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"Mute" plantar response: does the cortico-spinal tract "speak"?

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Dear Editor

Plantar reflex is elicited to determine the clinical integrity of the cortical-spinal tract. In normal adults, the toes curl down and inward, whereas Babinski sign occurs when the stimulation leads to big toe extension. Not rarely there is no response, called neutral plantar response (NPR) or "mute" plantar reflex. Although considered of uncertain clinical significance, NPR does not rule out central motor pathologies, and approximately 10% of patients with cortical-spinal lesions show normal or NPR [1]. Moreover, the underlying neurophysiological correlate is lacking, thus precluding a deeper understanding of its clinical value. Transcranial magnetic stimulation (TMS) non-invasively estimate *in vivo* and in real time the excitability of the motor cortex and the conductivity along the cortical-spinal tract [2–4]. In particular, motor evoked potentials (MEPs) to TMS showed clinical and radiological correlation with motor status [5,6].

From November 2018, we observed 88 consecutive patients with mono- or bilateral NPR from our out-patient clinic; 22 had no motor deficit based on neurological examination and brain and spinal magnetic resonance imaging (MRI). In these 22 patients, referred for subjective motor symptoms to rule out an occult central nervous system (CNS) pathology, we assessed and compared MEPs with 22 age- and height-matched healthy volunteers with bilateral normal plantar response. The other 66 patients were excluded due to a previous or current diagnosis of neurological disorder, the association of NPR with other signs, or contraindications to MRI or TMS. All participants gave informed consent for the study, which was approved by the Ethics Committee of the "Azienda Ospedaliero Universitaria Policlinico-Vittorio Emanuele" of Catania, Italy. All motor responses were obtained at 80% of the maximum output, based on the evidence that the threshold stimulation for a 2.0 T magnetic stimulator (as that used in this study) is about 50–65% of the maximal output [7]. This implies that the stimulus intensity was sufficiently high to excite the fast-conducting cortical-spinal neurons [8]. MEPs were recorded via standard surface EMG silver/silver chloride cup electrodes in a conventional belly-tendon montage. As recommended, cortical-muscular responses were acquired during mild tonic contraction, through a circular coil applied over the "hot spot" of the First Dorsal Interosseous and Tibialis Anterior muscles, bilaterally. Central motor conduction time was estimated as the difference between MEP cortical latency and the peripheral motor latency by cervical or lumbar magnetic stimulation [8]. Peak-to-peak MEP amplitude and right-to-left differences were also measured. Within NPR group, 7 patients underwent somatosensory evoked potentials (SEPs) from lower limbs. The two groups were compared with the Mann-Whitney test for skewed continuous data and the chi-square test for categorical variables. For inter-group analysis, the chi-square test and the Kruskal-Wallis test were used for comparison, followed by *post hoc* analysis. Correlation between TMS parameters and plantar response was performed by means of the Spearman's coefficient. A 95% of confidence level was set with a 5% alpha error.

No significant difference between the two groups was found, even when patients were divided in three subgroups according to NPR laterality (Table 1). The correlation analysis between NPR and TMS measures did not show significant results. Four out of 7 patients had SEP abnormalities that correlated with the NPR laterality.

Translationally, these data indicate that isolated NPR lacks of clinical significance and neurophysiological correlate, suggesting that the biggest and fastest conducting pyramidal axons are normal. However, these fibers represent the 5–10% of the total cortico-spinal bundle and, therefore, an involvement of smaller fibers cannot be excluded. Moreover, SEPs abnormalities in some of these patients support the hypothesis that normal MEPs do not devalue the role of NPR as a sign of potential CNS damage. Indeed, even if the reflex is mediated at the spinal level, it is influenced by higher centers, and the maintenance of territorial integrity of receptive fields (i.e. the cutaneous area from which the reflex is obtained) is one way in which the sensory-motor and the cortico-spinal tract normally exert its influence [1]. We propose that NPR alone should be interpreted as clinically and neurophysiologically "mute" as far as cortico-spinal tract is concerned, unless associated with other clinical or instrumental findings. Instead, NPR might suggest an involvement of the central somatosensory pathways, that alters sensory-motor integration. The small sample size, in particular of those who underwent both MEPs and SEPs, is the

Abbreviations: CMCT, central motor conduction time; CNS, central nervous system; FDI, First Dorsal Interosseous muscle; MEPs, motor evoked potentials; MRI, magnetic resonance imaging; NPR, neutral plantar response; PML, peripheral motor latency; SEPs, somatosensory evoked potentials; TA, Tibialis anterior muscle; TMS, transcranial magnetic stimulation.

