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High frequency repetitive transcranial magnetic stimulation over the motor cortex: No diagnostic value for narcolepsy/cataplexy

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Sirs: Narcolepsy is a disorder with two key symptoms: excessive daytime sleepiness and cataplexy (sudden attacks of paralysis triggered by emotions) [4]. As cataplexy is the only specific symptom, it is paramount to detect it correctly, so an objective diagnostic tool would be most welcome.

Hungs et al. applied high frequency repetitive transcranial magnetic stimulation (rTMS) over the motor cortex in three narcoleptic patients and eight healthy controls [2]. rTMS resulted in a transient loss of voluntary muscle activity in all three patients, but not in the controls. Unfortunately, the rTMS settings used were outside internationally accepted safety limits with respect to stimulus duration and intensity [6]. Here, we aimed to replicate the findings using adjusted rTMS settings within these limits.

We studied two female (age 31 and 36 years) narcoleptics with daily cataplectic attacks, both partial and complete, and eight healthy controls (mean age 39.6 ± 18.9 years, 4 women). All patients gave informed consent, and the study was approved by the local ethical committee. Patients were medication-free for three weeks. rTMS was performed with a figure-of-eight coil over the left hemisphere, at the 'hotspot' of the first dorsal interosseus muscle (FDI). EMG was recorded bilaterally from the FDI. Subjects contracted both FDIs at about 20 % of maximal voluntary force, using the EMG signal as visual feedback from 2 seconds before stimulation to 8 seconds afterwards. We kept close to the stimulation parameters used by Hungs et al. [2], but shortened the stimulus trains to remain within safety limits [6]. We stimulated at 20 Hz for 1.5 seconds at an intensity of 110 % of the resting motor threshold. rTMS trains were repeated three times, with one-minute intervals.

Suprathreshold rTMS during active muscle contraction resulted in extensive movements of the right arm, which startled several subjects, even though they had been warned of this possibility. In Fig. 1, three representative EMG traces during rTMS are shown. We did not find any cessation of voluntary EMG activity after rTMS in the two narcoleptic patients (Fig. 1A) or seven controls (Fig. 1B). However, one 24-year-old healthy man consistently showed an abrupt diminution of EMG activity in the contralateral FDI after the rTMS train, which lasted for about 2 seconds (Fig. 1C).

Our findings show that the cessation of EMG activity after rTMS is apparently not restricted to patients with cataplexy, and is therefore likely to be a physiological phenomenon. As the response was restricted to one side of the body and did not habituate, it cannot be regarded as part of the startle reflex. Still, startling might have caused the subject to cease the voluntary activation of the muscle. Another theoretical explanation is that the cessation of EMG activity represents a form of motor inhibition perhaps similar to the 'silent period' occurring after single-pulse TMS. One study reported that rTMS with trains of 20 suprathreshold stimuli at 15 Hz increased the duration of the silent period when compared to single-pulse TMS [5].

The differences between our findings and those of Hungs et al. might conceivably be due to medication effects. In the latter study, patients had been free from anti-cataplectic drugs for only 3 days. Short-term medication withdrawal can result in severe increases in cataplexy [1], and this may have led to a general increase in cataplexy frequency, and perhaps to cataplexy attacks triggered by the emotion linked to the uncomfortable TMS. Furthermore, it has been reported that clomipramine, one of the most potent anti-cataplectic agents, by itself alters the excitability of the motor cortex [3], so it is possible that short-term withdrawal may induce profound alterations in cortical excitability.

The explanations mentioned above might account for the existence of brief muscle atonia after rTMS, but do not invalidate our main finding that rTMS induced EMG depression is not specific for narcolepsy/cataplexy, and is likely

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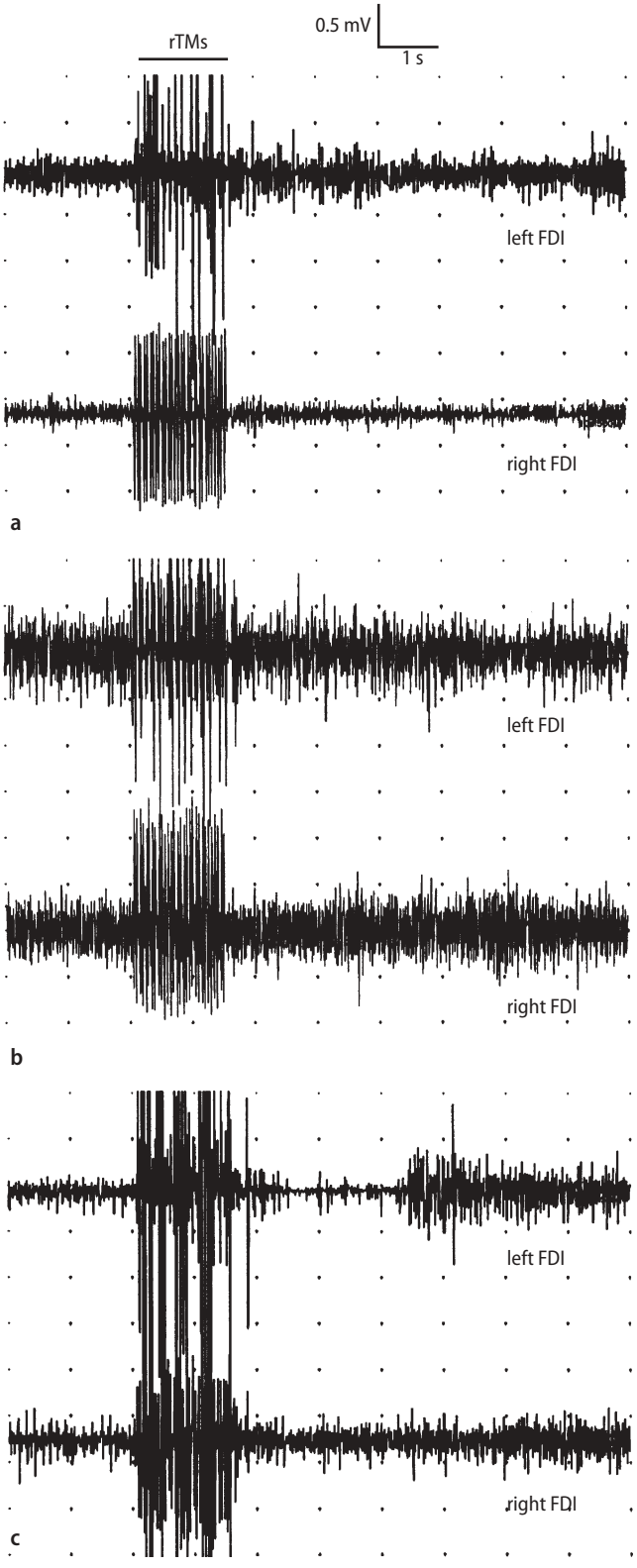

Fig. 1 Representative EMG registrations. Upper traces show EMG from the left FDI, lower traces from the right FDI. **A** EMG trace before and after a 1.5 second train of 20 Hz rTMS at 110 % of resting motor threshold in a medication-free narcoleptic patient with clear-cut cataplexy. No cessation of voluntary EMG activity is seen. **B** A similar EMG trace is observed for a control patient. **C** EMG trace in another healthy control subject. Here, voluntary EMG was clearly suppressed for about 2 seconds after the rTMS burst

to have little or no diagnostic value. Furthermore, we would like to stress adherence to safety restrictions posed on frequency and duration of rTMS [6].

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