# Absent motor evoked potentials to the lower limbs in progressive MS: is the standard stimulation method adequate?

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**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[1]. 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[2]. We compared the use 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 EDSS ranging between 4.5 and 6.5. Mean age of patients was 50 years and mean disease duration 15.9 years (IQR:9.3-21.5yrs). We recorded MEPs of Tibialis Anterior (TA) muscle with round and double-cone coil, both at rest and during a slight muscular pre-activation (about 10% of maximum effort).

**Results:** Round coil was able to elicit MEPs in 3/23(13.0%) and 9/23 patients (39.1%) at rest and after pre-activation respectively, while double-cone coil in 13/23(56.5%) and 17/23(73.9%) respectively. 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=0.0008), but not with double-cone coil (p=0.216).

**Discussion**: Using the standard coil for transcranial magnetic stimulation, muscle responses could not be evoked in almost 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.

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