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Slow pre-movement cortical potentials do not reflect individual response to therapy in writer's cramp

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ABSTRACT

Objective: To investigate whether movement-related cortical potentials (MRCP) provide a physiological correlate that indicates the response to treatment in patients with writer's cramp.
Methods: In 21 patients with writer's cramp, who underwent 4 weeks of limb immobilization followed by re-training for 8 weeks, we recorded MRCPs preceding a self-initiated brisk finger abduction movement. MRCP measurements of pre-movement activity were performed at baseline, after the end of immobilization and four and 8 weeks of re-training. We examined 12 controls, who received no intervention, twice 4 weeks apart.
Results: Patients benefited from the therapeutical intervention (Zeuner et al., 2008). They showed no abnormalities of the MRCPs at baseline. In controls, MRCPs did not significantly change after 4 weeks. In patients, immobilization and re-training had no effect on MRCPs. There was no correlation between the severity of dystonic symptoms or the individual treatment response and MRCPs.
Conclusion: MRCPs are stable measures for interventional studies. However, they do not reflect clinical severity of dystonic symptoms or improvement after therapeutic interventions.
Significance: This is the first study to investigate MRCPs in a large cohort of patients with writer's cramp compared to a control group at different time points. These potentials do not reflect the motor control disorder in patients with writer's cramp.

1. Introduction

Writer's cramp is a task-specific dystonia that presents clinically with co-contractions of antagonist muscles during handwriting in affected patients (Tolosa and Marti, 2004). Task-specific dystonia is thought to be associated with abnormal patterns of activity in cortical and subcortical areas during sensorimotor tasks (Garraux et al., 2004; Hallett, 1998, 2006; Lerner et al., 2004; Meunier et al., 2003; Peller et al., 2006) that may possibly result from maladaptive reorganization. This finding has been confirmed in several studies that investigated the dystonic (Bara-Jimenez et al., 1998; Elbert et al., 1998; Garraux et al., 2004; Meunier et al., 2003) or the non-dystonic side (Garraux et al., 2004; Meunier et al., 2001).

In writer's cramp movement-related cortical potentials (MRCPs) have been recorded to examine pre-movement activation of premotor and motor cortical areas and have found to be abnormal (Deuschl et al., 1995; Van der Kamp et al., 1995; Yoshida et al., 2003). The MRCP is a slowly increasing cortical negative electroencephalographic (EEG) potential preceding a self-paced brisk movement. As discussed by Shibasaki and Hallett (Shibasaki and Hallett, 2006) different terminologies have been proposed for identifiable components of the Bereitschaftspotential (BP). According to their nomenclature the BP1 reflects the early and BP2 the late phase of the BP (Shibasaki and Hallett, 2006). BP1 precedes self-initiated voluntary movements by 1–2 s. BP2 follows the BP1 and begins at about 500 ms before the EMG onset. Currently, it is the consensus that the BP1 starts first in the SMA, then shortly thereafter in the lateral premotor cortices, whereas the BP2 starts in the M1 and the premotor cortex mainly contralateral to the movement (Ikeda et al., 1992; Yazawa et al., 2000).

Beside the pre-movement potentials, the contingent negative variation (CNV) has been investigated. In contrast to the BP, the CNV is a slow negative EEG potential that arises between two stimuli triggering reaction time movement. The first stimulus serves as the warning stimulus, whereas the second stimulus after

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an interval commands the movement. The beginning of the CNV is related to the sensory processing of the warning stimulus, the end linked to motor preparation. Hamano et al. (1999) chose as the imperative stimulus (S1) a pair of tone bursts with fixed inter-stimulus interval and two different frequencies delivered through earphones. The motor task in response (S2) was either an extension of the fingers ipsilateral to the ear or a rotation of the head (Hamano et al., 1999). They reported decreased early and late CNV amplitudes for finger extension in the affected and non-affected hand of 11 patients with writer's cramp, while the CNV for neck turning was normal (Hamano et al., 1999). This study demonstrated that motor programming is abnormal for specific body parts, and clinical symptoms may result from a deficient compensatory mechanism.

In addition to abnormal movement initiation and execution, event-related EEG measurements suggest a deficient inhibitory control of motor programmes in task-specific dystonia of the hand (Berg et al., 2001; Hummel et al., 2002; Yazawa et al., 1999). For instance, the amplitude of the MRCP preceding voluntary relaxation is diminished over the left central area (Yazawa et al., 1999).

With the concept to reverse abnormal re-organization and normalize deficient inhibitory control of motor programmes novel therapeutic approaches included limb immobilization of the hand and forearm (Pesenti et al., 2004; Priori et al., 2001) and sensory or motor re-training (Zeuner et al., 2002, 2005; Zeuner and Hallett, 2003; Zeuner and Molloy, 2008). The therapeutic effect of immobilization followed by motor re-training has been reported recently (Zeuner et al., 2008).

