Title:

Left Hemispheric Gray Matter and Naming Task Performances in Chronic Left Hemisphere Stroke

Abstract:

In spite of continued research, the precise neural mechanisms underlying the recovery of language following left hemisphere strokes remain unclear. Scientific literature in this particular domain is strikingly inconsistent, particularly with regards to the role of the right hemisphere during recovery. While older evidence suggested that right hemispheric regions are compensatory in nature during recovery, another prevailing theory today contends that this same activity is insignificant or maladaptive. To offer insight into this contentious debate, our lab recently employed support vector regression-based lesion symptom mapping and voxel-based morphometry to determine whether grey matter volume in the right hemisphere contributes to aphasia outcomes following stroke. The current study extends this research to explore the relationship between written and oral naming tasks and brain structure. In contrast to the prior study, which implicated right hemisphere areas in recovery of speech, we found here that the gray matter structure of the left hippocampus, and middle and inferior temporal gyri relate to outcomes in written naming. Furthermore, no statistically significant associations were found for oral naming or the difference between the two naming tasks anywhere in the brain. These results indicate that recovery of written naming relies on different brain structures than speech production, specifically areas of the left hemisphere involved in memory and semantic knowledge. Going forward, more research must be done to unravel the mechanisms underlying language recovery following left-hemispheric stroke.

Introduction:

Aphasia is a broad term that encompasses deficits in language production and comprehension. While it can arise from progressive neurological disorders, brain tumors, or traumatic brain injury, aphasia most often manifests following stroke in the left hemisphere. Approximately one in three stroke survivors exhibit symptoms of aphasia, with two-thirds of this population never regaining their language faculties prior to their stroke. As such, just over twenty percent of stroke survivors have chronic aphasia: a crippling disability that diminishes quality of life by disrupting an individual's ability to communicate. The precise manifestation of aphasia drastically varies depending upon the nature of the stroke and may generate different kinds of linguistic deficits.

Agraphia is an acquired impairment in some aspect of an individual's ability to generate graphomotor visual representations of language through the use of an orthographic system that corresponds to the phonological form of a spoken language. Writing, like other language functions, is a complex cognitive function, although it may be subdivided into four distinct components: linguistic content, spelling of individual words, visuospatial organization of graphic symbols, and motoric components of handwriting. Since components that participate in writing are shared by other cognitive functions, agraphia is almost invariably accompanied by other disorders like alexia, apraxia, and agnosia. Discovering isolated deficits in the latter exclusively was once speculated to be impossible, as it was never observed in practice. Indeed, it was not until 1884 that Albert Pitres first published a case study that qualified as an example of pure agraphia: an individual who could speak, read, spell aloud, but not write letters or words spontaneously. From that point onward, clinicians surmised that significant dissociations exist between the expression of speech and the production of written language.

Neurologists in the late nineteenth century theorized the existence of a writing center in the brain analogous to Broca's area for speech. Models from this period often localized written language to the second frontal convolution, although Dejerine and others in the field rejected these notions. Subsequent investigations of language in the twentieth century seemed to support this idea, with agraphic disturbances being associated with damage in disparate areas of the brain. These findings contrast with other forms of aphasia like alexia without agraphia, which is characterized by the inability to read while demonstrating a normal capacity for writing. Alexia without agraphia is associated with distinct lesions in the dominant occipital lobe or to the lateral geniculate body and splenium of corpus callosum. In contrast, agraphia without alexia is linked to lesions across the left hemisphere. Implicated areas include, but may not be limited to, Exner's area (a region superior to Broca's area in left frontal cortex), the superior parietal lobe, as well as posterior perisylvian regions.

A recent meta-analysis of functional neuroimaging studies concluded that a minimum of twelve areas of the brain participate in writing. Of the implicated cortical and subcortical regions, it identified three as writing specific: the left superior frontal sulcus/middle frontal gyrus, left intraparietal sulcus/superior parietal area, and right cerebellum. Areas associated with general linguistic processes, including writing, included the ventral premotor cortex and posterior and

inferior temporal cortex. Another previous meta-analysis conducted two years prior uncovered similar results and linked written word production to the left inferior temporal and fusiform gyri, left inferior frontal gyrus, as well as the left posterior intraparietal sulcus. While these studies offer novel insights into the cognitive processes underlying writing, the scientific study of agraphia remains relatively understudied and therefore poorly understood. This study endeavors to continue research into the cerebral substrates responsible for this skill. A better understanding of how writing works in the brain should facilitate the development of more effective treatments for individuals with this form of aphasia.

