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TENS is harmful in primary writing tremor

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ABSTRACT

Objective: It is unclear whether primary writing tremor (PWT) is a tremulous form of dystonia or a tremor per se. Transcutaneous electrical nerve stimulation (TENS) at 50 Hz applied for 2 weeks was reported to improve the writing capabilities of patients with writer's cramp (WC). We explored whether such a beneficial effect can be obtained in patients with a PWT.
Methods: In a cross-over, double-blinded randomized study we tested whether 2-week periods of 5, 25 or 50 Hz TENS applied to wrist flexor muscles, improved the score of the Fahn–Tolosa–Marin scale of nine patients with PWT. Excitability of neurons and of various intracortical circuits in the motor cortex were also tested before and after TENS by using transcranial magnetic stimulation.
Results: TENS at 5 and 25 Hz did not have any effect while TENS at 50 Hz worsened the clinical condition and the cortical excitability.
Conclusions: TENS is not a new treatment alternative for PWT.
Significance: The beneficial effect in WC and the harmful one in PWT of TENS stresses that the two disorders are likely different nosological entities.

1. Introduction

Primary writing tremor (PWT) is considered to be a type of task-specific tremor in which a tremor predominantly occurs during and interferes with handwriting. Electromyographic (EMG) patterns show either alternating bursts of activity of forearm antagonist muscles or co-contraction of the muscles. Physiological investigations in PWT are scarce and conflicting (Bain et al., 1995; Modugno et al., 2002; Byrnes et al., 2005) and there has been a debate as to whether PWT represents a tremulous form of focal dystonia related to writer's cramp (WC). Pharmacologic treatments and injections of botulinum toxin have limited efficacy, thus, alternative approaches merit investigation. TENS (transcutaneous electrical nerve stimulation) is used routinely to alleviate pain. In the field of motor disorders/disability the use of TENS is less documented. TENS is able to induce effects that outlast the period of stimulation and involve both the somatosensory and the motor functions (Mima et al., 2004). When applied to wrist muscles, TENS-induced modulation of motor evoked potentials (MEPs) has opposite directions in the couple of forearm antagonist muscles (flexor – FCR – and extensor – ECR) and may be mediated by the inhibitory connections linking antagonist motoneuronal pools at the spinal and/or cortical levels (Tinazzi et al., 2005a, 2006). In secondary dystonia a beneficial effect of TENS at 20–30 Hz was suggested in two studies but not documented by a parallel physiological study (Bending and Cleeves, 1990). More recently, a modest but clear beneficial effect of TENS was demonstrated on the writing capabilities of patients with writer's cramp (Tinazzi et al., 2005b). Such a clinical beneficial effect was documented in a second study where TENS-induced modulation of FCR and ECR MEPs was compared between a group of healthy subjects and a group of dystonic patients. While in the control group 15 sessions of TENS did not have any additive effect compared to that of one unique TENS session, in the patient group the prolonged use of TENS led to reproduce a pattern of change sin corticomotoneuronal excitability of FCR and ECR muscles similar to that observed in healthy subjects after only one session of TENS (Tinazzi et al., 2006). Effect of TENS at high frequency was later questioned

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according to the high variability of TENS effects observed in one study of healthy subjects (Fernandez-del-Olmo et al., 2008). As PWT shares common features with WC, we explore the effects of TENS (using three different frequencies) in patients with PWT who have an EMG pattern with pure isolated rhythmic activity (tremor) involving the couple of wrist antagonist muscles, whereas the EMG pattern of WC patients is rather complex.

2. Subjects and methods

2.1. Subjects

Nine right-handed male patients (mean age: 61.6 years ± 13.4; range: 35–79) were enrolled in the study. Handedness was assessed by using the Edinburgh Handedness Inventory. They all completed the clinical screening and seven completed the physiological study. One subject who had a high resting motor threshold for TMS (see below) refused the stimulations and in another one it was impossible to get a sizeable MEP from FCR muscles. Diagnosis was made on the basis of clinical features: tremor interfering with writing in the absence of abnormal postures, postural tremor or other neurological signs. All medications for dystonia or tremor were stopped at least 2 weeks before starting the study. Botulinum toxin injections were not administered for at least 6 months before the study. Informed consent was obtained from each patient.

2.2. Experimental set-up (Fig. 1)

It was a cross-over, controlled, double-blinded randomized study. The study was approved by the Ethical Committee of the Salpêtrière Hospital, Paris, France. The experimental set-up is presented in Fig. 1. The study was divided in two phases. In phase 1, patients received a placebo or a 5 Hz TENS stimulation. In phase 2, patients received a 25 Hz or a 50 Hz TENS stimulation. The order of the stimulations was randomized across patients for each phase. Each phase lasted for 7 weeks with TENS stimulation for 2 weeks, wash-out for 3 weeks, TENS stimulation again for 2 weeks. A 3 weeks wash-out period was interposed between the two phases.

