

# Treating Congenital Mirror Movements with Botulinum Toxin

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Mirror movements (MMs) are simultaneous, contralateral, identical movements that accompany voluntary movements. They usually occur in the distal upper limbs, being of lesser amplitude than the voluntary activity; they can be unilateral or bilateral, but 1 side is generally more affected.<sup>1</sup> MMs are underlined by various causes and are sustained at least by 2 main pathophysiologic mechanisms: (1) coactivation of both primary motor areas (M1) in the majority of MMs associated with neurodegenerative diseases, and (2) the presence of an abnormal, ipsilateral, direct corticospinal pathway, as seen mostly in congenital MMs (CMMs). CMMs are characterized by MMs in isolation without other significant clinical signs and are associated in one-third of cases with a heterozygous pathogenic variant of the DCC or RAD51 genes.<sup>2</sup> Although MMs rarely cause disability, patients with CMMs may have strong and sustained synkinesis, which can interfere with complex bi-manual and repetitive movements.

Here, we report the case of a patient who had CMMs successfully treated with botulinum toxin (BoNT).

## Case Report

A left-handed, 24-year-old Caucasian man came to our Movement Disorders Clinic because of disabling, involuntary upper limbs movements, which occurred when performing precision tasks, like tying shoelaces or writing on the keyboard; these movements were first noticed in primary school (when he started writing), and they negatively impacted on his professional activity of computer service technician. Familial history was negative for MMs or any other neurologic disorders. He was born post term and had neonatal jaundice without sequelae, and he reached physiologic developmental milestones. Neurologic examination was videotaped after informed consent was obtained. There were MMs in the upper limbs, and they were more prominent on the right hand and were graded 3 on the Woods and Teuber scale<sup>3</sup>

(Video S1). He also had a brisk deep tendon reflex on the left hemibody and mild postural tremor in both hands. The remaining neurologic examination was unremarkable.

A brain magnetic resonance image (MRI) was normal, and a neck MRI showed a C5 through C6 disc protrusion, with minimal compression of the thecal sac. Nerve-conduction studies and needle electromyography did not reveal any abnormalities in the peripheral nervous system. Transcranial magnetic stimulation (TMS) was performed with a figure-of-8 coil in separate sessions stimulating at 130% over the resting motor threshold the left and right M1; motor-evoked potentials (MEPs) were recorded simultaneously from the right and left abductor pollicis brevis (APB). Bilateral MEPs were demonstrated when stimulating each M1; the mean ipsilateral MEP amplitude was higher than the contralateral MEP amplitude, especially when stimulating the left M1 (Fig. 1A) (left M1 TMS: ipsilateral MEP, 0.9 mV; contralateral MEP, 0.4 mV; right M1 TMS: ipsilateral MEP, 0.5 mV; contralateral MEP, 0.3 mV). Surface electromyography (EMG) polygraphs were recorded at rest and when performing self-paced, repetitive flexion-extension of the fingers and demonstrated simultaneous, bilateral bursts of EMG activity when performing unilateral flexion or extension movements (Fig. 1B). Incobotulinumtoxin A (20 U in total) was injected using EMG and ultrasounds guidance in the right extensor indicis proprius and extensor digitorum communis (component of the third finger). Botulinum toxin (BoNT) was injected only into the right forearm muscles to demonstrate clinical effects in noninjected muscles and allow the left upper limb to perform manual activities, if side effects developed. After a transitory period of reduced hand dexterity lasting 2 weeks, the patient experienced a reduction of MMs in the right hand, allowing him to easily perform his work and general bimanual activities. At 4 months after BoNT (Video S1), MMs on the right hand were still improved, scoring 1 on the Woods

