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Arcuate fasciculus variability and repetition: The left sometimes can be right

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ABSTRACT

Repetition ability is a major criterion for classifying aphasic syndromes and its status is helpful in the determination of the involved neural structures. It is widely assumed that repetition deficits correlate with injury to the left perisylvian core including the arcuate fasciculus (AF). However, descriptions of normal repetition despite damage to the AF or impaired repetition without AF involvement cast doubts on its role in repetition. To explain these paradoxes, we analyse two different aphasic syndromes – in which repetition is selectively impaired (conduction aphasia) or spared (transcortical aphasias) – in light of recent neuroimaging findings. We suggest that the AF and other white matter bundles are the anatomical signatures of language repetition and that individual variability in their anatomy and lateralisation may explain negative cases.

1. Introduction

At the beginning of the twenty first century the debate on localisation of aphasia is still alive with competition between holistic and localising positions (York, 2009). However, thanks to recent advances in neuroimaging it is possible to perform a close scrutiny of previous theories and predictions about the cerebral mechanisms underpinning language in normal and brain-damaged individuals. This seems likely through studies using positron emission tomography (PET) (Ohyama et al., 1996; Collete et al., 2001; Price and Crinion, 2005; Raboyeau et al., 2008), functional magnetic resonance imaging (fMRI) (Abo et al., 2004; Fernandez et al., 2004; Saur et al., 2008), and diffusion tensor imaging (DTI) tractography (Catani et al., 2005, 2007; Parker et al., 2005; Friederici, 2009a, 2009b; Thiebaut de Schotten et al., 2012; Catani et al., 2012). These methods have been used independently (Ohyama et al., 1996; Collete et al., 2001; Abo et al., 2004; Fernandez et al., 2004; Catani et al., 2005; Price and Crinion, 2005; Raboyeau et al., 2008), in combination (Saur et al., 2008; Propper et al., 2010; Bizzi et al., 2012), or even complemented with other ancillary procedures (neuropsychological testing, transcranial magnetic stimulation, intracarotid amytal testing) (Catani et al., 2007; Vernooij et al., 2007; Matsumoto et al., 2008) to obtain valuable information about the *in vivo* anatomy and function of brain areas devoted to language as well as about the white matter fibre pathways binding remote cortical areas in each cerebral hemisphere. Undoubtedly, the emergence of

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new empirical findings or the replication of previous anatomical observations using non-invasive tools is worthwhile, yet these advances open new questions and can eventually reactivate old debates (Yamada et al., 2007; Geldmacher et al., 2007; Bernal and Ardila, 2009; Friederici, 2009a, 2009b; Weiller et al., 2009; Ardila, 2010). Accordingly, refinement in the description of the anatomy, function and hemispheric asymmetry of white matter fibre tracts coupled with the identification of inter-hemispheric dissociation of major speech centres (lateralisation of Broca's area and Wernicke's area in different hemispheres) have aroused new controversies concerning the participation of the arcuate fasciculus (AF) and other white matter tracts in repetition (Bernal and Ardila, 2009; Ardila, 2010).

Below, we analyse the role of the AF and other white matter fibre pathways in conduction aphasia (CA) (Wernicke, 1966; Kohn, 1992) and transcortical aphasias (TAs) (Lichtheim, 1885; Berthier, 1999). Gaining additional knowledge on the role of neural pathways underpinning repetition in aphasia is important because it could directly inform prognosis (Hosomi et al., 2009) and rehabilitation (Schlaug et al., 2009). Available evidence indicates that the transformation of phonological input into output through repetition of non-words plays a role in learning new words (Jacquemot and Scott, 2006) perhaps by promoting synaptic modification in excitatory projections each time a stimulus is presented. Recent findings are in line with this argument. Repetition in errorless-learning therapies improves noun and verb naming in anomic patients presumably by enhancing reinforcement mechanisms (Conroy et al., 2009). Sentence repetition exercises alone (Kohn, 1990) or paired with the cholinesterase inhibitor donepezil improve not only repetition performance (Berthier et al., 2004), but gains are generalised to fluency and spontaneous speech in CA and to sentence comprehension in mild receptive aphasia (Francis et al., 2003). In addition, a computer-assisted aphasia therapy (IMITATE) combining audiovisual presentation of words and phrases with oral repetition of these stimuli is a promissory strategy to improve language function (Lee et al., 2010). Lastly, intensive therapies modulating intonation and rhythm through repetition (Melodic Intonation Therapy) ameliorate performance in production tasks amongst patients with chronic Broca's aphasia and most notably the observed benefits are associated with remodelling of the right AF (increases in number of fibres, length and volume) (Schlaug et al., 2009).

