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Movement preparation is affected by tissue damage in multiple sclerosis: Evidence from EEG event-related desynchronization

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Abstract

Objective: To investigate the impact of brain tissue damage in Multiple Sclerosis (MS) on the efficiency of programming of voluntary movement, assessed using event-related desynchronization of the EEG.

Methods: The onset latency of mu ERD (percent desyncronization of the mu rhythm preceding movement onset) to hand movement was studied in 34 MS patients. ERD onset was compared with normative data and correlated with T1 and T2 total lesion volume (TLV) at magnetic resonance imaging (MRI).

Results: ERD onset latency was significantly correlated with T1-TLV ($r=0.53$, $P=0.001$) and T2 lesion load ($r=0.5$, $P=0.003$), even after correcting for disability. Patients with higher T1-TLV had significantly delayed ERD onset compared with normal subjects and with patients with lower T1-TLV; patients with higher T2-TLV had significantly delayed ERD compared with normal subjects only. ERD onset latency was not correlated to clinical disability.

Conclusions: Our finding of delayed ERD onset in patients with more severe measures of brain damage, independently from clinical disability, suggests that functional cortico-cortical and cortico-subcortical connections underlying the expression of ERD during programming of voluntary movement are disrupted by the MS related pathological process. Further, studies are needed to evaluate the role of specific anatomical cortico-subcortical circuits in determining this abnormality.

Significance: The extent of brain lesion load in multiple sclerosis affects cortical changes related to motor preparation, detected by analysis of onset latency of event-related desynchronization (ERD) of the mu rhythm to self-paced movement.

Keywords: Multiple sclerosis; Voluntary movement; Magnetic resonance imaging; EEG; Event-related desynchronization

1. Introduction

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system of unknown etiology. Converging evidence suggests that the MS-related brain damage is related to disruption of neural connections among cortical associative areas and between cortical and subcortical structures, leading to the impairment of cognitive functions (Comi et al., 1993; Rao, 1990). The amount of subcortical brain lesions has been previously related to global impairment of functional cortico-cortical connections in MS patients as measured from the resting EEG (Leocani et al., 2000). The extent of brain tissue damage in MS patients also correlates with the pattern of activation to voluntary movement at functional magnetic resonance imaging (MRI), interpreted as the expression of cortical reorganization partially limiting the consequences of MS injury in the brain and spinal cord (Filippi and Rocca, 2003).

Another functional correlate of brain activity to voluntary movement is the event-related desynchronization (ERD; Pfurtscheller, 1977) of the electroencephalogram (EEG). Reduced expression of the mu and beta rhythms, observed over the contralateral sensorimotor cortex 1–2 s prior to voluntary movement (Leocani et al., 1997;

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Pfurtscheller, 1977) is considered an indicator of cortical activation. Delayed mu ERD onset, reported in basal ganglia disorders such as Parkinson's disease (Defebvre et al., 1994, 1996; Magnani et al., 1998, 2002), has been related to involvement of cortical circuits related to motor programming.

The aim of this study was to investigate the impact of accumulated brain damage in MS patients, assessed at conventional MRI measures of lesion load, on the efficiency of brain circuits involved in motor planning, assessed by mu ERD preceding voluntary movement.

2. Methods

2.1. Patients

Thirty-four right-handed patients (14 males, 20 females; mean age [$\pm$SD]: 35.3$\pm$7.0 years, mean disease duration: 9.2$\pm$6.1 years), followed-up in the MS Clinic of our Institution, were included. Twenty-three had the relapsing-remitting and 11 the secondary progressive form of MS, according to consensus criteria (Lublin et al. 1996). Their median Expanded Disability Status Scale (EDSS) score (Kurtzke, 1983) was 3.5 (range: 0–6.5; mean: 3.1$\pm$1.9), with the following Functional Systems (Kurtzke, 1983) scores: pyramidal: 2.3$\pm$1.5; brainstem 1.1$\pm$1; cerebellar 1.2$\pm$1.3; somatosensory 0.9$\pm$0.8; sphyncteric 0.8$\pm$0.9; visual 0.3$\pm$0.7; mental 0.5$\pm$0.8. Patients with a history of affective disorders, drug or alcohol abuse, or treated in the previous month with steroids or other psychoactive drugs, were not included, as well as patients with upper limb motor impairment, possibly interfering with performance at the electrophysiological examination. All patients gave their informed consent to participate in the study, which was approved by the local ethic committee.

