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RESEARCH ARTICLE

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# Physiological evidence for caudal brainstem projections of jaw muscle spindle afferents

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**Abstract** Retrograde transport and intra-axonal labeling studies provide convincing evidence that jaw-muscle spindle afferents project to the caudal medulla by way of Probst's tract. However, functional properties of this caudal projection are not well understood. Extracellular recordings were made in cats at the level of the subnucleus interpolaris (Vi) to identify single units that showed consistent responses to ramp-and-hold stretches of the jaw. In this report, we present data from 20 central units with properties indicating that they received input from trigeminal muscle spindle afferents. All units were activated by gentle palpation of jaw muscles, and none had superficial receptive fields. Two groups of neurons could be defined based on their responses to passive jaw movements. One group ($n$=12) showed an obvious dynamic response (i.e., a higher level of activity at the onset of stretch than during the hold period). Activity was maintained during the hold phase, and the units stopped firing (unloaded) for a brief period upon jaw closure. The other group ($n$=8) lacked a dynamic response. Instead, they showed an increase in firing with onset of stretch that was maintained during the hold phase. Thirteen units, which were tested with more than three different jaw stretch speeds and/or amplitudes, were further characterized by analyzing dynamic index (DI) and mean firing rate (MFR) during each phase of the ramp-and-hold movement as well as interspike interval (ISI) variability. All but one unit with a dynamic response showed a speed-sensitivity. In all cases, the MFR was a more sensitive indicator of changes in jaw speed than DI. Neurons in the other group (5/5 tested) showed a high position-sensitivity, i.e., their firing rates varied as a function of amplitude of jaw opening. The percent change in ISI variability for all neurons ranged from 37–84%. The response characteristics of these central neurons were compared to known physiological properties of muscle spindle afferents. The results provided compelling evidence for jaw-muscle-spindle afferent projection onto these neurons. Reconstruction of recording sites showed that medial Vi, and the adjacent reticular formation, are likely recipients for the caudal projections from jaw-muscle-spindle afferents. We suggest that muscle spindle input to this region is well suited for influencing the coordination of motor behavior during feeding and for the integration and processing of kinesthetic information.

**Key words** Trigeminal · Jaw movements · Muscle spindle · Vi · Reticular formation

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## Introduction

The perikaraya of jaw muscle spindles are located in the trigeminal mesencephalic nucleus (Vmes). Studies on the anatomical organization and functional properties of central connections of these neurons have demonstrated that they are intricately involved in the reflex control of a variety of oral and facial movements (Appenteng et al. 1978; Cody et al. 1975; Dessem and Taylor 1989; Kishimoto et al. 1998; Kolta et al. 1995; Larson et al. 1983; Luo 1991; Shigenaga et al. 1990; Taylor and Cody 1974). Most of these studies elucidated the role of central connections of jaw-muscle-spindle afferents onto the rostral trigeminal areas, such as trigeminal motor nucleus (Vmot), supratrigeminal nucleus (Vsup), intertrigeminal nucleus (Vint), and subnucleus oralis (Vo). However, our knowledge on the more caudal projections of these neurons is limited.

Vmes neurons have a relatively long descending processes, which collectively form Probst's tract (Corbin 1942). Anatomical studies have shown that this tract projects caudally to the spinal trigeminal nucleus and cervical spinal cord motor neurons (Matsushita et al. 1981; Mizuno and Sauerland 1970; Walberg 1984). Since Vmes innervates functionally different types of spindle afferents and also contains neurons innervating the periodontium,

the precise type of input from Vmes to caudal brainstem requires further study. Capra and Wax (1989) have found that Vmes cells innervating the masseter muscle project as far caudally as the trigeminal subnucleus caudalis (Vc). Although recent intra-axonal labeling studies have revealed more detailed topographic distributions of central axons from physiologically identified jaw-muscle-spindle afferents (Dessem et al. 1997), physiological properties of the caudal brainstem neurons that receive the muscle spindle inputs are still largely unknown.

We have previously described a group of neurons in Vi in the cat that respond to passively imposed jaw movements (Capra et al. 1994; Ro and Capra 1995). Jaw movement-related neurons received sensory inputs from the muscles of mastication, hair, and skin around the mouth, oral mucosa, and some combination of these structures. In addition, a few neurons were isolated that responded to low-threshold electrical stimulation of the masseter nerve and showed muscle spindle-like responses to jaw stretch. This study was conducted to determine whether these central neurons, which responded to passive jaw movements, may receive input from muscle spindles with more rigorous analytical criteria. Our examination included quantitative analysis of speed- and position-sensitivities by correlating dynamic index (DI) and mean firing rates to varying speeds and amplitudes of the jaw opening. ISI variability percent changes were also calculated and compared with those reported for muscle spindle afferents and the central neurons in Vsup (Miyazaki and Luschei 1987). Preliminary results from this study have been reported in an abstract form (Ro and Capra 1998).

## Materials and methods

The experiments were performed on adult cats weighing 2.5–4 kg anesthetized with a combination of ketamine (15 mg/kg) and xylazine (1 mg/kg) and maintained with sodium pentobarbital (38 mg/kg; i.v.). Arterial blood pressure, end tidal $CO_2$, and rectal temperature were monitored continuously during the experimental procedure. Body temperature was maintained between 37–39°C with a warming blanket. The animals were checked regularly to monitor the level of anesthesia. Additional anesthetic was administered when a firm pinch applied between the toe pads resulted in increased respiration and heart rate. For nerve stimulation, animals were paralyzed with Flaxedil (gallamine triethiodide 20 mg, i.v.; supplemented with 10 mg i.v. as needed) and artificially ventilated. Occasionally, gallamine effects were allowed to wear off and the depth of anesthesia was tested. All procedures were conducted within the NIH Guide for the Care and Use of Laboratory Animals.

An electrodynamic vibrator (Lab Works, Model 132; maximum displacement 8 mm) was attached to animal's mandible, contralateral to the side of the extracellular recording. The vibrator was controlled by a function generator to produce ramp displacements of the jaw with varying speeds and amplitudes. The resting interincisal distance was adjusted to 20–23 mm for all experiments.

