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Tremor and Other Hyperkinetic Movements

Case Reports

Mirror Movements Identified in Patients with Moebius Syndrome

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Abstract

Background: Moebius syndrome is a rare disorder with minimum clinical criteria of congenital facial weakness in association with impairment in abduction of one or both eyes. Mirror movements are not known to be associated with Moebius syndrome.

Case Report: We present three patients who meet minimum criteria for a diagnosis of Moebius syndrome and who also display mirror movements.

Discussion: This case series suggests that Moebius syndrome may be associated with mirror movements. Further investigation to delineate the genetic etiologies of Moebius syndrome is ongoing. Patients with Moebius syndrome and mirror movements may represent a specific subclass of this disorder.

Keywords: Mirror movements, Moebius syndrome

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Introduction

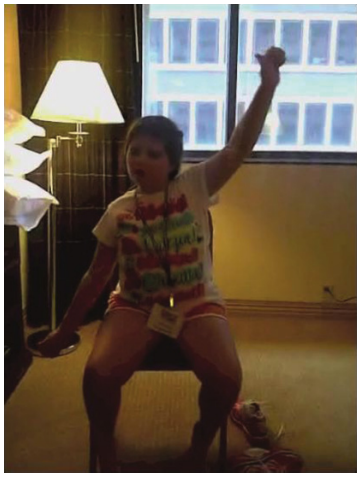
Mirror movements (MM) are defined as involuntary movements of one side of the body that occur simultaneously with intentional movements of the contralateral side. MM frequently are noted in the upper extremities, particularly in the hands and fingers, and their intensity often increases with the complexity of the voluntary movement. MM may be a normal neurological finding in young children, but their presence in older children, over the age of 10 years, and adults may suggest neurological disease. MM may be seen in isolation, may be inherited as an autosomal dominant condition, and may be associated with other motor abnormalities or genetic syndromes, including Kallmann and Klippel–Feil syndromes.[1,2] MM have not been associated with Moebius syndrome, a syndrome defined with minimum criteria of congenital, non-progressive facial weakness in association with limited abduction of one or both eyes, although bilateral horizontal gaze palsy (BHGP) may be a more common ocular finding.[3,4] Here we report three patients with facial weakness, impairment in ocular abduction, and MM. These patients were examined at a Moebius Syndrome Foundation conference, and MM were noted during detailed neurological examination after self-reported MM in one patient prompted examiners to assess all patients for MM.

Case report

Patient 1 is a 44-year-old Caucasian male with congenital bilateral facial paralysis (left more severe than right) and BHGP. Medical history is notable for significant developmental delay, autism, migraine headaches, and anxiety. The patient has had no prior surgeries.

Patient 2 is a 29-year-old Caucasian female with congenital left-sided facial weakness and BHGP. Surgical history is significant for smile surgery with sural nerve grafting and history of two revisions. History of prior strabismus surgery is denied. Neurological examination revealed abnormal tandem gait.

Patient 3 is a 9-year-old Caucasian female with congenital bilateral facial weakness and BHGP with additional mild left eye depression and right eye elevation defects. History is notable for three prior strabismus surgeries. Imbalance was reported and examination revealed mild arm weakness and an atrophic tongue with deep midline furrow. Video 1 shows Patient 3 exhibiting MM. Additional case details are provided in Table 1.



Video 1. **Video Demonstrating Mirror Movements in Patient 3.** Patient 3 is asked to raise her left arm above her head and open and close her left hand and then raise her right arm above her head and open and close her right hand. MM in the contralateral hand are witnessed during each of these tasks.