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Table 1
Demographic and TMS variables of controls and patients divided in three subgroups according to the neutral plantar reflex laterality.

Variable	Controls Median (I-III quartile)	Patients with neutral plantar reflex Median (I-III quartile) (n = 22)			*p* value
	Normal plantar reflex (n = 22)	Group 1 Right side (n = 11)	Group 2 Left side (n = 5)	Group 3 Bilateral (n = 6)	
Age (years)	55.00 (43.50–62.50)	5.00 (36.00-62-00)	55.00 (51.00–67.00)	54.00 (40-65.50)	0.97*
Gender, male (%) female (%)	8 (18.2) 14 (31.8)	3 (6.8) 8 (18.2)	3 (6.8) 2 (4.5)	2 (4.5) 4 (9.1)	0.65†
Height, cm	162.5 (158.00-169-75)	160 (155.00–172.00)	171 (157.00–174.00)	161 (157.50–164.25)	0.72*
Right FDI Amplitude, mV	6.95 (4.80–8.97)	6.10 (4.30–9.00)	7.60 (4.20–10.20)	4.05 (3.30–6.10)	0.17*
Right FDI Latency, ms	19.75 (18.47–20.80)	19.90 (18.10–20.90)	18.70 (16.40–20.75)	20.65 (19.47–22.42)	0.25*
Right FDI PML, ms	13.65 (12.70–14.62)	13.70 (12.60–14.60)	13.30 (11.65-15-65)	13.80 (12.87–15.82)	0.80*
Right FDI CMCT, ms	5.95 (5.17–7.12)	5.90 (5.00–7.10)	5.30 (4.20–5.70)	6.60 (6.37–6.90)	0.10*
Left FDI Amplitude, mV	7.40 (4.00–8.47)	5.70 (2.90–8.00)	8.20 (3.20–9.00)	5.50 (3.65–6.50)	0.46*
Left FDI Latency, ms	19.55 (18.45–20.50)	19.30 (18.10-21-20)	18.30 (17.50–19.95)	20.20 (19.20–21.75)	0.30*
Left FDI PML, ms	13.40 (12.70–14.40)	13.70 (12.30–14.40)	13.40 (11.95–15.15)	13.40 (12.80–14.70)	0.99*
Left FDI CMCT, ms	6.20(5.32–6.72)	6.00 (5.60–6.10)	5.30 (4.25–5.90)	6.65 (6.30–7.22)	0.10*
Right TA Amplitude, mV	5.20 (4.00–6.72)	5.20 (4.13–6.60)	4.50 (3.00–6.65)	4.95 (4.02–6.42)	0.86*
Right TA Latency, ms	26.30 (25.25–27.42)	26.29 (25.30–27.80)	27.40 (24.40–29.25)	25.30 (24.27–27.10)	0.63*
Right TA PML, ms	12.30 (11.60–13.80)	13.20 (12.40–14.10)	13.10 (11.25–13.55)	11.80 (11.05–13.07)	0.23*
Right TA CMCT, ms	13.50 (12.62–14.52)	13.50 (12.10–13.70)	14.30 (13.15–15.70)	13.60 (12.77–14.62)	0.40*
Left TA Amplitude, mV	4.55 (3.22–6.90)	5.40 (4.40–8.20)	4.10 (3.15–7.20)	3.75 (3.32–5.85)	0.40*
Left TA Latency, ms	26.65 (25.17–27.47)	26.00 (25.30–26.90)	28.10 (24.25–29.60)	25.60 (24.87–27.25)	0.82*
Left TA PML, ms	12.70 (11.55–13.95)	13.00 (12.49–14.10)	13.00 (11.00–13.35)	11.45 (10.87–14.50)	0.37*
Left TA CMCT, ms	13.80 (12.82–15.00)	13.00 (11.60–13.90)	15.00 (13.25–16.30)	13.80 (12.57–14.40)	0.40*

Legend: n = number of subjects; FDI = First Dorsal Interosseous muscle; TA = Tibialis Anterior muscle; PML = peripheral motor conduction time; CMCT = central motor conduction time; *Kruskal-Wallis test; † Chi Square test.

main limitation, followed by the lack of more detailed TMS measurements (i.e. cortico-motor threshold, MEP amplitude ratio, CMCT by F-waves, peripheral conduction velocity), although these go beyond a routine TMS exam [1].

Concluding, we intend to stimulate awareness on how to critically interpret a “mute” plantar reflex.TMS is a sensitive method for the quantitative evaluation of even “soft neurological signs”.

Conflicts of interest

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