

**LETTER TO THE EDITOR****TO THE EDITOR****Regarding the Significance of Non-Phase Locked Oscillatory Brain Activity in Response to Noxious Stimuli****Keywords:** Laterality, Endogenous Opioids, Analgesia

As a neurologist with an interest in epilepsy, migralepsy, and pain, I would like to make the following observations concerning the article by Rouleau and associates<sup>1</sup> published in the November issue of the *Journal*. The fundamental issue impeding a deeper understanding of the problems addressed by the authors is the absence of a credible model of cortical organization that underpins handedness (i.e. the unawareness of presence of directionality in callosal traffic).<sup>2</sup> For example, there was no mention of the handedness of the 23 subjects studied by Rouleau et al, at least two of which may have been behavioral left handers (10%), if the protocol did not exclude the sinistrals from participating in the study. The same consideration applies to the subjects investigated by Nahmias et al,<sup>3</sup> Babiloni et al,<sup>4</sup> Mouraux et al,<sup>5</sup> and Gaffau et al,<sup>6</sup> on all of whose contributions the authors relied to justify their findings. In fact, the article by Mouraux et al stated that only sites CZ, PZ, and C4 of the International 10-20 System were sampled for the purpose the study which involved stimulating the left median nerve. It is well-known, however, that moving the nondominant side of the body and sensing from it are bihemispherical events (requiring callosal participation).<sup>2</sup> The latter aspect had in fact been verified by Babiloni and coworkers, who reported bilateral cortical activation (both phase- and non-phase-locked) upon stimulating the left median nerve of their subjects.<sup>4</sup>

This issue of laterality of motor control is important not only because behavioral (declared) handedness of the subject imparts statistically significant information as to the laterality of his or her motor control and consciousness, but also because of the ease of determining a normal person's genuine (neural) handedness by a pen-and-pencil test (i.e. performing the bimanual simultaneous drawing task). Accordingly, in this test, the hand contralateral to the executive hemisphere draws the longer and straighter line, whereas the line drawn by the nondominant hand will be shorter and less linear. Now, because 10-15% of the population has a mismatch of neural and behavioral handedness,<sup>2</sup> Nahmias' comments<sup>3</sup> on the "variability of the [repetitive transcranial magnetic stimulation] response in healthy volunteers" find a potential anatomical answer, not forthcoming from the canonical teachings followed by the authors mentioned previously.

I now address the issue of pain perception upon which the authors concentrated their attention. According to the one-way callosal traffic circuitry, underpinning the lateralities of motor and sensory control (sketched previously), the nondominant side of the body is farther away from the seat of consciousness in both motor and sensory realms. Because there are no sensory communications from the major to the minor hemisphere, the signals (ipsilateral or bilateral) in response to the stimulated right sural nerve described by the authors are of dubious significance. The excitatory sensory connections from the minor to the major hemisphere (i.e. conscious hemisphere) occur through the

posterior aspect of the corpus callosum (splenium). All sensations (e.g. pain) arising from the nondominant side of the body and reaching the minor hemisphere must await transfer to the major hemisphere before reaching consciousness.<sup>2,4</sup> It is known that lesions affecting the minor hemisphere result in neglect of the nondominant side of the body/space as well a lack of awareness of the defect by the subject (anosognosia, denial of deficit).<sup>2</sup> On the other hand, as demonstrated by Brighina and coworkers in a study using repetitive transcranial magnetic stimulation (to which the authors referred),<sup>7</sup> "Left dorsolateral prefrontal cortex stimulation showed to exert antinociceptive effects on both right and left hands," corroborating the previously mentioned anatomical circuitry concerning sensory representation of both hands in the major hemisphere. Clinically, the relationship between consciousness and pain underlies the use of bedside techniques such as application of sternal rub or pinching of the pectoralis muscle in an attempt to awaken the subject. In this regard, an intracarotid injection of amyltal or propofol in the major hemisphere is known to alter consciousness (and cause coma), whereas the same maneuver applied to the minor hemisphere does not. This asymmetry also applies to the origination of seizures. It has been shown that only the major hemisphere can generate epilepsy because the minor hemisphere is devoid of a motor apparatus required to generate seizures.<sup>2</sup> The role of endogenous opioids in mediating analgesia in relation to the laterality of motor control was the subject of a recent study by Taylor and colleagues, using transcranial magnetic stimulation technique.<sup>8</sup>

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I dedicate this note to the loving memory of my beloved sister, Farkhondeh Derakhshan, who died in Australia in 2006.

**DISCLOSURES**

The author has no disclosures to report.

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