Changes in excitability at the level of M1, spinal cord and muscle during 3 minutes of finger tapping at the maximal possible rate

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Abstract
Linear mixed effects models were used to describe the dynamics of M1, spinal and muscle excitability during index finger tapping at the maximal possible rate, for 3 min. Our results show that tapping rate and amplitude decreased, following a triphasic pattern that seems to evolve parallel to changes in excitability measured by transcranial magnetic stimulation and electrical stimulation along the cortico-muscular axis.

1 Introduction

Repetitive rhythmic movements (RRM) are basic in activities of the daily living. The origin of fatigue induced by RRM is less understood that for those activities requiring isometric contractions, though it appears to be mixed: Peripheral (i.e., muscular) and central [1]. The central origin of fatigue induced by RRM might be potentially treated with non-invasive brain stimulation techniques. To optimize the use of these techniques it is needed to understand the changes in excitability along the cortico-muscular axis during RRM. For short-lasting RRM (30 s) the excitability of M1 inhibitory GABAb interneurons and spinal α-motoneurons increase [2, 3], but for longer RRM the profile is unknown. Our objective was to describe the changes in muscular, spinal and cortical excitability during the execution of 3 min index finger tapping (*ft*) at the maximal possible rate.

2 Methods

2.1 Participants

Nine young healthy participants took part in the experiments (age range 18–41 yrs, 5 men).

2.2 Procedure and Analysed Variables

Participants executed index-*ft* at the maximal possible rate for 3 min; *ft* rate and amplitude was recorded with a goniometer (sampling at 10 kHz). Transcranial magnetic stimulation (TMS) on M1 (single and paired-pulses with 2 ms ISI), cervicomedullary magnetic stimulation and percutaneous electric stimulation of the Erb's point evoked potentials (MEP, MEPc, CMEP and CMAP, respectively). Potentials were acquired before and during the execution of the task from the first dorsal interosseous muscle (extensor indicis, flexor digitorum superficialis, and abductor digiti minimi muscles were also

explored: analyses in progress). During *ft*, stimulation (automatically triggered) was applied every 4.5 s at the moment the finger tapped on the table (contact phase of the tapping cycle). This was done in two different sessions (S1 and S2, counterbalanced in order across subjects, >2 weeks apart). During S1, single and paired TMS pulses were alternated to test corticospinal excitability (CSE) with single pulse MEP, and short intra-cortical inhibition (SICI) with the MEPc. In S2, the acquisition of CMEP to test spinal excitability and CMAP to test muscle excitability were alternated. In the two sessions, *ft* rate and amplitude were computed along the task, considering the median score within the 2 s prior the stimulation pulses. This procedure resulted in the acquisition of 44 potentials evenly distributed along the 3 min *ft* task per session (22 MEP and 22 MEPc alternating in S1; and 22 CMEP and 22 CMAP alternating in S2). We also recorded *ft* frequency and amplitude at 44 timepoints, evenly distributed along the 3 min task.

2.3 Data Processing

For each subject, the *ft* rate along the task was computed by expressing the scores of the 44 time-points relative to the maximal frequency acquired during the task; for *ft* amplitude the scores were made relative to the maximum active range of motion (ROM) recorded before the tasks.

The peak-to-peak amplitude of MEP, MEPc, CMEP and CMAP during the task were expressed in relation to the median of 10 potentials (of each type) acquired at rest before the task. Subsequently, we also made the MEPc relative to the MEP value, the MEP relative to the CMEP value, and the CMEP relative to the CMAP value, by computing the corresponding ratios. MEP & MEPc potentials were alternated in their acquisition in S1 (i.e., event#1 MEP; event #2MEPc; event#3 MEP…), and CMEP & CMAP in S2. Therefore, for the analysis of the ratios at every time-point, we imputed the score of a MEP at a MEPc event time-point by calculating the mean score considering the time-points immediately prior and posterior: thus MEP for event #2, was the mean of MEP for event #1 & 3; and we proceeded likewise for imputing MEPc scores in S1; and CMEP and CMAP in S2.

