Journal of Clinical Neuroscience xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Clinical study

Assessment of the corticospinal fiber integrity in mirror movement disorder

Bilgehan Solmaz [a], Mustafa Görkem Özyurt [b], Demir Berk Ata [c], Fulya Akçimen [d], Mohammed Shabsog [b], Kemal Sıtkı Türker [b], Hakkı Dalçik [e], Oktay Algin [f], Ayşe Nazlı Başak [d], Merve Özgür [g], Safiye Çavdar [g,*]

[a] Department of Neurosurgery, Istanbul Education and Research Hospital, Istanbul, Turkey
[b] Department of Physiology, School of Medicine, Koç University, Istanbul, Turkey
[c] Department of Molecular Biology and Genetics, School of Medicine, Koç University, Istanbul, Turkey
[d] Neurodegeneration Research Laboratory, Suna and İnan Kıraç Foundation, Boğaziçi University, İstanbul, Turkey
[e] Department of Preclinical Science, Anatomy Unit, Faculty of Medicine, The University of the West Indies, St. Augustine, Trinidad and Tobago
[f] Department of Radiology, Bilkent University, Ankara, Turkey
[g] Department of Anatomy, School of Medicine, Koç University, Istanbul, Turkey

ARTICLE INFO

Article history:
Received 15 April 2018
Accepted 3 June 2018
Available online xxxx

Keywords:
Mirror movements
Corticospinal tracts
Neural tube defect
Electrophysiology

ABSTRACT

Mirror movements are unintended movements occurring on one side of the body that mirror the contralateral voluntary ones. It has been proposed that mirror movements occur due to abnormal decussation of the corticospinal pathways. Using detailed multidisciplinary approach, we aimed to enlighten the detailed mechanism underlying the mirror movements in a case subject who is diagnosed with mirror movements of the hands and we compared the findings with the unaffected control subjects. To evaluate the characteristics of mirror movements, we used several techniques including whole exome sequencing, computed tomography, diffusion tensor imaging and transcranial magnetic stimulation. Computed tomography showed the absence of a spinous process of C5, fusion of the body of C5-C6 vertebrae, hypoplastic dens and platybasia of the posterior cranial fossa. A syrinx cavity was present between levels C3-C4 of the spinal cord. Diffusion tensor imaging of the corticospinal fibers showed disorganization and minimal decussations at the lower medulla oblongata. Transcranial magnetic stimulation showed that motor commands were distributed to the motor neuron pools on the left and right sides of the spinal cord via fast-conducting corticospinal tract fibers. Moreover, a heterozygous missense variation in the deleted in colorectal carcinoma gene has been observed. Developmental absence of the axonal guidance molecules or their receptors may result in abnormalities in the leading of the corticospinal fibers. Clinical evaluations and basic neuroscience techniques, in this case, provide information for this rare disease and contribute to our understanding of the normal physiology of bimanual coordination.

1. Introduction

Mirror movements (MM) are involuntary movements of the one side of the body that mimic the voluntary movements on the other side. Two types of MM have been described: the first type is physiological and regarded as normal during the infancy of healthy children. This type of MM usually disappears in the first decade of life. The second type of MM is observed in the adult population and is congenital, often inherited autosomal dominantly and may also occur sporadically [1,2].

MM are observed in the distal parts of the extremities mostly in the hand and rarely in the forearm and toes [2,3], its occurrence is more common in males and in left-handed individuals [4]. Patients with MM usually have difficulties in bimanual coordination, causing difficulty in tasks that require each limb to act independently [3,4].

MM have been shown to be related to the abnormal crossing of the corticospinal tract in the medulla or upper cervical level or due to unintended excitations of the contralateral motor cortex through the corpus callosum [5,6]. Data collected from clinical cases showed considerable variations of the corticospinal tract size, myelination, decussation and the presence of aberrant fibers [7,8]. It has been shown that the decussation of this tract is asymmetrical. The fibers from the left hemisphere cross more extensively and more rostrally than those from the right hemisphere [7,8].

* Corresponding author at: Department of Anatomy, School of Medicine, Koç University, Rumelifeneri Yolu, 34450 Sarıyer, Istanbul, Turkey.
E-mail address: scavdar@ku.edu.tr (S. Çavdar).

https://doi.org/10.1016/j.jocn.2018.06.001
0967-5868/

Adult-type MM may accompany congenital disorders such as Klippel-Feil syndrome [9,10], X-linked Kallman's syndrome [11], or hemiplegic cerebral palsy [12,13]. They may also be acquired later in life as a result of either a neurodegenerative disease, such as amyotrophic lateral sclerosis [14], or an acute lesion after a hemiplegic stroke [15]. The presence of MM in Parkinson's disease has been studied in detail, and unlike congenital disorders, MM in Parkinson's disease were typically unilateral [16,17].

In the present case, we describe a patient with MM and aim to contribute detailed knowledge for the understanding of the MM using transcranial magnetic stimulation (TMS), Hoffmann reflex (H-reflex), computed tomography (CT), magnetic resonance imaging (MRI), diffusion tensor images (DTI) and the genetic background of the present case.

