Chronic Apraxia of Speech and "Broca's Area"

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Abstract

Background and Purpose—Apraxia of speech (AOS) is an impairment of motor planning and programming of speech articulation, and is often considered an important stroke syndrome, localizable to Broca's area. However, an influential study shed doubt on this localization, and reported that AOS is attributable to lesions of the anterior insula, based on an association between chronic AOS and anterior insula lesions. We hypothesized that chronic AOS is associated with large lesions (which include the insula) or lesions to Broca's area.

Method—We tested 34 participants with chronic left supratentorial stroke on an AOS battery and obtained concurrent MRI. We evaluated associations between AOS and locations and volume of infarct.

Results—The presence of chronic AOS (n=17) was associated with volume of infarct, but was also associated with infarct in Broca's area (and several other regions, but not anterior insula) in both volume-adjusted and age-adjusted linear regression and the dichotomous analysis. Carotid dissection was more common, and cardioembolism less common, as a cause of stroke in patients with AOS compared those without. Severity of AOS was also strongly associated with lesion volume.

Conclusions—Persistence of AOS after twelve months is associated with large left hemispheric stroke and strokes that involve Broca's area or other relatively anterior areas to which it is structurally and/or functionally connected. Patients with such lesions may benefit from early training in the use of technologies to support speech production and communication.

Keywords

Apraxia of speech; Broca's area; Stroke syndrome; [45] Acute Stroke Syndromes; [46] Behavioral Changes and Stroke

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Broca's area has long been thought to be important for orchestration of speech articulation. Localization of speech articulation to the posterior inferior frontal cortex by Paul Broca in the early 1860's was one of the earliest localizations of cortical functions[1] and has had a greater and more lasting impact on our thinking about localization of higher level function

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than almost any other lesion-deficit association study[2]. Disproportionately impaired orchestration of speech articulation has also long been an important vascular syndrome. Mohr et al.[3] reported that lesions to Broca's area give rise to "mutism that is replaced by rapidly improving dyspraxic and effortful articulation." This clinical syndrome of dyspraxic and effortful articulation – often called "apraxia of speech" (AOS) -- is thought by many to be an impairment in motor planning or motor programming,[4] although others have raised the possibility that it could be due to an impairment in holding the sequence of phonemes in a short-term store while the phonemes are articulated[5]. Norman Geschwind did not believe in the existence of AOS, as he considered apraxia to be a disconnection syndrome that excluded midline structures[6]. Most often AOS is diagnosed using specified clinical criteria. For example, widely recognized criteria for AOS include:

1. effortful trial and error groping with attempts at self-correction;

2. persistent dysprosody (abnormal rhythm, stress, and intonation);

3. articulatory inconsistency on repeated productions of the same utterance;

4. obvious difficulty initiating utterances.[7]

There has been less agreement between clinicians and investigators how many of these criteria must be fulfilled to "diagnose" AOS, although the more criteria the patient meets, the more confident the clinician can be that the patient has AOS. These criteria are applied because the syndrome can be difficult to distinguish from dysarthria (an impairment in speech articulation due to impaired rate, range, strength, or coordination of the muscles of articulation, phonation, and respiration) and phonemic or literal paraphasias (phoneme substitutions of which the aphasic patient is generally unaware). There has been only one attempt (of which the authors are aware) to formalize and quantify these criteria for AOS into a standardized and published battery, the Apraxia Battery for Adults[8].

