Mirror Movement in Children; A Single Center Experience

Çocuklarda Ayna Hayali Hareketler; Tek Merkez Deneyimi

Ozan Kocak, Kursat Bora Carman, Coskun Yarar

Eskisehir Osmangazi University Hospital, Department of Pediatric Neurology, Eskisehir, Turkey

Abstract: Mirror movements (MMs) are involuntary movements accompanying voluntary activity in contralateral homologous muscle. Mirror movements have been associated with a number of pathologic conditions, also it might occur physiologically in childhood and subside before the age of ten. In this study, we retrospectively evaluate etiologic and clinical features of the 27 patients with MMs.Clinical, demographic and laboratory data of the patients were obtained by evaluating medical records retrospectively. The Rasmussen scale was used to measure the severity of the MMs. Two children were diagnosed as physiologic MMs. Eleven children were unilateral spastic cerebral palsy and 14 patients were non-hemiplegic children. This study is one of the largest case series of MMs in children. We identified new disorders with MMs by using the Rasmussen scale. We suggest that an evaluation for MMs may be a part of neurologic examinations, at least in risk groups.
Key Words: children, mirror movement, cerebral palsy

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Özet: Ayna hayali hareketler(MMs), kontralateral homolog kaslarda istemli aktiviteye eşlik eden istemsiz hareketlerdir. Ayna hayali hareketleri, bir dizi patolojik durumla ilişkilendirilmiştir, ayrıca çocuklukta fizyolojik olarak, on yaşından önce ortaya çıkabilir. Bu çalışmada, ayna hayali hareket saptanan 27 hastanın etiyolojik ve klinik özelliklerini retrospektif olarak değerlendirdik. Hastaların klinik, demografik ve laboratuvar verileri retrospektif olarak değerlendirildi. Ayna hayali hareketlerin değerlendirmesi için Rasmussen ölçeği kullanıldı. İki hasta fizyolojik MMs olarak değerlendirildi. On bir hasta unilateral spastik serebral palsi ve 14 hasta ise hemiplejik olmayan çocuklardı. Bu çalışma, çocuklarda en büyük MMs vaka serilerinden biridir. Bu çalışmada ayna hayali hareketler ile birlikteliği ilk defa gösterilen hastalıklar da tanımlanmıştır. En azından risk gruplarında, ayna hayali hareketlerin saptanması için yapılacak bir değerlendirmenin, nörolojik muayenenin bir parçası olabileceğine inanıyoruz.
Anahtar Kelimeler: çocuk, ayna hayali hareketler, serebral palsi

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ORCID ID of the authors: O.K. 0000-0002-2285-7983; K.B.Ç. 0000-0002-4629-1873; C.Y. 0000-0001-7462-4578

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Yazışma Adresi / Correspondence Address
Ozan KOÇAK
mail: ozankocak79@gmail.com

1. Introduction

Mirror movements are defined as involuntary movements of one side of the body that mirror intentional movements on opposite side (1). MMs usually involve upper limbs, predominate in hands (2). Mirror movements may result in difficulty in bimanual activities of daily living (3).

Mirror movements have been classified into two general categories: physiologic and pathologic forms (4). Physiologic MMs are characterized mirror movements that subsides before the age of ten and normal neurological examination except MMs. In humans, there are homologous muscles that tend to work simultaneously, which is a result of complex interhemispheric interactions between wide ranges of cortical areas (5). Physiological MMs are prevented from restricting in order to spread the motor impulses from one side of the primary motor cortex (M1) to the contralateral M1 (4). The corpus callosum (CC) is the biggest white matter bundle of the brain, and its function is to connect both hemispheres (6). Immaturity of the CC may result in decreased interhemispheric inhibition, and physiological MMs can be explained by a reduction of this interhemispheric inhibition (7). Although there have been many attempts to elucidate the pathogenesis of MMs, the exact physiological mechanisms remain unclear. If physiologic MMs persist throughout adulthood, it is called as congenital MMs. It is inherited as autosomal dominant and might be familial. Mutations in deleted in colorectal carcinoma (DCC) and RAD51 genes have been reported in familial congenital MMs (4). The patients with congenital MMs have not other clinical complaint. Pathologic MMs can be acquired or associated with different syndromes or neurological diseases (Table 1).

In present study we aimed to evaluate the clinical and neurological features of children presented with MMs.

