nature neuroscience

In search of language genes

Ever since Chomsky suggested that humans have a 'language instinct', people have been debating the possible existence of genes that underlie our linguistic abilities. Now, in the first big triumph for the new field of 'cognitive genetics', such a gene has been identified[1]. The data seem clear-cut, and the discovery has been greeted with justifiable excitement; the deficit seems specific to language, and unlike the weak associations that are common in behavioral genetic studies, this gene shows a strong Mendelian pattern of inheritance. Nevertheless, the excitement should be tempered with caution. The explanatory gap between mutation and phenotype is wider in cognitive genetics than in any other area of biology, and bridging it will be a major challenge.

The new gene was identified based largely on studies of a single British family with a rare inherited disorder of speech and language. Now it has been cloned, and shown to encode a known transcription factor, FOXP2, a member of a large family of 'winged helix' proteins. The mutation is predicted to inactivate the FOXP2 protein, and the language deficit, which occurs in heterozygous individuals, presumably indicates that two copies of the gene are necessary for normal function.

Individuals who carry the mutant FOXP2 allele show a variety of deficits. Their speech is poor—sometimes to the point of being unintelligible—and they are also impaired in many other language tasks, including reading, writing, comprehension, and use of grammar. Their IQ is lower on average than unaffected family members, although there is enough overlap to exclude this as the cause of the language deficits. One of the most robust findings is that affected individuals have difficulty imitating mouth and face movements, and Faraneh Vargha-Khadem, one of authors of the new study, argues that this may be the core deficit; if the affected children cannot produce the complex sequences of movements necessary for speech articulation, they may be unable to acquire normal language skills. Consistent with this suggestion, the affected individuals show bilateral atrophy of the caudate nucleus, part of the basal ganglia that has been implicated in motor control.

Proving this hypothesis, however, will be difficult; rigorous methods to determine the site of gene action in experimental organisms cannot be applied to humans. FOXP2 is widely expressed in both mouse and human tissues, and although its brain expression has not been examined in detail, the available evidence offers no clue as to the basis of its remarkable behavioral effects. The mouse knockout phenotype is not yet known; the most interesting result might be a deficit in caudate function and/or orofacial movements, but—absent a talking mouse—it will be difficult to exclude the possibility that the human language impairment reflects pleiotropic effects in many brain regions. It should, however, be possible to determine how FOXP2 regulates the transcription of other mouse genes (it is thought to be a repressor), and this may lead to insights at the cellular level that will generalize to humans.

Can the identification of FOXP2 offer any broader lessons about the genetic basis of language? There are several questions to be addressed, and it will be important to keep them distinct. First, this study will encourage the search for additional mutations with language phenotypes; even if such cases are very rare, they may provide mechanistic insights into the neural basis of language that could not be obtained any other way. Second, we want to understand the basis for variation in language ability in the general population, including specific language impairment (SLI), a common condition that is partly hereditary and probably involves many genes. At least two loci have been linked to SLI through a whole-genome scan, and although the genes responsible have not yet been identified, neither locus corresponds to FOXP2 (ref. 2). It will of course be of great interest to identify these genes, and to determine whether and how they interact with FOXP2.

Finally, there is the question of the evolutionary origin of language. FOXP2 does not appear to be a recent evolutionary innovation, although closer examination may reveal differences in regulatory regions that could be related to a role in language. However, the genetic changes that led to the emergence of language may have become fixed in the population, and genetic studies of modern populations may therefore provide no information on their identity. How then might we understand how language evolved? Comparing the human genome and those of chimps and bonobos may reveal some clues, for instance the expansion and diversification of particular gene families in the human lineage. But equally plausibly, the linguistic uniqueness of humans may reflect the accumulation of diverse and subtle changes that will be hard to recognize, particularly if they are in regulatory sequences.

Further insights should come from identification of genes that are transcribed in brain areas known to be involved in language. This will not be easy, given the lack of clear anatomical landmarks, particularly in the cortex, but an important goal in the postgenomic era should be to generate a molecular map of the human brain, and to anchor it to existing anatomical and functional maps. A detailed molecular map could establish homologies between human brain areas and those of other species, including not only great apes but also macaques, where physiological experiments are feasible.

Chomsky suggested that the structure of language, with its universal grammatical rules, is somehow embodied in our brains and in our genes. It now seems realistic to hope that these genes can someday be identified; the discovery of FOXP2 represents an encouraging first step toward that distant goal.

1. Lai, C. S. L. *et al. Nature* **413**, 519–523 (2001).
2. Newbury, D. F. & the SLI Consortium (SLIC). Abstract presented at the American Society for Human Genetics 51st Annual Meeting, San Diego, California, October 12-16, 2001.