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Congenital Mirror Movements: Behavioral, Neural, Genetic, and Clinical Issues

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Non-syndromic congenital mirror movements (CMM) is a rare neurological condition, either inherited or sporadic, in which affected individuals lack independent dexterity of hand and finger movements. With all volitional movements of the hands and fingers, unintentional mirroring occurs in the opposite-side homologous effectors. A hallmark neural mechanism of CMM is abnormal, active, extra ipsilateral corticospinal tracts. Mutations in four different causal genes have been identified so far. The present review considers the physiology underlying CMM, including its implicated neural mechanisms and clinical relevance. The heterogeneous nature of the condition is highlighted, particularly in terms of the clinical importance of factors associated with the mirroring phenotype or phenotypes. Speculation about the possible effects of CMM on the somatosensory system is also included as a prospective direction for further study. Despite some inconvenience and occasional discomfort associated with CMM, the potential for highly positive life outcomes is illuminated. Lastly, CMM management is discussed as a key goal toward which future research should stride.

Keywords: congenital mirror movements, CMM, movement disorder, bimanual actions, volition

Les mouvements miroirs congénitaux (MMC) non-syndromiques sont une condition neurologique rare, héréditaire ou sporadique, dans laquelle les individus affectés manquent de dextérité indépendante des mouvements des mains et des doigts. Pour tous les mouvements volontaires des mains et des doigts, survient du *mirroring* involontaire dans les effecteurs homologues du côté opposé. Un mécanisme neuronal caractéristique des MMC consiste en des voies cortico-spinales extra-ipsilatérales anormales et actives. À ce jour, des mutations dans quatre gènes responsables ont été identifiées. Cette revue étudie la physiologie sous-tendant les MMC, en incluant les mécanismes neuronaux impliqués et son importance clinique. L'hétérogénéité de la condition est mise en évidence, particulièrement en ce qui concerne l'importance clinique des facteurs associés à son phénotype. Certaines spéculations à propos des effets des MMC sur le système somatosensoriel sont aussi proposées comme pistes prospectives d'études futures. Malgré quelques inconvénients et les inconforts occasionnels associés aux MMC, la possibilité de vivre des expériences de vie positives est soulignée. Finalement, la gestion des MMC est discutée en tant qu'objectif clé auquel les recherches futures devraient s'intéresser.

Mots clés : mouvements miroirs congénitaux non-syndromiques, MMC, trouble du mouvement, actions bimanuelles, volonté

Imagine pointing at something with a finger of the right hand and having the left hand's finger mimic the right hand's movements, or jotting down a note with your dominant hand while your non-dominant hand produces mirror writing. These are typical examples produced by people with congenital mirror movements (CMM), a rare condition in which involuntary movements of the hands and fingers on one side of the body occur with all intended unimanual movements of homologous effectors (Cohen et al., 1991; Franz, 2003). In addition, mirroring can occur in other effector systems such as the feet or upper arms (Franz et al., 2015; Schott & Wyke, 1981). Instances of the condition can be found in multigenerational families as well as in sporadic cases, with the prevalence estimated to be as low as 1

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in 1,000,000 people (Orphanet, 2018). However, Méneret, Trouillard, Depienne, and Roze (2015) and Marsh et al. (2018) propose that CMM could be underdiagnosed, particularly among individuals whose symptoms are mild; furthermore, subclinical evidence of mirroring has been reported (Franz et al., 2015).

CMM, as defined herein (and in other studies: Franz et al., 2015; Méneret et al., 2017) refers to the non-syndromic form in that isolated mirroring is the only behavioral symptom (at least, the only one known). However, it is important to point out that other syndromic mirroring conditions that feature mirror movements as a sign or symptom of more encompassing neurological disorders exist (e.g., Klippel-Feil syndrome, Usher's syndrome, agenesis of the corpus callosum [Schott & Wyke, 1981], Kallmann syndrome [Krams et al., 1999], Parkinson's Disease [Li et al., 2007], or following stroke [Nelles, Cramer, Schaechter, Kaplan, & Finklestein, 1998]), and typically pose further consequences for behavior and cognitive functioning.

