Neuroscience Letters 478 (2010) 141–145

Contents lists available at ScienceDirect

Neuroscience Letters

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

Post-movement beta rebound abnormality as indicator of mirror neuron system dysfunction in autistic spectrum disorder: An MEG study

Eiko Honaga[a,b], Ryouhei Ishii[a,*], Ryu Kurimoto[a], Leonides Canuet[a], Koji Ikezawa[a], Hidetoshi Takahashi[a], Takayuki Nakahachi[a], Masao Iwase[a], Ichiro Mizuta[c], Toshiki Yoshimine[d], Masatoshi Takeda[a]

[a] Department of Psychiatry, Osaka University Graduate School of Medicine, Osaka, Japan
[b] Department of Child and Adolescent Psychiatry, Osaka City General Hospital, Osaka, Japan
[c] Department of Human Sciences, Kobe College Graduate School of Human Sciences, Kobe, Japan
[d] Department of Neurosurgery, Osaka University Graduate School of Medicine, Osaka, Japan

ARTICLE INFO

Article history:
Received 23 March 2010
Received in revised form 26 April 2010
Accepted 1 May 2010

Keywords:
Magnetoencephalography (MEG)
Event-related synchronization (ERS)
Beta rebound
Autism spectrum disorder (ASD)
Mirror neuron system (MNS)
Beamformer

ABSTRACT

The mu rhythm is regarded as a physiological indicator of the human mirror neuron system (MNS). The dysfunctional MNS hypothesis in patients with autistic spectrum disorder (ASD) has often been tested using EEG and MEG, targeting mu rhythm suppression during action observation/execution, although with controversial results. We explored neural activity related to the MNS in patients with ASD, focusing on power increase in the beta frequency band after observation and execution of movements, known as post-movement beta rebound (PMBR). Multiple source beamformer (MSBF) and BrainVoyager QX were used for MEG source imaging and statistical group analysis, respectively. Seven patients with ASD and ten normal subjects participated in this study. During the MEG recordings, the subjects were asked to observe and later execute object-related hand actions performed by an experimenter. We found that both groups exhibited pronounced PMBR exceeding 20% when observing and executing actions with a similar topographic distribution of maximal activity. However, significantly reduced PMBR was found only during the observation condition in the patients relative to controls in cortical regions within the MNS, namely the sensorimotor area, premotor cortex and superior temporal gyrus. Reduced PMBR during the observation condition was also found in the medial prefrontal cortex. These results support the notion of a dysfunctional execution/observation matching system related to MNS impairment in patients with ASD, and the feasibility of using MEG to detect neural activity, in particular PMBR abnormalities, as an index of MNS dysfunction during performance of motor or cognitive tasks.

The mirror neuron system (MNS) is a subset of neurons of the visuomotor group in macaques and humans which operates not only during execution of specific biologically relevant motor actions (e.g., holding and grasping objects), but also during observation of analogous motions of a peer [27]. There is increasing evidence that the MNS is engaged in several cognitive processes such as imitation, action prediction, and understanding of action goals. Not surprisingly, MNS dysfunction is reported associated with impairments in a broad range of social-cognitive processes, including recognition of emotion, understanding of imitation, eye movement detection, language comprehension in autism spectrum disorders (ASD), and other neuropsychiatric conditions [11,26]. In general, individuals with ASD, with qualitative impairments of social interaction and communication, as well as with restricted, repetitive, and stereotype patterns of behavior, show the characteristic appearance of poor interpersonal skills, including lack of empathy, insensitive to other's feelings, inept metaphor, and difficulty in recognizing facial expressions, in greater or lesser degrees.

Since the first report of a potential relationship between clinical features and MNS impairment in ASD made by Williams et al. [31], it has been proposed that MNS dysfunction may provide an etiologic explanation for ASD [11], with a growing body of functional neuroimaging and neurophysiological data supporting a strong association between MNS deficits and ASD pathophysiology [25].

The mu rhythm, an 8–13 Hz oscillatory activity typically observed over the sensorimotor cortex in association with voluntary movements, can also be observed in the absence of actual movement, in situations like imagination [23], preparation [21], or observation of motor actions [23]. This demonstrates overlapping

* Corresponding author at: Department of Psychiatry and Behavioral Science, Osaka University Graduate School of Medicine, D3, 2-2, Yamada-oka, Suita, Osaka 565-0871, Japan. Tel.: +81 6 6879 3051; fax: +81 6 6879 3059.
E-mail address: ishii@psy.med.osaka-u.ac.jp (R. Ishii).

0304-3940/$ – see front matter © 2010 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.neulet.2010.05.004

of neural networks for perception and execution of actions. Therefore, mu rhythm has been seen as a physiological indicator of the human MNS [7,23].

Hari et al. [8] argued that in addition to an alpha 10- (8–13) Hz component, the mu rhythm also consists of a beta 20- (15–25) Hz component with different reactivities and source locations; the 10-Hz component seems to be of somatosensory origin whereas the 20-Hz signal also receives contributions from the motor cortex. The amplitude of the 20-Hz activity decreases prior to movement initiation following 10-Hz activity decrease, and sharply rebounds at movement termination compared to a modest recovery of the 10-Hz oscillations [7]. This power increase in beta activity following movement termination is known as post-movement beta rebound (PMBR), which typically appears after electrical nerve stimulation [2], and movement imagination [22] or observation [17] without motor cortex output or muscle activation, in the same manner as the mu rhythm. Nevertheless, neurophysiological evidence for MNS dysfunction in patients with ASD comes mainly from EEG studies looking at the mu rhythm in the 8–13 Hz during action observation/execution with few studies exploring beta oscillatory response [18,19,26]. Despite some conflicting results, it is generally accepted that mu rhythm and beta suppressions over somatosensory areas can be regarded as indicator of MNS function [19].

