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Investigation of the paradoxical painful sensation ('illusion of pain') produced by a thermal grill

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Abstract

A paradoxical painful sensation can be elicited by the simultaneous application of innocuous warm and cold stimuli to the skin. In the present study, we analyzed the conditions of production of this unique experimental illusion of pain in 52 healthy volunteers (27 men, 25 women). The stimuli were produced by a thermode composed of six bars whose temperature was controlled by Peltier elements. The temperature of alternate (even- and odd-numbered) bars could be controlled independently to produce various patterns of the 'thermal grill'. After measuring the cold and heat pain thresholds, a series of combinations of warm and cold stimuli, whose distance to the thermal pain threshold was at least 4 °C, were applied on the palmar surface of the right hand during 30 s. After each stimulus, the subjects had to describe and rate their sensations on visual analog scales. Paradoxical painful sensations, mostly described as burning, were reported by all the subjects but three. However, the phenomenon was less frequent in approximately one third of ('low responder') volunteers. The frequency and intensity of such painful sensations were directly related to the magnitude (i.e. 5–25 °C) of the difference of the temperature between the warm and cold bars of the grill. The combination of increasingly colder temperature to a given warm temperature induces similar effects as combining increasingly warmer temperature to a given cold temperature. These results suggest that pain can be the result of a simple addition of non-noxious warm and cold signals.

Keywords: Sensory systems; Psychophysics; Thermal sensation; Pain; Allodynia

1. Introduction

The simultaneous application of innocuous cutaneous warm and cold stimuli can induce a paradoxical sensation of 'heat'. This phenomenon was described more than a century ago by Thunberg (1896). Like other experiments performed at that time of development of experimental sensory psychology based on introspection, such experiments were devoted to the definition and analysis of the whole spectrum of sensations (Boring, 1942). In this context, it appeared to be important to determine whether warm and cold stimuli applied to the same place could evoke (i) two distinct sensations; (ii) only one sensation depending on intensity of each stimulus; (iii) a new and different sensation as a result of the fusion of cold and warm sensations. Soon after the description of this phenomenon, Alrutz (1898) concluded, on the basis of 'pure introspection', that 'heat' was a sensation qualitatively different from warmth or burning, that could be experienced without pain, 'although pain very often does accompany it'. He proposed that 'heat' depended on the excitation of warm spots and paradoxical activation of adjacent cold spots by warm stimuli. In subsequent years, researchers disputed whether 'heat' was a specific sensation or an analyzable mixture of warm and cold sensations and whether it was painful or not (Alston, 1920; Burnett and Dalenbach, 1927, 1928; Cutolo 1918; Ferral and Dallenbach, 1930; Jenkins, 1938a,b).

Surprisingly, the characterization of this paradoxical sensory phenomenon was completely discarded for decades.

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Although, a better analysis of its psychophysical properties and neurophysiological basis could largely contribute to our understanding of the mechanisms of both thermal and pain sensations. In particular, the production of a painful sensation by low-intensity thermal stimuli could represent a major challenge for the theories relying on the specificity of pain pathways. In this respect, Craig and Bushnell (Craig and Bushnell, 1994; Craig et al., 1996) were the first to clearly place the investigation of this phenomenon in the context of the study of pain (see also Frushtorfer et al., 2003). They reinvestigated its mechanisms in both animals and humans and concluded that the paradoxical sensation evoked by the thermal grill was painful and referred to this phenomenon as 'the thermal grill illusion of pain'. They proposed that this phenomenon resulted from central mechanisms involving the reduction of the inhibition normally exerted by the cold afferents on the nociceptive systems. Although these studies included a psychophysical analysis, the experiments were performed in a small number of healthy volunteers and only one combination of warm and cold temperatures was tested (i.e. 20 and 40 °C).

The goal of the present study was to further investigate the conditions of production of this paradoxical pain in a large population of healthy volunteers. In particular, we sought to provide information concerning the frequency, quality and intensity of this unique experimental illusion of pain and its relationship with normal thermal pain sensations.

2. Methods

Following approval by a local Ethics Committee, the experiments were performed on paid healthy volunteers who were carefully briefed about the experimental procedures and gave informed written consent. The volunteers were informed that they could feel various non-painful or painful sensations, but they were not informed as to the paradoxical nature of the sensations. All the participants were right-handed and had never participated in a psychophysical study previously.

2.1. Equipment

Thermal stimuli were produced using a thermode designed and built by SEICER (Mouy, France) (see Photograph). The thermode was composed of six bars (1.2×16 cm) covered with a copper plate, spaced 2 mm apart for thermal isolation, whose temperature was controlled by thermoelectric Peltier elements (three per bar). The temperatures of alternate (even- and odd-numbered) bars were monitored independently in the 5–50 °C range to produce various combinations of temperatures (i.e. patterns of the 'thermal grill'). Thermistors placed in each bar provided continuous temperature feedback of the thermode–skin interface (resolution ±0.3 °C).

2.2. Experimental procedure

All experiments were performed at constant room temperature (21 °C). Thermal stimuli were applied to the palmar surface of the right hand. Each stimulus was applied during 30 s with an interval of 3 min between two stimuli. The parameters of stimulation were chosen on the basis of both the analysis of the literature and pilot experiments in which we compared different durations (i.e. 5–40 s) of stimulation applied to the volar surface of the forearm or the hand. These experiments indicated that forearm and palm stimulation were similar and that a certain duration (up to 20–30 s), depending on the combinations of temperatures, could be necessary for stabilization of the sensation. We also compared the two modes used in early studies: changing the thermal temperatures while the palm was applied on the grill (i.e. 'dynamic stimulation') or setting the warm and cold temperatures before application of the palm on the grill (i.e. 'static stimulation'). Our data confirmed that both types of stimulation induced paradoxical sensations, but the sensations induced by the latter mode of stimulation were less variable and more easily analyzable by naive subjects.

Photograph. The volunteers applied their right hand palm on the thermode (i.e. thermal grill) orthogonally to the long axis of the bars. The thermode was composed of six bars (1.2×16 cm) covered with a copper plate, spaced 2 mm apart for thermal isolation. The control unit allowed to set the temperature of alternate (even- and odd-numbered) bars by means of Peltier elements (3 per bar).

At the beginning of each experiment, the neutral temperature (i.e. neither cold nor warm) was determined. Then the cold pain threshold (CPT) and heat pain threshold (HPT) were measured with a staircase algorithm. In this procedure, even-numbered bars were kept at the neutral temperature while the temperature of the odd-numbered bars was changed randomly (increased or decreased) by steps of 3–0.5 °C. After each stimulus, the subjects had to report whether they perceived the stimulus as painful or not. For a negative response, the next temperature step was 3 °C. After the first painful stimulus, successive stimuli were changed (increased or decreased) by 0.5 °C until the first non-painful sensation was reported.

Then, a series of combinations of simultaneous warm and cold stimuli were applied in a randomized order according to a paradigm based on the values of cold pain threshold (CPT) and heat pain threshold (HPT). Before each stimulus, the temperature of the cold bars was set at CPT +4, +6, +8 or +10 °C while the temperature of the warm bars was set at HPT −4, −6, −8 or −10 °C. The HPT −10 °C or CPT +10 °C stimuli were performed only if they did not exceed the neutral temperature.