Discussion

While MM may be seen sporadically in healthy individuals or may be inherited as an isolated trait, they may also signify pathologic neurological disease that is either congenital or acquired.[5] Recent studies of MM in adults with Parkinson disease and essential tremor revealed a much higher than anticipated prevalence of MM in adult healthy control subjects, ranging between 24% and 71%;[6,7] however, MM in the hands were much less common than MM in the feet, and pathologic MM tended to have worsened severity. Additional studies have shown that MM in healthy adults are subtle and require complicated movements for elicitation.[8] While we cannot fully exclude the possibility that MM in our patients represent an incidental finding, the presence of MM in the hands and the prominence and ease of elicitation of the MM in our patients suggest that they may be pathological and related to the diagnosis of Moebius syndrome. In addition, there is an emerging literature on widespread neurological involvement, including MM, in the group of congenital disorders of

Table 1. Additional Clinical History for Patients with Moebius Syndrome and Mirror Movements

	Patient 1	Patient 2	Patient 3
Hearing loss	Symptoms denied by patient	Symptoms denied by patient	Audiology examination notable for mild sensorineural hearing loss bilaterally
Additional cranial nerve abnormalities	XII: tongue atrophy	Decreased sensation in left V2 and V3 apparent, but patient has prior history of multiple smile surgeries.	XII: tongue atrophy
Limb anomalies	No	No	No
Poland anomaly [1]	No	No	No
Mental retardation/developmental delay	Yes	No	No
Psychiatric diagnosis	Anxiety, autism	No	No
Klippel–Feil anomaly	Neck X-rays reviewed and no evidence of Klippel–Feil anomaly	Neck X-rays unavailable, but patient has a long neck, normal range of motion, and a normal posterior hairline	Neck X-rays reviewed and no evidence of Klippel–Feil anomaly
Anosmia	No	No	No
Hypogonadotropic hypogonadism	No	No	No
Family history of mirror movements	No	No	No
Family history of Moebius syndrome	No	No	No
Family history of consanguinity	No	No	No

[1]Poland anomaly is defined as pectoral muscle hypoplasia ± ipsilateral hand or digit anomalies

axonal migration and cranial innervation to which Moebius syndrome belongs.[4,9]

None of the individuals presented here had a positive family history of MM, suggesting that MM segregating as an isolated autosomal dominant trait is unlikely. Neck X-rays available for two of the three patients reveal no evidence of Klippel–Feil anomaly. The third patient did not have a short neck, limited range of motion, or a low posterior hairline, and therefore exhibits none of the classic clinical triad for Klippel–Feil anomaly. None of the three individuals had symptoms of Kallmann syndrome. The three patients presented met minimum clinical criteria for diagnosis of Moebius syndrome. Patient 3 had a more complex ocular phenotype. This case series suggests that Moebius syndrome represents an additional developmental condition that may be associated with congenital MM.

MM are thought to result from two possible pathophysiological mechanisms. First, the signal for MM may arise within the *same* hemisphere as that of the voluntary movement via projections from an ipsilateral corticospinal tract or via branches of a crossed corticospinal fiber. Alternatively, MM may arise by aberrant activation of *both* hemispheres secondary to 1) decreased transcallosal inhibition and/or increased facilitation or 2) altered interhemispheric inhibition of intracortical facilitation in the primary motor cortex (M1) contralateral to the MM hand.[10] Interestingly, post-mortem analysis of the brainstem of one neonate with Moebius syndrome has revealed dysplastic pyramidal tracts with absent pyramidal decussation at the level of the cervical cord.[11,12] Such deficient decussation may lead to accessory or double-branched pathways and suggests that impaired corticospinal tract development may cause MM in patients with Moebius syndrome.

The genetic etiologies of Moebius syndrome are currently not well understood and the disorder appears to be molecularly heterogeneous. Patients who meet minimum clinical criteria may present with widely varying concurrent features including, but not limited to, abnormalities of other cranial nerves, limb anomalies, intellectual disability, and autism. Noting the presence or absence of MM in patients with this diagnosis may be helpful in clinical sub-classification.

Additional studies, including electromyogram, transcranial magnetic stimulation (TMS), and MR diffusion tensor imaging (DTI), will be useful for further characterization of MM in patients with Moebius syndrome.

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