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Mouse incising central pattern generator: Characteristics and modulation by pain

Charles G. Widmer[a,*], Joyce Morris-Wiman[b]

[a] *Department of Orthodontics, Box 100444, JHMHSC, University of Florida, Gainesville, FL 32610-0444, USA*
[b] *Biomedical Sciences, West Virginia School of Osteopathic Medicine, 400 North Lee St., Lewisburg, VA 24901, USA*

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ABSTRACT

Introduction: Vertebrate incising and chewing are controlled by a set of neurons comprising the central pattern generator (CPG) for mastication. Mandibular positioning and force generation to perform these tasks is complex and requires coordination of multiple jaw opening and closing muscle compartments located in muscles on both sides of the jaw. The purpose of this study was to determine the characteristics of the CPG by recording mouse incising forces in the home cage environment to evaluate changes in force characteristics with incising frequency and force direction. A second purpose was to evaluate the effects of jaw closing muscle pain on CPG output parameters.

Methods: Digitized incising forces were recorded for approximately 24 h using a 3-dimensional force transducer attached to solid food chow. Male and female CD-1 mice were evaluated during their last (fourth) baseline assessment and seven days after a second acidic saline injection into the left masseter muscle when maximum pain was experienced. Incising force resultants were calculated from the three axes data and force parameters were assessed including inter-peak intervals (IPI), peak amplitude, load time and unload time. Multiple regression analyses were conducted to identify incising episodes that had parameters of force that were significantly correlated ($p < 0.001$). These incising episodes were considered to represent the output of the CPG with a steady state of incoming sensory afferent inputs. Incising parameters were evaluated for each of the discrete incising frequencies (4.6, 5.3, 6.2, 7.6 Hz) and the predominant force directions: jaw closing ($-Z$), jaw retrusion ($+X$) and jaw protrusion ($-X$).

Results: A significant correlation between incising frequency (IPI) and the load time was observed. A significant decrease in peak amplitude was observed with higher incising frequency while the load rate significantly increased. The force peak amplitude and load rates were found to be statistically different when the force direction was considered, with smaller peak amplitudes and smaller load rates found in the jaw closing direction. The effect of pain on incising was to reduce the peak amplitude and load rate of incising compared to the baseline condition at lower incising frequencies.

Conclusions: Like the central pattern generator for locomotion, the CPG for incising controls rhythmicity, peak amplitude and force load duration/rate. However, unlike the CPG for locomotion, the amplitude of incising force decreases as the frequency increases. During incising, load rate increases with faster rhythm and is consistent with the recruitment of larger motor units. Muscle pain reduced the excitatory drive of the CPG on motoneurons and provides further support of the Pain Adaptation Model.

1. Introduction

Vertebrate incising and chewing requires a versatility of mandibular movement and force generation. For example, in humans, incising is performed to break off small pieces of food and this is accomplished by positioning the mandible in a more anterior position and generating a series of vertically-directed forces [1,2]. In rodents and lagomorphs, incising is utilized for both food acquisition/initial degradation and for maintenance of the incisor length since the incisors are continuously erupting. Once smaller pieces are acquired, the food is combined with saliva and the bolus is moved between the maxillary and mandibular molars by the tongue and buccinator muscles during the opening of the jaw. Finally, the mandible moves laterally in the horizontal plane to position the molars so that a shearing or grinding force can be

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* Corresponding author.
E-mail addresses: widmer@dental.ufl.edu (C.G. Widmer), jmorriswiman@osteo.wvsom.edu (J. Morris-Wiman).

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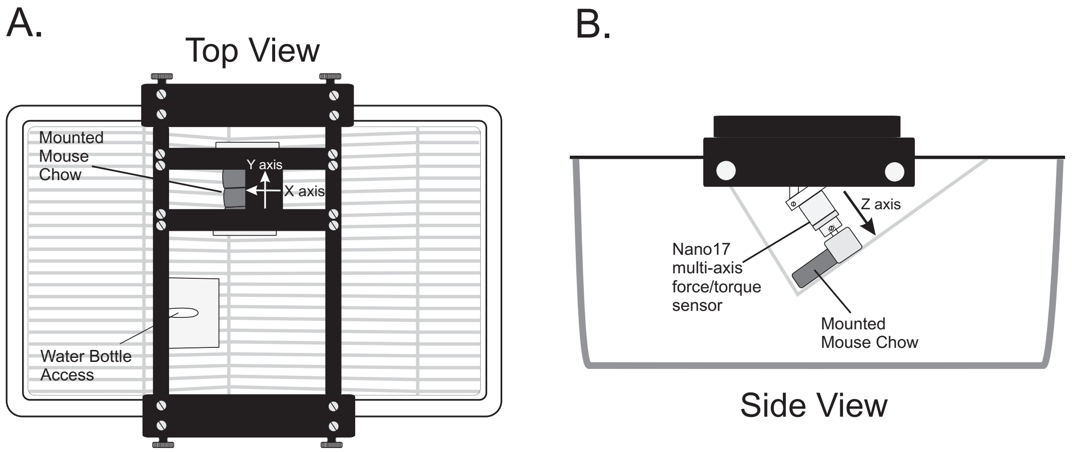

Fig. 1. Diagram of the 3-dimensional force transducer mounted on the wireframe cage top. Note the orientation of the X, Y and Z axes of the force transducer.