This common stroke symptom of AOS is thought to suggest a clot in the superior division of the left middle cerebral artery (MCA) or one of its branches[9]. However, an influential study attributed AOS to lesions of the anterior insula[10] (see also references 11 and 12), which would implicate a clot in the MCA stem. While an association between chronic AOS and lesions in the anterior insula clearly seems to exist, we have previously raised the possibility that this association might be accounted for by the facts that (1) AOS generally only persists beyond one year in cases of large MCA strokes, and (2) large middle cerebral artery strokes nearly always (in 94% of cases) involve the insula[13]. In a previously reported study we tested this hypothesis by testing patients with acute stroke (within 24 hours of onset) with and without insular damage, reasoning that if insular damage causes AOS, it should do so (at least) at the acute stage, even if the patients subsequently recover[14]. In patients who were tested within 24 hours of stroke onset we found no association between AOS and infarct (on Diffusion Weighted Imaging) or hypoperfusion (on perfusion weighted imaging) in the insula, or more specifically in the anterior insula[14], but we did find an association between AOS and acute infarct in Broca's area (Brodmann's area – BA – 44 and 45). However, we did not test chronic patients in that study. It is possible that the insula is essential for *recovery* from AOS, such that damage to the insula is associated with chronic AOS, independently of volume of infarct, and independently of damage to other areas of the left hemisphere. However, we expect that recovery of AOS would also be predicted by damage to left BA 44, 45, and lesion volume; because it seems likely that either BA 44/45 or one of the surrounding areas (e.g. anterior insula) might be essential for recovery of motor planning of fluent, well-articulated speech articulation. Large lesions that include both BA 44/45 and anterior insula, as well as other surrounding areas, may be the least likely to be associated with recovery from AOS because there is no nearby area to assume the function of damaged Broca's area (BA 44/45). In this paper we tested the hypothesis that chronic AOS is

associated with damage to BA 44 and 45 and the anterior insula, and also with lesion volume, but not independently of one another. If confirmed, the clinical implication is that patients with large lesions that involve these regions may be expected to have persistent AOS, and may benefit from introducing technologies to support speech production early in the course of rehabilitation.

Methods

Participants

We included a series of 34 adults from our database who were tested at least 12 months post onset of left supratentorial ischemic stroke with the Apraxia Battery for Adults II and had concurrent MRI. Additional inclusion criteria: proficient speaker of English, right handed, no previous neurological disease (including stroke), no uncorrected hearing or visual loss. The mean time post onset of symptoms was 19.1 months (sd = 16.1; range: 12–73). Nineteen (56%) were women. The mean age was 59.8 (sd = 14.7; range= 20–79 years). The mean education was 13.8 (sd 3.3; range= 9–25 years). All patients had some residual aphasia on standard language testing (the Western Aphasia Battery[15] and/or the Boston Diagnostic Aphasia Battery[16]). All were receiving or had received speech language pathology services. We were not able to control the quantity and type of rehabilitation.

Assessment of Apraxia of Speech

Apraxia Battery for Adults II[8] was administered to each participant. We used four subtests: Increasing Word Length, parts A and B (which scores the deterioration in performance with increasing word and phrase length; a higher score indicates greater deterioration with increased length or more severe apraxia), Repeated Trials (which scores errors in the repetition of the same polysyllabic word; incorrect words are subtracted from 30 possible points, so lower scores indicate more severe apraxia), and Inventory of Articulation Characteristics of Apraxia (which scores characteristics of AOS observed during spontaneous speech, reading, and automatic speech; higher scores indicate more characteristics of AOS). Tests were scored by an examiner blinded to the site of lesion. Audiofiles of the patients were reviewed by a second examiner (AH, who is both a behavioral neurologist and an experienced speech-language pathologist trained in recognition of AOS) for reliability measures. There was 90% point-to-point percent agreement on scores. Disagreement was settled by consensus.

We created a dichotomous variable for AOS, using all four subtests. If the participant had a score of 5 on the subtest of Inventory of Articulation, and either of the following: a score of <30 on the subtest Repeated Trials, or a score of 2 on either subtest of Words of Increasing Length, Part A or B, they were scored as having AOS on this measure.

Imaging

MRI scans (Fluid Attenuation Inversion Recovery, or FLAIR sequences) were analyzed by a technician masked to AOS results for presence or absence of ischemia in each of 11 Brodmann's areas (BA), using a published template[17] as well as the anterior and posterior insula (defined by the central sulcus of the insula). A second technician also rated the scans for inter-rater reliability. There was 95% point-to-point inter-rater agreement on the presence or absence of ischemia in each BA. When there was disagreement, a senior investigator (AH) served as a tie-breaker. The technician also conducted volumetric analysis on each MRI. Lesions were traced on T2 in ImageJ on each slice, then multiplied by the slice thickness, and the volume of infarct on each slice was added for the total volume of infarct. Volumes were recorded in cc.

