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Research report

Spinal dorsal horn neuron response to mechanical stimuli is decreased by electrical stimulation of the primary motor cortex

Arun K. Senapati, Paula J. Huntington, Yuan B. Peng*

Department of Psychology, P.O. Box 19528, University of Texas at Arlington, 501 S. Nedderman Drive, Arlington, TX 76019-0528, USA

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Abstract

Motor cortex stimulation (MCS) has been used clinically as a tool for the control for central post-stroke pain and neuropathic facial pain. The underlying mechanisms involved in the antinociceptive effect of MCS are not clearly understood. We hypothesize that the antinociceptive effect is through the modulation of the spinal dorsal horn neuron activity. Thirty-two wide dynamic range spinal dorsal horn neurons were recorded, in response to graded mechanical stimulation (brush, pressure, and pinch) at their respective receptive fields, while a stepwise electrical stimulation was applied simultaneously in the motor cortex. The responses to brush at control, 10 V, 20 V, and 30 V, and recovery were 11.5 ± 1.6, 12.1 ± 2.6, 11.1 ± 2.2, 10.5 ± 2.1, and 13.2 ± 2.5 spikes/s, respectively. The responses to pressure at control, 10 V, 20 V, and 30 V, and recovery were 33.2 ± 6.1, 22.9 ± 5.3, 20.5 ± 5.0, 17.3 ± 3.8, and 27.0 ± 4.0 spikes/s, respectively. The responses to pinch at control, 10 V, 20 V, and 30 V, and recovery were 37.2 ± 6.4, 26.3 ± 4.7, 25.9 ± 4.7, 22.5 ± 4.3, and 35.0 ± 6.2 spikes/s, respectively. It is concluded that, in the rat, electrical stimulation of the motor cortex produces significant transient inhibition of the responses of spinal cord dorsal horn neurons to higher intensity mechanical stimuli without affecting their response to an innocuous stimulus.

Theme: Sensory systems
Topic: Pain modulation: anatomy and physiology

Keywords: Motor cortex; Spinal cord; Electrophysiology

1. Introduction

Motor cortex stimulation (MCS) has been used in the clinical treatment of neuropathic pain [11,50,57], central post-stroke pain [22,28–30,56,62–65,69], and phantom limb pain [10,11]. These studies were conducted on human subjects who have undergone various other procedures to relieve the pain with little or no effect. The underlying mechanisms involved in the antinociceptive effect of MCS are not particularly understood.

Spinal cord dorsal horn neurons receive both inputs from primary afferents fibers and descending projections from supraspinal sources [6,21,40,44]. In the monkey and cat, activation of the corticospinal tract can modulate the activity of both afferent input [3] and dorsal horn neurons [16,20,24,32,38–42,49,68]. The corticospinal tract of the rat originates in the motor cortex [48], and descends in the base of the contralateral dorsal column [8], with some of these axons descending in the ipsilateral ventral funiculus [27]. The corticospinal tract axons terminate in all spinal laminae [4,8,13,37], making synapses with spinal cord interneurons [13,36]. The corticospinal tract also sends collaterals to the midbrain nuclei [2,14,31], which in turn projects to the spinal cord to modulate the activity of dorsal horn neurons. We hypothesized that activation of motor cortex would lead to inhibition of the spinal cord dorsal horn neurons. To test this hypothesis, we recorded spinal cord dorsal horn neurons in response to peripheral mechanical stimulation during MCS. Preliminary results have previously been reported [59].

* Corresponding author. Fax: +1 817 272 2364.
E-mail address: ypeng@uta.edu (Y.B. Peng).

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2. Materials and methods

Sixteen male Sprague–Dawley rats (300–350 g) were used in this project. All surgical procedures were approved by the University of Texas at Arlington Institutional Animal Care and Use Committee. The procedures were in accordance with the guidelines published by the Committee for Research and Ethical Issues of the International Association for Study of Pain [71].

2.1. Animal preparation

Animals were anesthetized using sodium pentobarbital (50 mg/kg, i.p.). As described previously [55], the spinal cord was exposed by performing a 3–4 cm laminectomy over the lumbosacral enlargement. A cannula was inserted in the trachea for artificial respiration. The anesthesia and paralysis of musculature were maintained by intravenous administration of a mixture of 50 mg of sodium pentobarbital and 5 mg of pancuronium bromide in 44 ml of 0.9% saline at a rate of 0.04 ml per minute. The pupillary reflex was monitored periodically to ensure proper depth of anesthesia. The spinal cord was immobilized in a stereotaxic frame and covered with mineral oil. The end tidal CO_2 was maintained at around 30 mm Hg and body temperature was maintained at 37 °C using a feedback controlled heating pad and rectal thermal sensor probe.

