論　文　内　容　要　旨

Event-related potentials evoked by skin puncture reflect activation of Aβ fibers: comparison with intraepidermal and transcutaneous electrical stimulations

（皮膚穿刺誘発電位は、Aβ 神経線維の興奮を反映する：表皮内電気刺激と経皮電気刺激との比較）

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Background. Recently, event-related potentials (ERPs) evoked by skin puncture, commonly used for blood sampling, have received attention as a pain assessment tool in neonates. However, their latency appears to be far shorter than the latency of ERPs evoked by intraepidermal electrical stimulation (IES), which selectively activates nociceptive Aδ and C fibers.

The reasons for shorter latency of ERPs evoked by skin puncture are considered to be the features of the lance stimulation device. Indeed, the blade of the lance stimulation device reaches a depth of 1 mm from the skin surface (the dermis layer); thus, it penetrates the 0.2 mm thick epidermal layer where the terminal ends of Aδ and C fibers are located. In addition, during the skin puncture procedure, the lance stimulation device is pressed against the puncture site and a button on the device is pressed to push out the blade. We speculate that these features and actions can cause a tactile or vibration sensation, resulting in the activation of the Aβ fibers, which consequently shortens the latency of the lance ERP. In addition, lance stimulation produces a click sound when a button on the device is pressed to push out the blade, which potentially affects the lance ERP. Therefore, in addition to the activation of the Aβ fibers, we speculate that the click sound produced by the lance device influences the ERP evoked by skin puncture. It is possible that the lance stimulation used commonly in clinical practice does not evoke ERPs reflecting nociceptive processing (i.e., Aδ and C fibers).

In the present study, to reduce the Aβ fiber activation, we created a condition in which tactile pressure and vibration were excluded as much as possible by making a base on which to fix the lance stimulation device and by having a shallower blade insertion depth than the depth used in clinical practice. We examined whether ERPs evoked by skin puncture reflect central nociceptive processing. We conducted two experiments. In Experiment 1, we investigated the effect of the click sound on the ERP evoked by skin puncture. In Experiment 2, we investigated whether Aβ fiber activation is associated with the lance ERP.

Methods. In Experiment 1, we recorded evoked potentials to the click sound produced by a lance device (BD Microtainer Quickheel™ Lancet 368102, Japan Becton, Dickinson, Japan) (click-only), lance stimulation with the click sound (click+lance), or lance stimulation with white noise (WN+lance) in eight healthy adults to investigate the effect of the click sound on the ERP evoked by skin puncture. In Experiment 2, we tested 18 heathy adults and recorded evoked potentials to shallow lance stimulation (SL) with a blade that did not reach the dermis (0.1 mm insertion depth); normal lance stimulation (CL) (1 mm depth); transcutaneous electrical stimulation (ES), which mainly activates Aβ fibers; and IES, which selectively activates Aδ fibers at low current intensities. White noise was

continuously presented during the experiments. The stimulations were applied to the hand dorsum. In the SL, using the device created, the lance device did not touch the skin and the blade was inserted to a depth of 0.1 mm into the epidermis, where the free nerve endings of Aδ fibers are located, which minimized the tactile sensation caused by the device touching the skin and the activation of Aβ fibers by the blade reaching the dermis. In the CL, as in clinical use, the lance device touched the skin and the blade reached a depth of 1 mm from the skin surface, i.e., the depth of the dermis at which the Aβ fibers are located.

Results. The ERP N2 latencies for click-only (122 ± 2.9 ms) and click+lance (121 ± 6.5 ms) were significantly shorter than that for WN+lance (154 ± 7.1 ms). In addition, the ERP P2 latency for click-only (191 ± 11.3 ms) was significantly shorter than those for click+lance (249 ± 18.6 ms) and WN+lance (253 ± 11.2 ms).

The ERP N2 latencies for the SL (146 ± 8.3 ms), CL (149 ± 9.9 ms), and ES (148 ± 13.1 ms) were significantly shorter than that for the IES (197 ± 21.2 ms). Likewise, the ERP P2 latencies for the SL (250 ± 18.2 ms), CL (251 ± 14.1 ms), and ES (237 ± 26.3 ms) were also significantly shorter than that for the IES (294 ± 30.0 ms).

Discussion. When a click sound was present (click-only and click+SL), the N2 latencies of ERPs in response to click-only and click+SL and the P2 latencies of ERPs in response to the click-only condition were within the range reported in previous studies investigating ERPs of auditory stimuli. Therefore, it is suggested that the click sound produced by the lance device appears to generate an auditory evoked potential and shortens the N2 latency of the ERP evoked by skin puncture.

The ERP latency for SL was significantly shorter than that for IES and was similar to that for ES. It has been reported that various clinically used needles produce a penetration force when they were inserted into the skin. It is likely that the SL also generated a penetration force when the blade was inserted into the skin, activating the Aβ fibers. Therefore, it is suggested that the penetration force generated by the blade of the lance device activates the Aβ fibers, consequently shortening the ERP latency.

Conclusions. The click sound produced by the lance device influences the ERPs evoked by skin puncture. Furthermore, the latency of the ERP of lance stimulation was shorter than that of IES and similar to that of ES, which suggests that Aβ fibers are activated by lance stimulation. Lance ERPs, therefore, may reflect the activation of Aβ fibers rather than Aδ fibers. A pain index that reflects nociceptive processing must be developed to improve pain assessment and management in neonates.