Single-unit activity was recorded extracellularly with glass electrodes filled with 2 M NaCl. Electrodes were directed rostroventrally at 30° to the vertical axis and advanced into the caudal brainstem. The caudal brainstem was explored systematically with stereotaxic coordinates derived from our previous studies (Capra et al. 1994; Ro and Capra 1995). Once a unit responsive to passive jaw movements was isolated, the receptive field was determined by mechanical stimulation of hair, skin, oral mucosa, teeth, and palpation of deep structures such as jaw muscles and the temporomandibular joint (TMJ). Units were considered to receive input from muscle or other deep receptors if they responded either to gentle muscle palpation or to light pressure on individual muscles of mastication. Muscle units were then tested by a series of ramp-and-hold jaw stretches at varying speeds (8–32 mm/s) and positions (1–8 mm). A minimum of 20 trials (ramp open, hold, ramp close) were presented for each speed and position. The jaw opening and closing speeds were identical for each trial. Units with superficial and intraoral receptive fields (RFs) were not studied further.

A stainless-steel concentric bipolar stimulating electrode was stereotaxically implanted in the contralateral ventroposteromedial nucleus (VPM) of the thalamus to test for antidromic stimulation of movement-related units. Neurons were considered to be antidromically driven if they exhibited an all-or-nothing response that consistently followed high frequency pulses (>200 Hz) with a short and fixed latencies at stimulus intensities <1 mA. In a few experiments, identification of muscle afferent input was complemented by electrical stimulation of the masseter nerve. The masseter nerve was exposed in the infratemporal fossa by reflecting the temporalis muscle laterally. A bipolar silastic cuff electrode was placed on the nerve just proximal to its entry into the deep surface of masseter muscle. Test stimuli consisted of single square-wave pulses (0.1 ms/1 Hz). Central neurons that were activated by masseter nerve stimulation were differentiated from primary afferent axons by their initial negative-going spikes and inability to follow high-frequency orthodromic stimuli (>200 Hz).

At the end of each experiment, animals were deeply anesthetized with a lethal dose of pentobarbital (100 mg/kg) and perfused with heparinized saline followed by a 4% paraformaldehyde in 0.2 M phosphate buffer (pH 7.2). One-centimeter thick blocks from the brainstem and thalamus that contained the recording/stimulation sites were made in situ. Serial sections (50 µm thick) were taken from each block with a vibratome. Recording sites were reconstructed from records of stereotaxic coordinates referenced to the location of the identified electrode tracks.

### Data analysis

Initial evaluations regarding movement responses were made based on peri-stimulus time histograms (PSTHs). Further analysis was performed on units recorded successfully during testing at least three different speeds and/or amplitudes. For units showing initial bursts of response at the onset of stretch, the dynamic index (DI) was assessed to examine speed-sensitivity. DI was calculated as the difference between the peak instantaneous frequency during the ramp stretch and the firing frequency taken 0.5 s later (Crowe and Matthews 1964). Units lacking initial dynamic response were excluded from this analysis. In addition, mean firing rate (MFR) was calculated during each stage of the ramp-and-hold trial. For each unit, a simple linear regression analysis was separately performed on mean DI and MFR from 15–20 trials. A linear regression line was obtained for each analysis; the slope of the line and correlation coefficients were calculated. The significance level of the statistical analysis was set as $P<0.01$.

Variations in interspike intervals (ISI) were examined by analyzing "ISI % change". This method, introduced by Miyazaki and Luschei (1987), was used to compare ISI variability between jaw movement-modulated primary afferents and second-order neurons in the trigeminal system.

## Results

Extracellular unit recordings were made from neurons that showed consistent jaw movement-related responses. Data were collected from six adult cats. We present here the results obtained from 20 jaw movement-related neurons that responded to light palpation of the masseter


**Fig. 1A, B** Jaw-movement related responses. Examples of two types of stretch-related responses elicited by passive ramp-and-hold movements of the jaw. The unit illustrated in (**A**) showed a dynamic response at the onset of the jaw opening, whereas the unit shown in (**B**) lacked a dynamic response. Upper deflections of the ramp wave indicate jaw opening. The duration for ramp-and-hold displacement was 4 and 2 s for the units shown in **A** and **B**, respectively

**Table 1** Summary of physiological properties of movement-related neurons. *ISI* Inter-spike interval, *RF* receptive field, *DI* dynamic index, *MFR* mean firing rate, *(r)* regression coefficient, *nt* not tested with more than three amplitudes/speeds. * denotes statistically significant relationship

| Cell ID | RF | Dynamic response | Speed sensitivity | | Length sensitivity | Mean ISI |
|---|---|---|---|---|---|---|
| | | | DI (r) | MFR (r) | MFR (r) | % Change |
| SMI 11–8 | Masseter | Yes | 0.580* | 0.796* | 0.778* | 70.2 |
| SMI 3–1 | Masseter | Yes | 0.623* | 0.923* | 0.490 | 37.4 |
| SMI 3–2 | Masseter | Yes | 0.636* | 0.790* | 0.814* | 40.6 |
| SMI 7–1 | Masseter | Yes | 0.620* | 0.670* | 0.180 | 57.3 |
| DST 4–7 | Temporalis | Yes | 0.370 | 0.850* | nt | 84.2 |
| DST 4–5 | Masseter | Yes | 0.326 | 0.372 | nt | 44.6 |
| DST 4–4 | Masseter | Yes | 0.303 | 0.790* | nt | 62.0 |
| SMI 5–3 | Masseter | No | – | 0.406 | 0.816* | 44.4 |
| SMI 6–4 | Temporalis | No | – | 0.488 | 0.917* | 74.6 |
| SMI 6–3 | Masseter | No | – | 0.050 | 0.816* | 41.6 |
| SMI 6–2 | Temporalis | No | – | 0.230 | nt | 37.7 |
| SMI 6–1 | Masseter | No | – | 0.310 | 0.904* | 34.5 |
| DST 9–8 | Masseter | No | – | nt | 0.961* | 37.1 |

(16/20) or temporalis muscle (4/20). Unlike movement-related neurons reported in our earlier work (Ro and Capra 1995), none of these neurons could be activated by mechanical stimulation of orofacial hair and skin, intraoral mucosa, or the teeth. Therefore, these neurons formed a distinct subpopulation of all jaw movement-related neurons recorded from Vi. Electrical nerve stimulation confirmed that six units received input from the masseter muscle. Stimulus intensity as low as 200 μA (range: 200 μA–900 μA) reliably activated these neurons with a mean latency of 3.7±2.2 ms (±SD). One unit also responded to antidromic stimulation of VPM of the thalamus.

