MedicalXpress

Genetic study provides new insights into molecular basis of language development

November 5 2008

Scientists have identified the first gene that is associated with a common childhood language disorder, known as specific language impairment (SLI). The gene – CNTNAP2 – has also been recently implicated in autism, and could represent a crucial genetic link between the two disorders.

Although most children acquire proficient spoken language almost automatically and with little conscious effort, a significant number develop unexplained difficulties in producing and understanding language. SLI is the most common such disorder, affecting up to 7% of pre-school children.

In a study published today in the *New England Journal of Medicine*, researchers at the Wellcome Trust Centre for Human Genetics, University of Oxford, discovered that particular variants of the CNTNAP2 gene were significantly associated with language deficits in a large sample of families with SLI.

"It has long been suspected that inherited factors play an important role in childhood language disorders," says Dr Simon Fisher, a Royal Society Research Fellow at the Wellcome Trust Centre, who led the research. "But this is the first time that we have been able to implicate variants of a specific gene in common forms of language impairment."

The trail to this new finding began with studies of another language-related gene, called FOXP2, previously found to be mutated in rare cases

of a severe speech and language disorder. Versions of FOXP2 are found in many animals, including primates, birds, bats and mice. In birds, for example, it has been linked to song, in mice to learning of sequences of movement, and in bats it may relate to echo-location.

FOXP2 acts to regulate other genes in the brain, switching them on and off. Dr Fisher and colleagues began analysing human neurons grown in the laboratory in order to search for these target genes. They identified CNTNAP2 as a key part of the network.

When the scientists went on to investigate CNTNAP2 in 184 families with common language impairments, they found that children who carried certain variants of the gene displayed reduced language abilities, most strikingly for a measure of nonsense-word repetition that is known to be a strong indicator of SLI.

Recent studies have also implicated CNTNAP2 in autism, a syndrome characterised by communication deficits, impaired social interaction, and repetitive behaviours. In particular, one investigation uncovered an association between variants of CNTNAP2 and delayed language development in children with autism.

"Our findings suggest that similar changes in the regulation or function of this gene could be involved in language deficits in both SLI and autism," says Dr Fisher. "This supports the emerging view that autism involves the convergence of a number of distinct problems underpinned by different genetic effects."

Professor Dorothy Bishop, a Wellcome Trust Principal Research Fellow at the University of Oxford, who specialises in the study of children's communication impairments, comments:
"All too often parents of language-impaired children are blamed for their children's difficulties, even though the evidence has been around for a

while that genes are implicated. These are important yet neglected disorders that can have long term effects on educational and social outcomes. This landmark study provides an important first step in unravelling the complex biological factors that determine susceptibility to language difficulties."

It is not yet known exactly how changes to CNTNAP2 interfere with language development, but there are some tantalising clues. The gene makes a type of protein called a neurexin, which sits in the membranes of neurons, controlling interactions between different cells during the development and wiring up of the nervous system. In early development, the protein appears to be strongly expressed in parts of the human brain which go on to become important for language processing, such as the frontal lobes.

The researchers are now investigating whether variations in CNTNAP2 contribute to natural variation in linguistic abilities in the general population.

"Genes like CNTNAP2 and FOXP2 are giving us an exciting new molecular perspective on speech and language development, one of the most fascinating but mysterious aspects of being human," says Dr. Fisher "There are likely to be more answers buried in our genome. This work promises to shed light on how networks of genes help to build a language-ready brain."

Source: Wellcome Trust