The severity in which CMM manifests has been shown to vary widely across individuals. For example, CMM may be undetectable upon visual observation, but when present can be measured in movements ranging from the fingertips to the shoulder girdle; it may or may not also be apparent in other effectors such as the toes (Franz et al., 2015). It can vary in extent across affected members of the same family (Fasano et al., 2014; Franz et al., 2015), yet it seems a commonality that mirroring occurs primarily in the distal upper limbs during active movements (i.e., voluntary or intentional, as opposed to passive movements which occur when someone or something else acts on the body). CMM is present during infancy with no apparent progression or regression in intensity throughout life and is not accompanied by other functional deficits as yet known, unless related to a form of disorder as listed above (Schott & Wyke, 1981). Whereas symmetrical bimanual movements are easy to perform by people affected by CMM, bimanual actions requiring distinct movements of the two hands (Franz, 2003; Franz, Zelaznik, & McCabe, 1991; reviewed in Franz, 2012) pose far more difficulty than in neurologically-normal samples. For example, skills such as playing the piano present a great challenge, although can become possible through practice with concerted effort/attention. However, applying effort or attention does not completely eliminate the mirroring (Schott & Wyke, 1981). Mirror movements also tend to be of lesser amplitude than the intended movements they mimic (Franz et al., 2015). Painful contractions of the muscles in the mirroring limb can occur in some individuals with CMM while attempting to suppress the involuntary movements (Cincotta et al., 2003) but typically, mirroring is linked to embarrassment and clumsiness more so than severe functional difficulties (Schott & Wyke, 1981). However, it is rather surprising that more focus has not been directed toward developing methods of CMM management, particularly in respect to control of unimanual and bimanual actions. At present, therapeutic strategies are largely limited to biofeedback (i.e., gaining awareness of muscle activity using electromyography readings; Schott & Wyke, 1981) and rehabilitative training (i.e., engaging in regular physical and mental practice of unilateral and separate bilateral finger movements; Cincotta et al., 2003), but their long-term effectiveness is questionable (cf. Interventions).

Isolated mirroring, as in CMM, can be quite difficult to detect, even to the trained clinical eye. Attempting to diagnose CMM in young children can be especially complicated given that young children normally demonstrate some mirroring of the distal upper extremities, possibly in association with neurodevelopmental processes such as maturation (including myelination) of the corpus callosum (Mayston, Harrison, & Stephens, 1999; cf. other examples below). Understanding the behavioral phenotype(s) of CMM is a step toward a better understanding of the condition but may also assist in its clinical diagnosis.

While the mirroring present in CMM can be a nuisance and interfere with everyday activities, people with CMM have seemed to cope with the condition quite well in many cases (Franz, 2003). Unfortunately, that is not the case for all affected individuals, some of whom have reported difficulties in work-related tasks, such as writing or typing on computer keys, or with skills that require coordinated movements of the two hands, such as playing musical instruments (Cohen et al., 1991). There are even reports of quite severe pain in the non-dominant arm while writing due to attempts to stifle the mirror movements (Cincotta et al., 2003; Franz et al., 2015). Thus, CMM poses some challenges that can influence well-being and typical daily activities, and can be particularly concerning, especially for parents of a young child who shows mirroring early in life, thus driving the family to seek medical help (Fasano et al., 2014). The present review covers some of the known details of relatively new findings linked to the neuroanatomical mechanisms and genetics underlying CMM, and then provides information more relevant to the clinical eye.

Neurodevelopmental Considerations and Related Neural Correlates

Given that CMM is thought to be present at birth, a number of neurodevelopmental effects have been

considered. Ipsilateral corticospinal tracts (ICSTs) can be observed in neurologically-normal newborns but are expected to withdraw during the first 18 months of life and become vestigial (Eyre, Taylor, Villagra, Smith, & Miller, 2001). However, evidence supporting the presence of ICSTs in adult CMM cases has been well documented. Whether fast-conducting ICSTs among individuals who have CMM are a result of genetic mutations that impact axonal guidance during gestation, or that influence the postnatal withdrawal (i.e., axon or synapse elimination) process, is not yet disentangled. In an initial study, Cohen et al. (1991) tested for motor evoked potentials (MEPs) in the thenar muscles of each hand (found at the base of the thumb) of two individuals with CMM using transcranial electric stimulation and transcranial magnetic stimulation (TMS). For both participants, stimulation by either transcranial electric stimulation or TMS resulted in bilateral thenar muscle responses that occurred at similar latencies. The researchers suggested that interhemispheric connections were not responsible for the bilateral muscle responses because conduction through the corpus callosum would have caused movements to be slightly delayed in the mirroring hand (rather than simultaneous as measured), a finding corroborated by others (e.g., Cincotta et al., 1994). Farmer, Ingram, and Stephens (1990) proposed the interesting alternative possibility that the contralateral corticospinal tracts have abnormal distal branches which connect to the ipsilateral side and might be the cause of mirroring (rather than ICSTs), but their theory has been questioned by others (Cincotta et al., 2003).