2.4 Statistical Analyses

Linear mixed effects models were applied to model the relation between the time and *ft* rates, amplitude values and the aforementioned ratios during the task, fitting fourth order polynomials where the subjects were modeled as random effect. For CMAP the linear model was adjusted without any ratio. Statistical analyses were carried out using the software R with package *nlme*. Significance was set at $p < 0.05$.

3 Results

The change in *ft* rate along the 3 min was significant ($p < 0.001$) and not different for S1 and S2; the rate dropped very rapidly in the first minute, more moderately in min 2, and made a plateau in min 3 (Fig. 1, left panel). The *ft* amplitude change along the task was borderline significant ($p = 0.057$) and was not different for S1 and S2. It reduced in the first minute more than in the second, and reached a plateau in the third minute (Fig. 1, right panel).

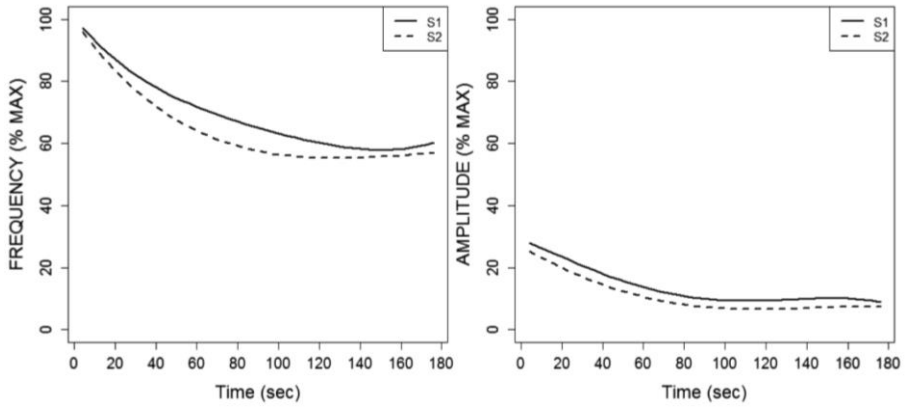

Fig. 1. Changes in *ft* frequency and amplitude (left and right panel respectively) along the task. 100% represent the maximal *ft* frequency and the maximal active ROM, the latter tested before the task. All figures represent the fitting of 4th order polynomials considering all participants.

Figure 2 (left panel) shows the modulation of the recorded potentials along the task, where y-axis unit represents the median score of each potential acquired at rest before the task. The right panel of the Fig. 2 shows the modulation of spinal excitability (i.e., CMEP) made relative to the changes of the CMAP along the task.

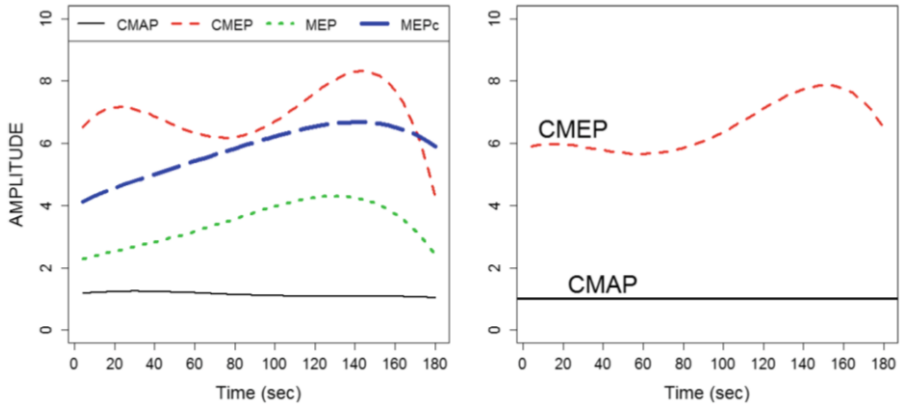

Fig. 2. The left panel shows the modulation of the recorded potentials along the task made relative to their sizes at rest before the task. The right panel shows the modulation of the CMEP made relative to the CMAP.

