



Contributions of the Insula to Speech Production

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20.1 Speech Apraxia and the Insula

Speech production is a complex physiological process involving the rapid and accurate coordination of nearly 100 different muscles [1]. Several muscle groups have been implicated in the production of speech including the respiratory muscles which enable voluntary expiration and maintain constant pressure below the glottis; the vocal cords which adduct and abduct to produce voiced and unvoiced sounds, respectively; and the articulators which modify expired air [2]. Speech apraxia is a motor speech disorder in which the muscles involved in speech production fail to produce the correct sounds of words in the appropriate order and with the appropriate timing; this differs from dysarthria which refers to weakness of the muscles involved in speech production [1]. It is characterized by speech with abnormal intonation or rhythm, significant

phonetic variability (i.e., articulation errors or distortions), syllable segmentation, impairments in initiation, and frequent false starts [3]. Given that muscle strength and range is unaffected, speech apraxia is believed to be a higher-level disorder of speech motor control distinct from Broca's aphasia, conduction aphasia, and dysarthria [4]. It has been reported as the first manifestation of neurodegenerative disorders such as corticobasal degeneration and nonfluent progressive aphasia [5]. The role of the insula in the production of speech has been investigated in several studies in the past, particularly to understand the pathophysiology of speech apraxia [1–4, 6]. The identification of a singular region in the brain resulting in speech apraxia has been controversial. Speech apraxia has been associated with lesions in Broca's area, the left frontal or temporoparietal cortices, subcortical structures such as the basal ganglia, and the left anterior insula [5]. Patients suffering from nonfluent progressive aphasia with speech apraxia show atrophy in all the aforementioned structures [7].

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20.2 Clinical Studies of Insular Speech and Language Function

Dronkers analyzed strokes in patients with and without speech apraxia. In the study published in *Nature* in 1996, he demonstrated that in 25

patients with speech apraxia, the location of the stroke overlapped with a region in the left precentral gyrus of the insula. In comparison to a group of 19 patients with left middle cerebral artery infarctions without speech apraxia, this area was completely spared, indicating an important role of the insular in the pathophysiology of speech apraxia.¹ The major limitation of the study is that it is not the likelihood of speech apraxia that is assessed in patients with the lesion but the likelihood of the lesion in patients with the deficit. Thus, it may be that all patients with apraxia of speech have insular infarction, but few patients with insular damage have speech apraxia [8]. Cerebral infarctions limited to the insular cortex may provide additional insight into the relationship with speech apraxia. These infarctions are incredibly rare, however. A registry of 4800 first-ever acute strokes only identified 4 such cases. In two of those cases, the lesion was located in the posterior intrasylvian cortex in the left hemisphere and resulted in articulatory deficits coupled with fluent and non-fluent aphasia [9]. Most strokes involving the insular cortex are embedded in larger middle cerebral artery territory infarctions. Thus, current evidence is limited to few case reports of isolated insula lesions reporting on speech and language deficits. Most do not fit the concept of speech apraxia [3]. In a study of patients with acute left-sided middle cerebral artery territory strokes with and without insular involvement, no association of speech apraxia and injury to the left insula was noted. Apraxia of speech was encountered in patients with damage or ischemia of the left posterior inferior frontal gyrus regardless of insula involvement [8]. In addition to cerebrovascular lesions, brain tumors limited to the insula represent another disease entity to elucidate the role of the insula in speech and language function. In a study of 30 patients with intrinsic tumors involving the insula, 3 had isolated involvement of the left insular cortex. No speech and language deficits were recorded after surgical resection [10]. Even removal of the entire language-dominant insula in a glioma patient did not result in speech apraxia [11].

Slowly evolving pathologies may trigger a compensatory mechanism in the contralateral insula, however [3]. In summary, reports of speech and language deficits associated with insular pathologies paint a rather inconclusive picture and may in part be related to injury of the adjacent frontal operculum and its connections.

20.3 Functional Imaging Studies of Insular Speech and Language Function

Initial positron emission tomography (PET) investigations of speech motor control showed hemodynamic activation in bilateral primary motor and sensory cortices, the supplemental motor area, the cerebellar hemispheres, and, surprisingly, in the depth of the Sylvian fissure [12]. This spot was later linked to the anterior insula in a more recent follow-up PET study [2]. Functional imaging from PET and MRI (fMRI) provides evidence for a “minimal brain network” critical for motor aspects of speech and language production. This network is lateralized to the left at the level of the insula and also includes the mouth region of the bilateral motor cortices, Broca’s area and the left inferior precentral gyrus, the left supplemental motor cortex, the basal ganglia, and the cerebellum [3, 13]. Another fMRI study assessing the temporal aspects of blood oxygen level-dependent (BOLD) activation during syllable repetition identified two clusters of cerebral structures involved in speech motor control. The preparative loop, consisting of BOLD signal in Broca’s area, the supplemental motor cortex, anterior insula, and superior cerebellum, showed significantly earlier hemodynamic activation than the executive loop made up by the primary sensory and motor cortices, thalamus, basal ganglia, and inferior cerebellum [14]. Another fMRI study localized the response to the junction of the insular cortex and the frontal operculum [13]. In summary, functional imaging studies found fairly consistent activation of the insula, predominantly in the dominant hemisphere, with tasks targeting higher-order articulation.

20.4 Autonomic Aspects of Speech Motor Control and the Insula

Functional imaging studies identified other distinct area in the insula, apart from the transition zone between the insula and the frontal operculum, during speech production. This raises the question as to whether the insula is involved in speech and language function not related to higher-order articulation. There is convincing evidence that the insula is an important regulator of autonomic functions such as the control of blood pressure or heart rate, for instance [15]. In speech motor control, the link to the autonomic system is its intimate relationship to the respiratory system [3]. Information on the state of the respiratory system is relayed to the insula as evidenced by functional imaging obtained in patients experiencing dyspnea [16]. In animal models, stimulation of the insular cortex has shown to result in respiratory slowing and respiratory arrest [17]. Still, respiratory depression is not a feature of speech apraxia [3]. Conclusively, insular cortical projections may have modulatory autonomic effects on respiratory activity while speaking and may act in parallel with existing corticobulbar and corticospinal systems that are under voluntary control. While motor and premotor cortical input may be responsible for phasic or brief linguistic adjustments of respiration, such as in between sentences, the tonic state of hyperventilation required while speaking may be under control by the insula [3, 18].

Conclusions

Speech apraxia, a higher-order articulation disorder, has been associated with injury to Broca's area, the left frontal or temporoparietal cortices, subcortical structures, and the left anterior insula. Isolated lesions of the insular cortex are very rare and, in most instances, do not resemble the symptomatology of speech apraxia. Functional imaging studies, however, demonstrate conclusive evidence for activation of the left anterior insula adjacent to the frontal operculum with

articulatory linguistic tasks. In addition to its role in articulation, the insula may also function as a relay center for autonomic signals pertaining to the linguistic respiratory state and may serve as a corollary to voluntary control of respiration during speech mediated by corticobulbar and corticospinal projections.

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