All neurons had increased discharge rates during the onset of jaw opening and continued to respond to maintained opening. Based on the observation of firing patterns, units were qualitatively categorized as one of two types. One group of neurons ($n$=12) exhibited a clear and consistent dynamic response, i.e., an initial burst of activity coincident with the onset of the ramp stretch followed by reduced, but relatively constant activity during the hold phase (Fig. 1A). The other group ($n$=8) lacked a

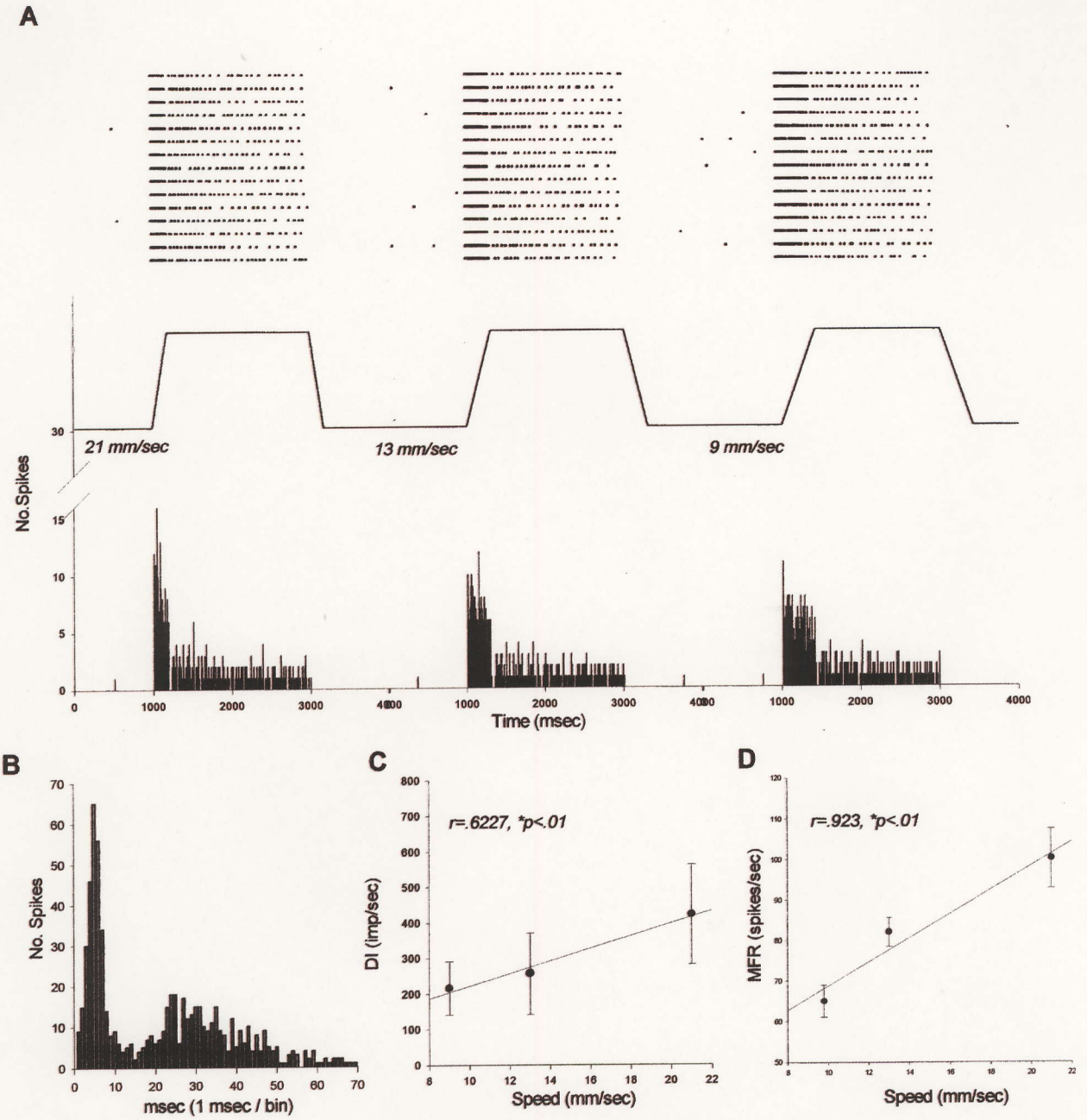


**Fig. 2A–D** Speed-sensitive response. **A** Raster displays and peristimulus time histograms of a dynamically sensitive unit aligned to ramp-and-hold stretches of the jaw. Reproducibility and stability of the unit's response to the jaw movements is evident over multiple trials and stretch velocities. Upward deflections of ramp wave represent 6 mm of jaw opening. **B** The distribution of interspike intervals reveals both dynamic and static responses of the same unit. **C, D** Both dynamic index (*DI*) and mean firing rate (*MFR*) were linearly related to the speed of jaw stretch. In all speed-sensitive units, MFR during the opening phase yielded a higher regression coefficient than DI and showed less variations between trials

dynamic response at the onset of stretch, but responded to maintained jaw opening (Fig. 1B). A few neurons in this group showed a weak dynamic response during some of the trials. For such responses, DI was not calculated.

All units successfully tested with at least three different speeds and/or amplitudes of jaw displacements (13/20) were selected for further analyses. The results from the quantitative analyses performed on these neurons are summarized in Table 1. All but one unit with a dynamic response could reliably signal changes in opening speeds with either DI or MFR, whereas units that lacked a dynamic response were highly sensitive to

