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Short Communication

The neuroanatomy of pure apraxia of speech in stroke

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ABSTRACT

The left insula or Broca's area have been proposed as the neuroanatomical correlate for apraxia of speech (AOS) based on studies of patients with both AOS and aphasia due to stroke. Studies of neurodegenerative AOS suggest the premotor area and the supplementary motor areas as the anatomical correlates. The study objective was to determine the common infarction area in patients with pure AOS due to stroke. Patients with AOS and no or equivocal aphasia due to ischemic stroke were identified through a pre-existing database. Seven subjects were identified. Five had pure AOS, and two had equivocal aphasia. MRI lesion analysis revealed maximal overlap spanning the left premotor and motor cortices. While both neurodegenerative AOS and stroke induced pure AOS involve the premotor cortex, further studies are needed to establish whether stroke-induced AOS and neurodegenerative AOS share a common anatomic substrate.

1. Introduction

Apraxia of speech (AOS) is a motor speech disorder characterized by slow speech rate, segmentation of syllables, sound distortions, distorted substitutions, trial-and error articulatory movements, and increased difficulty with increased length and complexity of utterances (Duffy, 2013). Although AOS is frequently grouped under the heading of aphasia, the two disorders are clinically distinguishable even though they frequently co-occur. Numerous synonyms for AOS exist including verbal apraxia, phonetic disintegration syndrome, and aphemia, adding to the confusion (Duffy, 2013).

The neuroanatomical correlates of AOS are controversial. In neurodegenerative disease, atrophy in premotor and supplementary motor cortices correlate with AOS (Josephs et al., 2006). Case reports of AOS due to stroke implicate Broca's area, the precentral gyrus or the insula (Schiff, Alexander, Naeser, & Galaburda, 1983; Shuren, 1993). Few larger studies have addressed the neuroanatomy of AOS in stroke. The insula was implicated in two studies with larger lesions corresponding to more severe apraxia (Dronkers, 1996; Ogar et al., 2006). The premotor region has been implicated in lesions with pure AOS, although these findings should be interpreted with caution because the study was a post hoc analysis of prior MRI lesion studies (Robin, Jacks, & Ramage, 2007). Another study, which took into account the relative vulnerability of the insula to middle cerebral artery thrombosis, concluded that the left posterior inferior frontal gyrus (Broca's area) was the neuroanatomical correlate of AOS (Hillis et al., 2004). The finding of Broca's area as the anatomical correlate for AOS were replicated in a large high-resolution structural and perfusion MRI study (Richardson, Fillmore, Rorden, Lapointe, & Fridriksson, 2012). Perfusion imaging can demonstrate areas outside the diffusion weighted abnormality identifying areas which are dysfunctional but eventually survive the ischemic insult. Therefore, studies which include only traditional MRI or CT scans may miss areas that were dysfunctional but subsequently recovered. Prior work has shown that Broca's area can be hypoperfused but not infarcted in some patients with apraxia of speech (Hillis et al., 2004).

Subjects with pure AOS due to stroke are rare because the commonest cause of AOS, middle cerebral artery infarction, often results in aphasia. Investigators have reported different neuroanatomical localizations of AOS because of different study designs (e.g. lesion analysis, perfusion-weighted imaging), different patient populations investigated (acute AOS, chronic AOS), the common co-occurrence between aphasia and AOS, and the possibility that more than one region is responsible for motor speech programming. The present study attempts to address the third issue (i.e. co-occurrence of aphasia with AOS) by studying participants with AOS but not aphasia. The area of infarction in patients with AOS but without aphasia

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may be smaller than AOS with aphasia and allow for more precise identification of the area or areas of the brain crucial to (or sufficient for) the development of AOS. Our objective was to determine the common area of infarction in patients with AOS with equivocal or absent aphasia.

2. Material and methods

2.1. Patients

All stroke patients who underwent evaluation by a speech-language pathologist between January 1st, 1998 and February 1st, 2012 were identified through a database kept by the speech-language pathologists. We identified a subgroup of patients with AOS from ischemic stroke. From these, by chart review, we identified those with "pure" apraxia of speech (i.e. absent or equivocal aphasia). Patients with hemorrhagic strokes were excluded.

