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Research Report

Interhemispheric interactions during sentence comprehension in patients with aphasia

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ABSTRACT

Right-hemisphere involvement in language processing following left-hemisphere damage may reflect either compensatory processes, or a release from homotopic transcallosal inhibition, resulting in excessive right-to-left suppression that is maladaptive for language performance. Using fMRI, we assessed inter-hemispheric effective connectivity in fifteen patients with post-stroke aphasia, along with age-matched and younger controls during a sentence comprehension task. Dynamic Causal Modeling was used with four bilateral regions including inferior frontal gyri (IFG) and primary auditory cortices (A1). Despite the presence of lesions, satisfactory model fit was obtained in 9/15 patients. In young controls, the only significant homotopic connection (RA1-LA1), was excitatory, while inhibitory connections emanated from LIFG to both left and right A1's. Interestingly, these connections were also correlated with language comprehension scores in patients. The results for homotopic connections show that excitatory connectivity from RA1-to-LA1 and inhibitory connectivity from LA1-to-RA1 are associated with general auditory verbal comprehension. Moreover, negative correlations were found between sentence comprehension and top-down coupling for both heterotopic (LIFG-to-RA1) and intra-hemispheric (LIFG-to-LA1) connections. These results do not show an emergence of a new compensatory right to left excitation in patients nor do they support the existence of left to right transcallosal suppression in controls. Nevertheless, the correlations with performance in patients are consistent with some aspects of both the compensation model, and the transcallosal suppression account for the role of the RH. Altogether our results suggest that changes to both excitatory and inhibitory homotopic and heterotopic connections due to LH damage may be maladaptive, as they disrupt the normal inter-hemispheric coordination and communication.

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1. Introduction

This study examines the role of interhemispheric connections in recovery from aphasia. One of the most prevalent questions in brain plasticity research considers the involvement of the right hemisphere (RH) in recovery from aphasia and specifically whether it plays a compensatory or maladaptive role in language processing after stroke. This question has clinical implications as well as theoretical significance for the understanding of brain lateralization in healthy individuals, and of mechanisms underlying brain plasticity after unilateral damage.

The adaptive account suggests that increased RH activation in post-stroke patients reflects compensatory recruitment of intact regions homologous to the lesioned areas, facilitating language processing and thus enhancing recovery (Abo et al., 2004; Blasi et al., 2002; Cappa et al., 1997; Winhuisen et al., 2005). In contrast, other studies argue that the RH involvement in language processing in post-stroke patients is maladaptive (Postman-Caucheteux et al., 2010) and is the result of a release from transcallosal lateral inhibition (Heiss et al., 2003; Naeser et al., 2004; Price & Crinion, 2005). According to this view, excitatory activity in the left hemisphere (LH) of the intact brain suppresses homotopic areas in the contralateral hemisphere via transcallosal pathways, resulting in the typical left lateralized pattern of activation in language tasks (Kinsbourne, 1974, pp. 239–259). When the LH is lesioned, transcallosal inhibition on the RH is released, resulting in increased RH activation (Selnes, 2000; Thiel et al., 2006). In turn, this increase in RH activation suppresses homotopic areas in the LH via transcortical inhibition, further interfering with language performance and impeding recovery (Naeser et al., 2004; Price & Crinion, 2005). However, it should be noted that maladaptive involvement of the RH in post-stroke aphasia is not necessarily mediated by direct transcallosal inhibition on LH homotopic regions. A negative effect of RH activity on language performance can also be a result of inefficient processing occurring in the RH and interfering with LH processing through excitatory coupling of both homotopic and heterotopic connections (Chiarello & Maxfield, 1996; Clarke et al., 1993). Therefore, directly measuring interhemispheric connectivity is important for understanding the role of the RH in aphasia recovery. Recently, several studies have measured task-related interhemispheric connectivity in patients with aphasia (Kiran et al., 2015; Meier et al., 2016; Schofield et al., 2012; Teki et al., 2013), and focused on naming tasks or on single word judgment tasks. In contrast to these tasks, which are typically left lateralized, sentence comprehension relies on bilateral activation in healthy individuals (Friederici, 2011; Price, 2010; Vigneau et al., 2011). Differences in lateralization between tasks are very likely to affect the value, strength, and direction of interhemispheric interactions in both healthy and brain damaged individuals (Price & Crinion, 2005). The current study examines interhemispheric connectivity in a sentence comprehension task performed by patients with chronic aphasia, seeking to clarify the role of the RH in language recovery.

