Comparative analysis of cortical activation associated to voluntary and electrically-evoked contractions

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Target audience: Researchers and clinicians working in the field of neuromuscular coupling.

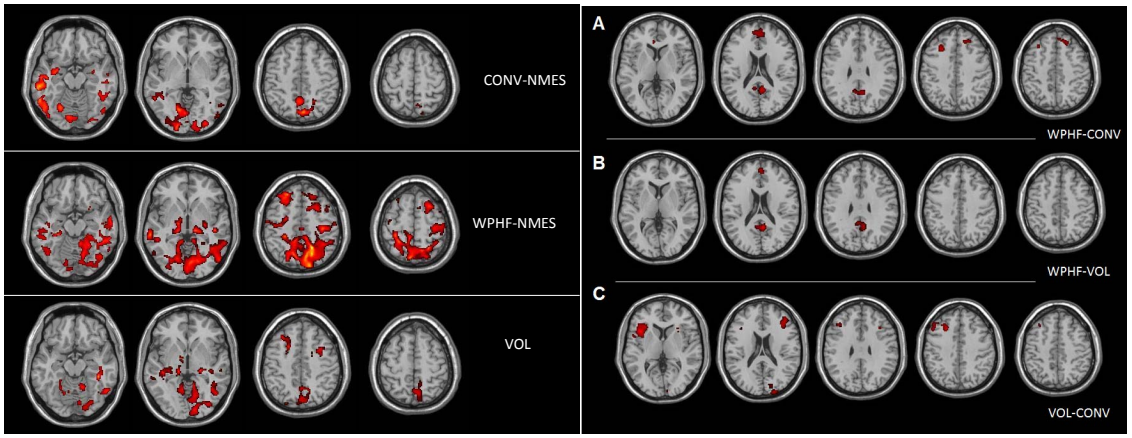
Purpose: Neuromuscular electrical stimulation (NMES) is commonly used in the field of training and rehabilitation in order to enhance, maintain and/or restore muscle mass. Conventional (CONV) NMES involves the application of narrow stimulus pulses (50- 400 µs) delivered at high current intensities and low frequencies (15-40Hz). Compared to voluntary contractions (VOL), the major limitation of NMES is the rapid onset of fatigue due to a non-physiological recruitment of motor units (i.e., the direct stimulation of motor axons beneath the surface electrodes) [1]. Interestingly, the use of longer pulse durations (1 ms), high frequencies (up to 100 Hz) (i.e., WPHF-NMES) and lower intensities has been reported to favor the recruitment of sensory axons and to minimize antidromic collision [2]. On that basis, it has been recently suggested that the motor unit recruitment linked to WPHF-NMES involves a higher central component, thereby resembling the physiological muscle activation profile of VOL [2]. In the present study, we aimed at comparing the brain activation patterns of CONV-NMES, WPHF-NMES and VOL using blood oxygenation level-dependent (BOLD) fMRI. We hypothesized cerebral activation to be higher for WPHF-NMES and VOL as compared to CONV-NMES.

Methods: 8 healthy subjects (24 ± 3 yrs) performed CONV- (25 Hz, 0.05ms), WPHF-NMES (100 Hz, 1ms) and VOL in a randomized order while lying in supine position inside a 1.5T scanner (Siemens Avanto, Erlangen, Germany). For both NMES protocols, electrodes were placed on the right triceps surae muscles and the intensity was adjusted to reach 10% of the maximal voluntary force (a visual feedback of the force intensity level was provided for VOL). Each protocol consisted of 20 isometric plantar flexions (20 sec on / 20 sec off) with 15-20 min of recovery in between protocols. Isometric force was continuously recorded and pain sensations were assessed immediately after each protocol using a visual pain rating scale ranging from 0 (no pain) to 10 (worst possible pain). BOLD fMRI data was acquired using single-shot gradient-echo EPI sequence (TE/TR = 60/3330 ms, FOV = 256^2 mm^2, matrix size 64x64, 30 continuous slices, resolution 4x4x4 mm^3, 12-channel head coil). An fMRI block design paradigm was performed with alternating activation-rest periods of 20 sec each. Measurements were repeated 20 times. Image post-processing, data analyses and visualization were performed using SPM8 software (London, UK). After realignment, images were normalized and smoothed. GLM was applied to obtain the activation map of each subject for each condition before second level analyses were performed to obtain group activation patterns for each condition. Repeated measurement ANOVA detected differences in activation patterns between conditions. A threshold of ($p<0.001$, $k=5$; FDR corrected $p<0.05$) was used to depict significant clusters located on the Talairach atlas after transformation from the Montreal Neurological Institute (MNI) coordinates.

Results: The force time integral was not significantly different between the three protocols (CONV: 1840 ± 155 Ns, VOL: 1756 ±29 Ns, WPHF: 1490 ± 525 Ns, p> 0,05). Pain sensation ratings remained low for all conditions (CONV: 1.93, WPHF: 1.82, VOL: 0.08, p>0,05). fMRI data for within-group analyses showed that relative to rest, all conditions produced significant brain activation in the lower limb somatosensory-motor network, the posterior cingulate and the temporal lobe. In addition, WPHF-NMES and VOL induced activation in prefrontal areas (Fig 1). The direct comparison between WPHF and CONV-NMES showed only increased activation during WPHF in the anterior and posterior cingulate cortex (BA 24, 30, 31, 32), the precuneus and the bilateral prefrontal areas (BA8, BA9) (Fig 2 A). Relative to VOL, WPHF activates more the anterior and posterior cingulate cortex (BA 24, 30, 31, 32) but not the bilateral prefrontal areas (Fig 2B) suggesting no decreased activation relative to this condition. Finally, the VOL condition showed higher activation relative to CONV in the dorsolateral prefrontal and premotor cortex (BA 44,45,46, 8, 9) (Fig 2C).

Fig. 1 (left): Within-group analyses *showing significant brain activation in the lower somatosensory motor network, the posterior cingulate and the temporal lobe*

Fig.2 (right): Between-conditions analyses: ***A)*** *higher activation in the bilateral frontal areas for WPHF vs. CONV-NMES,* ***B)*** *No decreased activation in the bilateral frontal areas for WPHF and VOL,* ***C)*** *higher activation in the dorsolateral prefrontal cortex and the bilateral frontal areas for VOL vs. CONV NMES*



Discussion & Conclusion: This BOLD fMRI study showed distinct cortical activation patterns between two different stimulation conditions (CONV-NMES and WPHF-NMES) and voluntary contraction (VOL). Despite the fact that no significant differences in force time integral and pain sensation were recorded for the three protocols, WPHF-NMES and VOL led to a stronger cortical activation response as compared to CONV-NMES. When directly comparing WPHF-NMES and VOL with CONV-NMES, the contrast images illustrate a higher activation in the prefrontal and premotor areas involved in the executive, and control motor system whereas the CONV-NMES condition illustrates a more passive sensorimotor stimulation. In addition, we found that WPHF-NMES hyperactivates different remote regions (precuneus, posterior cingulate) which are reported to belong to the default mode and/or saliency networks. In summary, the present study supports the hypothesis that brain activation is higher for WPHF as compared to CONV-NMES and closer to the physiological brain activation pattern of VOL.

References: [1] Gregory and Bickel, Phys Ther, 2005. 85(4):358-64. [2] Collins, Exerc Sport Sci Rev, 2007. 35(3) :102-9.