Abstract of Thesis

Name (Md Sams Sazzad Ali)	
Title	Orofacial Proprioceptive Thalamus in the Rat （ラットの口腔顔面領域の固有感覚が入力する視床部位の解明）

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Introduction

Proprioceptive sensation from the body is conveyed to the rostrodorsal shell or rostral (oral) region (or VPLo) of the ventral posterolateral thalamic nucleus (VPL). However, little is known about the thalamic relay of proprioceptive inputs from the orofacial area. Thus, the major aim of this study is to obtain detailed information on the thalamic relay of orofacial proprioceptive information. Fujio et al. (2016) have revealed that the proprioception arising form the jaw-closing muscle spindles (JCMSs) is conveyed by neurons in the the trigeminal mescencephalic nucleus to the supratrigeminal nucleus (Su5), and the Su5 receives only the JCMS proprioception among the orofacial sensations. In the present study, therefore, to identify the thalamic "orofacial proprioception-center" receiving JCMS inputs, we examined the thalamic projections from the Su5 by using neuronal tract tracing and electrophysiological recording methods in rats.

Earlier electrophysiological studies demonstrated that cutaneous and proprioceptive sensations from the body are separately encoded in different regions of VPL. Thus, the present study was designed to examine whether the JCMS proprioceptive sensation mediated via the Su5 neurons and the other orofacial sensations mediated via the neurons in the trigeminal sensory nuclear complex are encoded convergently or separately in the ventral posteromedial thalamic nucleus (VPM), by comparing thalamic projections of these distinct trigeminal neurons.

Materials and methods

Thirty male Wistar rats were used. All experimental procedures were approved by the Osaka University Graduate School of Dentistry Intramural Animal Care and Use Committee. The rats were anesthetized with sodium pentobarbital. In Experiment 1, after the Su5 was identified by recording large field potentials evoked by electrical stimulation of the masseter nerve or by passive, sustained jaw-opening movements, an anterograde tracer, biotinylated dextranamine (BDA), was injected into the Su5. In Experiment 2, electrophysiological mapping was done to find the VPM regions and its surrounding thalamus, which include neurons responsive to electrical stimulation of the masseter or lingual nerve. Soon after the mapping, horseradish peroxidase (HRP) was injected into the recording sites. In Experiment 3, a retrograde tracer, wheat-germ agglutinin conjugated horseradish peroxidase (WGA-HRP) or Fluorogold (FG), was injected into the VPM where the largest field potentials were recorded after the electrical stimulation of the masseter nerve and during passive, sustained jaw-opening movements. In Experiment 4, WGA-HRP or FG was injected into the core VPM where the largest field potentials were recorded after electrical stimulation of the lingual nerve. After a post injection survival, the animals were re-anesthetized deeply and perfused

with a fixative. The entire brain was removed and cut coronally at 60-μm thickness on a freezing microtome. To detect the labeling of BDA, HRP, WGA-HRP, and FG, the sections were reacted using ABC and DAB methods, or DAB method, TMB method, and anti-FG antibody and ABC and DAB methods, respectively.

Results

In Experiment 1, after BDA injection in the electrophysiologically identified Su5, many anterogradely BDA-labeled axon fibers and terminals were observed mainly in the caudo-ventromedial edge of the VPM (termed VPMcvm) bilaterally with a contralateral predominance to the BDA injection site. No terminals were observed in the core VPM.

In Experiment 2, in the VPMcvm, the largest negative field potentials with 4.0 msec latency were evoked by stimulation of the masseter nerve, and multi-unit discharges were induced during passive, sustained jaw-opening. However, no responses were evoked by stimulation of the lingual nerve. On the other hand, in the core of VPM rostrally adjacent to the VPMcvm, large negative potentials with 4.2 msec latency were evoked by stimulation of the lingual nerve, whereas no responses were evoked by stimulation of the masseter nerve.

In Experiment 3, after WGA-HRP or FG was injected in the electrophysiologically identified VPMcvm, many labeled neurons were contralaterally found in the Su5, especially in its caudal part, and in the dorsomedial edge of the principal sensory trigeminal nucleus (Pr5) laterally adjacent to the Su5. However, no neurons were labeled in the parabrachial nucleus, the Pr5 (except for its dorsomedial edge), and the spinal trigeminal nucleus (Sp5).

In Experiment 4, after WGA-HRP or FG was injected in the core VPM where large responses were evoked by stimulation of the lingual nerve, many retrogradely labeled neurons were contralaterally seen in the dorsomedial part of Pr5 (except for its dorsomedial edge) and dorsomedial part of Sp5. However, no neurons were labeled in the Su5 and the dorsomedial edge of Pr5.

Conclusion

The present study has for the first time revealed the detailed thalamic relay of JCMS proprioceptive inputs; the relay site was confined to a small region in the VPM (i.e., VPMcvm) which had not been predicted in previous studies. The present study also indicated that there exist two completely distinct trigeminothalamic pathways: the Su5 (and the dorsomedial edge of Pr5)-VPMcvm pathway conveying JCMS proprioception, and the core Pr5 and Sp5-core VPM pathway conveying orofacial sensations except for the JCMS proprioception. Therefore, the present study provides an important contribution to our understanding of the organization of ascending sensory proprioceptive pathways.

様式７

論文審査の結果の要旨及び担当者

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論文審査の結果の要旨

本研究により、ラットにおいて、閉口筋筋紡錘に生ずる固有感覚（閉口筋筋紡錘感覚）は、三叉神経上核(Su5)から、これまで考えられてきた視床腹側基底核群の吻背部(shell領域）ではなく、主に視床後内側腹側核の尾腹内側縁（VPMcvm）に反対側優位に投射することが明らかになった。また、この Su5-VPMcvm 路を閉口筋紡錘感覚が伝達されることが示された。VPMcvm は他の口腔顔面感覚が伝達される三叉神経感覚核群経由の投射は受けず、閉口筋筋紡錘感覚と他の口腔顔面感覚の視床投射は、並行しているが、別の経路であることも明らかになった。ヒトでも同様の感覚情報の伝達機構が存在すると考えられる。

以上より本研究は、運動に関与する固有感覚情報の脳内伝達機構を研究する上で重要な知見を与えるものであり、博士（歯学）の学位を授与するに値するものと認める。