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Gene discovery supports link between handedness and language-related disorders

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Scientists at the Wellcome Trust Centre for Human Genetics, University of Oxford, have identified a genetic variant which influences whether a person with dyslexia is more skilled with either the left or right hand. The finding identifies a novel gene for handedness and provides the first genetic evidence to support a much speculated link between handedness and a language-related disorder.

The majority of people worldwide are right-handed. Since the left side of the brain controls the right side of the body, and vice versa, this implies that for most people the left hemisphere of the brain is the dominant side for motor functions. It is also known from family studies that genetics strongly influences handedness.

Most individuals also have left-hemisphere dominance for language function, as demonstrated by language impairment in individuals with damage to certain regions of the left side of their brain.

It has since been suggested that the population bias towards right-handedness evolved as a consequence of the evolution of language. Therefore, scientists have thought that there may be a link between hand preference and disorders that affect language development, such as autism and specific language impairment (SLI). However, no convincing evidence has been found.

In a study funded by the Wellcome Trust, the Medical Research Council and the European Union, scientists scanned the genomes of 192 children

with reading difficulties. These children also had their left and right hand skill measured. The results of the study are published online today in the journal *Human Molecular Genetics*.

The scientists found a strong link between a variant of a gene called PCSK6 and relative hand skill in these children with reading difficulties. Specifically, while most people are better at using their right hand, those who carried the variant in PCSK6 were, on average, more skilled with their right hand compared to the left than those not carrying the variant. This result was also seen in two independent groups of children with reading difficulties.

The protein product of the gene PCSK6 is known to interact with another protein called NODAL. Previous experiments have shown that NODAL plays a key role in establishing left-right asymmetry early in embryonic development. This suggests that genetic variants of PCSK6 may have an effect on the initial left-right patterning of the embryo that in turn influences the development of brain asymmetry, and thus handedness.

Furthermore, as William Brandler, one of the study's authors explains: "Our closest relatives, the great apes, do not display the striking bias towards right-handedness seen in humans. So understanding the genetic basis of handedness may offer us significant insights into our evolution."

"This study provides the first genetic link between handedness, brain asymmetry and reading ability," says Professor Tony Monaco, leader of the group that made this discovery. "Despite the known biological function of PCSK6, this is the first study implicating it with handedness. The fact that this association also seems to be apparent in people with dyslexia provides an interesting clue to explore whether there is a link between handedness and language-related disorders."

One of the aims of this study was to understand the genetics of handedness, and the results should open up new avenues into exploring the biology of language-related disorders, and help identify whether the evolution of language and handedness did indeed go hand-in-hand.

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