Table 1.
Associated disorders with mirror movements (3,9,10,14)

• Klippel Feil syndrome (KFS) • Arnold Chiari malformation • Agenesis of corpus callosum • Kallmann syndrome • Usher's syndrome • Congenital hemiplegic cerebral palsy • Joubert syndrome • Phenylketonuria • Lissencephaly • Waldervanck syndrome • Porencephalic cyst • Spinal cord abnormalities • Diabetes insipitus • Mental retardation	• Parkinson's disease • Corticobasal degeneration • Huntington's disease • Friedreich's ataxia • Stroke • Amyotrophic lateral sclerosis • Schizophrenia • Tourette syndrome

2. Material and Methods

Twenty seven patients with MMs are evaluated retrospectively with the etiologic, clinical and neuroimaging findings between the dates of January 2009 and November 2015 that admitted Eskisehir Osmangazi University Hospital, Department of Pediatric Neurology. Written informed consent was obtained from the parents and/or legal representatives. The study protocol was approved by the Institutional Ethics Committee. Physical and neurological examinations of patients were reperformed and medical records reevaluated. Modified Ashworth scale (AS) and gross motor function classification system (GMFCS) were used to assess the severity of spasticity of children diagnosed as cerebral palsy.

Mirror movements were observed and recorded during three unimanual tasks; (i) fist opening and clenching, (ii) finger opposition (thumb sequentially touches other four digits), and (iii) finger tapping (fingers are sequentially lifted from the table surface).

The Rasmussen scale (8) composed of 11 tests, was used to measure the severity of the mirror movements. It is performed by applying passive, fast, and resistant movements on the proximal and distal muscle groups of the upper and lower limbs. The maximum score is 33 (Table 2).

Cerebral and spinal magnetic resonance imaging (MRI) examinations were performed on admission at 1.5 Tesla at various institutions, using T1 and T2-weighted spin-echo and inversion recovery sequences in the axial, sagittal, and coronal planes. The findings were evaluated by a neuroradiology specialist.

Statistical Analyses

All continuous variables were evaluated by the Shapiro-Wilk test for normality before use of the independent samples *t*-test. Categorical variables were analyzed using Yates's chi-square test. Pearson's correlation coefficient (*r*) was used to investigate the relationship between all continuous variables. Significance was attributed when $p < 0.05$. Statistical analyses were performed using IBM SPSS Statistics 21.0.

3. Results

Twenty-seven children were diagnosed as MMs. The youngest child was three years old age and the mean age of children was 10,5 years. Positive family history of MMS was present only in one child.

Two children diagnosed as physiologic MMs with normal neurological examination and brain magnetic resonance (MRI). Rasmussen Scale scores were 30 and 21 in physiologic cases. Their MMs was subsided within three years on following. Remaining twenty-five children were pathologic MMs.

Pathologic MMs was diagnosed in twenty-five children and 11 of them were unilateral hemiplegic cerebral palsy. Two patients were left hemiplegia. The mean Rasmussen score was calculated as 19.54 ± 2.42. No correlation was found between Rasmussen scale scores and gross motor function classifications of patients ($p>0.05$) (Table 2).

Pathologic MMs was present in 14 non-hemiplegic children (Table 3). The Mirror movements were mainly right-sided. The mean Rasmussen Scale score was 21.18 ± 6.89 in the non-hemiplegic group of children. There was no statistically significant difference between hemiparetic and non-hemiparetic children with MMs in the Rasmussen Scale score ($p>0.05$).

Chromosomal abnormalities related with 4^{th} chromosome were detected in three children. A seven-year-old girl was diagnosed as having Klippel-Feil syndrome with the fusion of vertebrae on cervical X-ray imaging and MMs were noticed in both her upper and lower limbs. A male patient presented with vocal and motor tic. His physical examination revealed tics and MMs in his left hand while moving his right hand. The results of cerebral and spinal MRIs were normal. Tourette syndrome was diagnosed.

A 15-year-old girl was diagnosed as CHARGE syndrome (square face with a broad prominent forehead; short, wide ears; and an ocular coloboma on the right eye). She had also been suffering from MMs of the right upper and lower extremities. Her cerebral MRI was normal and spinal MRI shows hemi-vertebra abnormalities on cervical region.

Brain investigations of all patients were performed. In six patients, the cerebral MRI was normal (two patients were defined as a physiological MMs, two patients had a chromosomal abnormality, one patient had CHARGE syndrome, and one patient had Tourette syndrome). Cortical migration anomalies (two with polymicrogyria and one each with pachygyria, schizencephaly, and band heterotopia) were detected in 5 children. Porencephalic cyst, cerebral atrophy, encephalocele with cervical syringomyelia, arachnoid cysts, corpus callosum abnormalities were other abnormalities determined. In hemiplegic cerebral palsy patients, the MRI showed sequel gliotic and encephalomalacia changes. Tractography investigation was not done in our patents because of technical facilities. The Clinical and neuroradiologic descriptions of patients were shown in Table 3.