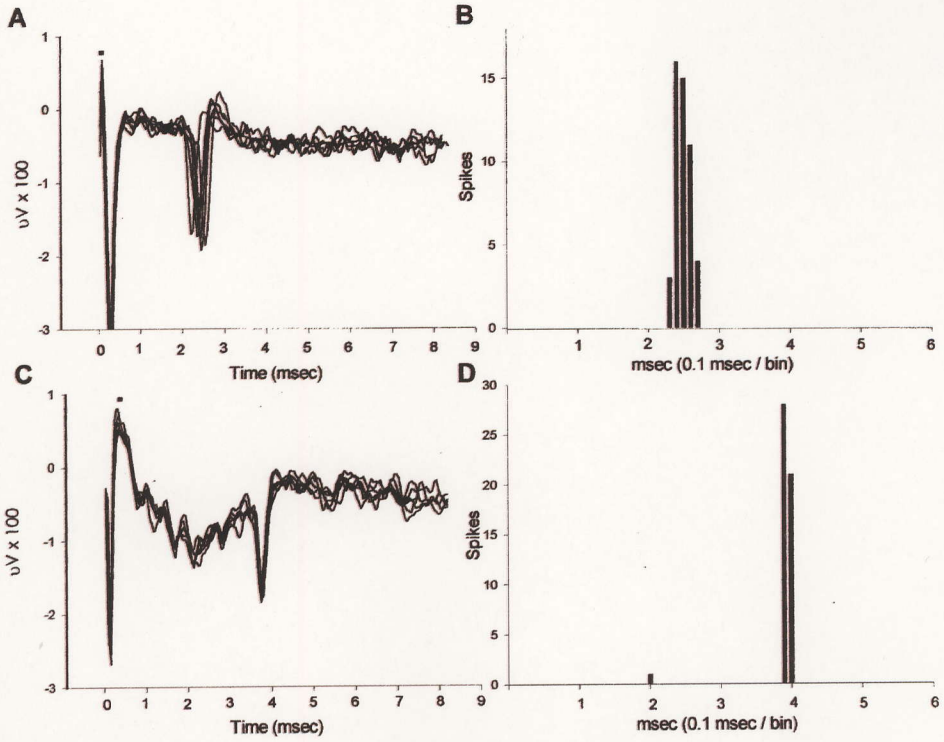


**Fig. 3A–D** Responses to electrical stimulation. **A** Examples of a stretch-sensitive unit responding to electrical stimulation of the masseter nerve. *Superimposed traces* show the unitary response to five consecutive stimuli (1 Hz; duration=0.1 ms; stimulus intensity=800 μA; latency=2–3 ms). **B** Peristimulus time histogram (PSTH) of the unit's response to nerve stimulation ($n$=50). **C** Examples of the same unit responding to antidromic stimulation of the contralateral ventroposteromedial nucleus (VPM) of the thalamus (10 Hz; duration=0.1 ms; stimulus intensity=900 μA; latency=4 ms). The responses to five consecutive stimuli are superimposed. **D** PSTH from 50 consecutive antidromic stimulation

changes in jaw opening amplitude. Based on these results, we classified these units as speed-sensitive and position-sensitive units, respectively. Two of the speed-sensitive units also showed position-sensitivity.

Figure 2 illustrates examples of a speed-sensitive neuron to three different speeds of jaw stretches. This unit was activated by gentle palpation on the anterior part of the masseter muscle. As illustrated in the rasters and histograms (Fig. 2A, B), the unit responded with bursts of activity as the jaw was stretched open and leveled off to a lower firing rate as the jaw reached the hold position. The duration of high activity corresponded with the duration of the dynamic open phase of a ramp-and-hold trial. Conversely, this neuron became completely silent during imposed closing of the jaw. Also evident was the presence of a deceleration response at the beginning of holding phase. The high firing rate of this unit halted transiently for a brief period as the stretch was completed and the hold phase began, then the unit resumed firing at a lower rate. Dynamic index of this neuron as well as MFR during opening phase were significantly correlated with the speed of jaw stretch (Fig. 2C, D).

The unit also responded to masseter nerve stimulation consistently without failure, but the latency varied between 2 and 3 ms when stimulated at 1 Hz (Fig. 3A, B). The stimulus intensity required to activate this neuron was 900 μA. The unit also responded to antidromic stimulation of the thalamus with a short and fixed latency (Fig. 3C, D) and followed a high frequency of thalamic stimulation up to 200 Hz.

Position-sensitive units lacked a dynamic response at the onset of stretch. The firing rate of these neurons varied as a function of amplitude of jaw opening. Figure 4A shows an example of a position-sensitive unit. The unit increased its firing rate from the basal level at the onset of jaw opening and maintained an elevated firing rate throughout the hold phase. The sustained stretch-related responses were consistent over multiple trials. However, the magnitude of firing changed as the opening amplitude was varied. The ISI distribution at each amplitude tested showed a slightly skewed, but regular pattern (Fig. 4B), which differed qualitatively from the ISI distribution of the speed-sensitive units (Fig. 2C). The mean firing rates during maintained hold were significantly correlated with the amplitude changes (Fig. 4C). In addition, a deceleration response following peak ramp stretch was not present in these neurons.

The mean percent changes in ISI, which was calculated for 13 units, was 51.3±16.7% (±SD) (Table 1). None of these units had a percent ISI percent change less than 25%, which is the value assumed to be associated with the recordings of muscle spindle afferents, but, instead, the observed range of ISI percent changes in this report was quite comparable to that recorded from a group of second-order neurons that received muscle spindle afferent inputs in the supratrigeminal nucleus (40±18.5%) (Miyazaki and Luschei 1987). Although interspike interval variabilities were high, these units could still reliably signal speed- and position-related information. In addition to DI, we also calculated MFR during the opening phase to examine the effect of speed changes in overall firing rates on all units with a dynamic response. All units that showed a significant relationship between DI and/or MFR, and the speed of jaw opening are illustrated

