

Summary of Thesis Examination

Report No.	Diploma No. 601		Applicant	Ashis Dhar
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The periodontium damage induces neuronal cell death in the trigeminal mesencephalic nucleus and neurodegeneration in the trigeminal motor nucleus in C57BL/6J mice

(歯周組織の傷害は C57BL / 6J マウスにおいて三叉神経中脳路核の神経細胞死および三叉神経運動核の神経変性を生じる)

Proprioception from masticatory apparatus and periodontal ligaments comes through the trigeminal mesencephalic nucleus (Vmes). In terms of absolute size, the human cells are considerably larger than the mouse cells. Considering the distribution of neurotrophic receptors and the cell size as one way of characterizing the general composition of DRGs, previously reported characterizations at this level showed no significant differences between human and mouse sensory ganglia. Trans activation responsive region (TAR)-DNA-binding protein 43 (TDP-43) was considered to be a disease-specific component of ubiquitin-positive and tau-negative inclusions in the brains of patients with frontotemporal lobar degeneration with ubiquitin-positive inclusions (FTLD-U) and amyotrophic lateral sclerosis (ALS). The distribution of TDP-43 immunoreactivity in the hippocampus and frontal cortex in Alzheimer disease appear to be different. Previous studies have been conducted into 3xtg mice for Vmes neuron death and tooth extraction, but 3xtg type has the A β formation disturbance. A β formation can also cause neuronal cell death in transgenic type of mouse. We evaluated the effects of tooth loss on neuro-degeneration of the Vmes and trigeminal motor nucleus (Vmo) in C57BL/6J mice. Bilateral maxillary molars of 2-month-old C57BL/6J mice were extracted under anesthesia.

As a result, the following findings were clarified in this study.

- 1) Neural projections of the Vmes to the periodontium were confirmed by injecting both retrograde and anterograde tracer (FG and AAV-GFP). Vmes neurons projecting to the PDL were significantly smaller than those projecting to the muscle.
- 2) At 1 month after tooth extraction, the number of Piezo2-immunoreactive (IR) Vmes neurons were decreased significantly. ATF3-IR neurons were detected on day 5 after tooth extraction. Dead cleaved caspase-3-IR neurons were found among Vmes neurons on days 7 and 12.
- 3) In the Vmo, neuronal cytoplasmic inclusions (NCIs) formation type of TDP-43 increased at 1 and 2 months after extraction.

These indicate the existence of neural projections from the Vmes to the periodontium in mice and that tooth loss induces the death of Vmes neurons followed by TDP-43 pathology in the Vmo. Therefore, tooth loss induces Vmes neuronal cell death, causing Vmo neuro-degeneration and possibly affecting masticatory function.

This study investigated changes in nerves after tooth extraction, and as a result, it was shown that neuronal death of the trigeminal mesencephalic nucleus and neurodegeneration of the motor nucleus of the trigeminal nerve occur after tooth extraction. It is noteworthy that tooth loss has an effect on the central nervous system. Therefore, this research was judged to be of sufficient value as a dissertation.