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Research report

Recovery of orthographic processing after stroke: A longitudinal fMRI study

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ABSTRACT

An intact orthographic processing system is critical for normal reading and spelling. Here we investigate the neural changes associated with impairment and subsequent recovery of the orthographic lexical processing system in an individual with an ischemic left posterior cerebral artery (PCA) stroke. This work describes a longitudinal case study of a patient, whose initials are MMY, with impairments in orthographic lexical processing for reading and spelling at stroke onset, and who recovered these skills within 1 year post stroke. We tested the hypothesis that this acute impairment to reading and spelling would be associated with a selective loss of neural activation in the left fusiform gyrus (FG), and that subsequent recovery would be associated with a gain of neural activation in this region. MMY's case provided a unique opportunity to assess the selectivity of neural changes because she demonstrated a behavioral recovery of naming as well; i.e., if there is neural recovery for reading and spelling, but not naming, then these neural changes are selective to the recovery of orthographic processing. To test our hypothesis, we examined longitudinal behavioral and functional magnetic resonance imaging (fMRI) data of reading, spelling, and visual object naming acquired acutely, 3 weeks, 5 months, and one year post stroke. In confirmation of our hypothesis, the loss and subsequent gain of orthographic lexical processing was associated with up-regulation of neural activation in areas previously associated with orthographic lexical processing: i.e., the left mid-FG and inferior frontal junction (IFJ). Furthermore, these neural changes were found to be selective to orthographic processing, as they were observed for reading and spelling, but not for visual object naming within the left mid-FG. This work shows that left PCA stroke can temporarily and selectively disrupt the orthographic lexical processing system, not only in the posterior region adjacent to the stroke, but also in relatively distant frontal orthographic processing regions.

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1. Introduction

Functional neuroimaging techniques can provide a window into the neural basis of orthography and allow us to track changes in structure–function relationships during recovery after a brain lesion. Thus, functional neuroimaging can be used not only to localize functional activity associated with a particular area, but also through careful analysis to determine whether the absence/presence of a functional activity in a region is associated with specific type of orthographic deficit.

In neurotypical literate adults, the ability to read and write relies on a complex set of interacting cognitive functions. Central to these functions are processes specifically associated with retrieving, maintaining, and expressing orthographic information; these include orthographic lexical, sub-lexical, and working memory functions. In the brain, these central orthographic processes are typically associated with a left hemisphere set of regions including the left inferior frontal gyrus (IFG), intraparietal sulcus (IPS), and fusiform gyrus (FG) (Martin, Schurz, Kronbichler, & Richlan, 2015 for reading; Purcell, Turkeltaub, Eden, & Rapp, 2011 for spelling). Recently, a study of acquired dysgraphia indicates that damage to the left IFG and FG are associated with impairments in orthographic lexical processing in spelling, and damage to the left IPS is associated with impaired orthographic working memory (Rapp, Purcell, Hillis, Capasso, & Miceli, 2015). The left FG in particular has long been studied in the neuroimaging literature and is consistently associated with visual word processing. The left FG has been referred to as the Visual Word Form Area (VWFA), due to: (1) its selective response to visual words in reading as compared to other non-word stimuli (e.g., Cohen et al., 2002; Dehaene & Cohen, 2011); (2) a clear association between activation in this area and development of literacy skills (Dehaene et al., 2010); and (3) an association between focal damage in this area and reading impairments (e.g., Gaillard et al., 2006). Specifically, the left FG has been associated with *orthographic lexical processing* in the neuroimaging literature in both reading (Glezer, Jiang, & Riesenhuber, 2009; Kronbichler et al., 2004; Szwed et al., 2011) and spelling (Rapp & Dufor, 2011; Rapp & Lipka, 2011).

That said, there is some debate regarding the selectivity of the left FG to orthographic lexical processing (for opposing views see Dehaene & Cohen, 2011; Price & Devlin, 2011). A unique perspective on this literature and debate involves an exploration of the neurotopographic changes across time associated with impairment and subsequent recovery of orthographic lexical processing after stroke. Such an investigation would allow for the testing of the hypothesis that transient impairment in orthographic processing in reading and spelling is associated with a transient decrease in activation specifically associated with orthographic tasks (i.e., reading and spelling) in the left FG and possibly other orthographic processing regions.

Although, to date, there is limited work examining written language longitudinally after stroke, there has been some work examining impairments in spoken language acutely. Generally, this previous work has indicated that recovery of language after a stroke involves multiple interacting mechanisms that are operative at different times over the course of recovery and vary across individuals. As such, the recovery of language after stroke is difficult to study, and therefore poorly understood. Some of these mechanisms are considered to include restoration of blood flow, recovery from diaschisis (i.e., impairment due to loss of input from a remote damaged brain area), and functional reorganization of a neural-cognitive system due to neuroplasticity (Jarso et al., 2013). Generally though, recovery of language function after stroke is considered to occur in three phases which occur within approximate time windows within the first year post stroke: acute phase is onset to 2–3 weeks post-stroke, subacute is 2–3 weeks to 4 months, and the chronic phase is greater than 4 months post stroke (Anglade, Thiel, & Ansaldo, 2014; Hillis et al., 2006). It is commonly understood that the bulk of cognitive, motor, or language recovery occurs within the acute and sub-acute phases post stroke (e.g., Kelly-Hayes et al., 1989). With respect to language function, this early post stroke recovery is thought to be primarily associated with a reperfusion of the indirectly damaged brain areas (e.g., Hillis et al., 2006, 2002; Jacquin et al., 2014). Late recovery of language function (i.e., in the chronic phase) is considered to be more marginal and is associated with a less well understood compensatory functional reorganization mechanisms (Anglade et al., 2014).

The functional neuroimaging literature on language recovery post-stroke is complex, and there has been difficulty identifying general principles of neural recovery. Some work suggests that recovery of language functions in aphasia is primarily accompanied by greater perilesional reorganization (e.g., Fridriksson, 2010; Perani et al., 2003; Postman-Caucheteux et al., 2010; Saur et al., 2006; Winhuisen et al., 2007), while other work suggests that good recovery is primarily associated with compensatory right hemisphere recruitment (Abo et al., 2004; Blank, Bird, Turkheimer, & Wise, 2003; Blasi et al., 2002; Turkeltaub et al., 2012). The diversity of these findings could be due to multiple factors such as the time post-stroke, severity of impairment, lesion location/size, and nature of the neural measure (Sebastian & Kiran, 2011). All of these factors may be differentially relevant across cases, and therefore influence recovery trajectories in vastly different manners across individuals.

At present, only a few studies have performed longitudinal functional neuroimaging in language recovery (Heiss, Kessler, Thiel, Ghaemi, & Karbe, 1999; Jarso et al., 2013; Saur et al., 2006; Sebastian et al., 2016). Heiss et al. (1999) examined patients with aphasia at 2 and 8 weeks post-stroke and reported that good recovery of language function may only be achieved if the language areas are preserved (but temporarily inactivated) and can subsequently be reintegrated into the original language network. Saur et al. (2006) used functional magnetic resonance imaging (fMRI) to examine the longitudinal reorganization in the language system after a stroke from the acute stage to the chronic stage. Saur et al. proposed that good recovery from aphasia is acutely associated with minimal activation, followed by an upregulation of the right homologue of language areas in the subacute phase, and finally a re-normalization shift back to the left hemisphere in the chronic phase. This previous work has focused primarily on the loss and recovery of spoken language. Only a nominal amount of work has examined the loss and recovery of orthographic