Despite Cohen et al.'s (1991) assertion that the production of mirror movements is not due to the transfer of motor signals across the corpus callosum, some evidence is suggestive of bilateral primary motor cortex (M1) activation. Cincotta, Lori, Gangemi, Barontini, and Ragazzoni (1996) assessed this possibility by recording the cortical silent periods of abductor pollicis brevis muscles (part of the thenar eminence) bilaterally using electromyography when an individual with CMM received unilateral TMS to M1. The participant demonstrated a bilateral silent period (as opposed to the typical unilateral) that was significantly shorter than in controls. That outcome led the researchers to propose that the mirror M1 causes early resumption of EMG activity at a lower amplitude once transient interhemispheric inhibition (due to the TMS application in the active M1) ceases. This interhemispheric inhibition refers to a neural process in which motor commands are prevented from spreading beyond the active hemisphere, thereby enabling movements to be performed strictly unilaterally (Cincotta & Ziemann, 2008; Shen & Franz, 2005). Thus, the study of Cincotta et al. (1996) suggests that the production of mirror movements may be attributable to both ipsilateral corticospinal tracts and bilateral M1 activity.

Gallea et al. (2013) assessed three possible hypotheses aimed at elucidating how mirror movements are produced on the basis of tests for 1) evidence of ipsilateral corticospinal tracts; 2) abnormal interhemispheric inhibition leading to motor commands emanating from bilateral M1; and 3) transfer of motor plans from the secondary motor areas to M1 in each hemisphere. Seven individuals with CMM underwent single-pulse focal TMS methods, which confirmed that contralateral and ipsilateral MEPs occurred in the hand muscles. MEPs measured in the mirror hand were significantly smaller than in the volitional hand, but no differences in latency were detected between hands, corroborating Cohen et al.'s (1991) and Cincotta et al.'s (1994; 1996; 2003) findings that individuals with CMM have functional ipsilateral corticospinal tracts even into adulthood. Additional evidence consistent with the presence of ICSTs was demonstrated by Gallea et al. (2013) using diffusion tractography. The ICSTs were found to be characterized by a higher proportion of fibers than the contralateral tracts for the CMM participants, which goes against expectations given that neurotypical adults should have vestigial ipsilateral corticospinal tracts (Eyre et al., 2001). A similar finding has recently been reported by Méneret et al. (2017).

To test interhemispheric inhibition (i.e., the restriction of motor output to the active hemisphere during performance of unilateral actions), Gallea et al. (2013) calculated fractional anisotropy (FA), an index of water diffusion along axons, which is used as a proxy measure of the density of neuronal fibers. FA values for the portion of the corpus callosum that connects homologous hand motor areas were significantly larger in CMM participants compared to controls. The FA values were interpreted as differences in connection probabilities, which are thought to contribute to abnormal interhemispheric inhibition. The larger the connection probability, the more precise the synchronicity of muscular activity during mirror movements. Such findings are congruous with the view presented in Cincotta et al. (1996; 2002), that both primary motor cortices contribute to the activity of the voluntary and mirroring hands (Gallea et al., 2013).

The supplementary motor area (SMA) has been associated with motor planning, which gave rise to the proposal in Gallea et al. (2013) that abnormalities of the SMA could impact how motor plans are transmitted to the primary motor areas, and as a consequence of such irregularities, mirror movements could result. Consistent with involvement of motor

planning areas, recent findings have revealed abnormal premotor processes in people with CMM (Franz & Fu, 2017; 2018). Furthermore, it has been acknowledged that subcortical processes, such as those comprising thalamo-basal-ganglia circuits, might play a part in SMA activity (cf. Franz & Fu, 2017; 2018, for more details). To test for possible SMA involvement, Gallea et al. (2013) analyzed people with CMM using functional magnetic resonance imaging while they performed sequential finger tapping movements either unilaterally or bilaterally. When tapping with just one hand, a larger than expected neural response was found in the ipsilateral SMA, but contralateral SMA activity was neurotypical. A positive correlation was also identified between mirror movement severity, as measured by EMG, and ipsilateral SMA activity (Gallea et al., 2013).

Connectivity between the primary and supplementary motor regions was another measure investigated by Gallea et al. (2013). In unimanual tapping conditions performed by those with CMM, greater degrees of connectivity between ipsilateral SMA and M1 (regions on the same side of the body as the intentional finger tapping movements) were demonstrated in comparison to connectivity between contralateral SMA and M1 (regions on the opposite side). However, based on structural measures, FA values of the neural pathways between each hemisphere's SMA and M1 were comparable, which suggests no differences in connection probabilities. The findings indicate that functional variations, rather than anatomical ones, are the more probable cause of the atypical neural activity patterns observed in individuals with CMM with respect to supplementary and primary motor areas (Gallea et al., 2013).

