

Editorial

Brain areas involved in speech production

The ability to produce accurate speech sounds in rapid succession is something we humans take for granted. In fact, speech production is an extremely involved process. Thoughts must be translated into linguistic representations (itself not a trivial feat), which are then sent to speech mechanisms that can coordinate, initiate, modify and execute the articulation of an utterance. Through the study of patients with disorders affecting this complex process, we have come to learn that numerous brain areas are recruited in speech production and that they hang in a precarious balance that is easily affected by neurological disease and dysfunction.

The coordination of articulatory movements, an end-stage component of speech production, has received increased attention in recent years. In order for sounds to be produced correctly, the lips, tongue, jaw, velum and larynx must make accurate movements at the right time or the intended sounds become distorted. For example, to say the simple word ‘gap,’ airflow must briefly be halted by raising the back of the tongue to the soft palate. This airflow is suddenly released, during which time the vocal cords must vibrate to create phonation. The tongue and jaw lower and the air should flow unobstructed to produce the proper vowel. The lips seal and the cords relax. All of this must be orchestrated perfectly in time and sequence so that the word ‘gap’ results. Given the many fine movements that are required for speech production, it is no wonder that the mouth area is so largely represented in the homunculus of primary motor cortex.

Patients with deficits in this ability to programme speech movements are said to have a disorder known as ‘apraxia of speech’. The disorder has been well studied in the realm of speech–language pathology, and treatment for the disorder has received equal attention (Wertz et al., 1984; Duffy, 1995; McNeil et al., 1997). The brain regions that might support this function had been less well investigated until the advent of neuroimaging techniques that allowed for the *in vivo* investigation of the brain areas affected in patients who had sustained injuries that resulted in apraxia of speech. In one such study (Dronkers, 1996), the computer-reconstructed lesions of 25 chronic stroke patients with left hemisphere lesions who had been diagnosed with apraxia of speech were overlapped to determine if a common area of infarction could be found in this group. The only region of overlap in 100% of the cases was found in the superior tip of the precentral gyrus

of the insula (SPGI). Since this region fell within the central-most area of the brain, it was possible that this common area merely reflected a vulnerable area in patients with left hemisphere strokes and was not specific to apraxia of speech. For that reason, the lesions of 19 patients who were similarly assessed but who did not carry the diagnosis of apraxia of speech were also overlapped. Their lesions spanned the same distribution of the left hemisphere but completely spared the same region that was affected in the patients with the disorder. This dissociation was taken to mean that the SPGI might play some role in the coordination of articulatory movements. Such lesion analysis methods serve not only to tie behaviours to brain areas, but also to take the complementary, reverse step of comparing the behaviour of patients with spared regions of interest. Other patient studies and some functional imaging studies have also implicated the insula in the process of speech production (e.g. Wise et al., 1999; Nestor et al., 2003; Gorno-Tempini et al., 2004).

In this issue of *Brain*, the relationship of the insula to apraxia of speech was examined by Hillis and colleagues in acute stroke patients by utilizing diffusion-weighted imaging (DWI) and perfusion-weighted imaging (PWI) within the first 24 h after stroke. Forty patients with and 40 without lesions and/or hypoperfusion to the insula were selected and given several short oral language tasks from which a diagnosis of apraxia of speech was later extracted. The authors found no reliable relationship between apraxia of speech and structural changes or low blood flow to regions of the insula, but instead found that 84% of patients with apraxia of speech had such changes in the posterior inferior frontal gyrus. The authors present an interesting and alternative method for identifying the relationship between behavioural deficits and affected regions of the brain, and raise questions concerning the best methods of lesion analysis.

The study of Hillis *et al.* makes a contribution to the field for several reasons. First, its starting point is the regions of interest that were lesioned and/or dysfunctional and evaluates whether patients with changes there show the expected deficit. This is the complementary approach to first selecting patients with the deficit and then evaluating if they demonstrate a common lesion. Secondly, the study evaluates patients in the acute stage of stroke and captures those who might have small lesions that could resolve quickly and might

be overlooked in a study of chronic patients. Thirdly, the study draws on the authors' earlier work that evaluates both dysfunctional and structural damage within the first 24 h. Few studies have assessed large numbers of patients with both techniques in this early stage after stroke and thus have not evaluated the effects of tissue dysfunction in addition to the effects of tissue loss.