In this study of a large cohort of 21 writer's cramp patients compared to 12 healthy controls we analyzed the pre-movement activity for the first time at different time points. MRCPs preceding self-initiated brisk finger abduction were recorded at baseline, after the end of immobilization and after four and 8 weeks of re-training. The control group received no intervention, and was examined twice 4 weeks apart. The questions addressed were whether immobilization for 4 weeks and 8 weeks of re-training normalizes MRCPs in affected patients, and whether the amplitudes of MRCPs correlate with clinical outcome.

2. Methods

2.1. Subjects

Twenty-one (10 females) patients with writer's cramp volunteered for the EEG analysis. The mean age was 48.7 ± 11.9 years (range: 26–71 years). Mean disease duration was 11.6 ± 7.9 years, ranging from 2 to 25 years. As a control group 12 healthy volunteers (age 47.2 ± 9.6) were included. Patients and controls gave written informed consent to the protocol, which had been approved by the local Ethics Committee.

Only patients received immobilization for 4 weeks followed by a daily re-training period for 8 weeks. All measurements in patients and healthy controls were conducted at baseline and after 4 weeks. Additionally, patients were investigated during the daily re-training period at weeks 8 and 12.

2.2. Electroencephalography (EEG)

EEG activity was recorded using a 32-channel electrode cap (Electrocap International, Eaton, OH, USA). Electrodes were positioned according to an extended 10–20 system with mastoids as reference. Electrooculographic activity was recorded to facilitate removal of eye movement artifact. Impedance was kept below 5 kΩ. EEG data were filtered from DC to 100 Hz and sampled at 500 Hz (Synamps, Neurosoft, Inc., Herndon, VA, USA).

Subjects were seated comfortably in an arm chair with the right arm relaxed on a resting pillow. The right hand was positioned with the palm down at the edge of the pillow so that the index finger could move freely. Right forearm EMG activity was recorded using bipolar tin surface electrodes over the first dorsal interosseus muscle. EMG was filtered between 10 and 100 Hz.

Patients and controls were instructed to make self-paced, brisk finger abduction, followed by relaxation approximately every 10 s. All subjects practiced the required movement before the EEG recordings started. This particular movement was chosen because the EMG of the FDI was easy to record, finger movements are mainly affected in writer's cramp patients and it represented a simple movement that all patients could perform without difficulty. None of the patients developed hand dystonia during the movements and the EEG recordings. Recordings were done six times in 5-min blocks for a total of at least 120–150 artifact free movements.

The EMG was digitally high pass filtered offline at 20 Hz, slope 6 dB/octave and rectified. The EEG was analyzed by visually marking the EMG onset of the first dorsal interosseus (FDI) muscle. Epochs were made lasting from −2000 to 2000 ms with respect to EMG onset. Epochs had the overall linear trend removed and were baseline corrected from −2000 to −1750 ms. Epochs with artifacts were removed and the average was calculated. The BP1 is defined as the mean voltage from −1500 to −500 ms. The BP2 is the mean voltage from −500 to 0 ms. The EMG peak amplitude, the EMG duration and the time to peak interval were measured.

2.3. Clinical evaluation

For clinical evaluation we used the Arm Dystonia Disability Scale (ADDS) (Fahn, 1989) and the Writer's cramp rating scale according to Wissel (Wissel et al., 1996) while patients wrote 10 times the sentence "Die Wellen schlagen hoch" ("The waves are surging high"). Scores were based on the blinded assessment of video tapes obtained during that standardized handwriting task. The higher the score the more severe were dystonic symptoms during handwriting (Wissel et al., 1996).

2.4. Immobilization and motor re-training

The wrist and fingers of the dominant hand were immobilized with a plastic splint that reached from just below the elbow to the tips of the fingers in all patients, but not in healthy controls as described before (Priori et al., 2001) (CAMP Handgelenksorthese halbzirkel, No. 8709 from Basko Healthcare, Germany). Additional material was used to individually build and adjust the splint (Ezeform Splint Material, thickness 3.2 mm, 1% perforated form Ludwig Betram GmbH, Lübecker Strasse, 1, 30880 Laatzen, Germany). Patients were allowed to take it off for 30 min per day for cleaning and specialized exercises.

The motor re-training is described in detail elsewhere (Zeuner et al., 2008). Patients trained for 8 weeks. In summary, we implemented two types of training: one group trained a task-specific finger exercise with finger Stax finger splints (Dj. Orthopedics, LLC; Vista, CA, USA) with a pen attached on the bottom of these splints to train drawing and writing movements as previously described (Zeuner et al., 2005). During the first week they practiced 25 min per day, in the remaining 7 weeks 50 min per day. The second group conducted a non-task-specific finger training using therapeutic putty. Exercises included the training of fingers (extension, flexion, adduction and abduction), hand and arm, but no writing or drawing movements. Duration of the training was daily 30 min in the first and 45 min in the remaining 7 weeks.