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The interactions between spatial summation and DNIC: Effect of the distance between two painful stimuli and attentional factors on pain perception

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ABSTRACT

The ability of a painful stimulus to suppress pain in another, remote area (DNIC) has been intensely studied. However, the effect of the distance between the two painful stimuli and the attentional factors during the measurement of pain perception received minimal treatment. We evaluated the effect of these factors on DNIC and on the interaction between DNIC and spatial summation (SS) of pain. Subjects rated the intensity of a test stimulus (applied to one hand) alone and simultaneously with conditioning stimuli applied to four different locations; 5 and 30 cm from the test stimulus on the same hand, the contralateral hand and contralateral leg. In each location, ratings were performed under three different instructions: summation, attention to test stimulus, attention to conditioning stimulus. The distance between the conditioning and test stimulus significantly affected pain perception ($p < 0.01$) regardless of the instructions; SS occurred only at a distance of 5 cm and DNIC occurred only in the remaining distances. DNIC's magnitude increased as the distance between the two stimuli increased ($p < 0.01$). However, the instruction to summate attenuated DNIC and the DNIC instruction attenuated SS of pain. Attention to the conditioning stimulus induced a stronger DNIC than attention to the test stimulus ($p < 0.001$). We conclude that (1) DNIC and SS of pain appear to be antagonistic processes. (2) DNIC is affected by the distance between two noxious stimuli and to a lesser extent, by attention. (3) The interaction between DNIC, SS and attention is complex and reflects the role of sensory–cognitive integration in pain perception.

1. Introduction

That pain in one body region can inhibit pain in another body region is a well-known phenomenon since ancient times [26]. Le Bars et al. (1979) termed this phenomenon as "diffuse noxious inhibitory controls" (DNIC) [22,23] and it was found to exist in both animals and humans [6,7,21,43]. In a standard DNIC experiment, a noxious stimulus is delivering to one body region ("conditioning stimulus" – CS) while measuring the pain evoked by another stimulus ("test stimulus" – TS) administered to another region [5,31]. A decrease of the latter is indicative of DNIC.

Although DNIC is extensively studied, several issues require further investigation. The critical distance between the TS and CS allowing for DNIC is one such issue. No consistent relationship was found between CS localization and its efficacy in attenuating the perceived intensity of the TS. The intensity of the TS has been shown to increase [19,38] and decrease [1] when the CS is administered to the ipsilateral homotopic site indicating either spatial summation of pain or DNIC, respectively. In other instances the intensity of the TS did not change [17,46].

The few attempts to study different, extra-segmental locations for the CS also yielded inconsistencies. While DNIC was stronger when the CS was applied to the ipsilateral heterotropic region compared with the contralateral [1,38], in another study DNIC was stronger in the contralateral-heterotropic region compared with the homotopic [40] and in another study, DNIC did not differ between homotopic and heterotopic regions [30]. Therefore studying the extent to which DNIC is affected by the distance between the test and conditioning stimulus is called for.

In the majority of DNIC experiments, as in those mentioned above, the characteristics of the TS are different than those of the CS in terms of modality, intensity and timing. Usually a combination of modalities such as electrical and thermal [5,20,21,39], hypertonic saline and electrical or mechanical [17,38,46] or heat and cold [16] is used. The intensity of the TS and CS is usually different as well [e.g. 28,48,49] as is their timing [e.g. 38,40]. The different stimulation parameters for TS and CS might produce an attentional bias towards one of them making it more prominent. Hence, DNIC might result from the changes in subjects' attention

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leading to a decreased rating capability. In order to test such a hypothesis the parameters of the CS and TS must be identical.

The variable results led us to conduct a systematic study of DNIC in which all sensory cues associated with differences between the TS and CS are eliminated and in this "neutral" condition (identical modality, relative intensity, stimulation area, and timing), to test the effect of the distance between them and the effect of attention. This condition also allowed us to further examine the interactions between DNIC and between the seemingly opposite phenomenons, i.e. spatial summation of pain. More specifically, we asked how spatial inhibition (DNIC) and spatial summation of pain are affected by the distance between the two stimuli and the instructions given to subjects.

2. Methods

2.1. Subjects

Seventeen healthy volunteers, eight males and nine females (mean age 27 ± 6 years), participated in the study by attending three testing sessions, separated by at least 1 week.

Subjects suffering from pain, diseases causing potential neural damage (e.g. diabetes), systemic illnesses, skin lesions of any kind, language problems, hearing or speech disorders and mental disorders were excluded. Informed consent was obtained from all subjects after receiving a full explanation of the goals and protocols of the study. The institutional review board of Tel-Aviv University approved the experiments.

