The Cerebral Neural System Responsible for Salivation: a Functional MRI Study

B. L. Hou[1], K. K. Peck[1], C. Kim[2], N. M. Petrovich[1], D. Bogomolny[3], D. Kraus[3], A. I. Holodny[1]

[1]Functional MRI Laboratory, Radiology, Memorial Sloan-Kettering Cancer Center, New York, New York, United States, [2]University of Cincinnati, Cincinnati, Ihio, United States, [3]Surgery, Memorial Sloan-Kettering Cancer Center, New York, New York, United States

Introduction: Understanding the role of the cerebral nervous system in controlling the generation of saliva is vital to both clinic and science. A few, early studies exist on the topic (1-2) but it remains poorly understood. The objective of this investigation was to define the cortical network responsible for salivation based on activation areas determined by functional MRI.

Materials and Methods: 10 right-handed healthy volunteers (9 males, 1 female, mean age 34.8 years) participated in this study. Two paradigms were applied. The first, ("Imagination") involved 6 activation and 6 rest periods, each 30 seconds in duration. During activation, volunteers were shown a picture of a lemon on the goggle screen and were asked to imagine eating the lemon. During rest periods they concentrated on the sound of the 1.5 T GE scanner. The second ("Drinking") also had 6 activation and rest periods and 30 seconds for each period. In each activation, 1 ml of 10 mM vitamin C solution was injected on the tip of the tongue of the volunteer by a power injector at a rate of 0.5 ml/ second, and the subject was asked to retain the liquid for the rest of the activation time, then to swallow the liquid during the first 2 seconds of the subsequent rest period. High resolution T1-weighted images were obtained using a SPGR pulse sequence (TR/TE=30ms/14ms, 90 degree flip angle, 256 x 256 matrix, 144-160 axial slices, 1.5 mm slice thickness with 0 cm gap for the whole brain coverage) and co-registered with the BOLD fMRI data which were acquired using a T2* weighted EPI sequence(TR/TE = 5000ms/40ms, 90 degree flip angle, 128 KHz bandwidth, 128 x 128 matrix size, 42-44 axial slices, 4.5 mm slice thickness with 0 cm gap). All 20 data sets for the 10 subjects and the two stimulations were analyzed using AFNI software. Individual and group analyses, using correlation coefficients to threshold the activation areas, were performed. The uncorrected p values were selected to be less than 0.005, and 0.05 for the individual and group analyses, respectively. To quantitate the amount of saliva generated during the "Imagination" paradigm, a 5cm*5 cm gauze sponge was placed into the subject's mouth prior of the fMRI acquisition. This sponge was collected from the mouth immediately after the scan. To normalize for the saliva produced naturally (i.e., without the lemon stimulation) during the scan time, one additional "Imagination" scan was run. This time the subject closed eyes with the gauze in the mouth, and did not imagine eating the lemon. The amount of saliva (in grams) generated due to the "Imagination" paradigm was determined using the equation: W(weight (g) of saliva) = W(the net increased weight of the sponge during "Imagination") - W(the net increased weight of the sponge during the eyes closed paradigm).

Results: The average amount of saliva induced by the "Imagination" was 0.798571 g with a standard deviation of 0.326904 g. During the "Drinking" paradigm, all volunteers reported that they were generating saliva during each period. Hence, the common activation areas in the conjunction maps determined from the group analyses should relate to salivation. There are three such areas, which appear to be associated with the cortical network of salivation. These are overlaid onto a Talairach Brain and shown in the Figures 1-3, with the corresponding coordinates in stereotaxic space (i.e., Talairach and Tournoux space) were listed in the Table1. All the three activation areas in the left hemisphere are more superior to the right.

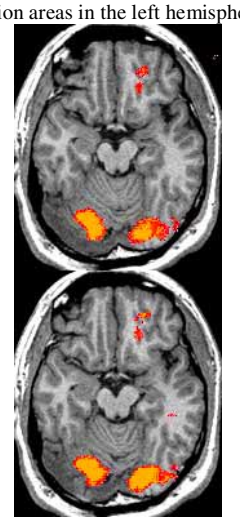

Figure 1. Left orbital gyrus.

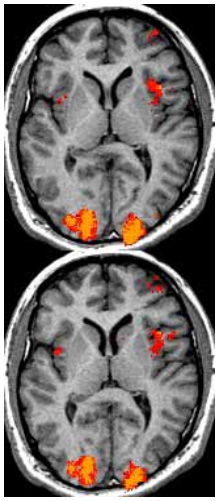

Figure 2. Insula.

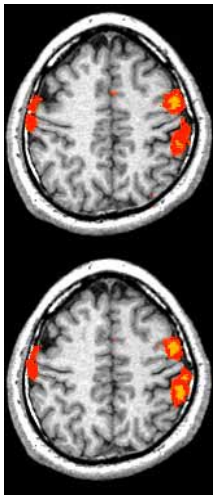

Figure 3. Post central gyrus.

	Left Orbital Gyrus (mm)	Left Insula (mm)	Right Insula(mm)	Left Postcentral Gyrus (mm)	Right Postcentral Gyrus (mm)
X (R-L)	20.00	35.00	-40.00	56.00	-58.00
Y (P-A)	-46.00	-15.00	-2.00	24.00	17.00
Z (I-S)	-10.00	6.00	7.00	43.00	43.00

Table 1. Talairach coordinates of orbital gyrus, insula, and postcentral gyrus.

Discussion: Functional MRI results demonstrates that the salivation stimulated by the "Imagination" and "Drinking" paradigms consistently activated three cortical areas. The first is the left orbital gyrus which is directly adjacent to the gyrus rectus - a crucial part of the olfactory system. The second, the left and right insula, is related to the gustatory (taste) system. The third is the postcentral (sensory) gyrus. These areas were activated even by the "Imagination" paradigm – when the subjects did not actually taste, smell or touch the lemon on the screen. This appears to represent the well-know Pavlovian response seen in animals and humans, where salivation occurs in anticipation of eating – either seeing food, thinking of food or (in the classical Pavlovian experiment) hearing a bell known to be associate with food. Here, we contributed evidence toward the determination of the neural network involved in salivation. This may have potential in determining the cause and the treatment for disorders in salivation such as xerostomia.

References: 1. Bogatch P.G. and Kosenko A.F, Fiziol Zh SSSR Im I M Sechenova 1963; 49:427-33. 2. Ishizuka K, et al., Shigaku. Odontology; Jounal of Nippon Dental College 1989; 77(3):904-9.