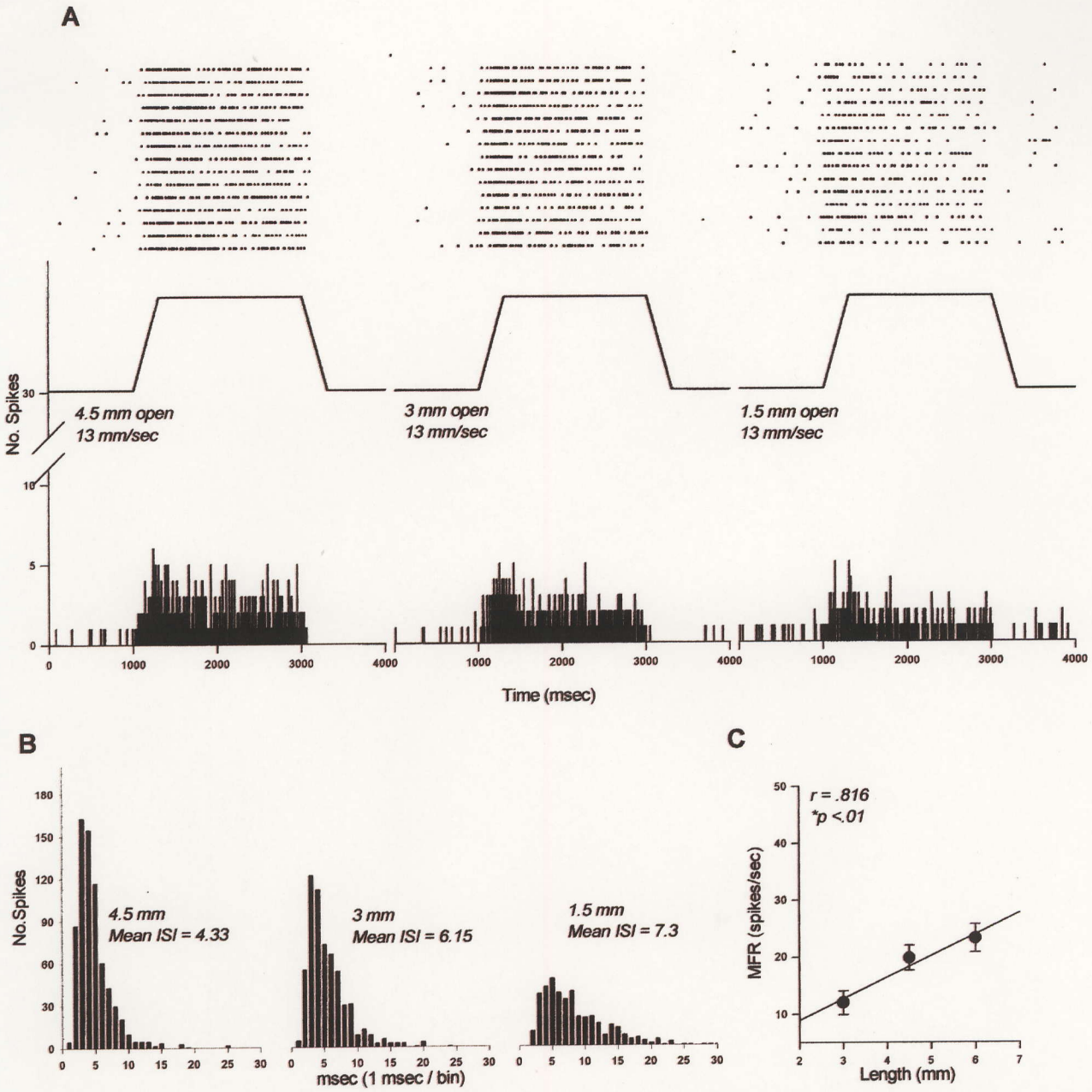


**Fig. 4A–C** Position-sensitive response. **A** Raster displays and peristimulus time histograms showing responses of an amplitude-sensitive unit to three different amplitudes. Upward deflections of each ramp wave denote jaw opening at 13 mm/s. Interspike interval histograms for different amplitudes tested are shown in **B**. **C** Mean firing rate during the holding phase of the ramp-and-hold movements was highly correlated with the amplitude of jaw opening

in Fig. 5. It is interesting to note that, in all cases, MFR yielded a higher regression coefficient than DI (Table 1). In some units, MFR alone showed a significant relationship to the speed changes. This result is presumably strongly influenced by high variability in the instantaneous firing rate among these neurons. The relationships of MFR and the length of jaw opening for all position-sensitive units are shown in Fig. 5C. All length-sensitive units showed a high correlation between MFR and the changes in jaw position.

Reconstructions of electrode penetrations revealed that these cells were concentrated 2–3 mm rostral to the obex, in the medial edge of Vi and in the adjacent reticular formation (Fig. 6). These cells were rostral and medial to the movement-related Vi neurons that receive low-threshold cutaneous inputs (Ro and Capra 1995) and dorsal to neurons that process nociceptive inputs from craniofacial muscles (Hayashi et al. 1984).

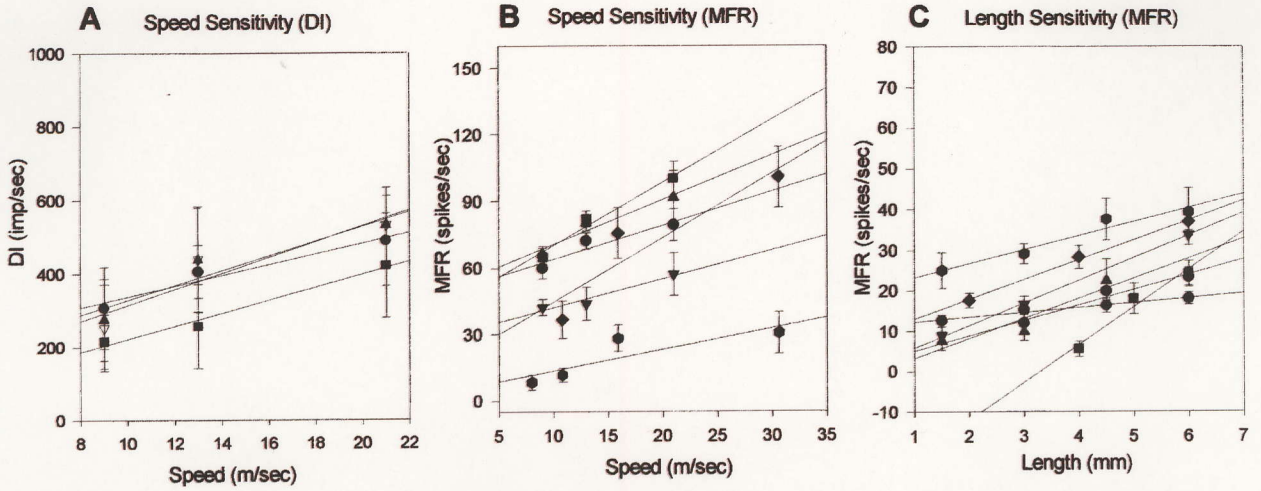


**Fig. 5A–C** Regression plots for all units. Speed-sensitivity of all units that showed the dynamic response. **A**, **B** Linear regression lines obtained with both dynamic index (*DI*) and mean firing rate (*MFR*) are plotted to compare the sensitivity of these measures. Similarly, amplitude sensitivity of all units that showed a significant relationship between MFR and the amplitude of jaw opening is evaluated (**C**)