Multiple conclusions about CMM can be drawn from the comprehensive study undertaken by Gallea et al. (2013). First, the presence of fast-conducting ipsilateral corticospinal tracts is strongly characteristic of the condition. Secondly, the connection probability of homologous hand motor territories (a reflection of interhemispheric inhibition deficiencies) seems to be especially large in cases of CMM. Gallea et al. (2013) proposed that this enhanced connection probability may be evidence of a compensatory mechanism (i.e., neuronal density is increased in an unsuccessful attempt to strengthen interhemispheric inhibition). Lastly, motor acts have been shown to be initiated by the supplementary motor area when it ceases inhibiting the primary motor cortex (Ball et al., 1991). As more activity was observed between the ipsilateral SMA and M1 than between those regions on the contralateral side, the implication is that the ipsilateral SMA may also play a role in the production of mirror movements. The integrated approach of Gallea et al. (2013) adds to the discoveries of Cohen et al. (1991) and Cincotta et al. (1994; 1996; 2002; 2003) while also showcasing the breadth of how CMM can impact the motor system.

Genetic Mutations

The intention of the present review is to focus primarily on the behavioral findings and consequences of CMM, and although we work with clinical geneticists, we ourselves are not geneticists. Hence our treatment (below) of genetics and neuroanatomy will be briefer than our treatment of the neurodevelopmental correlates of CMM (cf. Méneret et al. [2017] and Marsh et al. [2018] for more complete treatments of the genetics to date). As a quick overview of the genetics findings, at present, causative variants in three different genes with autosomal dominant inheritance have been discovered: *DCC* (Srour et al., 2010), *RAD51* (Depienne et al., 2012), and *NTN1* (Méneret et al., 2017); only one copy of the gene would be necessary for the condition to manifest in an offspring. A mutation in *DNAL4*, thought to cause an autosomal recessive form of the disorder, has also been reported (Ahmed et al., 2014): autosomal recessive means that two copies of the gene would be needed to manifest the condition in the child of an affected individual or genetic carrier. Other causal mutations are likely to exist, given that a number of affected people do not have mutations in the known causative genes (Fasano et al., 2014; Franz et al., 2015; Méneret et al., 2014; 2017).

Interestingly, *DCC*, *RAD51*, and *NTN1* all are linked with netrin-1 signaling, which has an important role during early nervous system development. Netrin-1 is notable for playing a part in axon guidance across the body's midline, thereby laying the foundations for the strong contralateral connectivity between the brain's hemispheres and the nerves running throughout the body in the normal nervous system (Serafini et al., 1996). Srour et al. (2010) studied members of a French-Canadian family and an unrelated Iranian family with CMM. Genetic analysis revealed a frameshift mutation of gene *DCC* and a truncated DCC protein. As a result of truncation, the ability of DCC to bind to the protein netrin-1 is limited (Srour et al., 2010). This reduction in netrin-1 binding is relevant because of the protein's role in attracting or repulsing axon populations during development (Keino-Masu et al., 1996; Serafini et al., 1996). The lack of netrin-1 availability is thought to be responsible for altering how the corticospinal tracts form in CMM cases, either because of protein instability or impairments in the secretion of netrin-1. This finding came to light after studying CMM families who have a mutation in *NTN1*, the gene that

specifically codes for the netrin-1 protein (Méneret et al., 2017).

With respect to discoveries of *RAD51*, Depienne et al. (2012) studied a French family with incomplete penetrance of CMM consistent with autosomal dominant heritability and discovered a nonsense mutation of *RAD51*. The researchers also identified a frameshift mutation of *RAD51* in a family from Germany. Both mutations result in haploinsufficiency of RAD51, meaning that there is less-than-normal availability of the protein and, consequently, the functionality of cells that rely on RAD51 may be affected. Depienne et al. (2012) proposed that CMM might occur in people whose functional RAD51 is lower than some critical level during development of the nervous system (cf. Franz et al., 2015 for details of another multigenerational family with a *RAD51* missense mutation).

