

Antonino Giordano¹, Stefano Gelibter¹, Marco Pisa¹, Raffaella Chieffo¹, Mario Fichera², Marco Vabanesi², Mauro Comola², Giancarlo Comi², Letizia Leocani¹

1. Magnetic Intracerebral Stimulation Center, San Raffaele Scientific Institute, Milan
2. Department of Neurology, San Raffaele Scientific Institute, Milan

Background and aims

Along with upcoming trials of drugs for progressive multiple sclerosis (PMS) a strong need for surrogate measures of efficacy is emerging. Motor Evoked Potentials (MEPs) may predict the extent of disease progression in patients with PMS. However, especially in most advanced phases, MEPs may be not clearly elicitable. In most cases, a round coil is used to elicit lower limbs MEPs in clinical routine. Double-cone coil is particularly useful to stimulate motor cortex of lower limbs in the interhemispheric fissure (fig.1A-1B). We compared the use and tolerability of round versus double-cone coil in evoking lower limbs MEPs in PMS to determine if it could represent a better alternative in clinical and research settings.

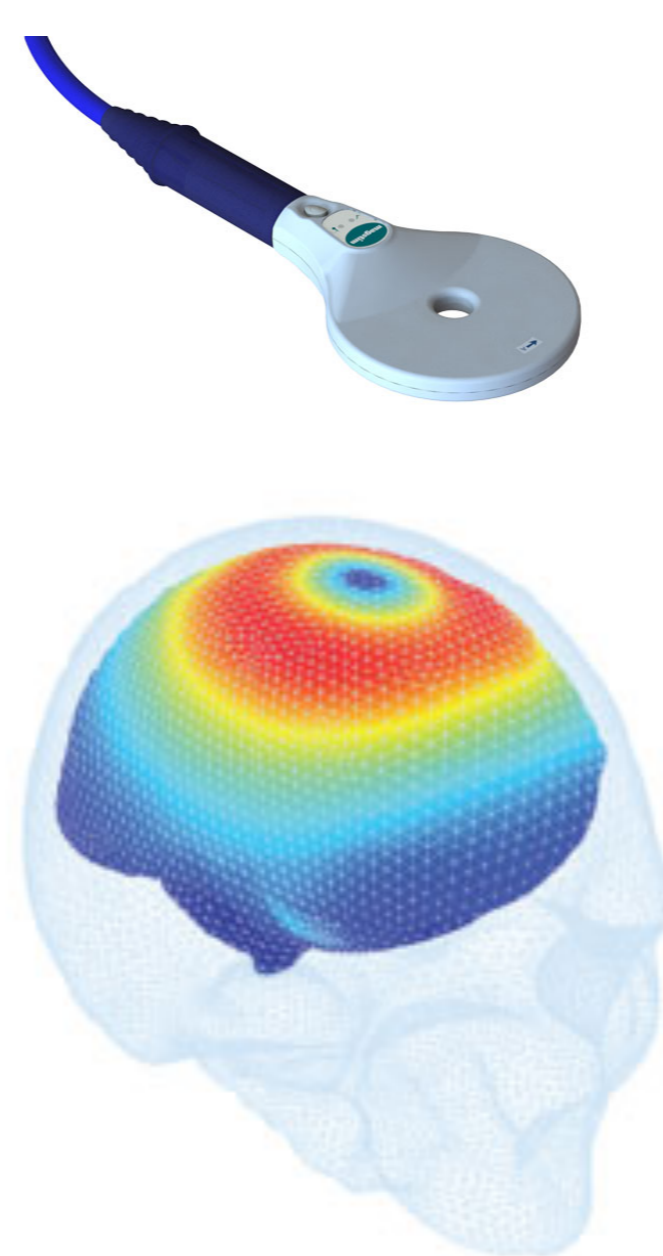
Materials and methods

We enrolled 23 PMS patients (PPMS n=7; SPMS n=16) with median EDSS=6.5 (range 4.5-6.5), mean age=50 years and mean disease duration=15.9 years. We recorded MEPs of Tibialis Anterior muscle at maximum stimulator output with round and double-cone coil, both at rest and during a slight muscular pre-activation (about 10% of maximum effort). We asked the subjects to rate the discomfort deriving from the two coils on a numerical rating scale (NRS), from 0 (no discomfort) to 10 (maximum discomfort).

