Motor evoked potentials as a clinically relevant outcome in progressive MS

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Introduction:
Trials of efficacy of anti-inflammatory therapies in people with non-relapsing progressive MS (PwPMS) have been often less promising than expected. The use of primary outcome measures focusing on neuronal pathways with exhausted functional reserve, as lower limbs (LL) pyramidal function, may have biased these results. Some recent trials on PwPMS have in fact shown better results testing upper limb (UL) function (9 hole peg test – 9HPT).

Objective:
To assess the association between motor evoked potentials (MEP) and clinical measures of motor impairment in a cohort of PwPMS with predominant cortico-spinal tract impairment.

Methods:
40 PwPMS with impaired ambulation and predominant pyramidal involvement (EDSS ranging 4.0 to 6.5; P>=3, C<=2) underwent:
- MEP at LL (recording tibialis anterior – TA bilaterally) and UL (right first dorsal interosseous - FDI) with assessment of resting motor threshold (RMT), latency and amplitude of MEP at 120% of RMT
- 6 minutes walking test (6MWT) and timed 10 meter walk test (T10WT)
- Clinical examination with EDSS, 9HPT, MRC (5 muscles for UL and 7 for each LL), MAS (3 per limb) and administration of Multiple Sclerosis Walking Scale (MSWS)

Results:
LL MEP were absent bilaterally in the 80% of PwPMS, and increased in latency in 7.35%.
Absence of evocable MEP (RMT > 100%) was associated with significantly higher T10WT (25.38 sec vs 14.78 sec; p=0.004) and lower 6MWT (152.2 mt vs 202.3 mt; p=0.065). LL MEP amplitude was associated with 6MWT (rho 0.745; p=0.013) and MSWS (rho -0.656; p=0.039).
Right UL MEP were absent in 12.5% of PwPMS and had increased latency in 70% of cases. In our cohort 55.6% had normal right UL strength (MRC mean 22.2/25); 94.6% had no spasticity (MAS mean 0.2/5) but 86.8% had impaired dexterity at 9HPT (mean 29.7 sec).
Abnormality of UL MEP was associated with absence of LL MEP (chi-square 6.3; p=0.018).
Moreover PwPMS with pathological MEP at FDI had significantly higher T10WT (22.39 sec vs 11.76 sec; p=0.011) and lower 6MWT (221.1 mt vs 165.31 mt; p=0.053).

Conclusion:
To the best of our knowledge, the association between MEP and ambulatory/dexterity measurements has not been previously described.
LL MEP are often absent in PwPMS limiting the possibility of a neurophysiological monitoring of progression due to ceiling effect. UL MEP despite mild clinical UL impairment are often delayed but measurable in PwPMS and may provide a better outcome measure to monitor cortico-spinal tract impairment.

Disclosures:
M. Pisa, S. Gelibter, Fichera M, Giordano A, Houdayer E, Chieffo R, Comola M: has nothing to disclose

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