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Research Report

Role of the lateral hypothalamus in submandibular salivary secretion during feeding in rats

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ABSTRACT

To evaluate the role of the lateral hypothalamic area (LH) in the masticatory-salivary reflex, we investigated submandibular salivary secretion and the electromyographic (EMG) activity of the jaw-closer masseter muscle in sham-operated rats and rats with unilateral LH lesions. One week prior to surgery and recording, the rats were given daily experience of eating pellets; powder; or hard, medium or soft mash, all of which were composed of laboratory chow. Salivary secretion was induced during eating and grooming behavior. During eating, the powdered food induced the highest salivary flow rate, and the soft (wet) mash induced the lowest salivary flow rate. Conversely, the amount of food consumed (dry weight) was greatest when soft mash was provided and lowest when the powder or pellets (a dry diet) were provided. The EMG activity of the masseter muscle during eating was greatest during consumption of the pellets and weakest during consumption of the powder. LH lesions that were ipsilateral to the examined submandibular gland reduced salivary secretion to about 20–30% of the control value, whereas contralateral LH lesions reduced it to about 40–50% of the control value. Neither masseter muscle EMG activity nor food consumption was markedly affected by the presence of an LH lesion. These results suggest that the texture of food, especially its water content, affects the flow rate of saliva and that the LH is heavily involved in the masticatory-salivary reflex.

1. Introduction

Salivary secretion is solely and entirely regulated by the sympathetic and parasympathetic autonomic nervous systems. The sympathetic nervous system is mainly responsible for protein secretion, whilst the parasympathetic nervous system controls fluid secretion. Profuse amounts of saliva are secreted during feeding, which is conventionally called the masticatory-salivary reflex. This reflex, which involves activation of the autonomic nervous system, is initiated and maintained by various oral and pharyngeal sensory afferents, including mechanoreceptors in the periodontal membrane and gingivae, and taste bud activation (for review, see Hector and Linden, 1999). In unanesthetized decerebrate rats, only a small amount of saliva is secreted in the presence of moderate sensory inputs, such as those induced by chewing, and relatively strong stimulation, such as pinching of the oral structures or the infusing of a rejectable solution of quinine

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and HCl, is required to induce the secretion of much greater amount of saliva (Matsuo et al., 1989; 2001). In a recent study of rats, we showed that electrical stimulation of the masticatory area of the cerebral cortex induced the secretion of a similar amount of saliva to that seen during chewing (Maeda et al., 2014). This cortical area is one of the two masticatory areas that partially overlap with the taste and oral sensory areas in the insular cortex. These findings suggest that a descending pathway from the cerebral cortex is involved in the masticatory-salivary reflex arc.

Neuroanatomical studies involving rats have demonstrated that corticofugal fibers from the masticatory area in the insular cortex terminate in the ipsilateral LH and the central nucleus of the amygdala (Zhang and Sasamoto, 1990), and moreover, have suggested that the superior salivatory nucleus (the parasympathetic neurons innervating the submandibular and sublingual salivary glands) mainly receives neural projections from forebrain areas such as the LH, the central nucleus of the amygdala, the hypothalamic paraventricular nucleus, and the cerebral cortex (Hübschle et al., 1998; Jansen et al., 1992; Matsuo, 1999). Among these forebrain regions, the rat LH possesses descending fibers that terminate in the ipsilateral superior salivatory nucleus (Hosoya and Matsushita, 1981; Hosoya et al., 1983). Our previous electrophysiological study demonstrated that electrical stimulation of the rat LH predominantly activated the ipsilateral parasympathetic neurons that innervate the submandibular and sublingual salivary glands (Matsuo and Kusano, 1984). These findings strongly suggest that the superior salivatory nucleus receives strong descending projections from the LH, which might play an important role in salivation during feeding.