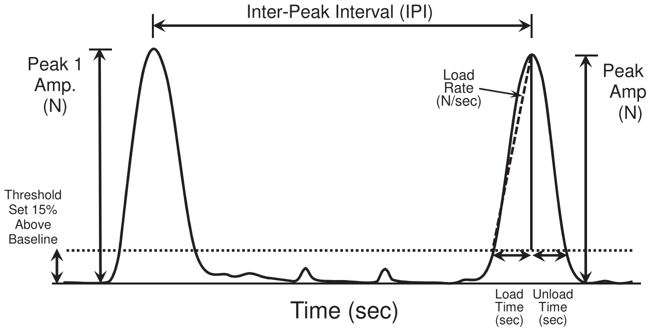

Fig. 2. Diagram of the incising force parameters that were calculated from pairs of peak forces. A threshold was set at 15% above the average baseline and peak amplitude, inter-peak interval and load and unload times were calculated. Load rate represented the slope of the load and was calculated by a line from the threshold of force onset to the peak amplitude.

generated as the mandible returns to its original position [2]. The motor control for mandibular positioning and force generation during incising and mastication is complex and requires the coordination of multiple jaw opening and jaw closing muscles located on either side of the mandible. The rhythmic coordination during incising and chewing is controlled by a central pattern generator (CPG) [3]. The masticatory central pattern generator consists of collections of neurons located in the trigeminal main sensory nucleus and reticular formation that control the recruitment and temporal rhythm of pre-motor neurons located in the supra- and intra-trigeminal nuclei necessary to perform the tasks of incising and chewing [4,5]. Both incising and chewing occur as a rhythmic activity with similar frequencies (incising: 4–10 Hz [6]; chewing: 5–10 Hz [7]) and the CPG neurons controlling these two activities are probably located in a similar region. The precise movement and force generation are modulated by intraoral and perioral sensory feedback that includes the jaw closing muscle spindles, Golgi tendon organs, periodontal afferents around the incisors and molars, mucosal afferents and temporomandibular joint receptors [8]. This motor pattern can be voluntarily modified through central descending drive or can reflexively respond to sensory perturbations such as with biting or incising a hard food [9], unexpected unloading of the jaw such as with biting through a hard object [10] or modifying the chewing rate and maximum biting force in response to pain in the masticatory system [6,11]. These responses are well-characterized and well established.

Masticatory and incising forces are also a product of intrinsic characteristics of muscle fibers and the motoneurons that innervate them. For example, motoneurons may have distinct temporal dynamics associated with their synaptic input [12] that may affect force production. Also, skeletal muscle demonstrates history dependence after shortening contractions that has been recognized for many years [13]. However, this dependence is eliminated when forces go down to resting levels. These intrinsic characteristics may not be a major influence on force production during rhythmic activities such as incising when compared to contributions of the CPG and sensory feedback but are described to demonstrate the complexity of masticatory motor control for force production.

An assessment of how sensory afferents influence masticatory motor control neurons such as pre-motor neurons or central pattern generator (CPG) neurons will enhance our understanding of the neurophysiological mechanisms of motor control [14–18]. It is well-established that some sensory inputs, such as those from muscle spindles located in jaw closing muscles, can have a monosynaptic effect on motoneuron excitation, but affect motoneuron inhibition using a disynaptic pathway [19–21]. The effects of low threshold afferents on the CPG for mastication, such as mucosal and skin receptor afferents in the inferior alveolar nerve activated by low levels of electrical stimulation, have been studied at the segmental level and multiple studies demonstrate the phasic modulation of motoneuron excitability [22–24]. Low threshold inputs such as those from periodontal afferents can have a mixed effect on motoneuron excitability, with low tooth force levels causing excitation, while high tooth forces elicit inhibition [25–29]. The influence of sensory afferents on rhythm generation and motoneuron activation in the home cage environment has not been examined. This is probably due to the difficulty of recording force or electromyographic activity without having the recording procedure influence the outcome parameters. One of the aims of this study was to examine the influence of one type of sensory experience, persistent pain, on rhythmicity and force production (as a proxy for motoneuron recruitment) during incising. Understanding the impact of persistent pain on motor control in the masticatory system is necessary to enhance our interpretation of clinical signs and symptoms in myofascial pain conditions.

Motor unit recruitment in masticatory muscles, like limb muscles, follows Henneman's principal where small motor units are recruited before large motor units [30–32]. This excitatory drive could be generated by descending cortical inputs, the basic excitatory rhythmic activity by the central pattern generator or as a CPG response to sensory feedback to accomplish a specific task such as incising harder foods [33]. In order to maintain the rhythmic activation of specific patterns of jaw openers and jaw closers, it has been shown that the CPG activates pre-motor neurons that then excite motoneurons that innervate the appropriate muscles to generate this temporally-coordinated rhythmic activation [4]. It would be expected that force generation parameters (loading time and magnitude and frequency of loading) would be interrelated during a steady state activity such as incising or chewing since these parameters are probably under the control of a common