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Asymmetry and time-course of cutaneous sympathetic reflex responses following sustained excitation of chemosensitive nociceptors in humans

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Abstract

Sympathetic reflex responses were elicited in human volunteers by sustained selective excitation of nociceptors by noxious chemicals, namely topical application of mustard oil which elicited burning pain, or histamine which induced itching in a skin area of 5 cm^2 on the volar aspect of one forearm. Stimulus-related sympathetic reflex responses were studied by means of computer-assisted infrared thermography of the palmar aspects of both hands. Nociceptive stimulation induced a decrease of skin surface temperature in both hands interpreted as vasoconstriction. The magnitude of the reflex cooling was correlated with the magnitude of the sensation ($r = 0.49$), but independent of the quality of sensation (itch or pain). The temperature reduction was maintained for more than 30 min and its time-course matched the time-courses of pain or itch sensations. It is concluded that the sustained and selective excitation of nociceptors elicits a sustained sympathetic reflex response, which adapts very slowly. The time-course of the reflexes suggests that these are not arousal responses, but may be indicators of nociceptive processing in conscious humans. Contralateral temperature decreases were consistently smaller than ipsilateral ones. Thus, sustained nociceptive-specific vasoconstrictor reflexes may be somatotopically organised with an emphasis on areas close to the painful stimulus (homotopic), which has so far only been shown in animals. The study thus demonstrates for the first time in humans the presence of a sympathetic reflex asymmetry, which is specific for nociceptive afferent input.

Keywords: Nociceptor; Pain; Itch; Infrared thermography; Somatosympathetic reflex; Vasoconstriction

1. Introduction

It has traditionally been assumed that the autonomic nervous system responds rather indiscriminately to painful, threatening, intense and novel stimuli with uniform general arousal reactions [10]. As a consequence of their non-specific nature the validity and reliability of autonomic responses as indices of sensory processing may be limited. In particular, autonomic reflex responses have been regarded inappropriate for pain assessment, at least as far as the sensory-discriminative dimension of pain is concerned [12]. This view is supported by experimental data which demonstrate that, like arousal responses, autonomic reflexes to painful stimuli adapt quickly and are prone to habituation upon repeated application [7,9]. Occasionally, a linear relationship was found between pain sensation and changes in skin resistance, but their thresholds differed [9]. Some confusion, however, may result from a restriction in experimental paradigms since commonly brief and transient forms of noxious stimulation, e.g., electrical or laser pulses, have been used for the induction of pain-related sympathetic reflexes in humans. Apparently, this type of stimulation with a duration in the millisecond to second range elicits predominantly transient startle or arousal-related sympathetic reflexes. In contrast, our group has recently demonstrated that a late and sustained phase of a vasoconstrictor reflex elicited by sustained painful squeezing of interdigital webs in conscious humans exhibits a remarkably slow adaptation rate and very little habituation [33]. Moreover, the reflexes were enhanced in sensitised (hyperalgesic) skin. This sustained reflex phase may thus

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