



Activating selectively and reliably nociceptive afferents with concentric electrode stimulation: *Yes we can! Provided that low stimulus intensities are used!*

Studying the neurophysiology of the human nociceptive system requires reliable methods to selectively activate nociceptive afferents. In the last decades, a large number of studies have relied on radiant heat stimuli, in particular, laser stimuli, to selectively activate heat-sensitive nociceptive afferents of the skin (reviewed in Plaghki and Mouraux, 2005). Over the last years, an alternative technique has been developed, based on the use of a small concentric bipolar electrode to deliver spatially restricted currents to the epidermis, in order to selectively activate the more superficial nerve endings (Inui et al., 2002; Kaube et al., 2000). As compared to methods based on thermal stimulation, this approach has several advantages, mainly related to the ease of its implementation.

Recently, de Tommaso et al. (2011) conducted a study in which they compared, within subjects, evoked potentials elicited by concentric electric stimulation (CES) to evoked potentials elicited by laser stimulation. They found that the latency of CES-evoked potentials was significantly shorter than that of laser-evoked potentials and, for this reason, concluded that CES-evoked potentials mainly reflect activity resulting from the activation of faster-conducting non-nociceptive A β -fibers, rather than the activation of nociceptive afferents. Therefore, they concluded that CES is not suited to explore the human nociceptive system.

We question this take home message. Indeed, we believe that the lack of selectivity of the responses elicited in de Tommaso et al. (2011) could be due to the use of relatively strong intensities of stimulation (1.6 ± 0.5 mA, corresponding to two fold the pain threshold estimated by their participants). Indeed, Mouraux et al. (2010) recently provided converging evidence that CES *can* be used to selectively activate nociceptive afferents, *provided that low intensities of stimulation are used*. Specifically, they showed that the selective denervation of nociceptive free nerve endings by capsaicin abolishes the behavioral and electrophysiological responses to both laser stimuli and low intensity CES (0.18 ± 0.25 mA, corresponding to two fold the *absolute detection threshold* of the participants), without affecting the responses to conventional transcutaneous electrical stimulation of large-diameter A β -fibers. Furthermore, they showed that, following a nerve pressure block of the superficial radial nerve, a technique known to preferentially affect large-diameter A β -fibers, the time course of the blockade of the electrophysiological responses to CES closely followed that of the responses to laser stimuli, but not that of the responses to transcutaneous electrical stimulation. Importantly, they reported that when higher intensities of stimulation were used (e.g. 2.5 mA), CES was no longer selective for nociceptive afferents, probably because the stimulus is then able to activate more deeply-located non-nociceptive A β -fibers afferents.

Taken together, the results of these studies emphasize a limitation of CES – the fact that its selectivity for nociceptive afferents is crucially dependent on the intensity of the delivered stimuli – but do not allow the conclusion that CES is not suited to study nociceptive pathways.

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Reply to “Activating selectively and reliably nociceptive afferents with concentric electrode stimulation: *Yes we can! Provided that low stimulus intensities are used!*”

The recent interest in mechanisms subtending chronic pain, increased the research for neurophysiological procedures to support clinical examination. However, the tools able to specifically activate nociceptive afferents, e.g., different types of laser equipments, remain quite expensive to be employed in routine examination. The concentric electrode (CE) with its peculiarities seemed a promising cheap and reliable alternative to more expensive procedures, enabling the selective activation of A-delta afferents to obtain nociceptive reflexes and cortical responses. The academic community was divided in regard to the possibility that an electric stimulus might exclude A-beta fibers co-activation, even if delivered in the superficial layer of the dermis. Some applications in clinical conditions of selective A-delta afferents involvement (Obermann et al., 2008) and comparative studies across evoked responses obtained by standard electrode, laser stimulus and CE (Inui et al., 2003) seemed to confirm the nociceptive specificity of this latter method stimulation. Our study (de Tommaso et al., 2011) aimed in origin to confirm that CE stimulation was specific for A-delta fibers, providing a comparison with laser evoked responses.