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Title: Inhibitory conditioning of the supplementary motor area with repetitive transcranial magnetic stimulation inhibits diaphragm motor-evoked potentials in healthy humans

Ms. Marie-Cécile 20318 Nierat m-cecile.nierat@wanadoo.fr [1], Dr. Louis 20319 Laviolette louis.laviolette@gmail.com [1], Dr. Anna 20320 Hudson a.hudson@neura.edu.au [1,2], Dr. Mathieu 20321 Raux mathieu.raux@psl.ap-hop-paris.fr MD [1], Mr. Étienne 20322 Allard etienne.allard256@gmail.com [1] and Prof. Dr Thomas 20323 Similowski thomas.similowski@psl.aphp.fr MD [1]. [1] Laboratoire de Physiopathologie Respiratoire, Université Paris 6, ER10upmc, Paris, France and [2] Neuroscience Research Australia, University of New South Wales, Sydney, Australia .

Body: Rationale: The supplementary motor area (SMA) has functional connections with the diaphragm. Facilitatory conditioning of the SMA using repetitive transcranial magnetic stimulation (rTMS) results in an increased excitability of the corticospinal pathway to the phrenic motoneurones (increased diaphragm motor evoked potentials, DiMEPs). This paves the way for rTMS respiratory applications, e.g. modulate respiratory sensations. However, whether DiMEPs can be inhibited through SMA manipulations is unknown. We stimulated the SMA using continuous theta burst stimulation, an inhibitory rTMS protocol (I-rTMS), and measured DiMEP amplitude. Methods: Eight naive healthy subjects (age 25 ± 3 years, mean ± SD, 3 men) were studied. DiMEPs (surface electromyogram) were elicited by single-pulse TMS over the diaphragm primary motor area (M1dia). DiMEPs were recorded at baseline and circa 5, 10 and 20 minutes after I-rTMS (post1, post2, and post3, respectively). Results: I-rTMS over the SMA reduced the amplitude of DiMEPs, from 328 ± 181 μV at baseline, to 239 ± 126 μV, 209 ± 114 μV and 212 ± 123 μV at post 1, post 2 and post 3, respectively ($F_{7,13}$, $p < 0,005$ vs. baseline). These changes were observed in the absence of any reduction in the amplitude of the pre-stimulus EMG ($F_{1,74}$, $p > 0.05$). Conclusions: Inhibitory theta-burst stimulation of the SMA decreases the excitability of the corticospinal pathway to the phrenic motoneurones. This suggests the existence of a tonic excitatory connection between the SMA and M1dia. The possibility of targeting this connection to interfere with respiratory sensations remains to be determined.