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Functional network architecture of reading-related regions across development

Alecia C. Vogel [a,*], Jessica A. Church [a], Jonathan D. Power [a], Fran M. Miezin [a,b], Steven E. Petersen [a,b,c,d], Bradley L. Schlaggar [a,b,c,e]

[a] *Dept. of Neurology, Washington University School of Medicine, St. Louis, MO, United States*
[b] *Dept. of Radiology, Washington University School of Medicine, St. Louis, MO, United States*
[c] *Dept. of Anatomy and Neurobiology, Washington University School of Medicine, St. Louis, MO, United States*
[d] *Dept. of Psychology, Washington University in St. Louis, St. Louis, MO, United States*
[e] *Dept. of Pediatrics, Washington University School of Medicine, St. Louis, MO, United States*

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ABSTRACT

Reading requires coordinated neural processing across a large number of brain regions. Studying relationships between reading-related regions informs the specificity of information processing performed in each region. Here, regions of interest were defined from a meta-analysis of reading studies, including a developmental study. Relationships between regions were defined as temporal correlations in spontaneous fMRI signal; i.e., resting state functional connectivity MRI (RSFC). Graph theory based network analysis defined the community structure of the "reading-related" regions. Regions sorted into previously defined communities, such as the fronto-parietal and cingulo-opercular control networks, and the default mode network. This structure was similar in children, and no apparent "reading" community was defined in any age group. These results argue against regions, or sets of regions, being specific or preferential for reading, instead indicating that regions used in reading are also used in a number of other tasks.

1. Introduction

Reading, as with many advanced human behaviors, is a complicated skill requiring the integrated functioning of a network of brain regions (Schlaggar & Church, 2009; Schlaggar & McCandliss, 2007). Several meta-analyses of functional MRI (fMRI) neuroimaging studies have attempted to define regional components of a reading network (Fiez & Petersen, 1998; Jobard, Crivello, & Tzourio-Mazoyer, 2003; Turkeltaub, Eden, Jones, & Zeffiro, 2002; Vigneau et al., 2006). Together these meta-analyses have described a group of generally left hemisphere brain regions consistently used in single word reading tasks. One such region, the visual word form area (VWFA, Cohen & Dehaene, 2004) is in the fusiform cortex near the occipital–temporal border. The VWFA has been reported to show more activity for words than consonant strings (McCandliss, Cohen, & Dehaene, 2003; Vinckier et al., 2007) and digits (Polk et al., 2002), though its specificity for processing words (and nonwords) is debated (see Dehaene & Cohen, 2011; Price & Devlin, 2003, 2011; Vogel, Petersen, & Schlaggar, 2012). The meta-analyses have also identified regions in the supramarginal gyrus (SMG), angular gyrus (AG), and middle temporal gyrus (MTG) as important for reading. Single studies have implicated regions in the SMG in phonological processing (Church, Balota, Petersen, & Schlaggar, 2011; Church, Coalson, Lugar, Petersen, & Schlaggar, 2008; Graves, Desai, Humphries, Seidenberg, & Binder, 2010) and the AG and MTG as possibly involved in semantic processing (Chou et al., 2006; Graves et al., 2010). Finally, regions in the inferior frontal gyrus (IFG), most commonly localized to the pars opercularis, have been identified as important in phonological processing (Fiez, Balota, Raichle, & Petersen, 1999; Gitelman, Nobre, Sonty, Parrish, & Mesulam, 2005; Mechelli, Gorno-Tempini, & Price, 2003; Pugh et al., 1996).

As has been argued elsewhere (e.g., Schlaggar & McCandliss, 2007), reading is a phylogenetically new skill, and it is unclear whether reading-related regions become dedicated to reading, or whether they serve more general processing demands. For example, a region that is used for orthographic (visual) processing of words could be dedicated to the visual analysis of words and letters, or it could be used more generally in the processing of words, objects, abstract shapes, etc. Although functional neuroimaging studies have converged on a general set of brain regions used during reading, it is not yet known whether reading related regions relate specifically to one another (consistent with dedication to reading), or whether reading regions are more closely related to non-reading regions (and are therefore likely to perform more general functions and not be specifically dedicated to reading).

A large and expanding literature suggests that functionally related brain regions tend to demonstrate high and specific correlations in spontaneous activity that are reflected in resting state

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* Corresponding author. Address: Petersen and Schlaggar Labs, Washington University School of Medicine, Box 8111, 660 South Euclid Ave., St. Louis, MO 63110, United States. Fax: +1 314 362 2186.

E-mail address: vogela@wustl.edu (A.C. Vogel).