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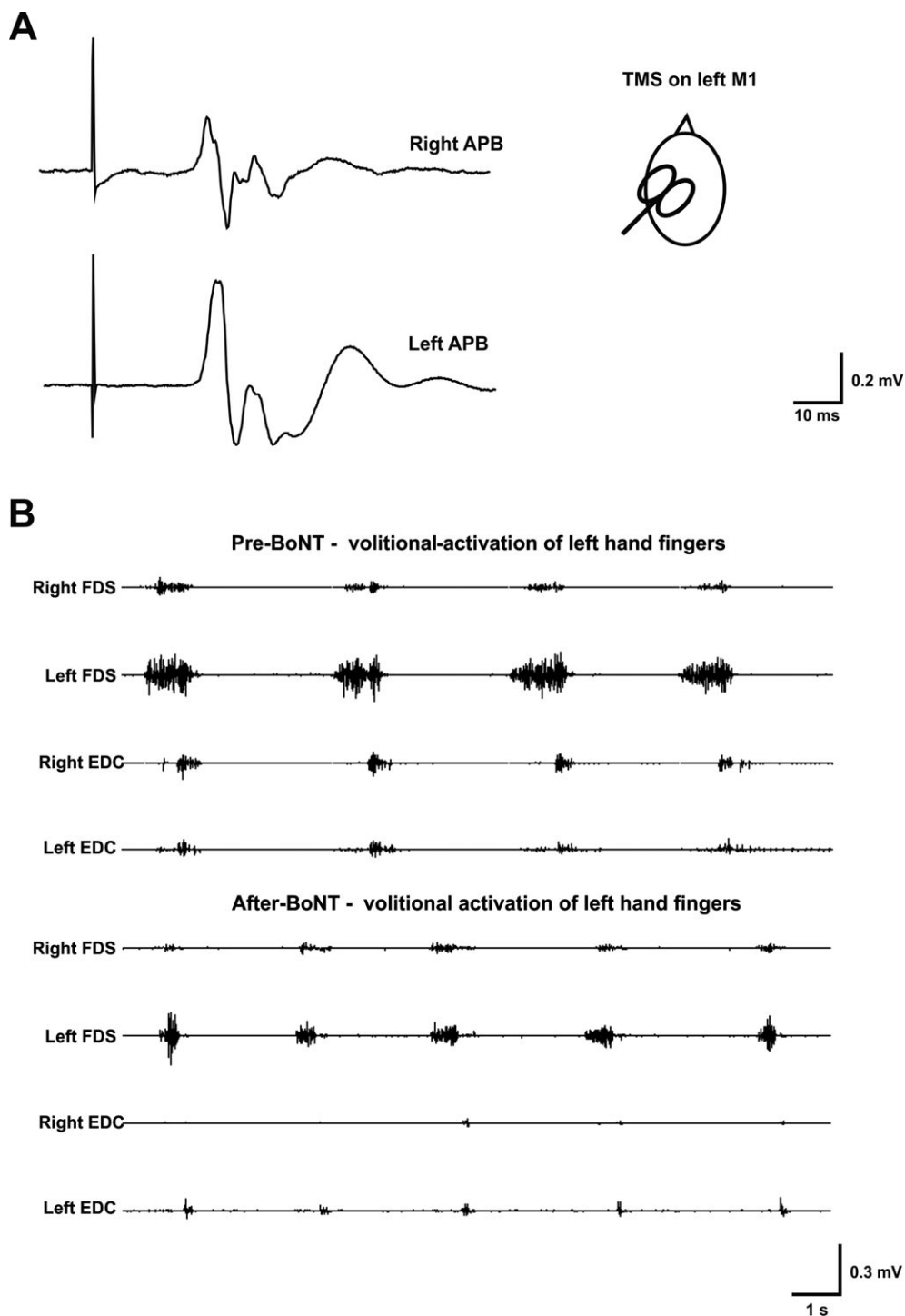
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Relevant disclosures and conflicts of interest are listed at the end of this article.

Supporting information may be found in the online version of this article.

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**FIG. 1.** **A:** Transcranial magnetic stimulation (TMS) of the left primary motor area (M1) induced a contralateral motor-evoked potential (MEP) (on the right abductor pollicis brevis [APB]) and an ipsilateral MEP (on the left APB). The mean amplitude of the ipsilateral MEP was larger than that of the contralateral MEP. Representative recorded MEPs are shown. **B:** Polygraph recordings from the right and left flexor digitorum superficialis (FDS) and extensor digitorum communis (EDC) were obtained while the patient was performing self-paced, repetitive flexion-extension movements of the fingers of the left hand. Simultaneous electromyogram (EMG) activity compatible with mirror movement (MM) was present on the right flexor digitorum superficialis (FDS) and extensor digitorum communis (EDC) before Botulinum toxin (BoNT) treatment. After BoNT treatment, the amplitude of the EMG bursts in the right FDS was decreased; and, overall, there was less EMG activity in the right EDC.

and Teuber scale. The improvement involved not only the injected extensor muscles but also the forearm flexors (Fig. 1B). He received another BoNT treatment at a 4-month follow-up visit, with injections into the forearm flexor and extensor muscles of both upper limbs, to achieve a larger functional improvement. We injected the right and left extensor indicis proprius, extensor digitorum communis, flexor pollicis longus, and flexor digitorum superficialis (5 U incobotulinumtoxin A in each). At 1-month follow-up, MMs were further improved in both hands (scores of 1–2 on the Woods and Teuber scale) to the extent that he could easily type on the keyboard. No side effects were reported.

## Discussion and Conclusion

Few case reports have focused on the treatment of MMs, and there are no studies on patient cohorts.<sup>1,4,5</sup> Zhu et al. reported a patient who had MMs associated with spastic cerebral palsy who improved after BoNT injection into the spastic arm.<sup>6</sup> Our case demonstrates that BoNT may be useful for treating MMs by targeting only specific muscles and also allowing a reduction in MMs in noninjected muscles. This approach was supported by the polygraph EMG recording, revealing a reduction in mirror EMG activity also in the right flexor digitorum superficialis muscle, which was not injected with BoNT. The mechanism of action of BoNT for MMs in noninjected muscles is speculative. We hypothesize that BoNT can modulate sensory afferents, changing the signal from muscle spindles,<sup>7</sup> ultimately modifying cortical networks, and improving the physiologic lateralization of the motor program over the abnormal ipsilateral pathways present in CMMs.

## Author Roles

1. Research Project: A. Conception, B. Organization, C. Execution; 2. Statistical analysis: A. Design, B. Execution, C. Review and Critique; 3. Manuscript preparation: A. Writing the First Draft, B. Review and Critique.

C.A.: 1B, 1C, 3A

P.G.: 1A, 3B

F.M.: 1A, 1B, 1C, 3B

## Disclosures

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## Supporting Information

A video accompanying this article is available in the supporting information here.

**Video S1.** *Segment 1:* Before botulinum toxin (BoNT) treatment, voluntary finger tapping movements were accompanied by prominent mirror movements (MMs) when performing the movement with either the right or left hand. *Segment 2:* Four months after BoNT treatment, extensor MMs of the right hand were markedly reduced. The second and third fingers of the right hand did not show clear extensor MMs, although some MMs were evident in the fourth and fifth fingers. Flexor MMs in the right hand were also decreased after BoNT treatment, although to a lesser extent.