Suppression of scratching-induced pleasurable sensation by compression nerve blocking and its association with itch relief

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Abstract

Itch can be suppressed by scratching. At the same time, scratching evokes a pleasurable sensation. In the present study, we investigated the peripheral mechanism of scratching-induced pleasurability and its association with itch relief using compression nerve block. We found that myelinated nerve fibers (A β -fibers and possibly A δ -fibers), are involved in transmission of scratching-induced pleasurability. We observed that itch relief effect was the same regardless of whether the pleasurable sensation was evoked by scratching an itch, indicating that pleasure is not a necessary component to induce itch relief. This is the first study to investigate the peripheral mechanism of scratching-induced pleasurability and itch relief.

Keywords: itch, scratch, itch relief, pleasurability, peripheral nerve fibers, nerve blocking

Introduction

Scratching behavior, which temporarily suppresses itch, is a prominent feature seen in chronic itch patients. It is also highly rewarding, evoking an intense degree of pleasure in most people. It is this rewarding nature that motivates and reinforces the behavior, which leads to more damage to the skin and further exacerbating the itch. This reward driven itch-scratch cycle is very distressing for patients, but the contribution of specific afferent peripheral nerve subtypes in driving the pleasantness of scratching an itch is not known. In addition, it is also unclear if the pleasurable sensation is a necessary component of itch relief. To address these questions, we used compression of the superficial radial nerve at the wrist to achieve a selective conduction block of myelinated fibers innervating the back of the hand, and investigated how this intervention influences scratching-induced pleasurability and itch relief in 10 healthy subjects.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Methods

Subjects

Ten healthy subjects (5 males and 5 females, age: 26 ± 3 y) participated in this study. This study was approved by the Temple University Institutional Review Board. A written informed consent was obtained from all subjects.

Time schedule of the experiment

First, baseline somatosensory tests (tactile threshold, mechanical pain threshold, warmth threshold, gentle brushing pleasure intensity, itch intensity, and scratching pleasure intensity) were performed on the test site (ie, the skin between the metacarpal bone of the thumb and index finger) of the control hand (either the left or right hand, counterbalanced between subjects). The order of the somatosensory tests was fixed for all subjects. Next, the same somatosensory tests, excluding itch sensation and scratching-induced pleasure, were performed on the test site of the opposite hand to the control hand (ie, the blocked hand). Then, the compression nerve block was performed. Similar to previous nerve blocking studies^[1,2], we assessed whether the light tactile sensation, mediated by thick myelinated fibers (A β -fibers), evoked by applying a monofilament with bending force of 4 mN was lost so as to check whether the nerve block successfully affected conduction of nerve fiber^[1,2]. After we confirmed loss of the light tactile sensation (50–60 min after starting the nerve block), all somatosensory tests were performed on the blocked hand. Details of somatosensory tests, compression nerve block, and statistical test are described in the supplementary information (Supplemental Digital Content 1, <http://links.lww.com/ITX/A1>).

Results

Tactile, pain, and warmth detection thresholds

The threshold of the light tactile sensation on the blocked hand before compression nerve block was 2 ± 1.5 mN. After the nerve

block, the threshold was 39 ± 42 mN. The difference in tactile threshold was significant ($P = 0.02$). The threshold of mechanical pain sensation on the blocked hand was 101 ± 72 mN before the nerve block. Six of 10 subjects showed increased mechanical pain thresholds during the nerve block, whereas the remaining 4 subjects did not show such an increase. The precise changes to the pain threshold and the Numerical Rating Scale (NRS) ratings of other somatosensory tests during the compression nerve block obtained from these 2 groups are described in the supplementary information (Supplemental Digital Content 1, <http://links.lww.com/ITX/A1>). Tactile and pain thresholds on the control hand were 2 ± 2.9 and 114 ± 69 mN, respectively. Warmth detection, mediated by unmyelinated fibers, was unchanged during the nerve block (before block: $34 \pm 0.7^\circ\text{C}$, after block: $34 \pm 0.7^\circ\text{C}$, $P = 0.35$).