In an attempt to better understand possible functional roles of *RAD51*, Depienne et al. (2012) studied the expression of RAD51 during the development of the mouse cortex. When the mice were two days old, RAD51 could be observed within the corticospinal axons of the pyramidal decussation, which suggests its involvement in the decussation process (i.e., the crossing of most corticospinal axons from one side of the brain to the opposite side of the body). Consequently, deficiency of the protein could create a situation in which robust ipsilateral corticospinal tracts might develop. Further findings of Glendining et al. (2017), also using a mouse model, suggested a novel function of *RAD51* linked to netrin-1 signaling. Specifically, the findings implicated RAD51 as a negative regulator of netrin-1-induced axonal branching. Thus, the mutated form of RAD51 is limited in its ability to regulate the effects of netrin-1 on neuritogenesis (i.e., the projection of an axon or dendrites from the cell body of a neuron).

Although most of the genetic research investigating the basis of CMM has focused on the inherited form, studies have also examined sporadic cases, particularly to corroborate familial cases. In one of the largest genetic studies of CMM, Méneret et al. (2014) managed to identify numerous novel mutations of either *DCC* or *RAD51* in many, but not all, of their participants, suggesting that additional causal genes likely exist. Only mutations that cause *DCC* or *RAD51* truncation had been isolated in families with CMM (Depienne et al., 2012; Srour et al., 2010) when Méneret et al. (2014) conducted their research, but most of the mutations in the study's sporadic cases were missense variants, leading the authors to suggest that mutation type could impact the penetrance of CMM inheritance (i.e., the likelihood that the condition will actually manifest in individuals who carry the mutated genes).

CMM resulting from *DCC* mutations is thought to have a penetrance rate of 42% (Marsh et al., 2017) and the rate could be as high as 50% in the French and German families with *RAD51* mutations (Depienne et al., 2012). Méneret et al. (2014) proposed that the apparently sporadic cases of CMM linked to missense variants may actually reflect inheritance at a lower penetrance rate than is associated with mutations causing gene truncation. This is because mutated proteins may still be expressed when missense variants occur. The researchers provided the alternative explanation that missense variants are responsible for affecting susceptibility to CMM, but that environmental factors determine if the condition develops.

Genotype-Phenotype Variability

To determine if differences in the phenotypic expression of CMM are present (i.e., how the condition physically manifests in the hands and possibly elsewhere around the body), Franz et al. (2015) recruited five families with CMM-affected individuals. A *RAD51* mutation and a *DCC* mutation were each identified in different families, but some affected individuals in the study were negative for *DCC*, *RAD51*, and *DNAL4* mutations. The researchers analyzed the CMM mirroring phenotype in detail using in-house accelerometer gloves, Dexterity Otago (DexterO, a newly developed package consisting of a device and software that is able to track subtle micro-movements during tasks performed by the hands). A standard tapping task in which participants are asked to tap unimanually through time (30 seconds per trial) was used for the CMM phenotyping. Based on measures of the index fingers, two types of mirroring were found: one referred to as "actual", in which the mirroring was of a smooth and continuous form that strongly resembled the intentional movements of the non-mirror hand; the other referred to as "fractionated", in which the mirroring was of a fragmented form, without precise resemblance to the intentional hand's movements (Franz et al., 2015). Although sample sizes were too small to reliably assess possible genotype-phenotype correlations, actual mirroring characterized affected individuals in the *RAD51*-CMM family, whereas fractionated characterized individuals in the *DCC*-CMM family (Franz et al., 2015). Furthermore, there were not clear left-right asymmetries across the sample in terms of the extent of mirroring found in affected members of the families tested, but larger sample sizes should shed important light on that issue. Another potentially revealing finding of Franz et al. (2015) is that in a small portion of the sample of individuals with CMM,

the mirroring could not be detected on the basis of visual inspection but was detected by DexterO. This is, of course, highly relevant to clinical diagnosis, as it might assist in the detection of CMM (in suspected cases including familial relatives with the visually-unobservable phenotype). DexterO is inexpensive, easily transportable, and relatively straightforward to apply. The use of this detection technique, and the subsequent identification of larger sample sizes with CMM, could improve estimates of the penetrance of the inherited version of the condition and of the overall prevalence of CMM.

Phenotypic differences in terms of gender and the penetrance of CMM have been proposed to exist, but again, large enough samples have not been tested to perform conclusive tests. CMM linked to *DCC* mutations was more prevalent among men in the studies of Srour et al. (2009; 2010) and Marsh et al. (2017). In contrast, only the female members of an Italian family were identified by Fasano et al. (2014) to have CMM, and all were negative for mutations involving *DCC* or *RAD51*. Notably, the Italian family experienced higher rates of mirroring in their feet and toes than had been reported in another family (Srour et al., 2009) and the individuals typically failed to notice their mirror movements. The only exceptions were the two oldest females: their mirroring was severe, but they attributed their unintentional actions to clumsiness. Unlike in other reports, which suggest that mirroring does not change with age, more extreme mirroring was found in the oldest members of the sample of Fasano et al. (2014). This again begs the question of whether different mirroring phenotypes exist, given that age-dependent effects have not previously been observed (Gallea et al., 2013). Overall, the findings of Fasano et al. (2014) showcase how diversely CMM can manifest (even within the same family) in terms of how strongly individuals are affected by the condition and in what secondary motor systems the mirroring occurs (in addition to primary mirroring in the hands/fingers).