Likewise, the Fig. 3 (left panel) shows the modulation of the CSE (MEP elicited by single TMS pulse) along the task, made relative to the changes of the spinal excitability. The right panel shows the amplitude of the conditioned MEP (MEPc, with ISI 2 ms) when made relative to the amplitude of the single pulse TMS-MEP). The CMAP amplitude at the beginning of the task was significantly larger than 1 ($p = 0.007$), i.e. large than at rest, since 1 is the median score at rest before the task. Along the task the change of CMAP amplitude with time was significant ($p < 0.001$), with a small but progressive reduction. The spinal excitability (CMEP amplitude) was about 6 times larger at the beginning of the *ft* than at rest (Fig. 2 left panel).

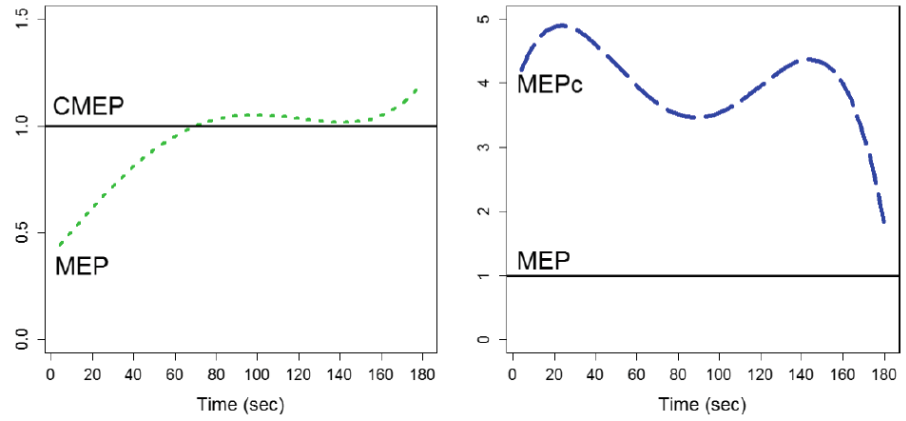

Fig. 3. The left panel shows the modulation of the MEP made relative to the CMEP. The right panel shows the modulation of the MEPc made relative to the MEP.

When making CMEP relative to CMAP amplitude change along the task, spinal excitability changed significantly ($p < 0.01$), remaining stable in the first third of the task, increasing in the second third, and dropping at the end (Fig. 2 right panel). At the beginning of *ft* the MEP amplitude was about twice its size at rest; during the task, its amplitude (relative to CMEP changes) also varied ($p < 0.001$): Increased, reached a plateau and increased further at the end. Finally, the change of the MEPc along the task (relative to the modulation of the MEP in the same period) was also significant ($p < 0.001$). It evolved following a sinusoidal-like pattern (increasing, decreasing, increasing, decreasing) embedded in a clear trend of reduction. Remarkably, MEPc was larger than MEP during the task, especially at the beginning, while it was smaller before the task, at rest. The conditioning TMS-pulse intensity and the ISI between the two pulses in the paired stimulation protocol, had been set to test intra-cortical inhibition, but it resulted that during the task the presence of the conditioning pulse produced facilitation, perhaps induced by an increased excitability of intra-cortical excitatory interneurons not recruited at rest, which become progressively less excitable during the task.

4 Conclusion

Our preliminary results suggest a triphasic pattern in the reduction of finger tapping rate and amplitude during the 3 min task, which might be coupled by changes in excitability along the cortico-muscular axis. Further analyses will explore this possibility and the excitability profile in some other muscles involved in the task.

References

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