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Neural Mechanisms of Swallowing Dysfunction and Apraxia of Speech in Acute Stroke

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Abstract

Speech and swallowing utilize overlapping anatomy and are thus inherently related processes. We sought to identify common neural mechanisms between risk of swallowing dysfunction and apraxia of speech (AOS). This was a retrospective analysis using data from a prospectively collected cohort. Left hemisphere stroke patients (68 subjects) tested with the Apraxia Battery for Adults II, a swallow screen, and MRI were included in the study. Main outcome measure was the presence of AOS or aspiration risk after stroke. We identified a significant association between AOS measures and increased aspiration risk (defined by failed swallow screen; $p = 0.04$; OR 5.2). Lesions in pars opercularis of Broca's area (BA 44) were associated with both AOS ($p = 0.044$; OR 9.7) and increased aspiration risk ($p = 0.04$; OR 5) but deficits rarely co-occurred in the same cases. Lesions in left premotor cortex (BA 6) were not significantly associated with increased aspiration risk ($p = 0.06$; OR 3.3) but were significantly associated with AOS ($p = 0.008$; OR 7). Impaired swallowing function was also associated with lesions in Wernicke's area (BA 22; $p = 0.05$; OR 3.5) and pars triangularis (BA 45; $p = 0.02$; OR 6.8). AOS and risk of aspiration are associated in patients with acute left hemisphere stroke. Acute infarct in the pars opercularis of Broca's area is associated with both deficits, though they rarely co-occur in the same individual. The co-occurrence of AOS and risk of aspiration likely reflects dependence on closely related neural structures.

Keywords

Apraxia of speech; Swallowing; Stroke; Dysphagia; Aspiration; Deglutition; Deglutition disorders; Broca's area

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Compliance with Ethical standards

Conflict of interest The authors have no conflict of interest to disclose.

Introduction

Neuroimaging has been used to identify activated cerebral regions during swallowing in healthy participants, including the primary motor cortex, the premotor cortex, the caudolateral sensorimotor cortex, the superior temporal gyrus, and Broca's area [1, 2]. Both cerebral hemispheres are activated during swallowing, with evidence for individualized patterns of hemispheric dominance [2, 3]. One limitation of these types of studies is that they reveal all areas activated during a behavior (swallowing, in this case), some of which may not be required for the execution and completion of the behavior [4–6]. Lesion studies are thus an important adjunct to functional imaging studies, to determine areas of the brain that are critical to the function to the extent that localized damage results in functional pathology at a defined time after stroke. Swallowing dysfunction (dysphagia) is present in approximately 50% of acute stroke survivors [7]. Dysphagia may occur after hemorrhagic and ischemic stroke and with cortical and subcortical lesions [7–9]. Additionally, the insula is a part of the network that controls swallowing function, and damage to the insula is likely to result in swallowing dysfunction [10, 11]. Swallowing impairments and aspiration incidence may differ by lesion location and hemisphere [12, 13].

A shared mechanism may underlie swallowing dysfunction and other types of motor control disorders such as apraxia of speech (AOS) [14]. AOS is a disorder of motor planning of speech that is often observed after stroke. AOS has been associated with lesions to left anterior insula [15]. Other studies report an association between AOS and lesions in Broca's Area in both acute and chronic stroke patients, independent of lesion volume [16, 17]. These authors have proposed that previous associations between the anterior insula and AOS may be due to the typically large areas of infarction in patients with chronic AOS and the high frequency of infarction in the insula in patients with large middle cerebral artery stroke [16].

While AOS and swallowing dysfunction are dissociable and occur in isolation, speech and swallowing utilize similar and overlapping anatomy and thus may be related neurophysiological processes. Both functions require precise motor programming/sequencing for adequate performance. The purpose of this study was to determine if there are common neural mechanisms associated with risk of aspiration and AOS in hyperacute left hemisphere stroke patients. We also sought to determine the frequency of their association within individuals. Double dissociations would indicate that these deficits depend on damage to overlapping neural structures in the left hemisphere.