Statistical Analysis

We identified associations between impaired performance on the AOS measures and presence of infarct in regions of interest as well as lesion volumes using age-adjusted linear regression models. We also evaluated the association between AOS and areas of infarct as dichotomous variables using chi square tests. Finally, we also evaluated the association between severity of AOS and volume of infarct using linear regression.

Results

A total of 17 patients had AOS using the Inventory of Articulation Characteristics of Apraxia (Score 5, an Indication of Apraxia, according to the test criteria); and 11 patients had AOS using our dichotomous variable using all 4 subtests. The mean number of behaviors on the Inventory was 9.5 (range=5–14, of 15 possible). The most common characteristics were: "exhibits visible/audible searching," "exhibits numerous and varied off-target attempts at the word," "exhibits abnormal prosodic features," "exhibits awareness of errors and inability to correct them," and "exhibits expressive-receptive gap." The least common were phonemic anticipatory errors (e.g. gleen glass for green glass), phonemic perseverative errors (e.g. dod for dog), and voicing errors (e.g. tog for dog), each shown by only one participant each. No patient had pure AOS. All patients with AOS had some component of Broca's aphasia (e.g. some agrammatic sentence production or impaired verb naming), except for one who had Global aphasia. For patients with AOS, the mean score on Words of Increasing Length Part A was 2.67 (range 0–7); the mean score for Words of Increasing Length Part B was 4.0 (range= 0–9). Only 38% of patients with AOS showed increasing difficulty with word length on Part A; 63.6% showed increasing difficulty on Part B. On the Repeated Trials subtest (repetitions of the same word), the mean score was 25.4 (range= 8–30); 90% of the participants with AOS showed some variability on this test.

There was a strong association between lesion volume and AOS, as measured by Inventory of Articulation (coefficient=1.48 more points (more characteristics) per 10 cc larger infarct; p=0.002, age-adjusted) and Repeated Trials (coefficient=−0.91 (worse score) per 10 cc increase; p=0.008, age adjusted). After finding a significant association between lesion volume and AOS, we adjusted for both lesion volume and age and found involvement of BA 44 and 45 (Broca's Area) to be significantly associated with AOS, as measured by Inventory of Articulation (coefficient=12.07, p=0.009 for number of points worse score associated with lesions in either BA 44 and 45). BA 20 and 38 were also associated with AOS, as measured by Repeated Trials scores (coefficient= −22.7, p=0.008 for both, age- and volume-adjusted). Additionally, there was a strong association between damage to the posterior insula and Inventory of Articulation scores (coefficient= 3.23, p=0.007, age- and volume-adjusted).

There were no regions of interest associated with the two subtests that looked for change in articulation for words of increasing length (e.g. but, butter, butterfly). Among the individuals with chronic stroke in this study, relatively few made more errors on longer stimuli on these subtests, especially Part A (the "easier" subtest).

Using our more stringent dichotomous measure of AOS (which requires errors in repeating polysyllabic words on at least one of three subtests), AOS was significantly associated with infarct in left BA 44 (χ^2= 4.04; p=0.04) and posterior insula (χ^2= 6.1; p=0.01), but not BA 45.

In light of the identified association between volume of infarct and chronic AOS, we were interested in the etiology of the strokes of the patients with AOS, using our dichotomous measure, and whether or not leukoaraiosis might have contributed to the persistence of AOS.

Table 1 shows that patients with AOS were younger (p<.01), were less likely to have cardiac embolism ($x^2 = 5$; p=.025), more likely to have carotid dissection ($x^2 = 6.9$; p=.008), and tended to have less leukoaraiosis (probably because they were younger, maybe because of higher rate of dissections). None had bilateral strokes, including lacunes, because single left hemisphere stroke was an inclusion criterion. None had small vessel atherosclerosis as the etiology; this was a series of patients with chronic aphasia, which is unlikely to be due to lacunar infarct.

