Stimulus-response evaluation of the antipruritic effect of homotopic, monophasic cold and TRP-agonist counter-stimulation on histamine-induced itch in healthy volunteers

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Hairless mice (HR-1) are useful to investigate the effects of topical drugs for various dermatological diseases such as atopic dermatitis and herpes simplex virus infection accompanied by itch and pain. We aimed to clarify the characteristics of itch-related behavioral and neuronal responses to pruritogens in HR-1 mice. Histamine (5–5,000 nmol), serotonin (5-HT, 10–300 nmol) and a PAR-2 agonist (SLIGRL-NH₂, 10–300 μg) were injected intradermally as a puritogen into the hindpaw in HR-1 and ICR mice, and biting behavior and spinal neuronal response were measured for 30 minutes. Biting behaviors were dose-dependently observed after 5-HT and SLIGRL-NH₂, but not histamine injections in HR-1 mice. The 5-HT and SLIGRL-NH₂-induced biting behaviors were more prominent in HR-1 mice than ICR mice. An excitation of spinal dorsal horn neurons were evoked by the 5-HT and SLIGRL-NH₂ injections in HR-1 mice, and the frequency of action potentials were also dose-dependently increased. There was a positive correlation between the duration of biting behavior and the frequency of action potentials. These results indicate that the present recordings of itch-related behavioral and neuronal responses elicited in HR-1 mice enable us to study detailed mechanisms for topical antipruritic drug action on histamine-independent itch.