At the same time, the paper opens the discussion concerning the assessment of lesion–symptom mapping in brain-injured patients. What is the best way to assess which areas are important for certain functions? How do methods of lesion analysis (lesion overlapping, DWI and PWI) contribute to this understanding? How do brain–behaviour relationships in acute patients using one set of methods reliably compare with those found using an alternative method in chronic patients? Should these relationships be pursued in acute patients before the brain has had the opportunity for reorganization of function, or should they be assessed in chronic patients when the physiological effects of the brain injury have passed and the behaviour has settled into a stable pattern? Should we be viewing structural changes or functional ones, and how do they compare? Should we constrain our search to regions of interest or open our investigation to all regions of the brain? Finally, how should behavioural deficits be investigated? Should we try localizing individual symptoms or search for syndromes and networks in the brain?

Clearly all of these approaches contribute to the study of brain–behaviour relationships in complementary ways. The difference in findings between the acute patients of Hillis *et al.* and the chronic patients of Dronkers is of great interest and questions what might be happening between these two stages that yields a shift in localization between Broca's area to the precentral gyrus of the insula for speech praxis. The ability to view both functional and structural lesions in the brain allows us to see which areas are recruited during a behavioural task and which ones are necessary to support the function. While lesion overlapping allows us to consider a wide area of brain in our search for localization of particular disorders (and has succeeded in yielding numerous associations throughout the brain, not just those in the insula), the *a priori* determination of regions of interest allows us to focus on the specific deficits that follow injury to that one area. Ideally, a mixture of both techniques would be advantageous and would allow for more detailed correlations between symptoms and brain regions. The new voxel-based methods such as VLSM (voxel-based lesion–symptom mapping; Bates *et al.*, 2003) in which well-defined continuous data can be evaluated at the voxel level are already making contributions in this area (e.g. Saygin *et al.*, 2003; Dronkers *et al.*, 2004)

Speech production is a complex process, involving a networked system of brain areas that each contribute in unique ways. Areas beyond Broca's area and the anterior

insula have been implicated in the complex process of producing speech movements. Future studies, associating even more specific apraxia of speech symptoms (e.g. pure motoric groping) with discrete brain areas, may further our understanding of such a distributed network. For the patients suffering from apraxia of speech, a better characterization of the disorder and its symptoms may ultimately help clinicians in planning for more effective rehabilitation. Perhaps using multiple methods, e.g. lesion overlap, DWI, PWI and functional MRI, to follow brain-damaged patients from the acute phase through early and late stages of rehabilitation will add to our knowledge of the time course of recovery, localization of function and the nature of reorganization after injury.

Nina Dronkers¹ and Jennifer Ogar²

¹*Center for Aphasia and Related Disorders
VA Northern California Health Care System
Martinez, CA, USA*

²*Departments of Neurology and Linguistics
University of California, Davis
Davis, CA, USA*

E-mail: dronkers@ucdavis.edu

References

- Bates E, Wilson SM, Saygin AP, Dick F, Sereno MI, Knight RT, Dronkers NF. Voxel-based lesion–symptom mapping. *Nature Neurosci* 2003; 6: 448–50.
- Dronkers NF. A new brain region for coordinating speech articulation. *Nature* 1996; 384: 159–61.
- Dronkers NF, Wilkins DP, Van Valin RD, Redfern BB, Jaeger JJ. Lesion analysis of the brain areas involved in language comprehension. *Cognition* 2004; 92: 145–77.
- Duffy J. *Motor speech disorders*. St Louis: Mosby; 1995.
- Gorno-Tempini ML, Dronkers NF, Rankin KP, Ogar JM, Phengrasamy L, Rosen HJ, *et al.* Cognition and anatomy in three variants of primary progressive aphasia. *Ann Neurol* 2004; 55: 335–46.
- Hillis AE, Work M, Barker PB, Jacobs MA, Breese EL, Maurer K. Re-examining the brain regions crucial for orchestrating speech articulation. *Brain* 2004; 127: 0000–0000.
- McNeil MR, Robin DA, Schmidt RA. Apraxia of speech: definition, differentiation, and treatment. In: McNeil MR, editors. *Clinical management of sensorimotor speech disorders*. New York: Thieme; 1997. p. 311–44.
- Nestor PJ, Graham NL, Fryer TD, Williams GB, Patterson K, Hodges JR. Progressive non-fluent aphasia is associated with hypometabolism centred on the left anterior insula. *Brain* 2003; 126: 2406–18.
- Saygin AP, Dick F, Wilson S, Dronkers NF, Bates E. Neural resources for processing language and environmental sounds: evidence from aphasia. *Brain* 2003; 126: 928–45.
- Wertz RT, LaPointe LL, Rosenbek JC. *Apraxia of speech: the disorder and its management*. New York: Grune and Stratton; 1984.
- Wise RJ, Green J, Buchel C, Scott SK. Brain regions involved in articulation. *Lancet* 1999; 353: 1057–61.