Recently, a number of studies looking at a potential relationship between PMBR and MNS function have provided evidence suggesting that, like mu and beta suppressions, PMBR especially over the motor cortex may also reflect MNS activity [15,17]. However, although MNS is thought to be dysfunctional in autism [19], few attempts have been made to assess the pattern of PMBR reactivity to observed and self-performed actions in patients with ASD. Avikainen et al. [2], for instance, explored MEG stimulus-locked responses or evoked potentials triggered by action observation in five Asperger subjects, and found no significant difference in PMBR around the 20 Hz range between patients and controls, although the patients exhibited a trend towards reduced PMBR. Overall, to date, little has been reported on PMBR related to movement observation and MNS dysfunction in ASD.

With the development of beamformers and other advanced time–frequency analysis methods, there has been growing interest in motor and cognitive task-related changes in brain oscillations. Indeed, beamformers have given us an insight into the dynamics of oscillatory changes across the cortex not explored previously with traditional analysis techniques that rely on averaged evoked responses [12,13]. In particular, Brain Electrical Source Analysis (BESA) [28] and its multiple source beamfomer (MSBF), a modified version of the linearly constrained minimum variance vector beamformer in the time–frequency domain, have proven to be of great value in the identification of source-power changes induced by cognitive tasks in neuropsychiatric disorders [4,16]. Moreover, BrainVoyager QX [6], originally developed for fMRI analysis, allows us to import data from BESA software and to perform between-group comparisons of 3D images. Recently, the combination of MSBF and BrainVoyager QX was successfully used for source imaging of MEG time–frequency data, especially in the alpha and theta bands, in psychiatric conditions like dementia and psychosis of epilepsy [4,16]. However, to our knowledge, there are no previous MEG studies of ASD focusing on source-power changes, particularly on PMBR, using beamformer and group comparison.

The purpose of the present study was to use BESA beamformer and BrainVoyager QX to explore neural activity related to MNS dysfunction, as indicated by PMBR abnormalities during observation of object manipulation in patients with ASD.

Seven patients with ASD (age range: 22–34, mean: 26.4 years; five males) with no other neurological/psychiatric illness, and ten normal subjects (age range: 28–35, mean 32.1 years; eight males) were enrolled in this study. All participants were right-handed. Patients with ASD were recruited from outpatient facilities of Osaka University Hospital, and diagnosed by experienced psychiatrists and/or clinical psychologists according to the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, APA 1994) criteria. Six patients were diagnosed with Asperger's disorder, and one with pervasive developmental disorder not otherwise specified (PDD-NOS). Intellectual ability of patients with ASD was assessed using the Wechsler Adult Intelligence Scale—Revised (WAIS-R). All patients scored 70 or higher on the full IQ scale (mean score 94.5 ± 14.7), as well as on the verbal IQ (101.8 ± 14.7) and performance IQ (86.0 ± 11.5) subscales. Participants received detailed information on the experimental procedures of this study, and written informed consent was obtained prior to the tests. The study was carried out in full compliance with the Declaration of Helsinki and approved by the hospital's Ethics Committee.

MEG data were recorded with a 64-channel whole head magnetometer (NeuroSQUID Model 100, CTF Systems Inc., Canada) in a magnetically shielded room. MEG signals were digitized at 625 Hz, and filtered using a combined 60-Hz notch filter and 200-Hz low-pass filter.

The experiment consisted of two tasks or conditions: (1) observation and (2) execution condition. During the MEG recordings, the participants were asked first to simply observe object-related hand actions performed by the experimenter (observation condition), and to execute the observed action at a later stage (execution condition), which ensured that participants paid attention during the observation task. Eight different objects were randomly used for their proper purposes, for example, picking up with chopsticks, cutting with a knife, brushing with a toothbrush, or grasping a ball, etc. All actions were performed using the right hand. Each condition comprised eight trials, each of 15-s duration, equally subdivided into three stages: (1) pre-movement, (2) movement, and (3) post-movement stage. During the pre/post-movement stages, participants were in a resting state, sitting still with their hands on their lap, and during the movement stage, they were asked to perform the tasks (i.e., observing or executing hand actions). Trials of the execution condition followed those of the observation condition.

For each trial in each condition, the beginning of the movement stage (5-s duration) was considered time zero ($t = 0$). The event-related time–frequency spectrum of PMBR was calculated by subtracting 4-s duration data of the time-window 0.5–4.5 s in the movement stage (control interval) from that of the time-window 5.5–9.5 s in the post-movement stage (active interval). Artifact rejection was performed off-line. Source imaging of MEG data in the time–frequency domain was performed using the MSBF implemented in BESA software. As an adaptive beamformer, the MSBF applies a spatial filter specific for each brain voxel that is fully sensitive to activity from the target voxel, while being as insensitive as possible to activity from other brain regions, thus suppressing interference from unwanted signals. We analyzed frequencies between 15 and 30 Hz (beta frequency band). The BESA beamformer applied complex demodulation to transform time-domain MEG data into time–frequency data. The complex demodulation consisted of a multiplication of the time-domain signal by a complex periodic potential function with a frequency equal to the frequency analyzed and an additional low-pass filter. In the resulting complex signal, its magnitude corresponded to half the envelope amplitude and its phase to the compound phase of the filtered frequency (beta) band. To obtain power values, the time-series MEG data were squared and averaged across all trials. Details on BESA time–frequency transformation are described elsewhere [9].

The beamformer 3D maps displaying q values as a measure of the magnitude change in the active (post-movement) interval relative to the control (movement) interval in percent, superimposed onto