# Soft-diet feeding impairs olfactory functions via changes in neural connections

Mastication ability correlates with cognitive impairment in elderly persons. A longitudinal study of aging and Alzheimer's disease indicates that participants with the fewest teeth had the highest prevalence and risk of incidence of dementia. There are abnormalities in the sense of smell having both raised olfactory thresholds and impaired odor identification in elderly subjects and patients suffering from Alzheimer's disease. The subventricular zone (SVZ) generates an immense number of neuroblasts even during adulthood. These neuroblasts migrate to the olfactory bulb (OB) via the rostral migrating stream and differentiate into interneurons, which modulate the information of various odorants received by the olfactory sensory neurons. Animal models have shown that a reduction of mastication by feeding only a soft-diet impairs both olfactory functions and neurogenesis in the SVZ.

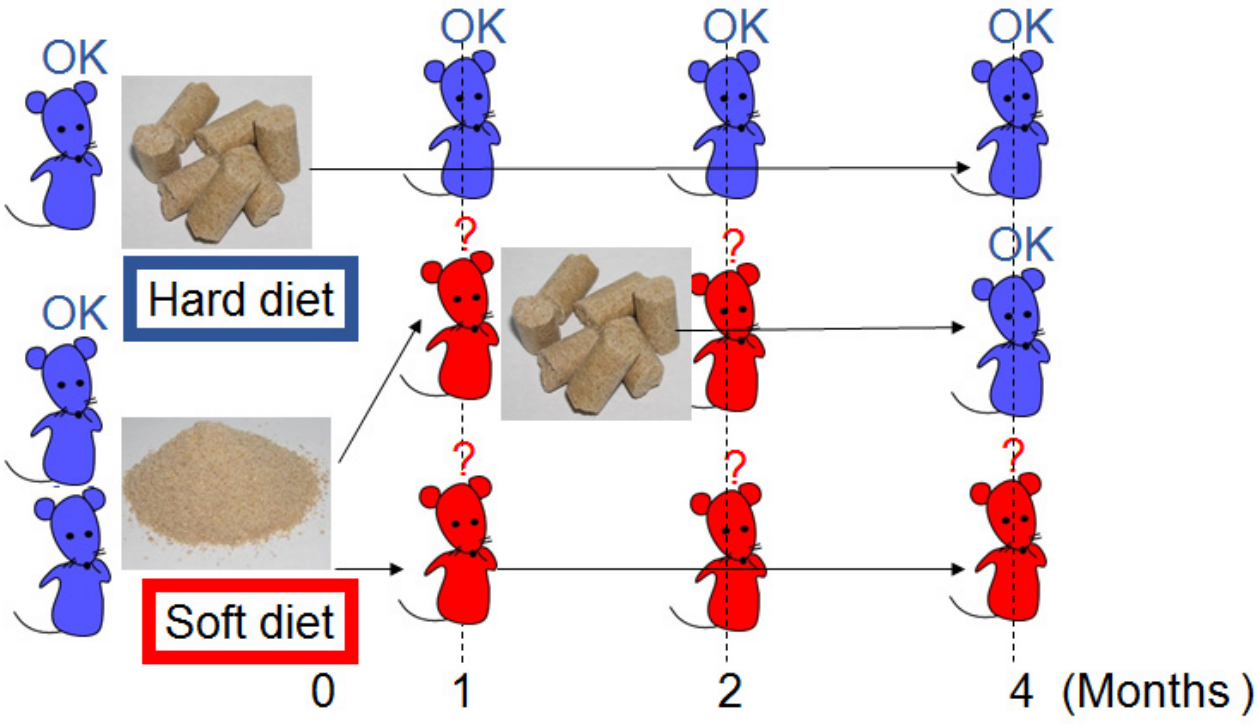


Fig. 1. Blue and red mice have normal and impaired olfactory functions, respectively.