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functional connectivity MRI (RSFC) (e.g., specific and high correlations within the visual system, auditory system, dorsal attention system, etc. (Biswal, Yetkin, Haughton, & Hyde, 1995; Dosenbach et al., 2007; Fox et al., 2005; Greicius, Krasnow, Reiss, & Menon, 2003; Lowe, Mock, & Sorensen, 1998)). RSFC seems to reflect a long history of coactivation across a large range of tasks and time (Bullmore & Sporns, 2009; Dosenbach et al., 2007;Fair et al., 2007; Fox & Raichle, 2007; Power et al., 2011; Vogel, Miezin, Petersen, & Schlaggar, 2011). RSFC has been used to characterize the network structure of regions across the brain. A primary result has been the classification of regions across the brain into groupings of regions with high correlations (these groupings are called communities, modules, sub-networks, or clusters in network analyses) (Power et al., 2011). The defined communities include many groupings of regions recognizable from prior functional imaging studies, such as selective groupings of default mode, front-parietal control, dorsal attention, ventral attention, motor, and visual regions (Power et al., 2011; Yeo et al., 2011). Given the idea that RSFC reflects a history of coactivation, the aforementioned reading regions, if they are used specifically or even predominantly in reading, should be closely related to one another using RSFC measures. Such close relationships would occur because the reading regions described above should be activated together almost always and rarely activated with other, disparate groups of regions. If, on the other hand, the reading regions described above are involved in reading, but reading is not their only, or even predominant, function, these regions will not necessarily be more related to one another than to more general use regions. The lack of a "reading network" will arise because these regions will be occasionally activated together, but more often each individual region will be activated with other, disparate, groups of regions. In this case each "reading region" will have closer RSFC relationships with whichever set of regions with which it is most commonly coactivated.

Of note, no dedicated "reading community" was seen in previous whole brain analyses (Power et al., 2011; Yeo et al., 2011). Instead, reading-related regions were dispersed among many different communities (dorsal attention, fronto-parietal, cingulo-opercular, etc.). These analyses included hundreds of brain regions, or the entire cortex, indicating that the lack of a reading community was not because reading-related regions were inadequately sampled. The lack of a reading community suggests that the strongest relationships of reading-related regions are not to one another but to other regions. However, there remains a possibility that a reading community was not found for methodological reasons. For example, algorithms have known difficulties finding small communities amidst larger communities (Fortunato, 2010), and perhaps a small reading community was difficult to define in a whole-brain context. Another way of stating this is that many strong relationships to a large community could overshadow equally strong relations among a smaller group of reading regions.

Here, in contrast to Yeo et al. (2011) and Power et al. (2011), we include for analysis only regions derived from a large set of single word reading-related tasks (see below), with the intent of providing the highest probability of finding a dedicated reading community. Importantly, the defined region set includes regions thought to be relatively specific for reading that have been derived from other meta-analyses. Accordingly, in this paper we examine the functional relationships of reading regions for evidence distinguishing between the hypotheses: (1) the reading regions described above are used predominantly in reading and thus will form a distinct and separate community demonstrable through graph analytic techniques, or (2) the reading regions described above are used in a large number of tasks outside of reading and, as a result, do not form a distinct community but are integrated into communities such as those found in prior large scale network analyses (Power et al., 2011; Yeo et al., 2011), reflective of each region's predominant function.

1.1. A large, distributed group of regions is used in single word reading

To determine the network structure of reading-related regions we must first define what will constitute a reading-related region. The aforementioned meta-analyses (Fiez & Petersen, 1998; Jobard et al., 2003; Turkeltaub et al., 2002; Vigneau et al., 2006) focused on regions identified by comparing reading to another task in an attempt to avoid identifying more "task general" processing. However, studies designed to identify all regions showing activity different from a baseline estimate or rest condition during a reading task find many more regions (Binder, Medler, Desai, Conant, & Liebenthal, 2005; Brown et al., 2005; Church et al., 2011; Graves et al., 2010). This abundance of regions with differential activity reflects the use of a number of different processes in reading. Visual, phonologic, semantic, and spatial processing (to appropriately direct visual attention to words or parts of words) are necessary for reading in general, whereas articulatory and motor output processing are necessary for reading aloud. Essential but non-specific task control processes to instantiate and maintain the reading task set and to evaluate performance are also part of reading. As we are interested in the network structure of all regions used in the conversion of written, visual input into spoken output, we have performed a meta-analysis of five single word reading aloud studies (some previously published in Brown et al., 2005; Church et al., 2011) and have included all regions with BOLD activity significantly different from baseline in a majority of the studies in our analysis. This approach allows us to test the hypotheses proposed above and to determine whether a large set of reading-related regions, including reading-predominant or reading-specific regions found in previous meta-analyses:

(1) form a discrete community (or sub-communities) dedicated to reading (or a sub-component thereof such as phonological or semantic processing), consistent with the idea that those regions are used predominantly in reading, or
(2) are integrated into other general use communities, as described in Yeo et al. (2011) and Power et al. (2011), consistent with the idea that they have more general functions that dominate their overall community relationships.

Additionally, while there is obvious interest in the network structure of reading-related regions in adults, this organization may well undergo developmental changes. Acquiring fluent reading requires considerable instruction and experience (see Schlaggar & McCandliss, 2007, for a review). Also, children show different functional activity for reading than do adults in both ERP (Brem et al., 2010; Maurer, Brem, Bucher, & Brandeis, 2005; Tarkiainen, Helenius, Hansen, Cornelissen, & Salmelin, 1999) and fMRI studies (Booth et al., 2004; Brem et al., 2010; Brown et al., 2005; Church et al., 2008; Puce, Allison, Asgari, Gore, & McCarthy, 1996; Schlaggar, Brown, Lugar, & Visscher, 2002). Therefore, studying the network structure across development may give additional insight into the organization of reading-related regions and possible age- or skill-related increases in skill specificity. For example, if regions were used preferentially for reading, we might expect to see the emergence of a reading community across development. However, studying the developing network structure requires a set of regions used for single word reading in both children and adults. Thus, as will be described further below, we added regions showing differential BOLD activity between children and adults in a reading fMRI study (Church et al., 2008) to our meta-analytic reading set.