Itch, pleasurability, and itch relief

The itch sensation was not significantly different ($P = 0.4$) on the blocked hand (NRS, 6.6 ± 3.64) compared with the contralateral control hand (NRS, 7.5 ± 1.72) (Figure 1A). However, the pleasurable sensation during scratching the skin where itch was induced was significantly lower for the blocked hand (NRS 2.9 ± 3.31) compared with the control hand (NRS 7.5 ± 2.17) (Figure 1B). Similarly, gentle brushing-induced pleasant sensation was also significantly reduced (before blocking: NRS, 4.8 ± 1.72 ; during blocking: NRS, 1.1 ± 1.1 ; $P = 0.0002$) (Figure 1C). We found no significant difference ($P \geq 0.1$) in scratching-induced itch relief between the blocked and control hands (Figure 2).

Discussion

This is the first study to investigate the peripheral mechanism of scratching-induced pleasurability and itch relief. Similar to previous studies^[1,2], the compression nerve block diminished conduction of myelinated fibers in the present study. In particular, conduction of light touch sensation was lost during the nerve block in all subjects. Thus, it was suggested that A β -fibers are involved in transmission of scratching-induced and gentle brushing-induced pleasurability. However, this is inconsistent with previous studies demonstrating that low-mechanotreshold unmyelinated fibers (C-tactile fibers) are a major pathway of pleasant sensation^[3]. We applied gentle brushing stimuli to the dorsum of the hand, whereas the previous studies applied the stimuli to the forearm. It has been reported that the most distal portions of the limbs (eg, the dorsum of the hand) have few C-tactile fibers^[4–6]. In addition, previous brain imaging studies have demonstrated that the posterior insula, which mainly receives projections from unmyelinated fibers, is associated with the pleasant sensation on the hairy skin; while the somatosensory cortex, that receives many projections from myelinated fibers, is associated with the pleasant sensation on the glabrous skin^[7,8]. These studies speculate that hedonic ascending pathways differ depending on the stimulated body site. Thus, it may be that myelinated fibers are primarily involved in transmitting a hedonic sensation in glabrous skin and its adjacent areas, whereas C-tactile fibers play an important role for that in hairy skin. In fact, a previous study reported that pleasant tactile sensation was preserved during compression blocking of myelinated fibers innervating the hairy skin of the leg^[9]. Currently, it is uncertain if

Figure 1. The itch and pleasurable sensations. A, The itch sensation immediately before scratching, and the pleasurable sensation during scratching (B) itch was compared between the blocked and control (ie, not blocked) hand. In addition, (C) the pleasurable sensation induced by gentle brushing was also compared between before and during compression nerve block. Statistical significance was set as $P = 0.05$.

Figure 2. Time course of the itch sensation. The graph shows mean time courses of the itch sensation obtained from all subjects. ●: The control hand (not blocked). ●: The blocked hand. Itch intensity was compared between the blocked and control hand using paired t test at each time point (ie, 30, 60, 90, 120, 125, 130, 140, 150, 160, 170, and 180 s after applying cowhage). At 120 seconds, scratching stimuli were applied for 10 seconds. Statistical significance was set as $P = 0.05$. P -value obtained by the paired t test at each time point was $P \geq 0.1$.

A δ -fibers are also associated with the pleasurable sensation evoked by scratching an itch. A further study will be needed to answer this question.

There was no significant difference in itch relief between the blocked and control hands (Figure 2), indicating that pleasurable sensation and itch relief are independent. Why, then, is a pleasurable sensation evoked during scratching an itch? When healthy skin is continuously scratched in the absence of itch, a weakly painful sensation can be elicited. However, this noxious sensation is not perceived or reduced while scratching an itch^[10]. It has been previously reported that pleasant somatosensory stimuli can reduce the perception of pain^[9]. Perhaps, the pleasurable sensation elicited by scratching in response to itch may serve to inhibit the weak painful sensation.

Compression nerve block creates a preferential blockade of myelinated fibers, which has been verified in human subjects by microneurography^[11–13]. Nonetheless, a limitation of the present study is the indirect evaluation. However, we could identify candidate myelinated nerve fibers associated with scratching-induced pleasurable sensation (eg, A β -fibers and possibly A δ -fibers). Thus, it would be necessary to confirm findings obtained in the present study using direct recording methods such as microneurography.

Taken together, these results provide new insights on the peripheral mechanism of scratching-induced pleasurable sensation and its role in relation to itch. Further studies will be needed to better understand these mechanisms.

Conflict of interest statement

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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