Results

Round coil was able to elicit MEPs in 3/23 (13%) and 9/23 patients (39%) at rest and after pre-activation respectively, while double-cone coil in 13/23 (57%) and 17/23 (74%) respectively (fig.2). Mixed linear model showed that both coil type and pre-activation were significant predictors of MEP presence. In particular, double-cone coil was associated to higher probability of evoking MEPs (OR=18.8 [95% CI:4.62 to 125.7], $p < 0.001$) compared to round coil. Pre-activation increased probability of evoking MEPs in overall analysis (OR=5.7 [CI:1.65 to 25.66], $p = 0.011$) and in coil-specific analysis with round coil ($p = 0.001$), but not with double-cone coil ($p = 0.216$). Patients rated the double-cone coil as causing more discomfort than round coil ($p < 0.001$ at two-tails Wilcoxon test).

Round coil



Double-cone coil

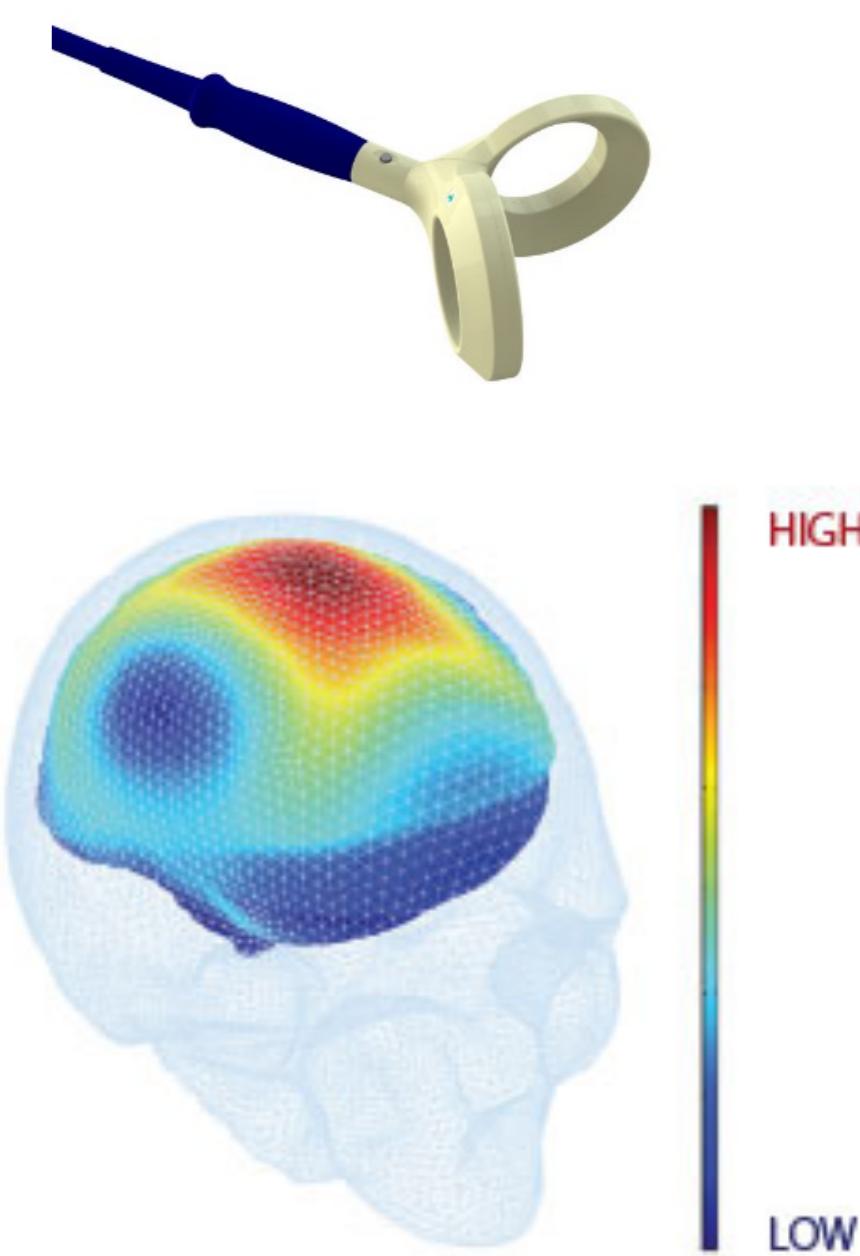


Fig.1A. Different magnetic field area with double-cone and round coil.