2. Methods

The Human Ethics Committee of Koç University approved the experimental procedure in accordance with the Declaration of Helsinki. Both control group and MM patient were asked to fill the informed consent form. The index patient is a 20-year-old right-handed male. He is a university student studying fine arts. The parents noticed the abnormal movements of the hands in the last six years. He has no relevant family history. He had no pre- and post-natal history. However, he had a febrile convulsion at the age of 2. His major complaint was the movement of one hand which was accompanied by the same movement of the unintended hand. No other movement disorder was present. He also had complications in bimanual activities such as; writing a message on his mobile telephone using both hands, tying up his shoe-laces, cutting vegetables, two-handed typing and buttoning up his shirts. He also complained of not being able to recognize an object in his pocket without looking (astereognosia). The general examination showed a deep dimple of the skin at the C2 level. The patient has no other gross abnormalities. Control subjects who had no known neurological disorders were recruited from Koç University. Further radiological, physiological, genetic assessments were made to clarify the case.

2.1. Radiology

Three-tesla MRI and DTI sequences were performed on all subjects (including the patient and controls) at Bilkent University. The examinations were performed by using a 3T unit (Trio with Tim; Siemens Healthcare AG, Erlangen, Germany) with 32-channel birdcage head coil. Multiplanar and curved reformatted images were obtained with Leonardo software (Neuro 3D, Siemens Healthcare AG, Germany). An experienced neuroradiologist evaluated the MRI data during acquisition. Details of the routine anatomical imaging sequences (except DTI sequence) are given in Table 1. The diffusion tensor and tractography images were acquired using a high-resolution diffusion tensor sequence (named as Diffusion High-Res, TE = 83 ms, and TR = 8200 ms). A DTI diffusion scheme was used, and a total of 49 diffusion sampling directions were acquired. The b-value was 700 s/mm^2. The in-plane resolution was 2.16 mm. The slice thickness was 1.8 mm. DTI data were analyzed with FSL, Medinria, and Leonardo programs for obtaining tractography images.

Table 1
Three Tesla MRI protocol used for the study.

Sequences/Parameters	3D-MPRAGE	3D-SPACE (with VFAM)
TR/TE (ms)	*2130/3.45*	3000/579
TI (ms)	*1100*	–
Slice thickness (mm)	*0.8*	0.6
FOV (mm)	*230 × 230*	240 × 240
Acquisition time (min)	*5*	5
NEX	*1*	2
Number of slices	*240*	240
Flip angle (°)	*8*	100
Imaging plane	*Sagittal*	Sagittal
Distance factor	–	–
PAT factor	*2*	2
PAT mode	*GRAPPA*	GRAPPA
Voxel size (mm)	*0.8 × 0.8 × 0.8*	0.6 × 0.6 × 0.6
FA mode	–	T2 variant

Abbreviations: time of inversion; 3D-SPACE: three-dimensional sampling perfection with application-optimized contrasts using different flip angle evolutions; 3D-MPRAGE: 3D T1W magnetization prepared rapid acquisition gradient-echo; STIR: short tau inversion-recovery; NEX: number of excitations; FOV: field of view; PAT: parallel acquisition technique; GRAPPA: generalized autocalibrating partially parallel acquisitions.

2.2. Genetics

The index case was subjected to whole exome sequencing (WES, Macrogen-Korea). Exomes were captured using the Agilent SureSelect Human All Exome V6, followed by paired-end sequencing on Illumina HiSeq 2500 platform. The bioinformatic analysis was done in-house at the NDAL laboratory of Boğaziçi University. Reads were aligned to human reference genome GRCh37 via Burrows-Wheeler Aligner (BWA) 1, downstream processing of the data was performed with SAMtools 2. Single nucleotide variations (SNV) and small indels were called for each sample by the HaplotypeCaller tool of Genome Analysis Toolkit (GATK) 3. Structural and functional annotation of the variations was performed by using ANNOVAR 4. Minor allele frequencies (MAF) of the variants were obtained from several data-sets consisting of dbSNP138, 1000 Genomes Project 18 and The Exome Aggregation Consortium (ExAC) 5. Variant filtration was performed based on the MAF values; variations present in the population with a frequency greater than 1% were considered as polymorphisms. Visualization of the sequence of interest was performed by Integrative Genomics Viewer (IGV) 6.

2.3. Electrophysiology

Electrophysiology results from the MM patient have been compared with health control subjects (n = 2). During the experimental protocols, all the subjects were blindfolded with an eye band to prevent visual feedback from the environment. Electrophysiology experiments were performed in Koç University Neurophysiology Laboratory.

2.3.1. Equipment

TMS was delivered using Magstim 200^2 stimulator (Magstim Co., Whitland, UK) with a figure-of-eight-shaped magnetic coil. Electrical stimulation was delivered using constant current stimulator (model DS7A, Digitimer Ltd, Hertfordshire, UK). Electromyography (EMG) analysis was done using Spike2 v7 (Cambridge Electronic Design, CED, UK). CED 1902 Quad System MKIII amplifier and CED 3601 Power 1401 MKII DAC were used for recording with 2000 Hz sampling frequency and recording was filtered with a band pass filter of 20–500 Hz. Force, on the other hand, was measured with Biopac Software (BIOPAC Systems Inc. CA, USA) using clench force transducer.

2.3.2. Preparation

Subjects were comfortably seated in an armchair where their forearm forms a 90-degree angle to the upper body which was vertical to the ground. The forearms were fixed to the armchair slightly to prevent the contribution of other muscle groups. The

Please cite this article in press as: Solmaz B et al. Assessment of the corticospinal fiber integrity in mirror movement disorder. J Clin Neurosci (2018), https://doi.org/10.1016/j.jocn.2018.06.001