

A Gene for Speech?

*What the FOXP2 gene can tell us about
the neural control of speech and language*

In contrast with all other animals, humans have evolved the ability to acquire spoken language. Humans' capacity for speech must, in some respect, be derived from our genes. What is it in our genes that enables us to acquire speech? What would such a gene *do*, and what neural structures would depend on its expression? What would happen if it were disrupted? There has been speculation about a genetic substrate for speech ability for a long time, but it wasn't until very recently that scientists were able to track down and identify a candidate gene, one that would be necessary for the acquisition of spoken language.

A speech-impaired family known as the KE family afforded geneticists a promising opportunity to look for the "speech gene." Half the members of the KE family have severe impairments in speech and language, implying a hereditary mutation that is passed on in a simple manner. Those with the disorder exhibit deficits in speech motor control: they have trouble with fine movements in the lower half of the face, disrupting their ability to speak. However, their disorder is not entirely articulatory: those with the mutation also have defects unrelated to verbalization, for example, a deficit in making a written list of words starting with a particular letter.¹

In 2001, after years of research with the KE family and CS, an unrelated patient with a similar speech abnormality, geneticists Lai and Fisher alighted on the FOXP2 gene on chromosome 7q31, a region known to be related to brain function. (The name FOXP2 comes from forkhead box, for the forkhead box protein family involved in transcription.) FOXP2 is expressed in many regions in the developing

brain, including the cortical plate, basal ganglia, thalamus, inferior olive, and cerebellum. A single base-pair mutation caused the FOXP2 mutation resulting in speech defects in both CS and the KE family.²

To determine FOXP2's contributions to speech ability – to establish what it actually does when it is expressed – recent studies have looked for differences in brain structure between normal humans and those with mutated copies of the gene. If we can determine what cortical structures the gene is regulating, and correlate structural irregularity with behavioral impairments, we can learn more about the neural circuits for speech processing and articulation. The papers I have proposed elucidate the role of FOXP2 with data about its expression in speech and motor centers in the brain, as well as the anatomical, functional, and behavioral consequences of its disruption.

PAPER 1: Liégeois et al., 2003³, neuroimaging (fMRI). The functional abnormalities in members of the KE family can be revealed in functional imaging studies. Results by Liégeois show a large discrepancy in brain activation between subjects with normal and mutant copies of the FOXP2 allele. Specifically, affected family members showed an atypical distribution of activation during both speech (nonword repetition) and language (word generation) tasks. Particularly striking was an abnormally broad activation throughout cortex and a simultaneous underactivation in Broca's area and other speech-related cortical and subcortical brain regions.^{4,5} The study also discusses morphological abnormality in these structures, principally the caudate nucleus and the putamen. Other related imaging studies¹ use voxel-based morphometry to show bilateral reductions in gray matter in the ventral cerebellum. All this is strong evidence that FOXP2 mediates cortical processes related to language.

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*PAPER 2: Shu et al. 2005⁶,
knockout mice & immunohistochemistry.*

Because FOXP2 is expressed in other animals, albeit in a slightly different form, we can induce mutations in the gene and examine the relations

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between gene irregularity and the resulting phenotypic differences. Shu et al. engineered two types of knockout mice, a type with two disrupted copies of FOXP2 (homozygous) and a type with one normal and one disrupted copy (heterozygous, the genotype of the affected members of the KE family). Heterozygous knockout mice made many fewer ultrasonic vocalizations in response to separation from the mother than did control mice, whereas homozygous knockout mice made no vocalizations at all. This result implies that FOXP2 plays a role in the development of a neural circuit employed in social communication, not uniquely related to human speech. In addition, heterozygous knockouts exhibited a delay in motor development, while homozygous knockout mice had a severe motor impairment, affirming the gene's involvement in motor and sequencing areas of the brain. Histological analysis of the mice illustrated irregular cerebellar sections in knockout mice, particularly in the Purkinje cells and in the external granular layer. FOXP2 therefore seems to be important for both cerebellar development and mechanisms of social communication.

PAPER 3: Teramitsu et al. 2004⁷, histology & vocal learning in songbirds. FOXP2 is also expressed in songbirds, and current research seems to suggest it plays a role in birds' vocal learning. According to Teramitsu et al., FOXP2 is localized to related subcortical structures in humans and birds (speech areas / song nuclei, cerebellar Purkinje cells). This colocalization suggests associated mechanisms underlying vocal learning in both humans (speech) and birds (song). FOXP2 and the related

gene FOXP1 show parallel expression in the human and songbird brain, predicting a possible role of FOXP1 in speech ability.

This topic is very relevant to studying the brain mechanisms for speech. The FOXP2 gene has the potential to be a powerful tool for exploring the neural circuits that allow us to communicate via spoken language. However, the field would certainly benefit from some spirited conversation about the limitations of these methods, as well as any unfounded conclusions that should be avoided. Furthermore, the function of the gene itself is an interesting topic of study. If FOXP2 is a “language” gene, what is it doing in mice, songbirds, and fungi? If it is merely a gene enabling fine motor movements such as those used in speech, what leads to defects in language development in individuals lacking the normal gene? What is the relationship between the motor mouth control FOXP2 may regulate and the language ability its disruption impairs? Does a hearing- or motor-feedback loop, such as that described in our speech motor control papers, play a part in any of this?

Finally, where did this gene come from? By comparing the gene’s expression in other animals, we can gain insight on when and how speech ability evolved in our species (and in no others).

The search for and evaluation of the speech gene, FOXP2, is an exciting and extremely recent issue, with broad-reaching implications for research on the evolution of human speech. Current research combines techniques from genetics, brain imaging, immunohistochemistry, and behavioral science to get at the function of FOXP2 in humans and animals. The FOXP2 gene is critical for the development of the neural substrates of speech and language, and will prove to be important to our understanding of circuits underlying speech and articulation.

References

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* proposed for discussion articles

** proposed for review/background articles