead to language deficits. Carl Wernicke (1874) described a syndrome resulting from a disconnection of Broca's and Wernicke's areas, that would later become known as ‘conduction aphasia’ (Catani & Mesulam, 2008). At the end of the 19th century, Lichtheim (1885), building on Wernicke's work, further extended the descriptions of disconnection syndromes in language and outlined two additional types of aphasia, transcortical sensory and transcortical motor, that resulted from disconnection of the concept center from other language areas, although he did not provide anatomical specifications for these syndromes in his work. Further, contemporary re-examination of classical cortical aphasia cases (e.g., Leborgne patient) using modern neuroimaging techniques have demonstrated extensive white matter involvement (Dronkers, Plaisant, Iba-Zizen, & Cabanis, 2007; Thiebaut de Schotten et al., 2015). Recent lesion studies repeatedly show that lesions associated with comprehension and production deficits in aphasia can be located in subcortical white matter (Bates et al., 2003; Kümmerer et al., 2013).

Still today, relatively little is known about the functional significance of fiber pathways in language processing, in general, and their contributions to aphasia syndromes, in particular (for review see Bajada, Lambon Ralph, & Cloutman, 2015; Dick, Bernal, & Tremblay, 2014). However, recent advances in diffusion imaging techniques now afford the opportunity to investigate microstructural tissue properties and white matter integrity *in vivo* in individuals with various brain pathology, including aphasia. Within this novel avenue of research, accumulating evidence shows that differential fiber pathway damage (Hosomi et al., 2009; Kim & Jang, 2013; Kim et al., 2011; Rosso et al., 2015) and premorbid anatomical variations in tract structure (Forkel, Thiebaut de Schotten, Dell'Acqua, et al., 2014) can serve as important prognostic factors for patterns of language recovery following stroke. Measured changes in the macro- and microstructure of fiber pathways have also been used as physiological markers of observed behavioral changes following training (Geva, Correia, & Warburton, 2011; Scholz, Klein, Behrens, & Johansen-Berg, 2009). To advance our knowledge of how language is processed in the brain and to gain insights into the neural mechanisms of language recovery in aphasia, further investigation of the functional roles of fiber pathways is required.

1.1. *Role of different white matter tracts in language processing*

1.1.1. *Dorsal tracts*

Historically, the arcuate fasciculus (AF) has been regarded as the main tract involved in language. The importance of this tract was highlighted in the first network model of language processing by Carl Wernicke (even though initially Wernicke was mistaken regarding its anatomical location) (Catani & Mesulam, 2008). The AF and the superior longitudinal fasciculus (SLF) are fiber bundles that run longitudinally within each cerebral hemisphere and connect frontal cortex with post-rolandic areas, the temporal and inferior parietal lobes, respectively. Once these fibers bundle together to pass over the ventricles, they become difficult to distinguish from one another and have previously been referred to by the same name. However, Petrides and Pandya (1988) – in the rhesus monkey brain using radiographic techniques – and later Makris et al. (2005) – in the human brain using diffusion tensor imaging (DTI) – isolated the two tracts and demonstrated their distinct trajectories. Specifically, Makris et al. (2005) delineated four separate segments of the SLF in the human brain, with the fourth subdivision being the AF. Based on recent neuroimaging techniques and electrostimulation studies, two- and three-pathway models of the AF have been proposed (Brauer, Anwander, Perani, & Friederici, 2013; Catani, Jones, & Ffytche, 2005; Glasser & Rilling, 2008). For instance, Catani et al. (2005) demonstrated functional segregation of the AF, with the direct (long) branch presumably supporting phonological processing and indirect (short) branches – lexical-semantic processing. Data no longer unequivocally support the classical depiction of this tract as directly and exclusively connecting Wernicke's with Broca's area. It has been shown that in the frontal lobe the tract actually reaches to the precentral gyrus rather than to the