Methods

A pilot study was conducted to identify possible associations between several brain locations, AOS, and swallowing dysfunction after stroke by performing a secondary analysis on data collected in a prospective parent study. Prior to subject recruitment, the study was evaluated and approved by the Johns Hopkins Institutional Review Board. Written consent was obtained from all participants.

Participants

We included a series of 68 native English speakers who underwent MRI within 48 h post-onset of a first acute left hemisphere ischemic stroke (per criteria of the parent study). The majority of subjects had strokes in the middle cerebral artery or posterior cerebral artery distribution. Subjects were also tested within 48 h for AOS and had an aspiration risk screening. Exclusion criteria were history of neurologic disease (other than the disease of interest), history of stroke prior to the current admission, and uncorrected hearing or vision loss. All subjects were admitted for stroke at a tertiary care academic medical center. Participation in the parent study required that participants be capable of following directions and completing the language battery.

Variables

Each patient was screened for aspiration risk upon admission to the hospital for stroke using a 3-step standardized swallow screen performed by trained nursing staff. Failure of any step resulted in nil per os status and recommendation for Speech-Language Pathology swallowing consultation. In the first step, patients were considered to have “failed” the screening if they met any of the following criteria: history of enteral feeding due to swallowing dysfunction; depressed level of arousal/alertness; recent history of swallowing dysfunction with known aspiration; and inability to manage oral secretions. If patients passed the first step, they progressed to the second step of swallowing 3 teaspoons of water. Failure of the second step was indicated if any of the following conditions were observed: no laryngeal elevation detected; cough/choke response immediately after the swallow; throat clearing after swallowing; wet/gurgly vocal quality with sustained “ah” after the swallow; or inability to complete the trial. If the second step was successfully passed, patients progressed to the third and final step of swallowing 3 oz. of water. The criteria for failure of this step were the same as for the second step. The 3 oz. water swallow test has been validated as a sensitive screening tool for identifying patients who are at risk of clinically significant aspiration (identified by videofluoroscopic swallow evaluation) [18, 19]. For the purposes of this study, patients who failed the swallow screen were considered to have high aspiration risk. The results of the swallowing dysfunction screening were abstracted from the medical record. We used the pass or fail result of the swallow screen as a dichotomous variable.

Each patient was also assessed for AOS with the Apraxia Battery for Adults II [20]. We used four subtests including increasing word length, parts A and B (which scores the deterioration in performance with increasing word/phrase length; higher scores indicated greater deterioration); repeated trials (which score the errors on the repetition of the same polysyllabic word; errors are subtracted from a total score of 30, thus a lower score indicates more severe apraxia); and inventory of articulation characteristics of apraxia following automatic speech, spontaneous speech, and reading (which totals characteristics of AOS observed throughout several activities; a higher score indicates more severe apraxia). Tests were scored by a technician blinded to the site of lesion. To develop a stringent criterion for diagnosis, we created a dichotomous variable for AOS from the 4 subtests. If a patient had a score of > 5 on the inventory of articulation subtest (highly indicative of AOS per test manual) and was impaired on 2/3 of the remaining measures (per test manual scoring), they were classified as having AOS for the purposes of this study. If data on any of the four

subsets were unavailable this variable was coded as missing. Audio recordings of a subset of 20 participants were reviewed by an experienced speech-language pathologist (blinded to test results and subsequent classification) who agreed with the diagnosis of AOS in all cases.

