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When your left hand mimics what your right hand does: It's in the genes

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Further work carried out on mice suggests that this gene plays a part in motor network cross-over. Cross-over is a key factor in the transmission of brain signals, because it allows the right side of the brain to control the left side of the body and vice versa. This research has been published in *The American Journal of Human Genetics*.

Congenital mirror movement is a rare disease transmitted from one generation to another by dominant inheritance. The affected persons lose the ability to carry out different movements with separate hands: when one hand moves in a certain way, the other hand is "forced" to copy the same movement, even if the person does not wish to do so. So people suffering from this disease are totally incapable of bimanual motor activities, such as piano playing for example. This phenomenon has been observed in children, but generally cleared up spontaneously before the age of 10, no doubt due to maturing of the motoneuron networks. However, in people who are affected by the disorder, the illness starts in early childhood and remains unchanged throughout life.

In 2010, research scientists from Quebec analyzed the genome from the members of a large Canadian family and discovered a gene responsible for the disease. Mutations had been detected in the DCC (Deleted in Colorectal Carcinoma) gene. Following this discovery, the team of researchers and doctors coordinated by Emmanuel Flamand-Roze began to search for mutations in this gene in several members of a French family who were also suffering from congenital mirror movements disease, but without success. "The DCC gene was intact", explained

Emmanuel Flamand-Roze. "We thought we were nearly there and instead we had to start searching for mutation in a different gene", he adds.

Using an approach that combines conventional genetic analysis and "whole exome" analysis (a new-generation genetic analysis technique that involves entirely sequencing the important part of the genome), scientists demonstrated that the RAD51 gene was responsible for congenital mirror movement disease in a large French family and went on to corroborate this result using the same techniques on a German family suffering from the same disorder.

"The RAD51 gene was already known to the scientific community as a potential catalyst for certain types of cancer and in problems of resistance to chemotherapy", explains Emmanuel Flamand-Roze. "So we wondered whether it had yet another function that could explain the motor symptoms of CMM disease".

In humans, the motor system is a cross-control system, which means that the left side of the brain controls the motor functions of the right side of the body and vice versa, with the cross-over taking place at the brainstem. While studying the expression of the RAD51 protein during development of the motor system in mice, the research scientists discovered that this gene could be implanted into the cross-over of the motor network that links the brain to the spinal fluid at the brainstem.

This discovery opens up a whole new field of investigation into the development of the motor system and to achieving better understanding of the cerebral mechanisms that control bimanual motricity. It could also shed light on other motricity disorders related to fine movement organization, such as dystonia or certain genetic neurodevelopmental diseases.

More information: RAD51 Haploinsufficiency Causes Congenital Mirror Movements in Humans, *The American Journal of Human Genetics*, dx.doi.org/10.1016/j.ajhg.2011.12.002