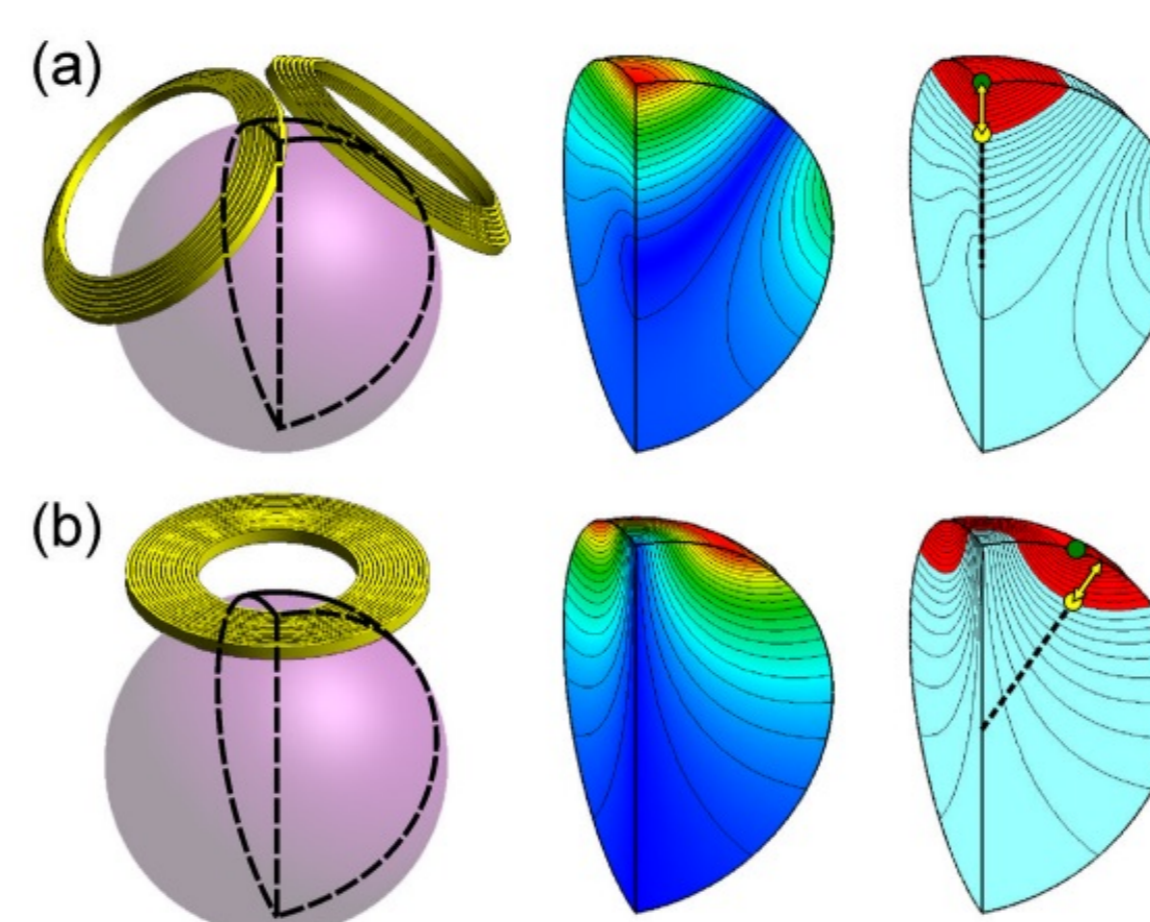


Fig.1B. Different magnetic field area with double-cone (a) and round coil (b). From Deng et al. *Brain Stim*, 2013.

