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Research report

Arterial spin labelling shows functional depression of non-lesion tissue in chronic Wernicke's aphasia

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ABSTRACT

Behavioural impairment post-stroke is a consequence of structural damage and altered functional network dynamics. Hypoperfusion of intact neural tissue is frequently observed in acute stroke, indicating reduced functional capacity of regions outside the lesion. However, cerebral blood flow (CBF) is rarely investigated in *chronic* stroke. This study investigated CBF in individuals with chronic Wernicke's aphasia (WA) and examined the relationship between lesion, CBF and neuropsychological impairment.

Arterial spin labelling CBF imaging and structural MRIs were collected in 12 individuals with chronic WA and 13 age-matched control participants. Joint independent component analysis (jICA) investigated the relationship between structural lesion and hypoperfusion. Partial correlations explored the relationship between lesion, hypoperfusion and language measures.

Joint ICA revealed significant differences between the control and WA groups reflecting a large area of structural lesion in the left posterior hemisphere and an associated area of hypoperfusion extending into grey matter surrounding the lesion. Small regions of remote cortical hypoperfusion were observed, ipsilateral and contralateral to the lesion. Significant correlations were observed between the neuropsychological measures (naming, repetition, reading and semantic association) and the jICA component of interest in the WA group. Additional ROI analyses found a relationship between perfusion surrounding the core lesion and the same neuropsychological measures.

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This study found that core language impairments in chronic WA are associated with a combination of structural lesion and abnormal perfusion in non-lesioned tissue. This indicates that post-stroke impairments are due to a wider disruption of neural function than observable on structural T1w MRI.

1. Introduction

The impact of a neural lesion extends beyond the site at which the lesion occurs (Feeney & Baron, 1986). Cognitive functions are supported through the integration of highly interconnected cortical and subcortical regions and, therefore, lesions to isolated network components can cause widespread dysfunction. As such, accounting for behavioural profile/impairment after stroke requires both the site of lesion as well as the functional status of remaining network components to be considered. In this study we investigate the relationship between stroke damage and the functional potential of wider neural regions in a group of individuals with chronic Wernicke's aphasia (WA) by exploring associations between structural lesion and residual cerebral blood flow (CBF). We further examine the relationship between these imaging profiles and neuropsychological impairment.

Within the first hours of an acute stroke, patients show regions of hypoperfusion, which often extend beyond the limits of the observable structural lesion (Neumann-Haefelin et al., 1999). This hypoperfusion can occur in the form of ischaemic penumbra, surrounding the area of core infarction (Croquelois, Wintermark, Reichhart, Meuli, & Bogousslavsky, 2003), or remote from the area of infarction, termed focal diaschisis (Carrera & Tononi, 2014; Feeney & Baron, 1986). Diaschisis most commonly occurs between cortical and subcortical regions; lesions to subcortical areas lead to cortical dysfunction and cortical lesions can lead to subcortical alterations (Bowler et al., 1995; Feeney & Baron, 1986; Hillis et al., 2002; Price, Warburton, Moore, Frackowiak, & Friston, 2001). Remote cortico–cortico hypoperfusion/hypometabolism is only rarely reported but is mostly transcallosal (Andrews, 1991; Carrera & Tononi, 2014). CBF supplies oxygen and glucose required for neuronal function and is associated with neuronal activity through neurovascular coupling (Girouard & Iadecola, 2006). Therefore, regional hypoperfusion indirectly indicates reduced functional capacity of associated neural tissue. These hypoperfusion patterns in the acute phase indicate that behavioural impairment emerges as a consequence of infarcted tissue and functional depression of intact tissue.

WA is an acquired language impairment which occurs at both the acute and chronic phases following lesions to the left posterior temporal lobe and inferior parietal lobe (Ogar et al., 2011; Robson et al., 2014b). WA is characterised by severely impaired language comprehension and repetition in the context of fluent speech and relatively well preserved mobility. This impairment profile is underpinned by a spectrum of neuropsychological impairments including verbal short term memory (Robson, Sage, & Lambon Ralph, 2012), acoustic (Robson, Grube, Lambon Ralph, Griffiths, & Sage, 2013), phonological (Baker, Blumstein, & Goodglass, 1981) and semantic (Cohen, Kelter, & Woll, 1980; De Renzi, Faglioni, Scotti, & Spinnler, 1972) processing impairments. The WA comprehension impairment at the acute phase has been associated with hypoperfusion of the left posterior superior temporal and inferior parietal regions (Hillis et al., 2001; Jodzio, Gasecki, Drumm, Lass, & Nyka, 2003) with reperfusion of these regions leading to improvements of language comprehension (Hillis et al., 2001). At the chronic stage, *structural* imaging investigations have found similar relationships between structural lesion and language comprehension impairments of the WA type, specifically following lesions to mid-posterior middle temporal areas (Dronkers, Wilkins, Van Valin, Redfern, & Jaeger, 2004).

Hypoperfusion investigations of WA at the chronic stage have not matched those undertaken at the acute phase. This may be because diaschisis and penumbral regions are frequently observed to re-perfuse or evolve to lesion (Binkofski et al., 1996; Butcher et al., 2005; Neumann-Haefelin et al., 1999; Seitz et al., 1999; Toni et al., 1997). There is, however, some limited evidence to suggest that hypoperfusion of structurally intact tissue can occur in chronic stroke (Barber et al., 2001; Brumm et al., 2010; Raynaud et al., 1987) and this has implications for understanding the mechanisms of recovery and source of impairments post-stroke.

In this study we investigated whether hypoperfusion of intact tissue, outside the lesion site, could be identified in chronic WA and explored the relationship between hypoperfusion and a range of neuropsychological symptoms observed in WA. Arterial spin labelling (ASL), a non-invasive measure of CBF, and structural T_1-weighted MRI data were collected in a group of 12 individuals with chronic WA. Statistical analysis used joint independent component analysis (ICA). Joint ICA is a multivariate analysis which combines multiple imaging modalities, enabling patterns across modalities to be detected (Abel, Weiller, Huber, Willmes, & Specht, 2015; Calhoun, Liu, & Adalı, 2009). This analysis enabled the identification of regions of hypoperfusion statistically related to areas of structural lesion. Correlational analyses then investigated the relationship between CBF and lesion distribution and neuropsychological profile.

2. Materials and methods

Ethical approval was provided by the North-West NRES committee, UK. Twelve individuals with Wernicke's aphasia (WA,