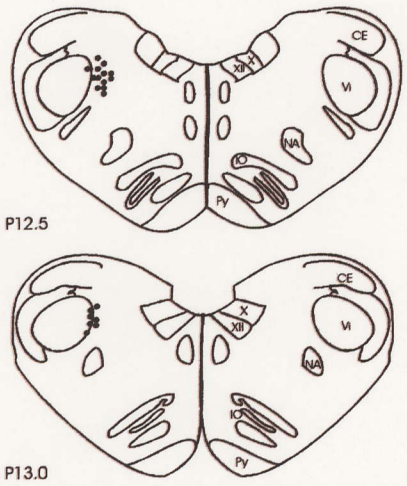


**Fig. 6** Histological reconstruction of recording sites for all 20 neurons. The neurons receiving jaw muscle-spindle afferent inputs were concentrated at the dorsal medial border of Vi and the adjacent reticular formation, between 1.5 and 2.5 mm rostral to the obex. *XII* Hypoglossal nucleus, *CE* external cuneate nucleus, *X* dorsal motor nucleus of the vagus, *NA* nucleus ambiguus, *IO* inferior olive nucleus, *Py* pyramidal tract

## Discussion

### Origin of the jaw movement-related responses

In this study we identified a group of neurons in the brainstem at the level of Vi that responded to passive jaw movements in a consistent and reproducible manner. Previous studies have shown that jaw movements can activate the receptors embedded in the skin (Appenteng et al. 1982; Ro and Capra 1995), muscles of mastication (Cody and Taylor 1973; Cody et al. 1975; Goodwin and Luschei 1975; Larson et al. 1981, 1983; Taylor and Cody 1974; Taylor and Davey 1968), and in the temporomandibular joint (TMJ) (Kawamura and Abe 1974; Klineberg et al. 1971; Lund and Matthews 1981). However, we believe that the most likely origin of the jaw movement-related activity described in this report is mechanical activation of jaw-muscle spindles. All units responded maximally during muscle lengthening and were even excited with minimal jaw movements, suggestive of muscle-spindle activation. Two basic response patterns were identified. One group had physiological properties similar to those described for muscle-spindle primaries in that they exhibited a clear dynamic response at the onset of stretch, deceleration response after the peak ramp stretch, and silence during closure (Cheney and Preston 1976; Crowe and Matthews 1964; Edin and Vallbo 1990; Harvey and Matthews 1961; Inoue et al. 1981). Firing patterns of these neurons were highly correlated with the changes in jaw opening speed. The second group lacked an initial burst at the onset of stretch and deceleration response at the onset of static hold. Instead, firing rates of these neurons were highly correlated to the amplitude of jaw stretch. These properties were comparable to those described for muscle-spindle secondaries (Cheney and Preston 1976; Cody et al. 1975; Inoue et al. 1981; Stein and Matthews 1965).

Furthermore, all of the units reported in this study were sensitive to gentle palpation of either the masseter or temporalis muscle. Some of the neurons that responded to palpation of the masseter muscle also responded to electrical stimulation of the masseter nerve (6/6 tested). Although we did not test all units with electrical nerve stimulation, no qualitative differences were evident in the response characteristics to jaw stretch between the masseter units identified by palpation only and the units identified by both mechanical and electrical stimuli. These units were not responsive to light mechanical

stimulation of the hair or skin overlying the muscle, or to mechanical stimulation of other oral and perioral tissues or of the region surrounding TMJ. Therefore, it is unlikely that the movement-related responses described in this report originated from cutaneous or joint receptors. The possibility that the stretch-evoked responses may have been generated from Golgi tendon organ was also considered unlikely since none of the units showed increased activity during muscle shortening (jaw closing) (Edin and Vallbo 1990). Admittedly, the identification of tendon-organ responses in jaw muscles is clearly a problematic issue (Taylor 1990).

## Caudal projections of jaw muscle spindles

The results of the present study provide the first physiological evidence that jaw muscle-spindle afferents project at least to the levels of Vi, where the recordings of these units were made. It is important to consider, however, whether the unitary responses described in this report were obtained from second-order brainstem neurons that process muscle-spindle inputs or from the axon collateral of Vmes muscle-spindle afferents that project more caudally. We believe that the responses described in this report were obtained from central neurons based on the following observations.

First, our analysis on ISI variability yielded values that are comparable to those obtained from second-order neurons in Vsup that received muscle-spindle inputs (Miyazaki and Luschei 1987). Miyazaki and Luschei showed that the Vsup neurons faithfully process first-order muscle afferent inputs and provide meaningful information about jaw movements. However, on a more quantitative basis, the second-order neurons in Vsup showed much higher interspike-interval variabilities when compared with the first-order muscle-spindle afferents. Similar results were obtained from the cells in Clarke's column that receive muscle-spindle inputs from the limb (Kröller and Grüsser 1982). The high ISI variability seen in central units may reflect convergence of multiple muscle-spindle afferents onto a single central neuron (Kröller and Grüsser 1982; Mann 1983). This may account for high DI variability of speed-sensitive units described in this report. The irregular firing patterns of these units resulted in unusually high DI values, even with a suppressed fusimotor activity by anesthetic and muscle relaxant. This may also explain the higher regression coefficients obtained using MFR in assessing speed-sensitivity. Although the information about jaw-speed changes was still preserved in DI, averaging firing rates, regardless of the temporal pattern of responses, provided a better measurement of speed changes.

Secondly, neurons that were activated by electrical stimulation of the masseter nerve displayed response properties suggestive of second-order neurons. The latencies to the masseter nerve stimulation ranged from 2.5–8 ms. This range was considerably longer than that reported by Shigenaga and his colleagues (0.7–1.3 ms), who made recordings from muscle spindles in the region between the Vmes tract and Vmot (Shigenaga et al. 1988), even if we consider the longer travel distance to the caudal brainstem. In addition, none of the six units followed electrical stimulation of the masseter nerve at a high frequency. In fact, all of these neurons yielded oscillating latencies even at stimulating frequency of 1 Hz (Fig. 3D).

Finally, anatomical studies provide further support for the neurons described in this report as central units. Vmes cells have been shown to project caudally to medial border of the descending trigeminal nucleus and the adjacent reticular formation (Luschei 1987; Walberg 1984). These areas were suggested as potential relay sites of jaw muscle-spindle afferents. Recently, Luo and Dessem (1996) reported that transneuronally labeled cells following intracellular injection of biotinamide into physiologically identified jaw muscle-spindle afferent axons were most frequently encountered in the dorsal-medial portion of Vi in the rat. This area is comparable to the recording site in the present study. Taken together, these results provide compelling evidence that the units described in this report are central units that receive jaw muscle-spindle input.

