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Disruption of oral sensory relay to brain increased anxiety- and depression-like behaviours in rats☆

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ABSTRACT

Objective: Sensory information plays an important role to determine psycho-emotional behaviours of individuals. Lingual nerve can be damaged by dental surgery or trauma, such as physical irritation, radiation, chemotherapy, or viral infection. This study was conducted to examine the psycho-emotional effects of lingual nerve damage in which oral sensory relay to the brain is disrupted.

Design: Male Sprague-Dawley rats were tested for anxiety and depression-related behaviours after bilateral transections of the lingual and chorda tympani nerves (Nx) or sham operation. Tissue contents of serotonin and its metabolite in the hippocampus, hypothalamus, and nucleus accumbens were analyzed by high-performance liquid chromatography.

Results: Sucrose preference was reduced in Nx rats compared with sham rats, suggesting the development of anhedonia, decreased pleasure seeking behaviour, by the lingual nerves transection. Ambulatory activity was decreased, anxiety-related behaviours during the activity test increased, time spent in the open arms during elevated plus maze test decreased, and immobility duration during forced swim test increased in Nx rats compared with sham rats. Serotonin level in the hippocampus of Nx rats was decreased significantly compared with sham rats.

Conclusions: Results suggest that aberration of oral sensory relay to brain may lead to the development of depression- and anxiety-related disorders, and decreased serotonergic neurotransmission in the hippocampus may play a role in its underlying mechanism.

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Abbreviations: Nx, bilateral transections of the lingual and chorda tympani nerves; 5-HT, 5-hydroxytryptamine; 5-HIAA, 5-hydroxyindoleacetic acid.

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1. Introduction

Sensory systems are responsible for generating an internal representation of the outside world, including its chemical (taste and olfaction) and physical (mechanical, sound, vision and temperature) features. Neuronal circuits in sensory system are closely connected with other nerve systems for efficient handling of sensory information.[1] For example, taste sensory information that reached the nucleus tractus of solitarius is principally relayed to the gustatory cortex via the parabrachial nucleus, but also targets to the other brain area such as the cerebral cortex, hippocampus, amygdala, hypothalamus and nucleus accumbens for the better storage or recall of taste memory or the innate and instinctive response such as preference and aversion.[2–4] Thus, it is suggested that the deprivation or disruption of taste sensory relays may affect the function of those brain regions.

Taste sensory system is in charge of evaluating the nutritious content of food and preventing the ingestion of toxic substances, and importantly also has the additional value of contributing to the overall pleasure and enjoyment of a meal. Eating has been viewed as a strategy to improve negative mood[5] and to mask stress,[6] and studies indicate that healthy, normal-weight persons regulate negative emotions by eating.[7,8] It has been reported that decreased responses in the reward network including the nucleus accumbens to palatable food may be a trait marker of vulnerability to depression.[9,10] In rodents, anhedonia, a reduced sensitivity to reward, which is a core symptom of major depression, can be measured by a decreased intake of and preference for sweet solutions. Indeed, sweet solutions have been shown to rapidly calm stress responses in human newborns,[11] and in adults, experimentally induced negative mood is improved immediately and selectively after eating palatable food,[12] suggesting that immediate positive affective reactions elicited by palatable foods diminish the impact of stress. Collectively, it is hypothesized that alterations in oral sensory information can modulate the psycho-emotional status of individuals.

Lingual nerve can be damaged by dental surgery or trauma such as physical irritation, radiation, chemotherapy, or viral infection. This study was conducted to define the psycho-emotional effects of the lingual nerve damage in which oral sensory relay to the brain is disrupted, and the rats were tested for anxiety- and depression-like behaviours after bilateral transections of the lingual and chorda tympani nerves. The chorda tympani nerve joins the lingual division of the trigeminal nerve, the lingual nerve, and distributes together to the fungiform papillae on the anterior two thirds of the tongue and may reach also the anterior portion of the foliate papillae. Axons of glossopharyngeal nerve supply both tastes buds and general sensory innervations to the vallate and foliate papillae, and also tastes buds in the pharynx.[13] Thus, it is expected that with bilateral transections of the lingual and chorda tympani nerves, rats may lose the sensory information from the anterior two thirds of tongue.

2. Materials and methods

2.1. *Animals*

Male Sprague-Dawley rats (200–250 g) were purchased (Orient, Co., Korea) and acclimated to the laboratory condition in a specific-pathogen-free barrier area where the temperature (22 ± 1 °C) and humidity (55%) were controlled constantly with a 12/12 h light/dark cycle (lights-on at 07:00 AM). Rats had ad libitum access to standard laboratory food (Purina Rodent Chow, Purina Co., Seoul, Korea) and tap water. All rats were habituated in the animal colonies at least for a week and were cared according to the Guideline for Animal Experiments, 2000, edited by the Korean Academy of Medical Sciences, which is consistent with the NIH Guidelines for the Care and Use of Laboratory Animals, revised 1996. All animal protocols were approved by the Committee for the Care and Use of Laboratory Animals at Seoul National University.

2.2. *Surgery*

Rats were anesthetized with an intraperitoneal injection of a 4:1 mixture of ketamine hydrochloride (100 mg/kg, Ketara®, Yuhan, Korea) and xylazine hydrochloride (25 mg/kg, Rumpun®, Bayer, Korea), and placed on the surgical plate equipped with a non-traumatic head holder. The surgical field was prepared by hair trimming and applying 10% povidone iodine, and then, a ventral–medial incision was made in the neck. Digastric and masseter muscles were bluntly dissected to allow the visualization of the chorda tympani nerve and lingual nerve as it bifurcated from the lingual branch of the trigeminal nerve. Transection of the lingual and chorda tympani nerve (Nx) was made using sharp microfine forceps; the proximal and distal stumps of the nerve cuts were visualized to verify complete transection. The wound was closed in a single layer by the use of 4-0 Nylon sutures (Ethicon®, UK). Sham surgeries were processed in an identical manner, but the nerves were not touched. Body weight gain and food intake were monitored during the post-operational recovery period.

2.3. *Sucrose drinking test*

Sucrose drinking test was performed after 10 days of post-operational recovery. Rats were divided into 4 groups ($n = 6$–8 in each group, total 28 rats); i.e., Nx groups that received either 1% or 5% sucrose and sham operated groups that received either 1% or 5% sucrose. Rats in each group were deprived from water, but not chow, for 20 h prior to the drinking test, and received free choices of sucrose solution and water for 30 min. The test sessions were repeated for 3 consecutive days, and the positions of sucrose and water bottles were exchanged daily.

2.4. *Ambulatory activity*

Another groups of Nx and sham operated rats ($n = 6$ in each group, total 12 rats) were subjected to the ambulatory test at 20 days after the surgery. On each trial, the rat was placed in the