2.3. Clinical assessment

We used the Fahn–Tolosa–Marin Tremor Rating Scale (TRS) as both part B and part C of the scale specifically assess tremor while writing and drawing whereas none of the scales used in dystonia specifically studied this type of functional disability. The primary endpoint of the study was the clinical score of the Fahn–Tolosa–Marin Tremor Rating Scale (TRS) (Fahn et al., 1993). Scores were performed at the beginning and at the end of each stimulation period (eight evaluations). This scale rates the severity of the tremor by body part from 0 (none), to 4 (severe). The scale is divided into three parts. Part A assesses examiner-reported tremor location and severity (amplitude). Part B assesses examiner-reported ability to perform specific motor tasks/functions (writing, drawing, and pouring; with the dominant and non-dominant hand). Part C assesses patient-reported functional disabilities resulting from the tremor (speaking, eating, drinking, hygiene, dressing, writing, working, and social activities). In this study, the total TRS score and the TRS sub-score B (dominant hand only) was calculated. The medical doctor performing the clinical assessment was unaware of patient's stimulation condition.

2.4. TENS stimulation

TENS was delivered to FCR by an electrostimulator (Cefar primo pro, Cefar Medical, Sweden). The current was an asymmetric rectangular biphasic waveform (pulse width: 250 μs). Electrical stimuli were delivered in 2-s trains separated by 2-s pauses. Each TENS treatment consisted of 14 sessions (7 days for per week for two consecutive weeks) lasting 20 min each (Fig. 1).

At baseline patients were taught how to place the electrodes over the FCR muscle and how to use the stimulator. All sessions were self-administered and reported in a booklet.

2.5. Electrophysiological testing

Electrophysiological assessment was done at baseline and at the end of each stimulation period (five evaluations) (Fig. 1). The experimenter was unaware of patient's stimulation condition. Electromyograph (EMG) signals were recorded from the right arm (all subjects were right-handed) through surface electrodes placed over the FCR and ECR muscles. The EMG signals were filtered (bandpass, 100 Hz to 1 kHz), rectified, and stored for offline analysis. A figure-of-eight shaped coil (7 cm inner diameter for each half) connected to a Bistim-module and two Magstim 200 magnetic stimulators (The Magstim Company, Dyfed, UK) was positioned on the scalp over the left M1. The hot spot for the right FCR muscle was defined as the lowest threshold site evoking a MEP response in FCR accompanied by a clear wrist flexion movement. The coil was positioned with the handle pointing backwards at an angle of 45° to the midline (Brasil-Neto et al., 1992). The hot spot was marked with a pen on the cap worn by the subject; this served as visual reference against which the coil was positioned and maintained by the experimenter.

In each physiological session we first calculated the resting motor threshold (rMT) for right FCR. We then drew the ascending part of the input–output curve of the FCR MEPs. Then conditioning

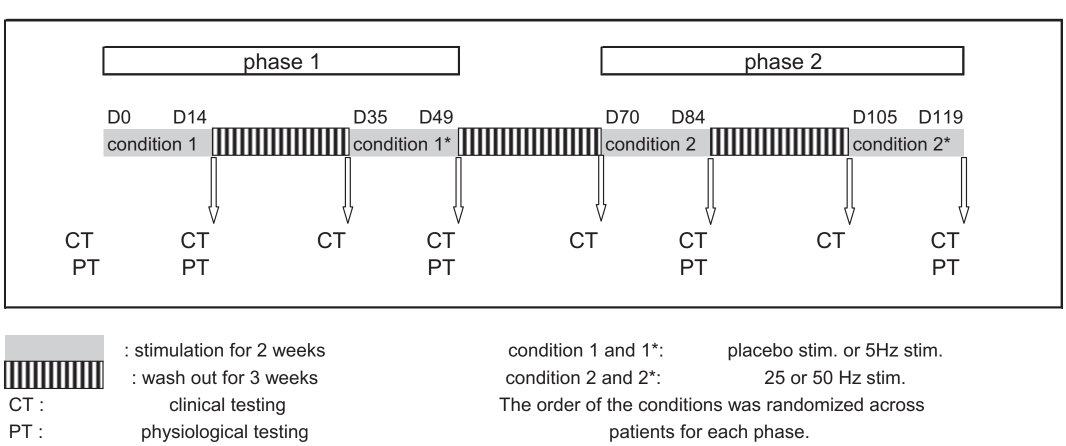

Fig. 1. Cross-over, controlled, double-blinded randomized study assessing the effects of TENS (placebo, 5, 25, 50 Hz) on clinical and physiological parameters.