Deficits in speech production and comprehension are also canonically associated with damage to areas of the brain localized to the left hemisphere. In individuals with aphasia, anomia is a particularly pervasive condition characterized by an inability to orally identify an object by its name after seeing it. Curiously, one common feature of anomia is that the inability to say the desired word does not signify that the associated concepts are lost from memory. People with anomia may identify an object by pointing to a visual representation of it or successfully produce the right name if primed with the initial phonemes of the word. Rather than being eradicated from a person's vocabulary, words are inaccessible to patients. This failure to fluently communicate in discourse is a source of extraordinary consternation for patients with aphasia, and a comprehensive explanation for this phenomenon still remains unfound.

Naming failures in anomia are extraordinarily diverse and presumably implicate different areas of the brain depending upon the precise deficit. Some patients with anomia have an inability to find the articulatory position for a word, whereas others will produce an off-target word when prompted to identify a given object. Other anomic individuals will substitute approximations for a required word, with these patients often being cognizant that their word selection is incorrect. Interestingly, a subset of aphasiacs with anomia can also supply a desired word through phonological priming, while others are hardly assisted by auditory cues. Clinicians have also noticed recurring trends in patients with anomia, particularly in the classes of words and concepts that are accessible. Some subjects in aphasia studies can identify colors readily but fail to name objects that are shown to them. Fascinatingly, others can name an object when it is described, but struggle immensely or fail entirely to do so if the entity is placed in front of them.

Another salient characteristic of anomia is the differential impairment of noun and verb production. This dissociation differs drastically, with nouns being relatively sparse in the speech of anomic aphasiacs. In stark contrast, agrammatic patients with Broca's aphasia will exhibit an aptitude for nouns while struggling to produce verbs necessary to link subjects with their predicates. Since differences in competence arise repeatedly in aphasic patients, it has been hypothesized that nouns and verbs are organized in different lexicons that are spatially distinct and hence separately impaired. Like semantic neighborhoods, in which certain ideas are grouped based on similarity, words may be clustered by their syntactic functions. Considering the complexity of this neural network, it is likely that oral naming capabilities are as diffuse as the regions participating in written naming, which tend to be localized to regions of the left hemisphere. That being said, recent findings also suggest roles for the right hemisphere in language processing.

In the scientific literature, there is significant disagreement over the brain basis of aphasia recovery. Much of the controversy in the domain centers on the role of the right hemisphere, along with identifying which brain regions are responsible for improved language outcomes following stroke. Multiple studies seem to suggest the right hemisphere is maladaptive during recovery, as their findings show that recruitment of right hemisphere cortex peaks early in recovery and diminishes over time as language capabilities improve. Transcranial magnetic stimulation studies support this hypothesis by demonstrating that controlled inhibition of the right inferior frontal gyrus improves language functions. Other studies, in contrast, reject the notion of right hemispheric recruitment as a source of interference. One compelling line of evidence comes from Yarnell et al., who first established an association between severe outcomes in aphasia and right hemisphere strokes. Another study strengthening this hypothesis demonstrated a worsening of language in aphasia patients following right carotid anesthesia. As previously noted by Xing et al., these older sources of evidence lacked fine spatial resolution to definitively implicate specific areas of the right hemisphere, but they collectively suggest that the areas are compensatory in nature following stroke. That said, the right hemisphere does not operate in isolation; several lines of evidence corroborate the notion that perilesional sites in left hemisphere language zones are activated and contribute to improved language outcomes.

In the present study, we addressed whether language outcomes in chronic left-hemisphere stroke relate to gray matter volume in brain regions spared by stroke damage. To achieve this objective, we

used support vector regression-based multivariate lesion-symptom mapping (SVR-LSM) to first identify critical left hemisphere areas for language functions. With this information, we calculated the amount of damage suffered in these areas for each stroke survivor. This value, the percentage of critical area damaged (PCAD), coupled with lesion size and demographic factors, were then used to predict written and oral naming scores on the Philadelphia Naming Test (PNT). Finally, we used voxel-based morphometry (VBM) to assess whether gray matter volume of unharmed brain tissue contributes to language outcomes independent of PCAD, lesion size, and demographic factors.