2.2. Image acquisition

On a 1.5 T scanner, each patient underwent dual echo turbo spin echo (TSE) (TR = 3300, TE = 16/98, echo train length = 5) brain MRI scans. Twenty-four axial 5-mm thick contiguous interleaved slices were obtained, with rectangular 188$\times$250 mm field of view and 194$\times$256 image matrix, thus obtaining approximately a 1$\times$1 mm in-plane resolution. T1-weighted magnetization-prepared rapid acquisition gradient echo (MP-RAGE) scans were also obtained in the same session (TR = 10, TE = 4, TI = 700, flip angle = 10°, number of acquisitions = 1), with the acquisition of a 3D sagittal slab (194$\times$256$\times$160 image matrix, 250 mm field of view) covering the entire brain. The original MP-RAGE data were reformatted to obtain 24 axial contiguous 5-mm thick slices, with the same orientation and offsets as the corresponding TSE slices. Patients were positioned in the scanner following published guidelines for MS studies (Miller et al., 1991).

2.3. Image analysis

MS lesions were first outlined by agreement by two experienced observers, unaware of patients' clinical characteristics, on proton density (PD)-weighted and T1-weighted MPRAGE image hardcopies; T2-weighted scans were always used to increase confidence in lesion identification. Only areas with signal intensity close to that of the CSF and corresponding hyperintensities on PD and T2-weighted images were considered as hypointense lesions. Total T2-hyperintense and T1-hypointense lesion volume (T2 TLV and T1 TLV, respectively) measurements were then performed by a trained technician, who was also unaware of patients' clinical characteristics. A local thresholding technique (LTT) was used for lesion segmentation on computer-displayed images, keeping the marked hardcopies as a reference. The LTT is based on the assumption that, on MR images, MS lesions have a different signal intensity compared with the normal-appearing brain tissue. Using a mouse-controlled cursor, the rater first chooses a point on the lesion boundary and the algorithm starts contouring the lesion, following from the strongest edge point in the neighbourhood (i.e. by searching it over a 5$\times$5 pixel square area with the manually-selected point in its center). Once the starting point has been found, the program searches in all directions and chooses the next contour point, which must have at least as strong a gradient as the starting one. By following the same principle from the most recent point, the contour is complete when it traces back to the starting point. Lesions are delineated as regions of interest (ROIs) and for each sequence the lesion volume can be simply calculated by multiplying the total ROI area for the slice thickness. Further, details about this image analysis method are extensively reported elsewhere (Rovaris et al., 1997).

2.4. EEG recording

Patients performed about 60 self-paced extensions of the right thumb at a rate of one every 5–10 s, while seated on an armchair in an electrically and sound-shielded room, their hands pronated and resting on a pillow. Twenty-nine EEG channels with binaural reference were recorded with scalp electrodes mounted on an elastic cap (Electro-cap International, Eaton, OH) according to the 10–20 international system of electrode placement, with additional electrodes placed along the longitudinal axis (FC3, FCz, FC4, CP3, CPz, CP4, FT3, FT4, TP3, TP4) and bipolar electrooculogram. The EEG signal was amplified (Synamps Amplifiers, Neuroscan, Inc., Herndon, VA), filtered (DC to 50 Hz), and digitized (250 Hz sampling frequency). Bilateral bipolar EMG from the right extensor pollicis brevis muscle was recorded to detect movement onset and to monitor for contralateral complete relaxation. Subjects were asked to perform brisk movements while keeping their eyes open and fixated on a point in front of them.