Imaging Protocol

Imaging was performed on a 1.5 Tesla scanner with a standard quadrature transmit–receive head coil. Scans included time-of-flight MRA, conventional T1- and T2weighted images, FLAIR MRI, and isotropic DWI images ($b_{\max} = 1000 \text{ s/mm}^2$; TR/TE of 10,000/120 ms). MRI scans were analyzed by experienced technicians for the presence or absence of ischemia in each of 12 Areas (BAs: 4, 6, 20, 21, 22, 37, 39, 40, 44, and 45; the anterior and posterior insula) using a published template [21]. These BAs were selected as they have previously been associated with swallowing dysfunction in the literature [22]. The volume of each lesion was calculated from DWI using ImageJ software (<http://rsb.info.nih.gov/ij>) as previously reported [23–26]. Infarcts were manually traced on each slice, multiplied by the value for slice thickness, and summed across the entire brain to yield a total stroke volume. Volumes were recorded in cubic centimeters.

Statistical Analysis

We identified associations between a failed swallowing screening and AOS (both as dichotomous variables) using Fisher's exact tests. We identified associations between a failed swallowing screening, AOS, and the presence of infarct in regions of interest using logistic regression. Significance level was set at $p < 0.05$. Data analysis was performed using Intercooled Stata version 11 (StataCorp, College Station, TX).

Results

In this 68-subject sample, we identified 14 cases with high aspiration risk as defined by a failed swallow screen and 24 cases with AOS as defined by our dichotomous variable. The mean age of the group was 58.4 years (± 14 ; range 17–91) and mean education was 13.6 years (± 4.2 ; median 12; range 4–28). Detailed sample characteristics by group are presented in Table 1.

There was a significant association between failed swallow screen and AOS ($p = 0.04$; OR 5.2, 95% CI 1.1–32.8). Lesions in pars opercularis of Broca's area (BA 44) were associated with both AOS ($p = 0.044$; OR 9.7, 95% CI 1.1–89.4) and impaired swallowing ($p = 0.04$; OR 5, 95% CI 1.1–23.4). Lesions in left premotor cortex (BA 6) were not significantly associated with failed swallow screen ($p = 0.06$; OR 3.3, 95% CI 0.9–11.7) but were significantly associated with AOS ($p = 0.008$; OR 7, 95% CI 1.7–29.5). Lesions in Wernicke's area (BA22) and pars triangularis (BA45) were significantly associated with increased aspiration risk but were not associated with AOS (+ aspiration risk: BA 22 $p = 0.05$; OR 3.5, 95% CI 1.1–12; and BA 45; $p = 0.02$; OR 6.8, 95% CI 1.3–35.2). Areas of ischemia associated with AOS, positive swallowing screening, or both are detailed in Table 2. Deficits in the pars opercularis of Broca's area resulted in AOS or + aspiration risk but rarely occurred simultaneously.

Discussion

The results of this pilot study suggest that AOS and swallowing share common neural substrates but that no single region is critical for speech and swallowing. In this study, damage to the pars opercularis of Broca's area was associated with AOS and a failed swallow screen. These areas may be important for the motor programming of both speech and swallowing. Previous studies have reported an association between damage to premotor cortex and AOS [27] and between Broca's Area and AOS [16, 17, 28, 29]. In contrast to previous studies [11, 15, 30], we failed to find an association between insular damage and either AOS or swallowing; this discrepancy may be due to fewer patients with insular lesions and a smaller average lesion size in our study sample. Additionally, the insula may be over-represented in large strokes, as 87% of strokes in the 90th percentile for volume include the insula [31]. The mean volume of infarct in the current study was 14.5 cc, with a maximum volume of 130.6 cc, whereas the mean lesion volume in another study was 141.5 cc, compared to mean lesion volume of 68.3 cc in patients without AOS [30].

Although pars opercularis was associated with both AOS and increased aspiration risk, these deficits rarely cooccurred in patients with lesions in this region, perhaps because AOS and dysphagia result from damage to distinct portions of pars opercularis. Pars opercularis of the inferior frontal gyrus has many connections with premotor, motor, and sensory cortex, as well as subcortical and brainstem nuclei. It is plausible that damage to different parts of this region (Brodmann area 44) might disrupt distinct connections, and differentially affect motor speech programming versus swallowing. Future studies that examine damage to white matter tracts would be helpful in evaluating this possibility.