2.2. Speech and language testing

AOS diagnosis was based on the presence of the perceptual features of the disorder described in the Introduction and summarized in Table 1; these diagnostic features are consistent with those described in the literature (Duffy, 2013). AOS and aphasia diagnoses were determined by one of two speech-language pathologists (JRD and EAS) who examined each patient with a speech and language protocol designed to elicit features of aphasia (e.g., spoken or written language comprehension errors; semantic or phonologic errors; word retrieval delays or reduced rapid word retrieval; grammatical errors, spelling errors) and AOS, including picture description, word and sentence repetition, comprehension of language, naming and writing. Prior studies have established reliability in determining AOS between these examiners (Josephs et al., 2006). All patients consented to the use of their clinical records for the purpose of research and the study was approved by the Mayo Clinic IRB.

2.3. Neuroimaging methods

The brain magnetic resonance imaging (MRI) studies performed closest to the time of the infarction were used for the lesion analysis (range: 1–10 days). The MRI scanners and acquisition parameters varied widely across the 14 years surveyed in this analysis commensurate with the clinical workflow in place at the time of the individual study's acquisition. Field of view ranged from 20 to 22 cm with an in-plain matrix of 256 × 256 and slice thicknesses ranging from 4 to 5 mm. Field strength varied from 1.5-3T. With this protocol variability and the small number of subjects identified with pure AOS, a detailed morphometric analysis would not provide valid results. However, given the well circumscribed lesions identified in patients presenting with pure AOS, the data were well suited to be subjected to a lesion tracing analysis focusing on the frequency of involvement of large-scale functional brain areas.

There are several circumstances in which large functional regions of interest may be preferred rather than analyzing on a millimeter-scale. One of the most common rationales for such an approach is avoiding type I error by limiting the multiple comparisons problem. Another common rational is to reduce type II error by using a priori anatomic and functional information (e.g. Brodmann's areas) to increase the sensitivity of the analysis to identify large-scale functional brain regions at the expense of millimeter level resolution. In addition, given that the information processing units in the brain span multiple spatial scales (e.g. neuron, column, circuit, and large-scale systems of brain areas), it is important to consider the scale of observation that is best suited to the available data and the scientific question under consideration. In this study, we aim to investigate the lesional disruption of the large-scale motor-language network at the spatial resolution of large-scale functional brain areas.

The T2 weighted sequences were reoriented, normalized and resampled to the resolution of the SPM8 T2 template using the unified segmentation and normalization procedure in SPM8. All resampled and normalized images were visually inspected and confirmed to have undergone high quality normalization. Each subject's lesion was then manually traced using the MRIcron software package (Rorden & Brett, 2000). Lesion location was verified with diffusion weighted images when available. The Brodmann's areas (BA) template available within the MRIcron software package was used to identify the location of maximal lesion overlap and regional topographic frequency of lesion occurrence. The regional topographic frequency was defined as the number of lesions located within a functional brain region (BA) relative to the number of lesions examined ($n = 7$).

3. Results

3.1. Patient characteristics

Seven patients met entry criteria, median age 68 (range: 49–72). Two had mild right upper extremity weakness, and two had mild right facial weakness; neurological examinations were otherwise unremarkable. Patients were evaluated at a median of 3 days after stroke (range: 1–17 days) by a speech-language pathologist. Language and AOS features for each patient are summarized (Table 1). No patients had non-verbal oral apraxia or significant dysarthria. Five had "pure" AOS, while two had AOS and equivocal evidence of aphasia. In patient 1, aphasia was considered equivocally present based on reduced rapid word retrieval and written

Table 1
Speech and language characteristics in each patient.

Case number	Slow rate	Distorted substitutions	Vowel distortions	Increased sound errors with increased complexity	Segmentation of words and/or syllables	Self-correction of sound level errors	Articulatory groping	Verbal comprehension errors	Naming (semantic or phonemic paraphasias)	Reading comprehension errors	Writing errors (spelling, semantic or grammatic)	Word retrieval delays
1	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Normal	Normal	Normal	[a]Abnormal	Occasional
2	Yes	Yes	Yes	Yes	Yes	Yes	No	Normal	Normal	Normal	[b]Abnormal	None
3	Yes	Yes	Yes	Yes	Yes	No	No	Normal	Normal	Normal	Normal	None
4	Yes	Yes	Yes	No	Yes	No	Yes	Normal	Normal	Normal	Normal	None
5	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Normal	Normal	Normal	Normal	None
6	Yes	Yes	Yes	No	No	Yes	Yes	Normal	Normal	Normal	Not tested	None
7	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Normal	Normal	Normal	Normal	None

[a] Self-generated writing was normal, but written sentences to dictation contained spelling errors (e.g., plese/please).
[b] Normal to dictation, some mild difficulty starting self-generated sentence.