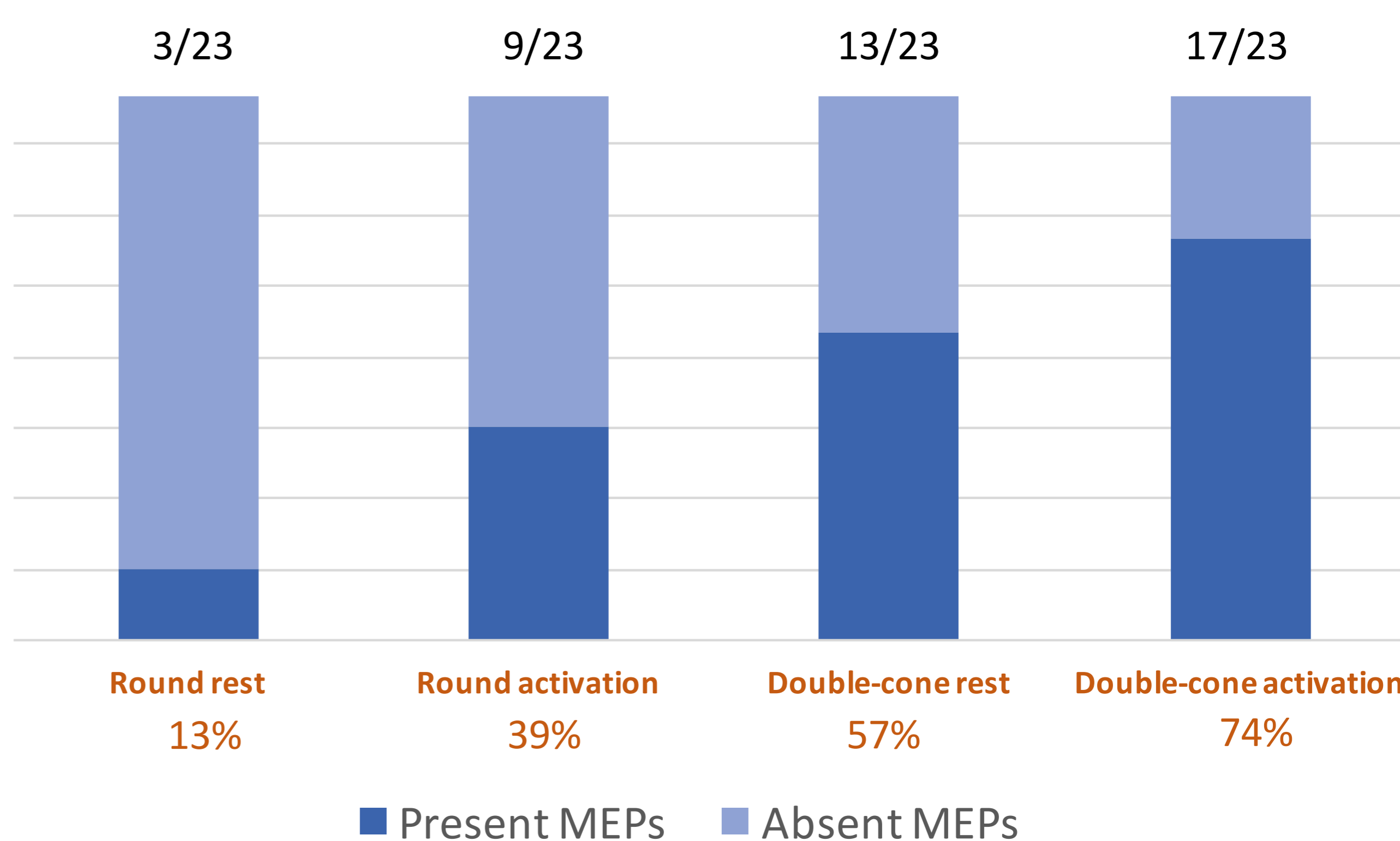


Fig.2. MEPs presence with round and double-cone coil at rest and during muscular facilitation.

Discussion

Using the standard coil for transcranial magnetic stimulation, muscle responses could not be evoked in more than half of PMS patients. Considering its higher success rate in evoking MEPs, double-cone coil represents a promising tool to better assess corticospinal involvement in PMS. Therefore, it may be helpful for assessing the therapeutic effects on neuroprotection and demyelination/remyelination in PMS.