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Effects of isometric exercise on pain are mediated by blood pressure

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Abstract

Sensitivity to pain is reduced during exercise. The underlying mechanism has yet to be established. One possibility is that a baroreceptor-related mechanism may contribute to this exercise-induced hypoalgesia phenomenon. Accordingly, this study examined whether increases in arterial blood pressure during graded isometric exercise, which activate baroreceptors in the aortic arch and carotid sinus, could account for any effects of exercise on pain in 24 normotensive young men. Electrocutaneous stimuli were delivered to the sural nerve while participants performed isometric handgrip exercise at 1%, 15%, and 25% of their maximum voluntary contraction (MVC). Participants provided a pain intensity rating immediately following the delivery of each stimulus. Nociceptive flexion reflex (NFR) responses and thresholds were also determined to provide objective physiological correlates of pain. Pain ratings were attenuated by graded isometric exercise in a linear fashion, whereas nociceptive flexion reflex responses and thresholds were unchanged by exercise. Blood pressure increased in proportion to the force of the contraction. Mediational analyses using analyses of covariance indicated that the reduction in pain with exercise was substantially accounted for by the magnitude of the blood pressure response. These findings are consistent with an arterial baroreceptor inhibition mechanism for exercise-induced hypoalgesia.

Keywords: Arterial baroreceptors; Pain; Pressor response; Nociceptive flexion reflex; Exercise-induced hypoalgesia

1. Introduction

Human studies have established that dynamic exercise is associated with a reduction in electrical, thermal, and mechanical pain (Koltyn, 2000), however, the mechanism for this phenomenon has not been established. Although endogenous opioids have been suggested as mediators of hypoalgesia (i.e., reduction in pain) induced by stress such as exercise, the evidence from pharmacological blockade experiments is mixed (e.g., Janal et al., 1984; Olausson et al., 1986). Thus, other mechanisms seem more likely. Examples of such mechanisms are activation of ascending (e.g., via stimulation of skin or muscle afferents) and descending (e.g., via cognitive distraction) pain inhibition pathways by stress. Specifically, stress experiences, such as exercise, may induce hypoalgesia by increasing blood pressure which will activate arterial baroreceptors resulting in increased supraspinal inhibition (Ghione, 1996; Koltyn and Umeda, 2006).

Arterial baroreceptors are stretch receptors in the aortic arch and carotid sinus naturally stimulated during the systolic upstroke of the pulse pressure wave and sensitive to both absolute pressure and rise in pressure (Eckberg and Sleight, 1992). Pain can be reduced during activation of baroreceptors by vasoactive drugs that increase blood pressure (Larbig et al., 1985; Rockstroh et al., 1988), maneuvers that increase blood pressure (Agarwal et al., 2005), and suction of the neck region that stretches the receptors (Rau and Elbert, 2001). Evidence suggests that the nociceptive flexion reflex (NFR), a spinal reflex that facilitates withdrawal from noxious stimuli and that has been advocated as an objective physiological correlate of pain, is attenuated by natural (Edwards et al., 2001; McIntyre et al., 2006) but not artificial (Al'Absi et al., 2005; Edwards et al., 2003) baroreceptor activation. Further, electrophysiological studies have found that pain-related evoked potentials are attenuated by natural (Edwards et al., 2007) and artificial (Angrilli et al., 1997; Mini et al., 1995) baroreceptor stimulation. These human findings are broadly consistent with an extensive animal literature showing that baroreceptors are involved in pain modulation (Randich and Maixner, 1984; Ghione, 1996). For example, responses to noxious stimulation are reduced by increases in blood pressure during phenylephrine infusion only in animals with intact baroreceptors (Dworkin et al., 1979). In sum, evidence has accumulated to support a baroreceptor-related pain modulation mechanism.

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Several studies have found that isometric exercise, which increases blood pressure in proportion to the percentage of the maximum voluntary contraction (MVC) (Lind, 1984), reduces mechanical (Koltyn et al., 2001; Kosek and Ekholm, 1995; Kosek et al., 1996; Kosek and Lundberg, 2003; Staud et al., 2005) and thermal (Staud et al., 2005) pain. The current study examined electrocutaneous pain when participants contracted hand flexor muscles at 1%, 15%, and 25% of their MVC. Contractions at the higher intensities were expected to stimulate arterial baroreceptors by increasing blood pressure by approximately 10 and 25 mmHg, respectively (Boushel et al., 1998; Williamson et al., 1996). Preliminary evidence suggests that the NFR, an objective physiological correlate of pain (Sandrini et al., 2005), is attenuated by dynamic exercise (Guieu et al., 1992). Accordingly, the present study also examined the NFR during isometric exercise.

The aims of the present study were twofold. First, to assess the effects of graded isometric exercise upon pain ratings and the NFR, a physiological correlate of pain. Second, to determine the extent to which any exercise-induced hypoalgesia was mediated by increases in arterial pressure. As such, the study makes important contributions to the literature by being the first to examine the effects of isometric exercise on electrocutaneous pain and the NFR, and, importantly, the first to determine the contribution of a baroreceptor-related mechanism to reduced pain sensitivity during exercise.