Discussion

We confirmed our hypothesis that chronic AOS was strongly associated with larger infarcts. That is, people who fail to recover from AOS are those who have large infarcts involving most of the territory supplied by the superior division of the left MCA. This finding may indicate that many areas of the left frontal and anterior temporal cortex in the MCA territory are capable of assuming the role of the damaged components of the network underlying speech articulation, so that if nearly any of these areas are left intact, the network will be able to recover. If all of this territory is damaged, the network may not be able to recover.

Nevertheless, we did find that certain measures of AOS are associated with damage to particular areas of the brain, even after controlling for infarct size. For example, BA 44 and 45 (comprising Broca's area) were associated with measures of AOS, independently of lesion volume, as proposed by Mohr[2]. In chronic stroke patients, damage to anterior temporal cortex (BA 38, 20), as well as posterior insula, was also associated with AOS, regardless of lesion size. These areas, which all have both anatomical and functional connections with BA 44 and 45[17–19], may be important for recovery of motor speech planning. They may be components of a network critical to relearning of motor speech planning or areas that assume the role of BA 44 or 45 when these areas are damaged. It is not possible from this sort of lesion study to determine the role of these areas in recovery. These areas are on the border of the MCA territory, and while the association was independent of infarct volume, they may be associated with particular types of stroke, such as carotid dissection, that have poorer prognosis.

We failed to identify the anterior insula as an area associated with chronic AOS, after controlling for lesion volume, in contrast with some previous studies. There are several differences in our study and the Dronkers[10] study that might account for the differences in the results. First, AOS in this study was evaluated with scores on a standardized battery for AOS; and AOS was identified using a speech sample and Motor Speech Evaluation in the Dronkers study. Use of a standardized battery may or may not provide a more valid measure of AOS. Secondly, lesions were identified on MRI FLAIR sequences in this study, and were identified on either CT or MRI (T1) in the Dronkers study (FLAIR was not available at that time). Our patients also had smaller lesions on average. Finally, we controlled for lesion volume using multivariable regression. The Dronkers study reported lesion overlap in patients with AOS (compared to lesion overlap in a control group without AOS).

Other studies have also reported an association between AOS and anterior insula in chronic stroke[11], but have not controlled for lesion volume. Mean lesion volume of patients with AOS was 141.5 cc, compared to mean lesion volume of 68.3 cc in those without AOS. The association between AOS and infarct in the anterior insula in these studies of stroke might reflect the strong association between damage to the anterior insula and large strokes due to occlusion of the middle cerebral artery[13]. The authors also noted that areas neighboring anterior insula were associated with more severe forms of AOS and aphasia, consistent with our study. Likewise, in a very recent study, using a voxel-based analysis and a different

method of assessment of AOS (but not controlling for volume of infarct), Richardson and colleagues[20] also found that chronic AOS was associated with lesions in Broca's area.

Functional imaging studies of motor speech planning have been mixed with regard to localization of activation. Some show activation in anterior insula[21], some show activation in BA 44 and/or 45[22, 23] or other areas in healthy participants. One study used dynamic causal modelling (DCM) to model the neural architecture underlying motor speech; this study yielded a system architecture in which the insula is positioned between BA 44 and two parallel nodes (the cerebellum and basal ganglia), from which information then converges onto premotor and motor cortex[23]. Connectivity between cerebellum/basal ganglia and insula is primarily driven by preparation, while connectivity between insula and the cortex is driven by rate of word production (execution). This study of normal subjects, along with the acute and chronic lesion studies, is consistent with the hypothesis that orchestrating speech articulation normally depends on a network of brain regions that includes at least BA 44, premotor and supplementary motor cortex, basal ganglia, cerebellum, and part of the insula.