Somatosensory Irregularities

What little attention the somatosensory system has received in the context of non-syndromic CMM research has revealed no clear evidence of sensory-related developmental anomalies. Schott and Wyke (1981) studied seven individuals with mirror movements, two with CMM (i.e., one inherited and one sporadic) and five whose mirroring was associated with an alternative disorder (e.g., Usher's syndrome). Sensory responses in the hands were assessed and found to be normal, with the exception of one report of an individual with apparent impairments in postural sense of the fingers when they were moved by the experimenter in different directions. Upon further inspection, however, the proprioceptive abnormalities experienced by that individual could have been due to a cranio-cervical anomaly that was thought to be the cause of the mirroring (Schott & Wyke, 1981).

To measure somatosensory evoked potentials (SEPs), the median nerves in the wrists of two people with CMM were electrically stimulated by Cohen et al. (1991). That study found no significant differences in SEPs between those with CMM and controls. Cincotta et al. (1994) conducted a similar experiment with one individual who had non-syndromic CMM. As in Cohen et al. (1991), SEPs were contralateral to the stimulated nerve and of typical latency, leading the researchers to conclude that CMM does not cause the somatosensory afferent pathways to develop or function abnormally (Cincotta et al., 1994). Capaday, Forget, Fraser, and Lamarre (1991) also stimulated the median nerve (H reflex) and index finger (cutaneous reflex) of three people with non-syndromic CMM, none of whom claimed to have perceived sensations in the hand contralateral to the stimulation. That study found contralateral SEPs, as in the previous studies, indicative of normal sensory function.

Anecdotes suggestive of somatosensory abnormalities have appeared in the CMM research literature, but they have garnered little attention. In 1914, a study by H. Drinkwater (cited in Pratt, 1967) featured a young boy with CMM, perhaps the earliest documented case. In addition to the synchronized bimanual movements typical of CMM, it was also reported that the child perceived some unilateral sensations as being bilateral. However, Pratt (1967) questioned the authenticity of the boy's claim. Guttmann, Maclay, and Stokes (1939) documented a family in which some members reportedly experienced passive mirroring (i.e., when mirror movements are initiated by an outside force acting on only one hand of an affected individual) that was of lesser amplitude and slightly delayed in comparison to the movements caused by the researchers. Even more uniquely, one man's passive movements were observed to be parallel, rather than mirrored, under some conditions. For example, when the researchers supinated one hand, the other might pronate instead of supinate. That effect could be produced by either physical or electrical stimulation. Based on their observations, the researchers postulated that passive and active mirroring were likely caused by the same nervous system pathways. Reports by Schott and Wyke (1977; 1981) about an unrelated case of CMM in an otherwise normal teenage boy who also experienced passive and parallel mirroring add further curiosity about the potential of CMM to influence the somatosensory system.

The hypothesis that the somatosensory system is affected in some way by CMM, even to a subclinical degree, is in our view still open to rigorous investigation. If aspects of proprioception, haptic perception, and/or other features related to sense of touch are in any way altered in people with CMM, these abnormalities have either gone unnoticed or have been disregarded in the research literature thus far. Discovering how and why the somatosensory system is impacted in cases of CMM (if so) would likely inform on the physical manifestations of the condition and perhaps subtle somatosensory functions.

Living with Congenital Mirror Movements

In some individuals with CMM, the presence of mirroring has been noted by a parent, caretaker, or professional, by the time the individual has reached one year of age (Ahmed et al., 2014; Cohen et al., 1991; Fasano et al., 2014; Srour et al., 2009). Cohen et al. (1991) reported on an adult male with CMM whose bilaterally synchronized limb movements prevented him from crawling and delayed learning to walk because of balance issues. An adult woman with mirror movements was also studied by Cohen et al. (1991). She was thought to have delayed motor development as a child because of the difficulties caused by her mirror movements. Although CMM is typically considered a stable condition across the lifespan (i.e., the severity of the mirror movements does not change with time; Gallea et al., 2013; Schott & Wyke, 1981; Fasano et al., 2014), mirroring may become more obvious as early development progresses, due to an increased dependence on skilled bimanual actions, particularly those requiring strong grasps and fine motor control (e.g., buttoning a shirt). Evidence of a struggle with bimanual actions might make the mirroring seem more noticeable and disruptive over time (Cohen et al., 1991).