Testing took place in a quiet room. Temperature in the room was maintained at 22 ± 2 °C. The subjects were seated in a comfortable armchair with the hands and legs supported. Measurements were conducted on the hands and legs. All subjects were trained in perceived pain intensity (PPI) measurements prior to the experiments. The results obtained in the training sessions were discarded.

2.2. Thermal stimulator

Thermal stimuli were delivered using two Peltier-based computerized thermal stimulators (TSA 2001, Medoc Ltd., Israel), with a 3 × 3 cm contact probes. The principles of the Peltier stimulator were already described [11,42,47]. Briefly, a passage of current through the Peltier element produces temperature changes at rates determined by an active feedback system. As soon as the target temperature is attained, probe temperature actively reverts to a preset adaptation temperature by passage of an inverse current. The adaptation (baseline) temperature was set to 35 °C. The two TSA machines were synchronized via a communication cable and special software and could be operated simultaneously.

2.3. Determination of the test and conditioning stimuli

Our purpose was to establish, for each subject and in each testing session, identical test and conditioning stimuli in terms of modality, intensity, and timing. Test and conditioning stimuli were determined at the beginning of each testing session by matching the temperature level to a score of 5 in a 0–10 visual analog scale (VAS). These temperatures were interpolated from stimulus–response functions created for each subject in each of the four body regions tested (the three regions of the hand and the leg).

For the stimulus–response functions, subjects received a series of heat stimuli and were asked to rate the intensity of perceived pain following each stimulus on the (VAS) by moving the inner slider of a 15 cm plastic ruler with end points set as "no pain sensation" and "the most intense pain sensation imaginable". The stimulus intensities used for these magnitude estimations rose from a baseline temperature of 35 °C to a destination temperature ranging between 37 °C to the temperature eliciting eight on the VAS at which it remained for 3 s and then returned to baseline. An inter-stimulus interval of at least 30 s was maintained to avoid any changes in skin sensitivity and to allow for adequate VAS scoring. We repeated this procedure in each of the three testing sessions for each subject.

2.4. Procedures

The study comprised of two separate experiments.

2.4.1. Experiment I (n = 7)

The aim of experiment I was to evaluate the effect of distance between test and conditioning stimulus and the instructions on DNIC and on spatial summation. As previously mentioned, the test and conditioning stimuli were identical in terms of modality (contact heat-pain), intensity (VAS 5), stimulation area and shape (3 × 3 cm) and duration (3 s in destination). The locations of the test and conditioning stimuli are depicted in Fig. 1. The test stimulus was always on the distal part of the forearm and the conditioning stimuli were placed in four different body regions with varying distances; (1) 5 cm from the test stimulus on the same arm (ipsilateral homotopic), (2) 30 cm from the test stimulus on the same arm (ipsilateral heterotropic), (3) on the distal part of the contralateral forearm (contralateral-homotopic) and (4) on the lower lateral part of the contralateral leg (contralateral-heterotropic). The test and conditioning stimuli were always administered simultaneously.

Subjects were asked to rate the amount of pain perceived as produced by the test stimulus (applied to the distal part of the forearm) in the absence and in the presence of the conditioning stimulus. The conditioning stimulus was administered to the four body regions three times, following three different instruction: (1) "rate the *total* amount of pain evoked by the two stimuli together" (a "spatial summation instruction"), (2) "concentrate only on the *test stimulus* (pointed out by the examiner) and rate the amount of pain caused by it" ("DNIC-A instruction" = attention to the test stimulus), (3) "concentrate only on *the conditioning* stimulus (pointed out by the examiner) and rate the amount of pain caused by the test stimulus" ("DNIC-B instruction" = attention to the conditioning stimulus). The order of the instructions was random.

As a control condition, subjects also rated the test stimulus in the presence of an innocuous conditioning stimulus (36 °C) applied to the four body regions.

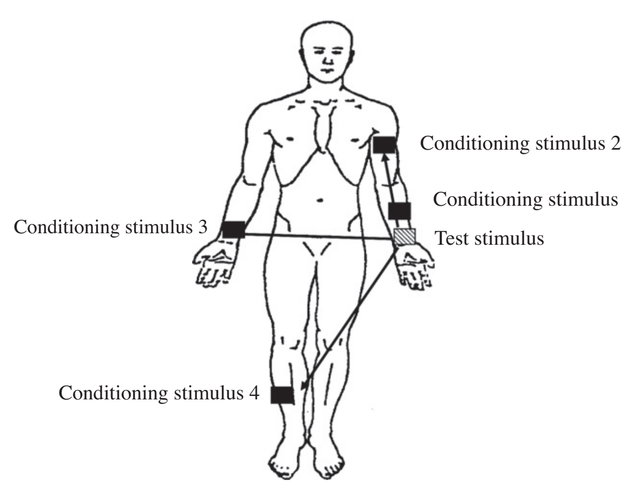

Fig. 1. The locations of the test and conditioning stimuli.