Limitations

Patients with larger lesions may have been excluded from participation due to inability to speak or reduced level of consciousness at the acute stage of stroke. This is a potential limitation of our study, as we were only able to include patients who were capable of completing the Apraxia Battery within 48 h of stroke onset. Because we included small strokes, we had 18 patients with lesions involving the posterior insula and only 7 patients with lesions involving the anterior insula. It is imperative to test insular stroke patients as soon as they are functionally able to participate in future studies to determine the role of the insula in AOS and swallowing function. Additionally, the current sample was limited to left hemisphere strokes, as speech is typically controlled by the left hemisphere; though the swallowing neural network is bilateral, and dysphagia may result from left, right, or bilateral acute infarction [32]. By limiting our participants to left hemisphere infarcts, we focused on the potential overlapping mechanism of AOS and aspiration risk, though with limited representation of and generalization to all manifestations of dysphagia after stroke.

Another limitation of our study was that we classified patients by pass/fail of the swallow screen protocol which is the standard of care for all stroke patients admitted to this medical facility. These results may include false positives (reported sensitivity and specificity: 96.4 and 46.4%, respectively) [19]. Subsequent investigation should include a more thorough evaluation of swallowing physiology and bolus management. Although Broca's Area and the premotor cortex may be involved in the control of speech and swallowing, the precise role of

these cerebral areas in swallowing function remains unclear. Instrumental examination (videofluoroscopy or videoendoscopy) would be necessary to determine which components of swallowing are impaired in patients with acute stroke and to describe the specific physiologic changes after damage to specific parts of the brain. We are currently investigating the results of videofluoroscopic swallow studies within 48 h of stroke onset in all consenting patients with concurrent AOS testing and MRI to further delineate correlates of function and lesion properties.

Conclusions

In this cohort of left hemisphere stroke patients, AOS and dysphagia were associated with damage to left pars opercularis. However, a given lesion affecting left pars opercularis was typically associated with only AOS or high aspiration risk, indicating that different sub-regions (likely with distinct connections) may control motor programming of speech versus swallowing. Similarly, other areas were associated with speech or swallowing, suggesting complex functional cortical-subcortical networks. The potential association between the left premotor cortex and increased aspiration risk did not meet the criteria for statistical significance, likely because of low power. Our findings indicate the need for more detailed prospective research using instrumental swallowing evaluation to determine the precise role of these areas, as well as inclusion of more patients with insular stroke.

Clinically, this research informs the development of treatment interventions, as treatment of one deficit may be improved by targeting the preserved function that is also associated with that location in patients with left frontal strokes.

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Table 1

Demographic and other sample characteristics, *n* = 68

Variables	Stroke cases <i>n</i> = 68
Age, years, mean (SD)	58.4 (13.9)
Female, count (%)	35 (51.5)
Education, years, mean (SD)	13.6 (4.2)
Lesion volume, cc, mean (SD)	14.5 (25.8)
Apraxia of speech, count (%)	24 (35.3)
(+) Aspiration risk, count (%)	14 (20.6)
Both Apraxia of speech and (+) aspiration risk, count (%)	6 (8.8)

Table 2

Aspiration risk and AOS by brain region, $n = 68$

BA	No AOS no aspiration risk $n = 36$	AOS only $n = 18$	Aspiration risk only $n = 8$	Both AOS and dysphagia $n = 6$	p value
4	4	4	3	0	0.18
6	2	8	5	1	<0.001
20	1	0	0	0	1
21	1	2	1	0	0.38
22	6	6	5	2	0.05
37	5	5	3	0	0.18
39	7	4	1	1	1
40	6	4	3	1	0.61
44	0	4	3	1	0.002
45	1	2	4	0	0.005
Ains	2	3	2	0	0.19
Pins	7	7	3	1	0.38

AOS Apraxia of Speech, Ains Anterior insula, Pins Posterior insula