Although the majority of people in our own CMM cohort have suggested that the mirroring is of no real consequence to their happiness or ability to achieve success in work and family life, a number have commented on the challenges that the mirroring can pose. This is particularly the case with learning new skills using hands, such as typing, playing a musical instrument, and even tying shoes (for those who remember learning that skill, as the majority of our cohort has interacted with us only during their adult lives). The man with CMM featured in Cohen et al.'s (1991) study reportedly could not go up a ladder, struggled with learning the guitar, and could not run until high school due to the challenge of alternating swings of his arms. As a student in medical school, performing percussion during physical examinations (i.e., having to tap body parts with the fingers) was said to be a hurdle and, one can assume, might have interfered with his ability to adequately do his job later on.

As for the woman with CMM in the study of Cohen et al. (1991), even simple actions, such as opening and closing one hand or tapping a knee, could be enough to induce mirror movements. Although she had no issues with swimming using the breaststroke, it took her four years to learn the crawl because she apparently struggled with moving each arm independently. Like many other individuals with CMM, her mirror movements also interfered when trying to write or type (Cincotta et al., 1994; 2003; Cohen et al., 1991).

While some people with CMM reportedly experience no social or functional impairments due to their condition, other than perhaps clumsiness (Fasano et al., 2014), others face pain (Cincotta et al., 2003), embarrassment (Schott & Wyke, 1981; Srour et al., 2009), or potential limitations in their career prospects (Schott & Wyke, 1981). A young girl claimed that trying to control her mirror movements caused her pain in the muscles in her left shoulder when she wrote using her right hand (Cincotta et al., 2003) and others have also made mention of such pain associated with writing (Franz et al., 2015). A teenage boy mentioned being highly self-conscious at school when he mirrored while writing, and there was some worry over his ability to become a diamond cutter in the future. When stressed and anxious, an adult male with inherited CMM stated that his mirroring seemed to become enhanced. However, he still claimed that, overall, the mirror movements did not negatively impact his daily activities (Schott & Wyke, 1981).

Interventions

Although mirroring can make performing unimanual and bimanual tasks especially difficult, some people with CMM are able to overcome certain bimanual hurdles if they engage in concentrated effort and practice of those skills. Franz (2003) made mention of two individuals within a CMM family, one of whom could ride a motorcycle even though separate hand movements are necessary to operate the throttle and the brake. The other was talented at playing a twelve-string guitar, a feat that would be impressive even without the mirror movements. Srour et al. (2009) pointed out that CMM has not prevented two members of a French-Canadian family from becoming an electrician and a secretary, professions that both require dexterous skills of the hands and fingers. Clearly, having CMM does not guarantee that an individual will be held back from successfully pursuing their wants in life (and the talented sample of people we work with further emphasizes that fact).

While CMM is largely tolerated by the individuals who have it, that in no way negates the need to further explore the more practical consequences of the condition. If children who experience mirroring are embarrassed by their involuntary movements, they may be teased at school or otherwise fail to thrive in some way, which may have long-term implications for their personal and educational achievement. The same could be said for adults in the workplace and their potential for upward mobility, assuming they are even able to pursue their desired careers given the interference of mirror movements in their hands. There is also the issue of everyday hindrances, such as the possible difficulty of engaging in recreational activities like playing instruments or participating in sports. Struggling with an act as commonplace as typing on a computer keyboard may have rather severe social consequences in this modern era, which again points to the need to develop accurate diagnoses and further seek solutions for those with CMM.