2.2. Data acquisition

A 10–12 MΩ tungsten microelectrode (FHS, Brunswick, ME) was used for electrophysiological recordings in the L5 and L6 region of the spinal cord dorsal horn. By mechanical stimulation of the receptive field in the plantar region of the hind paw, spinal dorsal horn neurons were searched for single unit extracellular recordings. Responses to intensity-coded mechanical (brush, pressure, and pinch) stimulation were recorded using SPIKE2 computer software program (CED, UK).

2.2.1. Measurement of mechanical stimulation responses

Following the identification of a differentiable cell, three mechanical stimuli of increasing intensity (brush, pressure, pinch) were applied to the receptive field. Each stimulus was applied once for 10 s, with an inter-stimulus interval of 20 s. The response to each mechanical stimulus was measured as the number of action potentials per second. Wide dynamic range (WDR) spinal dorsal horn neurons were selected for this study [15].

2.2.2. Motor cortex stimulation

After craniotomy, a bipolar stimulating electrode was placed in the motor cortex (0.26 mm rostral to bregma, 2.0 mm lateral to the midline) [51]. Stimulation was delivered at 300 Hz, 0.1 ms, and 10, 20, and 30 V.

2.2.3. Histological verification of stimulation site

The brain was obtained and immerged in 10% formaldehyde solution. Serial coronal sections of the brain in 80 μm were stained with thionin for histological verification of the stimulating electrode track. The site of the stimulating electrode was localized under light microscope (Fig. 2A).

2.3. Data analysis

The stored digital record of unit activity was retrieved and analyzed off-line. For single neuron recordings, responses to mechanical stimuli applied to the receptive field for 10 s, with or without MCS, were calculated. Statistical significance was tested by ANOVA followed by post hoc Tukey HSD test for significant change (STATISTICA, StatSoft, OK). A change was judged significant if $P < 0.05$. All values are presented as mean ± SEM.

3. Results

Thirty-two wide dynamic range spinal dorsal horn neurons from 16 animals were recorded in response to graded mechanical stimulation (brush, pressure, and pinch) at their respective receptive fields, while a stepwise electrical stimulation (300 Hz, 0.1 ms, at 10, 20, and 30 V) was applied in the motor cortex. Among them, 22 spinal dorsal horn neurons from 16 rats were tested for ipsilateral MCS, and 10 spinal dorsal horn neurons from 7 rats were tested for contralateral MCS. The depth from which dorsal horn neurons were recorded was 488 ± 38 μm (range from 117 to 839 μm). The responses of a representative spinal dorsal horn neuron to brush, pressure, and pinch, while either ipsilateral or contralateral electrical MCS was delivered, are shown in Fig. 1.

Data were analyzed by ANOVA to test differences between sides of MCS (ipsilateral and contralateral), among effects of stimulation intensity (control, 10 V, 20 V, and 30 V, and recovery), and among effects of mechanical stimuli (brush, pressure, and pinch). The results indicated no effect of stimulation side, $F(1, 29) = 0.39$, $P = 0.54$, a main effect of electrical stimulation, $F(4, 116) = 10.07$, $P < 0.01$, and a main effect of mechanical stimuli, $F(2, 58) = 7.27$, $P < 0.001$. A significant interaction (electrical intensity × mechanical intensity) was found, $F(8, 232) = 3.91$, $P < 0.001$.

3.1. Effect of ipsilateral motor cortex stimulation

The responses to brush at control, 10 V, 20 V, and 30 V, and recovery were 12.5 ± 3.0, 15.6 ± 6.7, 11.8 ± 5.4, 11.6 ± 5.6, and 16.5 ± 6.3 spikes/s, respectively. The responses to pressure at control, 10 V, 20 V, and 30 V, and recovery were 25.0 ± 5.3, 18.9 ± 3.8, 16.4 ± 3.7, 13.3 ± 2.4, and 25.0 ± 4.3 spikes/s, respectively. The responses to pinch at control, 10 V, 20 V, and 30 V, and recovery were 28.4 ± 5.1, 20.6 ± 4.1, 18.9 ± 4.3, 17.0 ± 2.9, and 26.2 ±