Table 2.
Unilateral Spastic Cerebral Palsy (USCP)patients' clinical and neuroradiological descriptions

Patient No	**Sex**	**Age**	**MMs side**	**Clinical signs**	**MRI**	**MMs score**	**GMFCS/AS**
1	F	4	L	Right hemiparesis, epilepsy, IDD	Encephalomalacia on left MCA region	24	1/+1
2	M	6	L	Right hemiparesis, epilepsy, IDD	Left PVL	30	2/3
3	F	11	R	Left hemiparesis, epilepsy, IDD	Right PVL	13	2/3
4	F	11	L	Right hemiparesis, epilepsy, IDD	Left PVL	12	1/2
5	F	12	L	Right hemiparesis, epilepsy, IDD	Encephalomalacia on left MCA region	14	3/3
6	F	13	L	Right hemiparesis, epilepsy, IDD	Left PVL	28	3/3
7	F	13	L	Right hemiparesis, epilepsy, IDD	Left PVL	22	2/1
8	F	12	R	Left hemiparesis, epilepsy, IDD	Right PVL	11	2/2
9	M	14	L	Right hemiparesis, epilepsy, IDD	Left PVL	28	2/2
10	F	16	L	Right hemiparesis, epilepsy, IDD	Colpocephaly on left ventricule	20	1/1
11	M	17	L	Right hemiparesis, epilepsy, IDD	Left PVL	10	2/+1

***F:** female, **M:** male, **MCA:** middle cerebral artery, **PVL:** periventricular leukomalacia, **R:** right, **L:** left, **IDD:** intellectual and developmental disabilities**, GMFCS:** gross motor function classification system, **AS:** Ashworth scale*

Table 3.
Clinical and neuroradiologic descriptions of patients without hemiplegia

Patient No:	Age	Sex	Affected Side/ Handedness	Cerebral/spinal MRI	Clinical signs	MMs score
1	4	M	R/R	Schizencephaly, CC agenesis	IDD, epilepsy	20
2	9	M	R/R	Polymicrogyria, arachnoid cysts, CC dysgenesis	Epilepsy, IDD	33
3	11	F	R/R	Polymicrogyria, CC agenesis	IDD, epilepsy	27
4	12	M	L/R	Pachygyria, CC agenesis	IDD, epilepsy	16
5	15	M	L/L	Band heterotopia,Dandy Walker, , CC agenesis	4q deletion syndrome, epilepsy, IDD	30
6	9	F	R/R	Normal	IDD 46 XX del(4) t(4,10) q35p123	17
7	14	M	R/R	Normal	IDD 46 XY del(4) t(4,10) q35p123 (Brother of Patient 6)	18
8	15	F	R/R	Hemivertebra on C5,Cerebral MRI normal,	CHARGE syndrome	22
9	7	F	R/R	Cervical X-Ray: fusion of C2–C3 and C4–C6 levels Bilateral temporal arachnoid cysts;	Klippel Feil Syndrome	30
10	7	M	R/R	cervical syringomyelia Occipital encephalocele, , CC agenesis	IDD	19
11	5	M	R/R	Normal	Physiological MMs	30
12	3	F	L/R	Normal	Physiological MMs	21
13	8	M	R/R	Normal	Tourette syndrome	16
14	14	F	L/R	Porencephalic cysts on right side	Incontinentia pigmenti, epilepsy, IDD	11
15	12	M	L/R	Cerebral atrophy	IDD	11
16	11	M	L/L	Porencephalic cysts	Epilepsy, IDD	18

***F:** female, **M:** male, **PVL:** periventricular leukomalacia, **R:** right, **L:** left, **IDD:** intellectual and developmental disabilities **CC:** corpus callosum*

4. Discussion

Humans have a natural tendency towards symmetrical contraction of homologous muscles, which are known to require less cortical activation than alternated bimanual movements or unilateral movements. The motor system has a hierarchical organization based on the cytoarchitectonic properties of cortical motor areas and their anatomical connections (9). Within the cerebral hemisphere, the M1 is mainly involved in motor execution and it is the origin of the corticospinal or pyramidal tract. Secondary motor areas are involved in higher-ordered functions than the primary motor cortex, such as motor planning and movement preparation. Anatomical connections between these two

motor areas allow the ipsilateral transmission of motor plans to the M1 regions involved in limb control (10,11). The interhemispheric transfer of information between the left and right motor areas through the corpus callosum is also possible. At this point, mirror movements are defined as involuntary movements executed on one side of the body occurring simultaneously with unprompted movements of the homologous contralateral muscles.