## Functional considerations

A potential role of the caudal projection can be envisaged as providing a neural pathway for signaling mandibular kinesthesia. While electrophysiological and anatomical studies have characterized the neural pathways for limb and digit kinesthesia (for reviews, see McCloskey 1978; Weisendanger and Miles 1982) a comparable pathway for jaw kinesthesia has not been described. Electrophysiological studies of the cerebral cortex have shown that movement-related information from the muscles of mastication and other deep structures reach cerebral cortex in subhuman primates (Huang et al. 1988; Sirisko and Sessle 1983) and in cats (Landgren and Olsson 1980; Lund and Sessle 1974). Langren and Olsson (1980) also demonstrated the projections of low threshold afferents from the oral cavity and the face to the cerebral cortex in the cat. These studies showed that area 3a of the cortex is the main cortex of low-threshold muscle-afferent input, consistent with data from the spinal system. However, it has not been clearly demonstrated how jaw muscle-spindle afferent information reach the thalamus and, ultimately, the cerebral cortex.

Miyazaki and Luschei (1987) offered the possibility that cells in Vsup or dorsal principal sensory nucleus may relay muscle spindle information to the ipsilateral thalamus for cranial proprioception in cats. However, we found little evidence to support a substantial relay of muscle afferent input from these areas to thalamus (Ro and Capra 1994). Recently, we reported a group of neurons in Vi that provided reliable information about the status of the jaw to the thalamus for further processing (Capra et al. 1994; Ro and Capra 1995). These neurons received inputs from a variety of peripheral structures in-

cluding muscle. The presence of a small group of jaw movement-related neurons with muscle spindle-like properties, located in close proximity to movement-related neurons with convergent receptive fields, strongly suggest that Vi and adjacent reticular formation are potential sites for processing and relaying of proprioceptive inputs from jaw muscle spindles and other afferents to the thalamus.

Another important role that this caudal projection may play is the provision of muscle-spindle inputs to the cerebellum. The cerebellum performs a delicate coordination of multiple peripheral structures in order for complex motor behaviors to be performed properly. Such coordination depends on temporally and spatially organized sensory inputs to the cerebellum (Welsh et al. 1995). Numerous studies have demonstrated Vi as a major projection site to the cerebellum in the trigeminal system (Bukowska 1996; Ikeda 1979; Kruger 1979; Ohya et al. 1993; Somana 1980; Woolston et al. 1982). Although trigeminocerebellar connections are not exclusive to Vi, they have long been considered to be the cranial homolog of the spinocerebellar system (Kruger 1979). Therefore, the caudal projection from Vmes muscle spindle afferents is well suited to provide relevant information to the cerebellum after a relay in Vi and adjacent reticular-formation neurons (Ikeda 1979; Somana 1980) or via olivocerebellar projections (Walberg 1982) for coordination of complex oral motor behaviors, such as mastication and swallowing.

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## References


Appenteng K, O'Donovan MJ, Somjen G, Stephens JA, Taylor A (1978) The projection of jaw elevator muscle spindle afferents to fifth nerve motoneurones in the cat. J Physiol 279:409–423

Appenteng K, Lund JP, Seguin JJ (1982) Behavior of cutaneous mechanoreceptors recorded in mandibular division of Gasserian ganglion of the rabbit during movements of lower jaw. J Neurophysiol 47:151–166

Bukowska D (1996) Trigeminocerebellar projection to the paramedian lobule with emphasis on the climbing fiber zones: a retrograde tracing study in the rabbit. J Hirnforsch 37:159–172

Capra NF, Wax TD (1989) Distribution and central projections of primary afferent neurons that innervate the masseter muscle and mandibular periodontium: a double-label study. J Comp Neurol 279:341–352

Capra NF, Ro JY, Wax TD (1994) Physiological identification of jaw-movement-related neurons in the trigeminal nucleus of cats. Somatosens Mot Res 11:77–88

Cheney PD, Preston JB (1976) Classification and response characteristics of muscle spindle afferents in the primate. J Neurophysiol 39:1–8

Cody FW, Taylor A (1973) The behavior of spindles in the jaw closing muscles during eating and drinking in the cat. J Physiol 231:49–50

Cody FW, Harrison LM, Taylor A (1975) Analysis of activity of muscle spindles of the jaw-closing muscles during normal movements in the cat. J Physiol 253:565–582

Corbin KB (1942) Probst's tract in the cat. J Comp Neurol 77:455–467

Crowe A, Matthews PB (1964) The effects of stimulation of static and dynamic fusimotor fibers on the response of stretching of the primary endings of muscle spindles. J Physiol 174:109–131

Dessem D, Taylor A (1989) Morphology of jaw-muscle spindle afferents in the rat. J Comp Neurol 282:389–403

Dessem D, Donga R, Luo P (1997) Primary- and secondary-like jaw-muscle spindle afferents have characteristic topographic distributions. J Neurophysiol 77:2925–2944

Edin BB, Vallbo AB (1990) Dynamic response of human muscle spindle afferents to stretch. J Neurophysiol 63:1297–1306

Goodwin GM, Luschei ES (1975) Discharge of spindle afferents from jaw closing muscles during chewing in alert monkeys. J Neurophysiol 38:560–571

Harvey RJ, Matthews PB (1961) The response of de-efferented muscle spindle endings in the cat's soleus to slow extension of the muscle. J Physiol 157:370–392

Hayashi H, Sumino R, Sessle BJ (1984) Functional organization of trigeminal subnucleus interpolaris: nociceptive and innocuous afferent inputs, projections to thalamus, cerebellum and spinal cord, and descending modulation from periaqueductal gray. J Neurophyiol 51:890–905

Huang CS, Sirisko MA, Hiraba H, Murray GM, Sessle BJ (1988) Organization of the primate face motor cortex as revealed by intracortical microstimulation and electrophysiological identification of afferent inputs and corticobulbar projections. J Neurophysiol 59:796–818

Ikeda M (1979) Projections from the spinal and the principal sensory nuclei of the trigeminal nerve to the cerebellar cortex in the cat, as studied by retrograde transport of horseradish peroxidase. J Comp Neurol 184:567–585

Inoue H, Morimoto T, Kawamura Y (1981) Response characteristics and classification of muscle spindles of the masseter muscle in the cat. Exp Neurol 74:548–560