Avoidance of butyric acid, which has a stink odor, is reduced in mice feeding only the soft-diet for 1 month. Neural responses at the OB and pyriform cortex to odors are also reduced by the soft-diet feeding. Release of GABA from inhibitory interneurons at the OB induces inhibitory currents at the

mitral cells, which are output neurons from the OB. The soft-diet feeding extends the intervals between spontaneous inhibitory postsynaptic currents of the mitral cells, which are induced by GABA released from inhibitory neurons at the OB, and reduced their peak amplitudes, indicating that soft-diet feeding in mice attenuates the neural functions of inhibitory interneurons at the OB. The density of newly generated cells in the SVZ and OB is lower in the soft-diet-fed mice than in the hard-diet-fed mice. At 3 months of hard-diet feeding, avoidance of butyric acid was reversed and responses to odors and neurogenesis in the SVZ of mice impaired by soft-diet feeding are recovered. This indicates that feeding with a hard diet improves neurogenesis in the SVZ, which in turn enhances olfactory function at the OB.

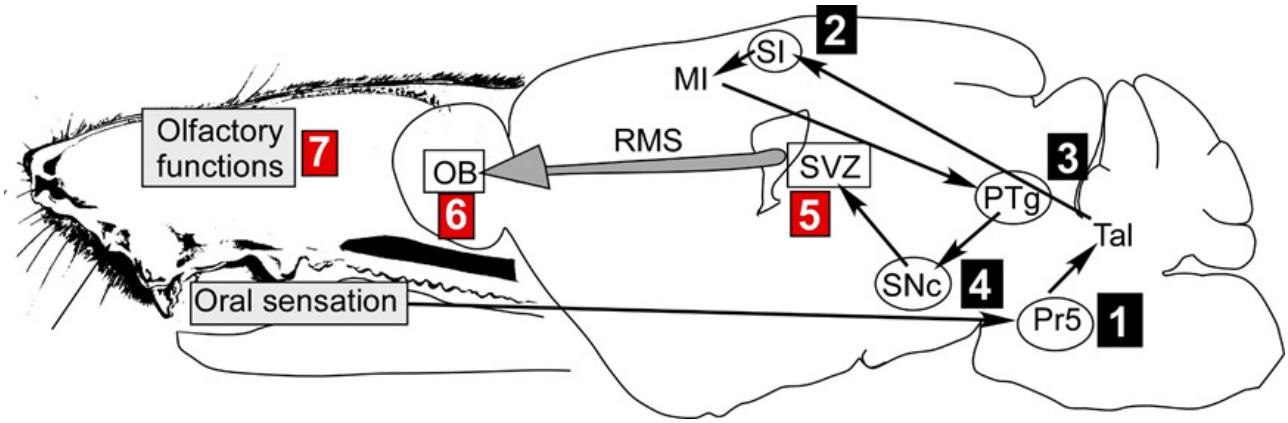


Fig. 2. Neural circuit regulating olfactory functions. Pr5: principal sensory trigeminal nucleus; Tal: thalamus; S1: somatosensory cortex; M1: motor cortex; PTg: pedunculopontine tegmental nucleus; SNc: substantia nigra pars compacta; SVZ: subventricular zone; RMS: rostral migrating stream; OB: olfactory bulb.

At this time, it is unclear how impaired mastication decreases and how hard-diet feeding recovers neurogenesis at the SVZ. Ingestion of a hard diet induces greater neural responses at the principal sensory trigeminal nucleus (Pr5), which receives intraoral touch information via the trigeminal nerve, than does a soft diet or no diet (Fig. 2). Sensory information from ingestion of the hard diet receives at the Pr5 is transmitted to the pedunculopontine tegmental nucleus (PTg) via the thalamus (Tal), somatosensory cortex (S1), and motor cortex (M1). Ingestion of a hard diet induces remarkable neural excitation at the PTg. Cholinergic and glutamatergic neurons of the PTg innervate to the substantia nigra pars compacta (SNc). Neurons at the SNc are activated by ingestion of a hard diet. Proliferative precursors in the SVZ express dopamine receptors and receive dopaminergic afferents. Dopamine increases the proliferation of SVZ-derived cells by releasing epidermal growth factor in a PKC-dependent manner *in vitro*. Dopaminergic neurons in the SNc innervate to the SVZ. Therefore, it is possible that the feeding with a hard diet maintained neurogenesis at the SVZ via the Pr5, PTg and SNc to keep olfactory functions.

***Makoto Kashiwayanagi***
*Department of Sensory Physiology, Asahikawa Medical University, 078-8510 Asahikawa, Japan*

## Publication

Soft-diet feeding impairs neural transmission between mitral cells and interneurons in the mouse olfactory bulb.
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