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Research report

Modulation of jaw reflexes induced by noxious stimulation to the muscle in anesthetized rats

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Abstract

Previous studies have shown that jaw reflexes and activity patterns of the jaw muscles were modulated in the presence of jaw muscle pain. However, there is no study comparing the modulatory effects on the jaw reflexes induced by noxious stimulation to the jaw muscle. To clarify this, effects of the application of mustard oil (MO), an inflammatory irritant, into the temporalis (jaw-closing) muscle on (1) jaw-opening reflex evoked by tooth pulp stimulation (TP-evoked JOR) as a nociceptive reflex, (2) jaw-opening reflex evoked by inferior alveolar nerve stimulation as a non-nociceptive reflex and (3) jaw-closing reflex evoked by trigeminal mesencephalic nucleus stimulation as a proprioceptive reflex were investigated in anesthetized rats. The MO application induced suppression of all reflexes, and the effect on the TP-evoked JOR was more prominent than on the other reflexes. To elucidate the involvement of endogenous opioid system for the suppressive effect, a systemic administration of naloxone following the MO application was conducted. The MO-induced suppressive effect on the TP-evoked JOR was reversed by the naloxone administration. The results suggest that noxious stimulation to the jaw muscle modulate jaw reflexes particularly for the nociceptive jaw-opening reflex, and the modulatory effect includes both facilitatory and inhibitory aspects. The results also suggest that pain modulatory systems such as the endogenous opioid system play a crucial role in the suppression of the nociceptive transmissions related to nociceptive reflexes, and in some pathological states, defense reflexes may not be evoked properly.

Theme: Motor systems and sensorimotor integration
Topic: Reflex function

Keywords: Jaw-opening reflex; Jaw-closing reflex; Inflammatory pain; Jaw muscle; Rat

1. Introduction

The jaw reflex is one of the important neuronal mechanisms controlling jaw movements in various oral functions such as ingestion, digestion and vocalization. There are two types of jaw reflexes, namely the jaw-opening reflex (JOR) and the jaw-closing reflex (JCR). The JOR is evoked by the activation of either nociceptive (i.e., high threshold) orofacial receptors (nociceptive JOR) or non-nociceptive (i.e., low threshold) orofacial receptors (non-nociceptive JOR). In the animals, the JOR consists of both an excitation of the jaw-opening muscle and an inhibition of the jaw-closing muscle, whereas the latter is dominant in man [18,20,33,59,60,68]. The JCR is evoked by the activation of non-nociceptive intraoral mechanoreceptors or muscle spindles of the jaw-closing muscles [15,18,20,33]. For the latter, sensory fibers innervating the muscle spindles have their cell bodies in the trigeminal mesencephalic nucleus (MesV); the MesV neurons send their central axons directly onto the motoneurons and evoke the proprioceptive JCR or the so-called jaw-jerk reflex [18,20].

Various studies have shown that the jaw reflexes are modulated under various physiological states such as

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mastication [21,32,34,67], swallowing [36] and sleep [25]. In addition, recent studies have suggested that these reflexes are also modulated under pathophysiological states such as jaw muscle pain, which is one of the major symptoms of the temporomandibular disorders [19,51–53,61–65] (also see Ref. [15] for review). It has been found that the inhibitory response of the jaw-closing muscles (i.e., the major components of the JOR in man) evoked by noxious stimulation to the peri-oral tissue was suppressed by the unilateral noxious chemical stimulation to the jaw-closing muscle [61]. It has also reported that the facilitation of a jaw-jerk reflex (i.e., proprioceptive JCR) was induced by the same noxious conditioning stimulation in man [62–65]. These findings suggest that noxious stimulation to the jaw muscle induces different modulatory effects on the JOR and JCR. However, we cannot deny the possibility that such a difference was due to the difference in the experimental conditions (e.g., chemicals for noxious stimulation to the muscle). In addition, it is still uncertain whether two types of JORs (i.e., nociceptive JOR and non-nociceptive JOR) are modulated in the same manner following noxious stimulation to the jaw muscle. To clarify these issues, the present study was conducted to compare the effects of unilateral noxious stimulation to the jaw muscle on the nociceptive JOR, non-nociceptive JOR, and proprioceptive JCR. As a noxious stimulus to the jaw muscle, MO was injected into the temporalis muscles (i.e., one of the jaw-closing muscles). MO is a small-fiber excitant and inflammatory irritant which is commonly used as algesic chemical [23,27,28,40,66,70] and its algesic mechanisms were recently revealed on the molecular basis [30].