2. Method

2.1. Participants

Twenty-four healthy adult Caucasian right-hand dominant men with a mean age of 21 years (S.D. = 3), mean weight of 74 kg (S.D. = 7), and mean height of 180 cm (S.D. = 6) participated in the study. Their mean (S.D.) resting systolic and diastolic blood pressures were 121 (9) and 63 (6) mmHg, respectively; all participants were normotensive. Participants were asked to refrain from analgesic medication for 3 days and from strenuous physical activity for 12 h prior to testing. The local research ethics committee approved the study protocol, and volunteers gave informed consent to participate.

2.2. Physiological measurements

Participants sat upright in a comfortable chair with their left ankle supported so the knee was flexed at 35°. A computer and Micro1401 (CED) were programmed in Spike2 to present stimuli and record responses. Blood pressure was measured using an oscillometric sphygmomanometer (Dinamap, Critikon) and a brachial cuff attached to the participant's upper left arm. Electromyographic activity of the left biceps femoris muscle was recorded at 2000 Hz using a Bagnoli-2 amplifier (20–450 Hz, 10,000×) and single differential surface electrode (Delsys) with a separate reference electrode (for further details see Edwards et al., 2001). The sural nerve was stimulated using a constant current stimulator with 400 V compliance (DS7A, Digitimer) and bar electrode (Nicolet) that was secured posterior to the ankle. Sites were prepared using alcohol swabs and abrasive gel until electrode impedance was <10,000 Ω. Conductive cream was applied to electrode contacts.

2.3. Pain

Pain was assessed concurrently using a 0–100 numerical rating scale, with anchors of 0 (no pain) and 100 (maximum tolerable pain). A version of the scale was located on the wall in front of participants. After each sural nerve stimulation had been delivered, participants were asked to rate the intensity of the sensation associated with each electrocutaneous stimulus by calling out a number between 0 and 100. Previous research in our laboratory indicates that the pain sensation associated with sural nerve stimulation is typically described by participants as sharp, shooting and stabbing.

2.4. Nociceptive flexion reflex

Electrical stimulation of the sural nerve of sufficient intensity to stimulate small diameter A-delta nociceptive fibers is used to elicit a withdrawal response from the ipsilateral biceps femoris muscle (Willer, 1983). This polysynaptic spinal reflex subserves withdrawal from noxious stimuli to avoid tissue injury, and accordingly, there is a close correspondence between the thresholds for nociceptive withdrawal and pain perception (Hugon, 1973; Willer, 1977). The NFR threshold was determined using a 4-2-1 adaptive up–down staircase procedure. The sural nerve was stimulated by five 1 ms square-wave pulses at 250 Hz, 200 ms into each 1 s trial. The NFR response was operationally defined as a mean rectified electromyographic response in the 90–150 ms post-stimulus interval that exceeded mean rectified electromyographic activity during a 60 ms pre-stimulus baseline interval (−65 to −5 ms) by at least 1.5S.D. Stimulus intensity increased in 4 mA steps, starting at 0 mA, until the NFR was first detected, and then decreased in 2 mA steps until the NFR was no longer detected. The staircase continued in 1 mA steps for four more reversals, which were averaged to yield the NFR threshold (mA). A variable (15, 20, and 25 s) inter-trial interval was used.

2.5. Procedure

Participants completed a single testing session. First, they performed three maximal contractions using a handgrip dynamometer (Lafayette) while resting their right arm on a support at a constant angle (Kahn et al., 1986). The peak forces were recorded and the MVC was determined as the largest (M = 48.5, S.D. = 7.7 N) of the three contractions (Kilbom et al., 1983). After instrumentation and instruction (30 min), they sat quietly and rested for 5 min while their blood pressure was measured three times; these measures were obtained during 1, 3, and 5 min.

Participants were then familiarized with the NFR procedure by having their sural nerve stimulated at various intensities. Next, their NFR threshold was determined under three isometric exercise conditions expected to produce graded increases in blood pressure: 1% MVC, 15% MVC, and 25% MVC (see Goldberg et al., 1982). In each condition, the participant was required to squeeze the dynamometer continuously. The required force was indicated to participants by placing a bright green strip on the dynamometer's analog force output scale; participants were asked to squeeze the dynamometer so that the black analog pointer, whose position indicated the current force output, was aligned with the green strip. The 1% MVC condition served as a control condition. Based on previous research showing that 25% MVC is associated with a time to fatigue of approximately 6 min (Kilbom et al., 1983), the intensity of the 25% MVC condition was chosen to allow sufficient time for an NFR threshold to be determined.

Each condition lasted as long as required to obtain an NFR threshold; the mean number of trials needed for this was 13 (S.D. = 3) trials and the mean duration of each NFR determination was 4.5 (S.D. = 1) min. Conditions were counterbalanced across participants to prevent order effects (Goldberg et al., 1982); analyses confirmed that there were no significant order effects for pain or the NFR. Participants were instructed to breathe normally while exercising to prevent the Valsalva maneuver (Mancia and Mark, 1983) that can also increase blood pressure. Blood pressure measurements were initiated 30, 90, 150, and 210 s into each condition, which was followed by a 5 min rest to allow blood pressure to return to baseline levels (Boushel et al., 1998; Fontana et al., 1993). Finally, participants rested for 5 min while their blood pressure was again measured three times; the measurements were obtained in 1, 3, and 5 min.

2.6. Data reduction and analysis

The pain ratings associated with each of the electrocutaneous stimulations (M = 13, S.D. = 3 ratings) were averaged to produce an overall pain intensity rating for each exercise condition. In addition, the ratings associated with the three peak stimulus intensities (i.e., the reversal points in each staircase) were