Pathologic MMs can be associated with many neurological disorders. In present study eleven children were presented with MMs and diagnosed as USCP. The pathogenesis of MMs in cerebral palsy is not yet fully understood. One potential hypothesis could be the activation of bilateral primary motor cortices due to deficient interhemispheric inhibition caused by the underlying brain lesion. Conversely the persistence of ipsilateral corticospinal projections between the non-lesioned motor cortex and the paretic hand has been also proposed as a possible mechanism for mirror movements. This reorganization of the corticospinal tract is unique in children with USCP, and depends on both timing and extend of the lesion. The importance of timing is further supported by the fact that children with congenital USCP show more mirror movements compared to those suffering from childhood stroke. Mirror movements causes some difficulties during daily life of children with CP. Adler C et al.(3) reported that MMs have a specific negative impact on bimanual performance and the time needed to perform typically bimanual activities of daily living in children with USCP. In our research group, except two physiologic cases, remaining 14 children were non-hemiplegic children. The mean Rasmussen Scale scores of hemiplegic and non-hemiplegic patients groups were statistically indifferent. It might be speculated that the organic lesion is not the only factor that determines the severity of MMs.

Mutations in deleted in colorectal carcinoma (DCC) and RAD51 genes have been reported in familial congenital MMs, but their implication has yet to tested in simplex cases. Although one of our cases was familial, genetic analysis was not performed in none of patients.

Cortical malformations have been reported in patients with MMS. Schizencephaly, pachygyria and polymicrogyria were detected in our cases.

Chromosome 4, the fourth largest chromosome, contains 6.4% of the human genome (12). In our study three patients had chromosome 4 abnormalities and two siblings had the same abnormalities. The siblings has *del (4) t(4,10) q35p123*, mild intellectual disability, and dysmorphic appearance (hypertelorism, long philtrum, anteverted nostrils). Both patients' cerebral and spinal MRI was normal. Other patients with 4q deletion syndrome and cerebral MRI showed Dandy-Walker Syndrome malformation, band heterotopy, and corpus callosum hypogenesis. To the best of our knowledge, there is no reported 4q deletion syndrome with MMs, although some subjects had cerebral malformation and CC hypogenesia and these signs may explain MMs pathophysiology.

MMs can be associated with spinal cord abnormalities, such as syringomyelia, spina bifida occulta, and spina bifida meningocele (13,14). In our study three patients had different spinal cord abnormalities. One patient have fusion of cervical vertebrae (KFS), one patient have cervical hemivertebra (CHARGE syndrome) and one non-syndromic patient with cervical encephalocele and syringomyelia. MMs have been reported in 20% of patients with KFS (15,16). Incomplete pyramidal decussation has been found in autopsies of patients with KFS who presented with MMs (17). However there is no previously reported case concerning MMs and CHARGE syndrome. There were patients with two different syndromes and one non-syndromic patient, but all patients had spinal cord abnormalities and MMs. To explain this association, there may be a need to focus on the developmental stages of spinal cord and corticospinal tract.

Tourette syndrome is defined by the chronic presence of both multiple motor tics and one or more vocal/phonic tics and it may related

with MMs (8,18). Although the exact pathophysiology of tics is still unknown, transcranial magnetic stimulation studies have indicated the possible involvement of the primary motor cortex and Broca's area in the performance of repetitive behaviors, as well as abnormalities of intracortical/ interhemispheric inhibition that may cause tics (19,20). In our study, one patient was diagnosed as having Tourette syndrome. His cerebral and spinal MRI was normal. This may be a result of reduced interhemispheric cortical inhibition.

Although present study is one in the largest series on MMs in children, it was conducted retrospectively and this is the main limitation of the research. Lack of neurophysiological investigations, such as EMG, might be considered other limitations. Lack of neurophysiological investigations, such as EMG, seems to be limitation for the study. EMG can detect all movements that may not be detected by physical examination. However we couldn't detect MMs especially with patients whose mirror movements are based on CNS causes, or Tourette syndrome, because the EMG would not be indicated for these disorders. Also special training and special equipment are needed to perform EMG.

In conclusion, present study emphasizes that clinical examination is the most important tool to use in detecting MMs, while physiological tests can help in analyzing MMs. Our opinion, if the clinicians consider MMs, MMs will be reported more frequently.

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