Are There Nociceptive-Specific Brain Potentials? Reply to Baumgärtner and Treede

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REPLY: In a recent commentary, Baumgärtner and Treede questioned the conclusion of our recent study, in which we show that laser-evoked brain potentials (LEPs) are not able to isolate nociceptive-specific cortical processing (Mouraux and Iannetti 2009). Here, we will show that the three points raised by Baumgärtner and Treede are unjustified and that our conclusion is entirely valid.

1. Baumgärtner and Treede state that we “focused on late evoked potential components that are known to reflect mostly nonspecific multimodal processing steps, whereas modality-specific activity is reflected in early components.” This statement is simply incorrect, since we examined the entire LEP waveform—i.e., the time interval ranging from 0 to 500 ms after stimulus onset. As shown in Fig. 3 of our study, we observed that the early N1 LEP wave reflects a combination of multimodal and nociceptive-specific processing. This somatosensory-specific processing was not nociceptive specific because it contributed equally to both the LEP elicited by nociceptive stimuli and the somatosensory-evoked potential (SEP) elicited by nonnociceptive stimuli. Crucially, these findings do not imply that LEPs and SEPs should necessarily have identical scalp topographies and are thus entirely compatible with the different scalp distributions of LEPs and SEPs reported by Treede et al. (1988). In fact, we also found topographical differences between LEPs and SEPs resulting from neural processing contributing uniquely to the SEP waveform (i.e., nonspecific somatosensory-specific activity; see fifth row of Fig. 2) and from differences in the relative contribution of multimodal processing and somatosensory-specific processing to the LEP and SEP waveforms. Therefore observing a difference in the scalp topography of LEPs and SEPs does not constitute any evidence that nociceptive-specific processing contributes to LEPs.

2. Baumgärtner and Treede claim that the electrical stimulus used in our study may also have activated nociceptive fibers, suggesting that our inability to isolate nociceptive-specific processing could be explained by the fact that nociceptive-specific processing also contributed to the SEP waveform. The following four pieces of evidence indicate that their claim is unjustified. First, the short latency of the different SEP peaks is compatible only with the direct activation of fast-conducting large-diameter nonnociceptive Aβ axons (Inui et al. 2003). Second, at the intensity used in the present study (9.9 ± 2.1 mA), the sensory action potential elicited by stimulation of the sural nerve is not contributed by Aδ fibers (Willer et al. 1978). Third, to substantiate their claim, Baumgärtner and Treede highlight that the duration of our stimulus (1 ms) was identical to the stimulus duration reported in a number of recent studies attempting to activate nociceptive fibers preferentially using an electrical stimulus (Inui et al. 2002; Kaube et al. 2000). However, they fail to mention a fundamental difference: that these studies did not deliver the stimulus using conventional large bipolar electrodes placed on the skin surface but, instead, relied on a completely different device consisting of a needle cathode inserted within the epidermis and surrounded by a small cylindrical anode, so that strong currents are delivered to a spatially restricted area of the epidermis, in which only nociceptive fiber endings lie. Thus the ability of this technique to activate nociceptors does not rely on the duration of the electrical pulse, but only on the spatial configuration of the generated electrical current. In fact, most of the latter studies from the same groups have applied intraepidermal stimuli using electrical pulses of a much shorter duration (e.g., 0.5 ms; Inui et al. 2006; Obermann et al. 2008). Fourth, even assuming, for the sake of academic discussion, that the electrical stimulus we used concomitantly activated nociceptive and nonnociceptive fibers, it is well known that the elicited event-related potential would be uniquely related to the arrival of the first, Aβ-related somatosensory input, and that there would be no response related to the arrival of the second, Aδ-related input (Boulou et al. 1985; De Broucker and Willer 1985; Garcia-Larrea 2004). This last consideration does not only constitute an additional argument against Baumgärtner and Treede’s suggestion that nociceptive-specific processing contributed to the SEP recorded in our study, but also indicates that the neural generators underlying LEPs are not required to perceive pain. Indeed, when LEPs are suppressed by the concomitant activation of nonnociceptive fibers, the nociceptive input still elicits a clear painful percept.

3. Baumgärtner and Treede quote a single-cell electrophysiological study performed in the primary somatosensory cortex of monkeys to suggest that, at the macroscopic level of the electroencephalogram (EEG), “responses [of nociceptive-specific neurons] may be spatially indistinguishable from those of tactile neurons in the same regions (Kenshalo et al. 2000).” We entirely agree with this statement, which we also make in our report: “a second possibility is that the postsynaptic activity of nociceptive-specific neurons does translate into a measurable scalp EEG response but that this response is spatially indistinguishable from the response generated by nonnociceptive-specific somatosensory neurons.” Obviously, this possibility is not sufficient to assume that LEPs isolate nociceptive-specific processing. Furthermore, Baumgärtner and Treede fail to mention a finding that indicates that this possibility is extremely unlikely: in all of these single-cell studies, the number of neurons identified as nociceptive-specific is always extremely low, a notion that led Patrick Wall (1995) to state that “it
remains an act of faith to continue searching the brain for some still undiscovered nest of cells whose activity reliably triggers pain.”

REFERENCES