2. The neural basis of normal language repetition

Before examining the role of the AF in repetition in aphasia, it is pertinent to briefly summarise how the normal brain mediates language repetition. The functional anatomy of repetition has been firmly established in normal subjects using $H_2\,^{15}O$ PET (Ohyama et al., 1996; Price et al., 1996; Castro-Caldas et al., 1998; Collete et al., 2001; Klein et al., 2006) and fMRI (Burton et al., 2001; Abo et al., 2004; Saur et al., 2008). Repetition of single words and word lists produces a strong activation of both cerebral hemispheres in superior temporal and premotor cortices, whereas the same pattern of activation holds for non-word repetition, but only in the left hemisphere (Weiller et al., 1995; Collete et al., 2001; Saur et al., 2008). Complementary studies combining fMRI with DTI further show that superior temporal and premotor areas activated during sublexical repetition interact via the AF, whereas foci of activation in temporal and frontal cortices elicited by semantic comprehension paradigms are connected by the ventral stream (Saur et al., 2008). The scenario is wholly different in aphasic patients with left hemisphere lesions because of network reorganisation. PET and fMRI studies revealed that aphasic patients use different strategies to compensate for impaired repetition performance which in part depend upon the localisation of the structural lesion (Turkeltaub et al., 2011); some patients recruit networks surrounding the infarction in the left hemisphere (e.g., Heiss et al., 1999), whereas in others word and non-word repetition is mediated by the right hemisphere (Weiller et al., 1995; Ohyama et al., 1996; Abo et al., 2004).

3. Conduction and TAs: two sides of the same coin

CA and TAs represent paradigmatic examples of impaired and preserved repetition, respectively (Geschwind, 1965; Brown, 1975; Kohn, 1992; Berthier, 1999). Traditionally, impaired repetition in CA has been linked to involvement of the left AF and other white matter tracts (Wernicke, 1966; Geschwind, 1965; Kohn, 1992), whereas TAs have been attributed, but not always (Niessl von Mayendorf, 1911; Stengel, 1947; Berthier, 1999), to lesions that spare the left perisylvian area and the AF (isolation of the speech area) (Geschwind, 1965, 1968) (Fig. 1). In CA, a disproportionate deficit in repetition occurs in the context of fluent paraphasic verbal production and relative sparing of auditory comprehension (Geschwind, 1965; Goodglass, 1992). At least two types of CA have been described, *reproduction* and *repetition* (Shallice and Warrington, 1977; Nadeau, 2001). The reproduction subtype is characterised by phonemic paraphasias in all verbal domains and recurrent production of sequential phonemic approximations to self-repair errors (*conduit d'approche*) (Shallice and Warrington, 1977; Nadeau, 2001). Reproduction CA has been variously attributed to deficits in verbal praxis (Ardila and Rosselli, 1990), disrupted speech programming (Bernal and Ardila, 2009), poor output phonological encoding (Kohn, 1992; Bernal and Ardila, 2009), or a combination of abnormal sensory-motor integration and reduced phonological short-term memory (Buchsbaum et al., 2011; Hickok et al., 2011) which may result from cortical damage without obligatory involvement of the AF. The repetition subtype shows virtually isolated repetition deficits which have been linked to a selective impairment in auditory–verbal short-term memory and cortical damage that extend deeply to affect the AF (Shallice and Warrington, 1977; Kohn, 1992; Nadeau, 2001).

Note, however, that a clear-cut distinction between both forms of CA may be difficult to establish as they usually share some language deficits (e.g., phonological paraphasia, reduced auditory–verbal short-term memory) (Sakurai et al., 1998). Indeed, at present there is a true spectrum of syndromes meeting the diagnostic criteria for CA which could be, at least in part, explained by differences in aphasia severity, time of aphasia evaluation (acute *vs* chronic), type of repetition tasks