The LH relates to many different functions such as food intake, drinking, motor/motivation, metabolism, and autonomic responses including salivation (Bernardis and Bellinger, 1993; Berthoud, 2002; Yamamoto, 2006). The earlier studies have reported that rats with bilateral LH lesions showed prandial drinking similar to the surgically or pharmacologically desalivated rats suggesting interruption of salivary secretion (Epstein, 1971; Kissileff and Epstein, 1969; Teitelbaum and Epstein, 1962). Subsequent reports have shown that LH lesions, after recovery from severe aphagia and adipsia, yield a low salivary flow from the parotid gland during feeding in dogs (Rozkowska and Fonberg, 1972) and a reduced salivation measured by insertion of cotton into the mouth in rats (Schallert et al., 1978). In these studies, the salivary function was examined while animals' food intake was still smaller than normal one's, because bilateral LH lesions need the long recovery time of a few months (Teitelbaum and Epstein, 1962). Thus, in the present study we employed rats with unilateral LH lesions and sham-operated rats, and aimed to evaluate the role of the LH in the masticatory-salivary reflex and involved the recording of feeding-elicited submandibular salivary secretion and the electromyographic (EMG) activity of the masseter muscle. To analyze the effects of food texture on the abovementioned parameters, rats were trained for one week to eat five kinds of food; that is, solid pellets; powdered food; or soft, medium, or hard mash, all of which were composed of laboratory chow. Here, we report that the flow rate of saliva depends on the moisture content of food, and unilateral LH lesions, especially ipsilateral LH lesions, markedly reduce salivary secretion, but do not affect the amount of food consumed or the EMG activity of the masseter muscle. Based on these findings, we discuss the importance of the LH for the masticatory-salivary reflex.

2. Results

2.1. Lateral hypothalamic lesions

After the rats had been fed for one week in the test box, some rats had one side of their LH electrically coagulated. The coagulating electrode was introduced into the brain 2.5 mm caudal and 1.7 mm lateral to the bregma and 8.5 mm below the surface of the brain according to the stereotaxic atlas produced by Paxinos and Watson (1998). Fig. 1A and B show the areas affected by the left ($n=10$) and right ($n=10$) LH lesions, respectively. The lesions included most of the LH, as defined in the abovementioned stereotaxic atlas. Fig. 1C shows a photomicrograph of a left LH lesion.

2.2. Behavior and salivation in the test box

Salivary secretion was recorded from the left submandibular salivary gland. The rats frequently groomed and ground their teeth before and after feeding in the test box. In addition, they often drank water after consuming the powdered food. The rats secreted small amounts of saliva when they were drinking water or grinding their teeth, and this was also true of the sham-operated rats after they had consumed the powdered food during the recording session (Fig. 2A). In the test box, the greatest left masseter muscle EMG activity was usually seen during tooth grinding. Large amounts of saliva were secreted during feeding and grooming. The flow rate of saliva in the test box was highest during grooming; however, the masseter muscle EMG activity induced by grooming was far weaker than that induced by tooth grinding (Fig. 2B).

The LH lesions generally reduced salivary secretion during both feeding and grooming. Thus, we checked for alterations in the secretory function of the submandibular gland itself at the end of the experiment. Under anesthesia, electrical stimulation was applied to the parasympathetic nerve, and the flow rate of saliva was measured (Fig. 2C). At a stimulus frequency of 10 Hz, the salivary flow rates of the sham-operated rats and those with left and right LH lesions were 41.2 ± 3.9 μl/min ($n=6$), 40.1 ± 4.4 μl/min ($n=6$), and 39.8 ± 4.3 μl/min ($n=5$), respectively. There was no significant difference among these values ($F(2,14)=0.155$, NS).

2.3. Salivation and masseter muscle EMG activity during feeding

Five kinds of feed were provided in the test box: pellets; powder; and hard, medium, and soft mash, all of which were made from laboratory chow. Fig. 3 shows the submandibular salivary secretion and EMG activity of the masseter muscle at the beginning of the eating process in one sham-operated rat. The rats usually sniffed and nibbled the food, before chewing it with their incisors and molars. All these movements happen within a few seconds, and the associated bursts of masseter muscle EMG activity were of various durations and amplitudes. Thus, chewing cycles were calculated from