There are a number of limitations of this study. First, AOS is difficult to reliably assess. As mentioned, not all aphasiologists or neurologists even agree on the existence of AOS, much less the criteria for identifying AOS. However, we used the only published battery of AOS of which we are aware, and settled any disagreement in scoring through consensus after review of taped evaluations. We also used a ROI approach to analyzing MRI scans, using a Brodmann Area map to identify ROIs. We recognize the variability across individuals in BAs, although this variability is no greater than the individual variability in brain size and shape, sulci and gyri or other anatomical landmarks. Although voxel-based approaches to lesion-deficit analysis are currently widely used, given the individual variability in brain structure, it is not possible to be confident that a given cluster of voxels in an odd-shaped brain that has been registered to a "normal" brain has the "same" function or cytoarchitecture as that cluster in differently shaped brain registered to that "normal" brain (because that cluster of voxels may not have been registered correctly, not because it functions differently). There is currently no perfect or agreed-upon method to parse the brain. If we had access to an individual's cytoarchitectural fields in vivo, it would be an ideal way to parse the cortex, as the various cytoarchitectural fields likely correspond in some way to the functions of each area (as has been well described for some BAs, such as BA 17, striate cortex)[24]. Our patients also did not have pure AOS, but had some language impairment as well. Lesions associated with selective AOS would be of interest.

Future longitudinal fMRI studies of motor programming of speech articulation during recovery of AOS will be essential for determining the specific roles of BA 44, 6, 38, 20, and anterior and posterior insula in recovery of speech articulation in individuals with AOS after stroke. Nevertheless, this study provides additional support for the traditional notion that Broca's area is one of the areas critical for orchestrating speech articulation. Although subcortical strokes can also be associated with AOS[25], cortical hypoperfusion often contributes to the clinical syndrome in subcortical infarcts.[26] Results of the present study suggest that the presence of persistent AOS at twelve months indicates either a large stroke or damage to at least a subset of critical areas that may comprise components of a network supporting speech articulation (e.g. BA 44, 45, 6, 38, 20, posterior insula) or damage to critical areas that are capable of assuming the function of damaged Broca's area many months after stroke. The etiology is more likely embolism from the carotid (e.g. dissection) than cardioembolism. It has been previously observed that cardioembolism is more likely to cause inferior than superior division MCA stroke[27]. Another important clinical implication of our study is that it points to the relationship between large left (particularly frontal) MCA strokes and persistent AOS at one year. This result indicates that patients with this type of stroke, even young ones, are at high risk for persistent AOS at one year, and therefore might

benefit from introducing instrumentally guided feedback to support speech production, technology to augment verbal communication, and other innovative techniques in speech and language rehabilitation[28]. Results also point to the importance of controlling for lesion volume in lesion-deficit association studies, as all areas of the brain are not equally vulnerable to ischemia.

Acknowledgments

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Table 1

Stroke Characteristics and Subtypes (by TOAST Criteria[30]) in Patients with and without AOS

	Patients who met our Dichotomous Criteria for AOS (n= 11)	All other Patients in our Study (n=23)	Alpha Level for Test for Significant Difference between Patients with and without AOS (Chi Square or T-test)
Age (mean, SD)	51.2 (13.2) years	64.0 (13.9) years	p<0.01
Volume of infarct (mean, SD)	58.7 (62.8) cc	29.8 (49.6) cc	p<0.002
Moderate to severe Leukoaraiosis (% of group)	0%	21.7%	p =0.09 (ns)
Stroke Subtype[30] (% of group)			
Cardioembolic	0%	34.7%	p<0.03
Large Vessel Atherosclerosis Stenosis	27.3%	34.7%	Ns
Carotid Stenosis	(9.1%)	(17.4%)	Ns
Intracranial Stenosis	(18.2%)	(17.4%)	Ns
Stroke of Other Determined Etiology	63.6%	21.7%	p<0.02
Carotid Dissection	(27.3%)	(0%)	p<0.01
Coagulopathy (e.g. cancer)	(9.1%)	(13.0%)	Ns
Other (e.g. vasculitis; Hbss)	(27.3%)	(8.7%)	Ns
Stroke of Undetermined Etiology	9.1%	8.7%	Ns