When the modulation of the reflex was observed following the MO application, the possible neural mechanisms underlying the MO-induced modulatory effect were also studied. Since endogenous opioids play important roles in modulating central and peripheral nociceptive transmission associated with injury or inflammation of peripheral tissues [6,38], we tested the effects of the systemic administration of naloxone, the opiate antagonist, on the MO-induced modulatory effect on the reflexes.

2. Materials and methods

2.1. Surgical procedures

The experiments were carried out in a total of 60 male rats (Wistar albino, 250–270 g) in accordance with the "Principles of Laboratory Animal Care " (NIH publication #86-23, revised 1996). The animal protocols were approved by the Intramural Animal Care and Veterinary Science Committee of the Niigata University. The animals were initially anesthetized with 2–3% halothane. Two percent lidocaine was injected into the skin to minimize surgical pain before the incisions were made. Cannulae were inserted into the trachea and the femoral vein for respiration and drug administration, respectively, and then the anesthesia was maintained with the mixture of α-chloralose (50 mg/kg) and urethane (500 mg/kg) injected via the femoral vein. Depth of anesthesia was checked repeatedly throughout the experiment by pinching the paws. A supplementary dose of chloralose–urethane mixture was administrated when a withdrawal reflex was elicited. The rectal temperature was measured and maintained between 37 °C and 38 °C with a heating pad.

A midline incision was made along the ventral aspect of the mandible. Paired copper wire electrodes (0.12 mm in diameter, 3 mm interpolar distance) with an exposed tip (1 mm) were implanted bilaterally into the masseter (Mas) as a jaw-closing muscle and the digastric (Dig) as a jaw-opening muscle to record electromyographic (EMG) activities. EMG electrode locations in each muscle were confirmed by post-mortem dissection.

In the present experiment, electrical stimulation of the tooth pulp (TP) of the rat's lower incisor was conducted to evoke the nociceptive JOR (TP-evoked JOR). The electrodes were placed on the apical part of the crown of the right lower incisor. Two holes were made on the labial surface of the crown of the incisor by the use of a low-speed dental drill with a round tungsten carbide bur (#1/2) and water cooling: one hole was made 2 mm away from the gingival margin (for the cathode), and the other hole was 4 mm away from the gingival margin (for the anode). The holes were rinsed with saline, and the custom-made bipolar stimulating electrodes with two gold-coated metal pins (0.4 mm in diameter, 2 mm interpolar distance) were implanted in the holes. For the purpose of limited stimulation of the pulpal fibers within the tooth crown, the position of the electrode tips was adjusted to be the border of the dentin and the pulp chamber, and the electrodes were fixed to the tooth with the use of adhesive dental acrylic (SUPERBOND C&B, SUN MEDICAL, Shiga, Japan). To stimulate the inferior alveolar nerve (IAN) to evoke the non-nociceptive JOR (IAN-evoked JOR), a pair of Teflon-coated stainless-steel wire electrodes (0.1 mm in diameter, tip exposure 0.5 mm) was inserted into the right mental foramen 1 mm deep for the anode and 3 mm deep for the cathode and fixed on the adjacent bone with the use of adhesive dental acrylic.

Then, the rat's head was placed in a stereotaxic frame. The skin over the dorsal surface of the skull was reflected, and four screws were implanted into the frontal and parietal bones. These screws were attached to a vertical support bar with dental acrylic (UNIFAST II, GC, Tokyo, Japan), and the ear bars were removed. A part of the occipital bone overlying the cerebellum was removed to enable the microelectrode penetrations (glass-coated tungsten microelectrode, 0.2–0.6 MΩ at 1 kHz) for MesV stimulation to evoke the proprioceptive JCR (MesV-evoked JCR). The microelectrode was introduced stereotaxically through the cerebellum into the MesV. Neuronal responses evoked by passive jaw opening or probing the belly of the masseter muscle were used to confirm that the electrode tip was located within the MesV.