Numerous neuroimaging studies show enhanced RH activation during language tasks in patients with aphasia following LH lesions (Abo et al., 2004; Basso et al., 1989; Blank et al., 2003; Buckner et al., 1996; Calvert et al., 2000; Gold & Kertesz, 2000; Ohyama et al., 1996; Rosen et al., 2000; Thulborn et al., 1999). The finding that such RH activation is correlated with better language performance in patients (Abo et al., 2004; Blasi et al., 2002; Cappa et al., 1997; Winhuisen et al., 2005) supports the view that the RH plays a compensatory role in language recovery. Furthermore, it was shown that compensatory changes in RH activation following language therapy in these patients are more likely in RH regions homologous to the LH lesion (Abel et al., 2015).

In contrast to these findings, other neuroimaging studies suggest that recovery-related language reorganization in patients with aphasia occurs only in perilesional areas in the LH, while RH activation during language tasks is an epiphenomenon which does not contribute to performance (Heiss et al., 1997; Rosen et al., 2000; Thiel et al., 2001; Warburton et al., 1999). Moreover findings showing that RH activation is associated with incorrect naming responses in patients with LH lesions suggest that RH activation is not only unnecessary but is actually interfering with language recovery (Fridriksson et al., 2009; Postman-Caucheteux et al., 2010). Other studies suggest that RH activation may play a compensatory role, but may occur in different non-homologous regions, reflecting the use of an alternative cognitive strategy rather than homologous disinhibition. For example, a magnetoencephalography (MEG) study that used a sentence comprehension task showed that although aphasic patients activated RH areas homologous to the temporal lobe region in which lesions predicted comprehension deficits, functional activation was correlated with performance not in that homologous region but rather in bilateral dorsal fronto-parietal regions (Meltzer, Wagage, Ryder, Solomon, & Braun, 2013).

The apparent contradiction between findings supporting the compensatory or the maladaptive accounts may be settled by other explanatory factors such as the time since injury (Fernandez et al., 2004; Saur et al., 2006), the specific RH regions involved (Crosson et al., 2007), or the nature of the tasks used for measuring language recovery (Heiss et al., 2003; Price & Crinion, 2005). Price and Crinion (2005) suggest that RH activation is compensatory in speech comprehension tasks (Sharp et al., 2004), but plays a maladaptive role in speech production tasks (Fernandez et al., 2004; Heiss et al., 1997; Postman-Caucheteux et al., 2010; Rosen et al., 2000; Saur et al., 2006).

Neuroimaging studies using PET and FMRI can only provide correlational findings, so even a negative correlation between RH activation and language recovery across participants does not provide causal evidence for a maladaptive role of the RH. Increased RH involvement may be the consequence of a more severe or extensive LH damage which results in a poor outcome for recovery not directly caused by the RH (Heiss et al., 1997; Karbe et al., 1998). In contrast, numerous transcranial brain stimulation studies in the last decade overcome this weakness by showing a causal effect of RH inhibitory or excitatory stimulation on language function within subjects (Baker et al., 2010; Floel et al., 2008; Monti et al., 2008; Naeser et al., 2005; Sandars et al., 2016; Winhuisen et al., 2005). For example, a meta-analysis of 9 randomized control trials, including 215 patients with post-stroke aphasia, tested the