Kawamura Y, Abe K (1974) Role of sensory information from temporomandibular joint. Bull Tokyo Med Dent Univ [Suppl] 21:78–82

Kishimoto H, Bae YC, Yoshida A, Morotani M, Takemura M, Nakagawa S, Nagase Y, Wada T, Sessle BJ, Shigenaga Y (1998) Central distribution of synaptic contacts of primary and secondary jaw muscle spindle afferents in the trigeminal motor nucleus of the cat. J Comp Neurol 391:50–63

Klineberg IJ, Greenfield BE, Wyke BD (1971) Afferent discharges from temporomandibular articular mechanoreceptors. Arch Oral Biol 16:1463–1479

Kolta A, Lund JP, Westberg K-G, Clavelou P (1995) Do muscle-spindle afferents act as interneurons during mastication? Trends Neurosci 18:41

Kröller J, Grüsser OJ (1982) Convergence of muscle spindle afferents on single neurons of the cat dorsal spinocerebellar tract and their synaptic efficacy. Brain Res 253:65–80

Kruger L (1979) Functional subdivision of the brainstem sensory trigeminal nuclear complex. Adv Pain Res Ther 3:197–209

Langren S, Olsson KÅ (1980) Low threshold afferent projections from the oral cavity and the face to the cerebral cortex of the cat. Exp Brain Res 39:133–147

Larson CR, Smith A, Luschei ES (1981) Discharge characteristics and stretch sensitivity of jaw muscle afferents in the monkey during controlled isometric bites. J Neurophysiol 46:130–142

Larson CR, Finocchio DV, Smith A, Luschei ES (1983) Jaw muscle afferent firing during an isotonic jaw-positioning task in the monkey. J Neurophysiol 50:61–73

Lennerstand G (1968) Position and velocity sensitivity of muscle spindles in the cat. I. Primary and secondary endings deprived of fusimotor activation. Acta Physiol Scand 73:281–299

Lund JP, Matthews B (1981) Responses of temporomandibular joint afferents recorded in the Gasserian ganglion of the rabbit to passive movements of the mandible. In: Kawamura Y, Dubner R (eds) Oral-facial sensory and motor functions. Quintessence, Tokyo Berlin Chicago, pp 153–160

Lund JP, Sessle BJ (1974) Ora-facial and jaw muscle afferent projections to neurons in cat frontal cortex. Exp Neurol 45:314–331

Luo P (1991) Morphological characteristics and terminating patterns of masseteric neurons of the mesencephalic trigeminal nucleus in the rat: an intracellular horseradish peroxidase labeling study. J Comp Neurol 303:286–299

Luo P, Dessem D (1996) Transneuronal transport of intracellularly injected biotinamide in primary afferent axons. Brain Res Bull 39:323–334

Luschei ES (1987) Central projections of the mesencephalic nucleus of the fifth nerve: an autoradiographic study. J Comp Neurol 263:137–245

Mann MD (1983) Clarke's column and the dorsal spinocerebellar tract: a review. Brain Behav Evol 7:34–83

Matsushita M, Okado N, Ikeda M, Hosoya Y (1981) Descending projections from the spinal and mesencephalic nuclei of the trigeminal nerve to the spinal cord in the cat. A study with the horseradish peroxidase technique. J Comp Neurol 196:173–187

McCloskey DI (1978) Kinesthetic sensibility. Physiol Rev 58:763–820

Miyazaki R, Luschei ES (1987) Responses of neurons in nucleus supratrigeminalis to sinusoidal jaw movements in the cat. Exp Neurol 96:145–157

Mizuno N, Sauerland EK (1970) Trigeminal proprioceptive projections to the hypoglossal nucleus and the cervical ventral gray column. J Comp Neurol 139:215–226

Ohya A, Tsuruoka M, Imai E, Fukunaga H, Shinya A, Furuya R, Kawawa T, Matsui Y (1993) Thalamic- and cerebellar- projecting interpolaris neuron responses to afferent inputs. Brain Res Bull 32:615–621

Ro JY, Capra NF (1994) Receptive field properties of trigeminothalamic neurons in the rostral trigeminal sensory nuclei of cats. Somatosen Mot Res 11:119–130

Ro JY, Capra NF (1995) Encoding of jaw movements by central trigeminal neurons with cutaneous receptive fields. Exp Brain Res 104:363–375

Ro JY, Capra NF (1998) Jaw muscle spindle-like responses in the caudal brainstem. Soc Neurosci Abstr 24:2080

Shigenaga Y (1988) The central projection of masticatory afferent fibers to the trigeminal sensory nuclear complex and upper cervical spinal cord. J Comp Neurol 268:489–507

Sirisko MA, Sessle BJ (1983) Corticobulbar projections and orofacial and muscle afferent inputs of neurons in primate sensorimotor cerebral cortex. Exp Neurol 82:716–720

Somana R (1980) Cerebellar afferents from the trigeminal sensory nuclei in the cat. Exp Brain Res 38:57–64

Stein RB, Matthews PBC (1965) Differences in variability of discharge frequency between primary and secondary muscle spindle afferent endings of the cat. Nature 208:1217–1218

Taylor A (1990) Neurophysiology of the jaws and teeth. Macmillan, London

Taylor A, Cody FW (1974) Jaw muscle spindle activity in the cat during normal movements of eating and drinking. Brain Res 71:523–530

Taylor A, Davey MR (1968) Behavior of jaw muscle stretch receptors during active and passive movements in cats. Nature 220:301–302

Walberg F (1982) The trigemino-olivary projection in the cat as studied with retrograde transport of horseradish peroxidase. Exp Brain Res 45:101–107

Walberg F (1984) The medullary projection from the mesencephalic trigeminal nucleus. An experimental study with comments on the intrinsic trigeminal connections. Exp Brain Res 56:377–383

Weisendanger M, Miles TS (1982) Ascending pathway of low-threshold muscle afferents to the cerebral cortex and its possible role in motor control. Physiol Rev 62:1234–1270

Welsh JP, Lang EJ, Sugihara I, Llinás R (1995) Dynamic organization of motor control within the olivocerebellar system. Nature 374:453–457

Woolston DC, La Londe JR, Gibson JM (1982) Comparison of response properties of cerebellar- and thalamic- projecting interpolaris neurons. J Neurophysiol 48:160–173