In terms of managing CMM, some individuals with CMM reported a perceived ability to exercise a measure of control over their mirroring (Schott & Wyke, 1981; Srour et al., 2009) and a couple of methods for training to overcome mirroring have been encouraging. For example, Schott and Wyke (1981) worked with an individual with CMM by collecting EMG biofeedback from his forearm extensor muscles and playing tones alongside a visual display of a calibrated meter to indicate when muscular activity occurred in the mirroring arm. After training with the auditory and visual feedback for sessions lasting up to twenty minutes, mirroring could be suppressed in both hands for a few minutes, but the suppression was not permanent or even long-lasting. The young girl featured in the study of Cincotta et al. (2003), who suffered from shoulder pain while writing, went through seven months of rehabilitative training in an attempt to produce unilateral finger movements. For fifteen to twenty minutes per day, she performed symmetrical finger movements, then non-symmetrical finger movements that were designed to increase in difficulty over time, and lastly, she engaged in mental imagery of her finger movements occurring unilaterally. After completing all of the training, she mirrored less frequently while making unilateral finger movements. In addition, the painful muscle contractions no longer affected her left shoulder. However, her abductor pollicis brevis muscles, which were not included in the training, were unchanged in their mirroring frequency. As suggested by those results, rehabilitative training can be helpful, but the effects do not appear to generalize to untrained muscles. Unfortunately, whether the benefits persisted after training ceased is unknown (Cincotta et al., 2003). Further exploration by the research community of both biofeedback and rehabilitative training as possible methods of CMM management could prove beneficial, but, given the lack of knowledge about long-term potential, we caution that neither method should be viewed as a way of treating or reversing the condition.

Future Studies

As discussed earlier, EMG biofeedback (Schott & Wyke, 1981) and rehabilitation training of the distal upper limb muscles (Cincotta et al., 2003) have shown moderate success in reducing the incidence of mirroring in the immediate/short-term, but there is a lack of follow-up studies. The mirroring community might benefit from an increased awareness of the condition and most people we have worked with are eager to learn more about the possible management of CMM, but access to people with CMM for experimental purposes can be extremely limited. However, researchers may be able to investigate involuntary movement control by working with young children who display associated (i.e., extraneous) movements of one part of the body while exerting effort with the homologous muscles of the opposite side (e.g., a twitch of the right eyelid while trying to wink with the left), a minor and commonplace effect that declines with age and may be suggestive of nervous system maturity (Connolly & Stratton, 1968). Perhaps studying the manner in which their naturally-occurring mirroring changes through development, and testing methods to actively decrease the prevalence of it, will inform on potential strategies for suppressing abnormal forms of mirroring such as CMM. Lazarus and Todor (1991) studied young boys with associated movements and demonstrated that audio feedback could significantly reduce the incidence of the movements in the childrens' hands by simply using a tone to call attention to the hand that is meant to remain stationary (should any unintentional muscular activity occur). Even after the tones were removed, fewer associated hand movements were observed. If those methods could be expanded and evaluated for their long-term potential, they could prove helpful to individuals who have CMM, perhaps more if such people were to begin feedback training while still young. Clearly, learning and attention are viable intervention options for reducing non-volitional movements.

A more widespread use of objective and quantifiable measures, such as those based on the use of accelerometer gloves (Franz et al., 2015), might assist in the earliest possible identification of mirroring in individuals. That might pave the way for the development of interventions aimed at minimizing interfering movements, which could then be introduced when the affected individuals are young and have nervous systems that are still highly

malleable. We have no doubt that the multidisciplinary scope of present investigations will continue to progress and lead to a better understanding of CMM and methods to approach management of the condition.

Conclusion

As a condition, CMM is far from being well understood. However, great strides have been made in recent decades to expand the knowledge base for its understanding by researchers, diagnosticians, clinicians, and most importantly, the people who experience mirror movements every day. The range of subtle central nervous system irregularities attributable to CMM has been thoroughly documented as including the ipsilateral corticospinal tracts (e.g., Cohen et al., 1991), connections between primary motor cortices (e.g., Cincotta et al., 1996), and circuitry of the supplementary motor areas (Gallea et al., 2013), but more certainly remains to be uncovered, and the somatosensory system offers nearly untrodden ground. Since 2010, mutations in four different genes have been isolated and suggested to lead to the development of CMM (Ahmed et al., 2014; Depienne et al., 2012; Méneret et al., 2017; Srour et al., 2010), opening the door to numerous other questions related to whether specific genotypes are related to distinct phenotypes (Franz et al., 2015). If there are indeed distinct phenotypes, clinicians could gain from not only being more cognizant of the condition in general, but also from knowing which signs to look for according to phenotypes. The development of better diagnostic tools, such as DexterO, the accelerometer gloves used by Franz et al. (2015), could be of additional aid toward that aim. Perhaps with greater understanding of how each individual with CMM is uniquely affected by having the condition, new CMM management strategies might be designed, and existing ones improved, to allow for broader application and effectiveness beyond the short-term (Cincotta et al., 2003; Schott & Wyke, 1981). CMM is relatively rare, and therefore the community with CMM is small, but the impressive resilience displayed by people with CMM and their generosity and openness to participate and learn about research, is inspiring. We hope that their patience will continue to be rewarded.

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