Multimodal Neurophysiological and Neuroimaging Evidence of Genetic Influence on Motor Control: A Case Report of Monozygotic Twins

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Abstract: Considering genetic influence on brain structure and function, including motor control, we report a case of right-handed monozygotic twins with atypical organization of fine motor movement control that might imply genetic influence. Structural and functional organization of the twins' motor function was assessed using transcranial magnetic stimulation (TMS), fMRI with a motor-task paradigm, and diffusion tensor imaging (DTI) tractography. TMS revealed that both twins presented the same unexpected activation and inhibition of both motor cortices during volitional unilateral fine hand movement. The right ipsilateral corticospinal tract was weaker than the left contralateral one. The motor-task fMRI identified activation in the left primary motor cortex and bilateral secondary motor areas during right-hand (dominant) movement and activation in the bilateral primary motor cortex and secondary motor areas during left-hand movement. Based on DTI tractography, both twins showed a significantly lower streamline count (number of fibers) in the right corticospinal tract compared with a control group, which was not the case for the left corticospinal tract. Neither twin reported any difficulty in conducting fine motor movements during their activities of daily living. The combination of TMS and advanced neuroimaging techniques identified an atypical motor control organization that might be influenced by genetic factors. This combination emphasizes that activation of the unilateral uncrossed pyramidal tract represents an alternative scheme to a "failure" of building a standard pattern but may not necessarily lead to disability.

Key Words: mirror movements, transcranial magnetic stimulation, functional magnetic resonance imaging, diffusion tensor tractography, interhemispheric inhibition

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ACE–R = Addenbrooke's Cognitive Examination—Revised. **AI** = asymmetry index. **APB** = abductor pollicis brevis. **CST** = corticospinal tract. **DTI** = diffusion tensor imaging. **FA** = fractional anisotropy. **HADS** = Hospital and Anxiety Depression Scale. **IHI** = interhemispheric inhibition. **M1** = primary motor cortex. **MEP** = motor-evoked potential. **ptA** = participant A. **ptC** = participant C. **R** = rest. **ROI** = region-of-interest. **S1** = primary sensory cortex. **SMA** = supplementary motor area. **SP** = silent period. **T** = task. **TMS** = transcranial magnetic stimulation.

The heritability of, and genetic influence on, cognitive functions and intelligence has been proven in twin and family studies for decades (DeFries et al, 1976; Toga and Thompson, 2005) and has also been observed in studies of brain structure (Chen et al, 2013; Panizzon et al, 2009; Peper et al, 2007; Thompson et al, 2001) and function (Colclough et al, 2017; Fu et al, 2015; van Beijsterveldt et al, 1996). Genetic influence has also been reported regarding motor functions in studies of monozygotic and dizygotic twins (eg, motor control [Maes et al, 1996] and motor learning [Fox et al, 1996; Missitzi et al, 2013; Williams and Gross, 1980]). Recently, a collaborative network of researchers (ie, Enhancing Neuroimaging Genetics Through Meta-Analysis) and large-scale data sets (eg, Human Connectome Project) investigated associations between genetics and (a) volumes of cortical and subcortical structures, (b) white matter microstructure (Thompson et al, 2014), and (c) patterns of functional connectivity (Miranda-Dominguez et al, 2018).

Fine motor movements that are executed by peripheral muscles in the upper extremities are mediated by

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