LETTER TO THE EDITOR

Congenital mirror movements: lack of decussation of pyramids

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Sir, We have read with great interest the article published by Gallea et al. (2013), in the November 2013 issue of Brain, regarding the pathophysiological basis of the rare disease named congenital mirror movements (Srour et al., 2010; Depienne et al., 2012), that might serve as a model to recognize new aspects of bimanual motor control (Gallea et al., 2011).

We have recently seen a patient with congenital mirror movements and have coincidentally studied this disorder using a clinical, neurophysiological and neuroimaging protocol similar to those used by Gallea et al. (2013). This case was presented as a video session at the 5th Meeting of the Movement Disorders Scientific Department of the Brazilian Academy of Neurology, in August 2013, but has not yet been published.

Our patient is a 32-year-old right-handed male, with synkinetic distal movements of distal limbs since early childhood, with stable course, and no other movement disorders or neurological abnormalities. The involuntary movements led him to labour impairment as he works as a postman and has difficulties in performing bimanual tasks such as writing on a clipboard or handling a mobile telephone or keyboard. Interestingly, a late acquisition of running abilities was his only neurodevelopmental delay; his parents reporting a preference for jumping instead of running in early childhood [which may be similar to the Kanga mice hopping gait, with spontaneous mutation in the deleted in colorectal carcinoma (Dcc) gene] (Finger et al., 2002). His clinical manifestations were classified in the Woods and Teuber Mirror Movements Scale (Woods and Teuber, 1978) as 3 of 4 (strong and sustained repetitive mirror movements), and are shown in Fig. 1.

We made sure to exclude alternative diagnoses, such as Klippel-Feil or X-linked Kallman syndrome, with cervical spine imaging and hypophyseal hormone dosing, which were normal.

The patient underwent a functional MRI with blood oxygen level-dependent protocol and 3.0T diffusion tensor imaging (DTI) tractography and, subsequently, focal transcranial magnetic stimulation (TMS), to induce motor evoked potentials and measure their amplitudes and latencies.

The TMS focal stimulus was delivered to the optimal scalp position related to the hand area of the primary motor cortex (M1) and the evoked response recorded by superficial electromyography over the abductor digiti minimi hand muscle. The magnetic stimulator was a MagPro® and the electromyograph a Keypoint® (Meditronic).

The motor evoked potentials were elicited bilaterally, and exhibited a 2.5 ms difference in latencies between both sides (22.7 ms in ipsilateral abductor digiti minimi recording and 25.2 ms in contralateral abductor digiti minimi recording). The amplitudes of the elicited motor evoked potentials were also slightly asymmetric, showing higher values for contralateral motor evoked potentials (0.14 mV) when compared with the ipsilateral motor evoked potentials (0.085 mV). The shorter latency in ipsilateral motor evoked potentials might suggest a direct cortico-motor neuronal projection in the ipsilateral corticospinal tract.
and, possibly, a polysynaptic connection in the crossed corticospinal tract—although this conclusion may be elusive as only one subject was studied. The ipsilateral motor evoked potential was, in addition to smaller in amplitude, also not systematically induced in each stimulus, a feature that agrees with data presented in Gallea et al. (2013), and does not confirm the ones described in previous studies (Cohen et al., 1991; Cincotta et al., 2003a, b; Ueki et al., 2005; Verstynen et al., 2007; Cincotta and Ziemann, 2008).

The MRI scanner used was an Ingenia 3.0 T (Philips Healthcare). DTI tractography protocol was performed with 15 diffusion directions isotropically distributed on a sphere, 128 × 128 matrix, 2.5 × 2.5 × 2.5 cm voxel size, echo time 89 ms, repetition time 3470 ms, b-value of 800 s/mm², for 7 min. The blood oxygen level-dependent functional MRI sequence was performed with T₂*-weighted single-shot echo-planar imaging sequence with voxel size 2.4 × 2.4 × 4 mm, 128 × 128 matrix, field of view 230 × 230 mm², echo time 35 ms, repetition time 3000 ms, 60 phases, stimulus every 10 stages with ‘finger tapping test’.

The MRI results exhibited similar results to those by Gallea et al. (2013). The blood oxygen level-dependent functional MRI signals are shown in Fig. 2, showing blood flow in both primary motor cortices and supplementary motor areas during finger tapping of either the right hand (Fig. 2A), or left hand (Fig. 2B). The corticospinal tractography shows, in Fig. 3, lack of the decussation of pyramids (Fig. 3A), as compared to a control subject (Fig. 3B).

**Figure 1** Synkinetic contralateral movements (mirror movements) with distal motor task of the upper limb: (A and B) voluntary hand grip of the right hand, (C–F) intentional alternating finger tapping of the left hand, using from second to fifth hand digits.

**Figure 2** Bilateral functional MRI blood oxygen level-dependent response over precentral, post central gyrus and supplementary motor area during unimanual task. The patient was asked to perform a finger tapping task with either (A) the right hand or (B) the left hand.
To accurately confirm the complete absence of the normal crossed corticospinal tract, and to overcome technical limitations of DTI in regions with intense axonal crossing, another analysis of the MRI data of the patient with congenital mirror movements was made. Deterministic and probabilistic tractography were reconstructed, using an algorithm for fibre orientation distribution function estimation on the corticospinal tract, based on high angular resolution diffusion imaging (HARDI) and Q-ball imaging (QBI), in a technique already described elsewhere (Descoteaux et al., 2009; Fortin et al., 2012). Six regions of interest were segmented for each side, using the software FiberNavigator (Open-source software: http://scilus.github.io/fibernavigator/): the hand cortical area (in precentral gyrus), posterior limb of internal capsule, cerebral peduncle, ventral pons, ipsilateral anterior

![Figure 3](image1.png)

**Figure 3** 3.0 T MRI DTI tractography, (A) missing decussation of pyramids, with strictly unilateral non-crossing corticospinal tracts, and (B) a control subject, with normal crossing corticospinal tracts.

![Figure 4](image2.png)

**Figure 4** HARDI/Q-ball fibre tracking through orientation distribution function estimation of the corticospinal projection of the patient with congenital mirror movements. Strictly non-crossed corticospinal tract is shown in (A and B). A crossed corticospinal fibre bundle is not found when the region of interest is segmented to the contralateral lateral funiculus in (C).
funiculus of upper spinal cord (to track the non-crossing corticospinal fibre bundle) and contralateral lateral funiculus (to determine the crossing corticospinal tract). The tractography, derived from this algorithm and region of interest, is shown in Fig. 4, where only abnormal uncrossed corticospinal tracts are tracked at each side, confirming previous DTI findings of a lacking decussation of pyramids and lack of a normally crossed corticospinal tract.

The above results, in addition to those in the referred paper, also raise other interesting questions: (i) may the supplementary motor area be a potential target for repetitive TMS (with therapeutic aims? (ii) might the abnormal pyramidal decussation be an adequate biomarker for diagnostic purposes? and (iii) could the described abnormal interhemispheric inhibition be artificially ‘rebalanced’ with neuromodulation strategies such as repetitive TMS or anodal transcranial direct current stimulation?

To address this last question, it would be interesting to try to modulate the excitability of the motor cortices; we are now conducting a series of transcranial direct current stimulation experiments on the patient to ascertain whether his mirror movements could be thus diminished.

The paper by Gallea et al. (2013), in an elegant experimental setting, provides evidence for the importance of studying this rare disease using basic and clinical neurosciences in ways to better comprehend unimanual and bimanual motor control as well as to give insights into corticospinal tract neurodevelopment.

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References


