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Neurobiology of the Gustatory–Salivary Reflex

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All neural information resulting from chemical stimulation of taste buds in the oral cavity, pharynx and larynx travels via the facial (VII), glossopharyngeal (IX) and vagus (X) nerves to terminate in the nucleus of the solitary tract (NST) in the brainstem. The NST is responsible for initial processing and distribution of chemosensory information. At higher relays in the central nervous system the processes of detection, discrimination and affective responses occur resulting in the sensation we call taste and the behavioral reactions to that sensation. In addition, the NST connects to efferent motor systems involved in oral facial motor reflexes and systems controlling the initiation and flow of saliva. Thus, the NST plays a pivotal role in the neural processing of chemosensory information derived from stimulation of taste buds.

Beginning in 1961 (Pfaffmann *et al.*, 1961) a large number of investigators in different laboratories have examined the NST using anatomical, and neurophysiological techniques. The topographical projections of the VII, IX and Xth nerves conveying sensory information to the NST have been determined using different methods in several species (Torvik, 1956; Norgren, 1981; Whitehead and Frank, 1983; Hamilton and Norgren, 1984). The morphology of the NST has been studied and the neuronal architecture defined (Whitehead, 1988). Neurons in the NST have been described as belonging to three major anatomical types—multipolar, elongate and ovoid (Whitehead, 1988; Lasiter and Kachele, 1988; King and Bradley, 1994; Mistretta and Labyak, 1994), and using immunocytochemistry the presence of GABA and other neuropeptides has been described (Lasiter and Kachele, 1988; Barry *et al.*, 1993).

Responses of NST neurons to chemical stimuli applied to the tongue have also been examined many times in different species (e.g. Doetsch and Erickson, 1970; Hill *et al.*, 1983; Smith *et al.*, 1983a). Because stimulation is almost always restricted to the anterior 2/3 of the tongue, only neurons with input from the VIIth nerve have been extensively characterized. Moreover, because the recordings have been accomplished with extracellular electrodes, the type of neuron and its projection pattern are often undetermined. Thus, it is not known if the NST neurons recorded from send information rostrally, or to brainstem areas, or to both terminations. Regardless, these neurons are invariably called 'taste neurons' presumably because the information passed on will result in a taste perception. However, these so called 'taste neurons' could be interneurons involved in local circuits, neurons involved in reflex muscle activity, or neurons involved in salivary secretion. Despite the problem of knowing exactly what a particular neuron that receives input from taste buds actually does with that information, the assumption is made that they are involved in taste sensation. Furthermore, despite this lack of basic knowledge of the role of these NST neurons in chemosensory processing, theories of their roles in taste coding have been formulated (e.g. Smith *et al.*, 1983b; Di Lorenzo and Lemon, 2000).

It is obvious therefore that to make progress in understanding sensory processing at the level of the NST more information is needed about the network of neurons in the NST that process chemosensory information derived from stimulating taste buds. In an attempt to make progress we have made intracellular recordings in horizontal brainstem slices of the NST. Using this methodology we have been able to define that glutamate is the neurotransmitter between the primary afferent synapse and the second order neurons in the NST (Wang and Bradley, 1995), that GABA-mediated inhibition plays a major role in synaptic processing by NST neurons (Wang and Bradley, 1993; Grabauskas and Bradley, 1998) and that neurons in the NST have different biophysical and repetitive discharge characteristics (Bradley and Sweazey, 1992). Some of these *in vitro* results have been confirmed *in vivo* (Li and Smith, 1997; Smith and Li, 1998). More recently in an attempt to understand NST circuits, we have examined neural elements of the gustatory–salivary reflex circuit responsible for taste-initiated secretion of saliva, assuming that this is a relatively simple circuit. The reflex is typified by a high flow rate secretion of a bicarbonate-containing saliva in response to sour or low pH stimulation of taste buds. The reflex involves relatively few synapses and the overall details of the circuit are well understood, making it amenable for the study of NST circuits that process neural information originating in taste buds. Our previous investigations of NST neurons and synaptic characteristics of the NST have focused on the input circuit and now we are concentrating on neurons of the output circuit.

Parasympathetic preganglionic neurons controlling the salivary glands form a column of cells closely associated with the medial border of the NST (Contreras *et al.*, 1980). The most rostral extension of the salivatory nuclei innervating the submandibular and sublingual salivary glands has been studied in some detail (Matsuo and Kang, 1998; Mitoh *et al.*, 2004). The caudal extension of this column, the inferior salivatory nucleus (ISN), innervates the von Ebner and parotid glands. While the general topography of the parasympathetic neurons is known, detailed analysis of their morphology has only recently been studied (Kim *et al.*, 2004). Neurons innervating the parotid gland are significantly larger than those innervating the von Ebner glands although the neurons innervating either of these glands have similar repetitive discharge characteristics. Measurements of the latency of response of postsynaptic potentials (PSP) recorded from the ISN neurons indicate a multisynaptic pathway between the primary afferent synapse and the ISN neurons. In addition all the PSPs recorded are a mixture of both excitatory and inhibitory activity. Recently we have examined the effect of a number of neuropeptides on the ISN neurons and have found that Substance P depolarizes and excites the ISN neurons.

These results indicate the complexity of the NST and suggest caution in interpreting the role of the NST in coding before more details of the network of neurons responsible for processing chemosenory information are available.

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