Location of the Primary Gustatory Area in Humans and its Properties, Studied by Magnetoencephalography

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The precise location of the primary gustatory area (PGA) in humans has not been determined conclusively, regardless of intensive studies with various non-invasive brain imaging. Analysis of brain function by fMRI and PET is based on changes in the regional cerebral blood flow (rCBF) several seconds after electrical neural activity. Thus, these techniques are not suitable for the location of the PGA, the cortical area activated at the shortest latency after gustatory stimulation, though most studies have localized the putative PGA in the middle dorsal insula and the frontal operculum (Small *et al.*, 1999, 2003; O'Doherty *et al.*, 2001; De Araujo *et al.*, 2003) by analogy to the PGA in monkeys. However, the anatomical structure of the human brain does not always present in the location corresponding to that of the monkey; for example, the human primary visual area is located on the medial surface of the occipital lobe, whereas that of subhuman primates is on the lateral surface. Thus, it is possible that the human PGA and monkey PGA reside in different locations.

Börnstein (1940) investigated three patients with hematoma at the base of the postcentral gyrus caused by gunshot wounds. The patients with hematoma close to the lateral sulcus showed ageusia or hypogeusia. The patient with hematoma dorsal to the lateral sulcus showed parageusia. Penfield and Jasper (1954) evoked gustatory sensation by electrical stimulation of the dorsal middle-posterior insula and fronto-parietal operculum inside the lateral sulcus during the brain surgery and found the foci of gustatory aura in similar regions. Hausser-Hauw and Bancaud (1987) reported two foci related to gustatory hallucination: one at the dorsomedial region of the temporal lobe and one at the parietal lobe superior to the lateral sulcus. The parietal focus causes gustatory hallucination only in contrast to the temporal focus generally inducing both olfactory and gustatory hallucinations. The parietal lobe is, therefore, considered to be a taste-specific area. Although Faurion *et al.* (1999) and Zald and Pardo (2000) reported activity in the Rolandic operculum, which partially overlaps with the parietal lobe, few fMRI and PET studies have reported activity in the parietal lobe. A clear discrepancy is noted between most fMRI and PET results and clinical observations.

MEG, on the other hand, can measure brain activity with a time resolution of 1 ms. Additionally, MEG can locate the active area with high spatial resolution when the number of cortical areas activated within a given latency is limited. Suk *et al.* (1991) reported that the regions activated by electrical stimuli at the index finger and little finger were 5.8 mm apart in the primary somatosensory cortex and clearly statistically distinguishable. Likewise, Pantev *et al.* (1995) reported that areas activated by pure tones of 500 Hz and 1 kHz were 6 mm apart in the primary auditory cortex. These reports demonstrate that MEG can locate activated areas in the primary sensory cortex with both high temporal and spatial resolutions.

Kobayakawa *et al.* (1996, 1999) developed a gustatory stimulus presentation device characterized by a short rise time of the taste stimulus avoiding tactile component to measure gustatory evoked magnetic fields (GEMfs). The taste delivery system has previously been described in detail (Kobayakawa *et al.*, 1996). Deionized water was always presented to participant's tongue and short duration taste stimuli were inserted repeatedly in the constant water flow with the two fluids separated by air bulbs. The participant covered a small hole opened in the wall of a tube with the tip of his/her tongue and the air and liquid did not leak into participant's mouth. The stimulation area was approximately the same as the filter-paper disk, clinically used to evaluate the gustatory function (Tomita and Ikeda, 2002). Solutions of 1 M NaCl and 3 mM saccharin were used as tastants. The earliest activation was most frequently found at the transition area between the posterior insula and parietal operculum (area G in humans), followed by the bottom of the central sulcus (CS). The average latency of activation in area G was 155 ms and 267 ms for NaCl and saccharin, respectively and the difference between these latencies was significant. No activation was observed at the CS for saccharin stimulation. Following area G and the CS, late activation was found in several cortical regions, e.g. the hippocampus, parahippocampal gyrus, superior temporal sulcus, intra-parietal sulcus, frontal operculum and anterior insula. These last two regions were denominated as the putative PGA by fMRI and PET studies. Kaneda *et al.* (2004) also discovered the first cortical activation in area G with the average latency of 327 ms after the presentation of isohumulones-enriched decarbonated beer. The results also show that the activity latency in area G varies with different taste stimuli, probably because of the different transduction mechanisms in taste receptors. Mizoguchi *et al.* (2002) recorded gustatory-evoked potentials (GEPs) together with GEMfs using the aforementioned taste delivery system. Each participant received a total of 240 stimulus presentations in six sessions. Three components—P1, N1 and P2— were observed in GEPs. ECD corresponding to P1 was localized in area G in all participants and no significant GEPs activity was detected preceding the P1, suggesting the presence of no cortical activity other than that detected by MEG.

Findings based on MEG at a high temporal resolution and clinical studies indicates that area G in humans and the CS are the most likely candidates for the PGA in humans. The mid-frontal operculum and anterior insula, reported as the putative PGA by fMRI and PET studies, are more likely to be high-order gustatory regions, because they were activated with longer latencies in MEG experiments.

The reason is still unclear as to why the activation of the parietal region has rarely been observed by PET or fMRI studies. Frequent repetition of stimuli with short duration, e.g. quick reverse of checker pattern in vision experiments, is probably required to observe rCBF changes in the primary sensory cortices. In gustation, however, long-lasting stimuli have been used in PET and fMRI studies. The present authors, therefore, attempted to examine whether fMRI detects cortical activation by repetitive stimulations of the tongue tip with NaCl

by using a computer-controlled stimulator and found the activation of area G in nine out of eleven participants in individual analysis. The results indicate that changes in the rCBF in area G in humans are observable in fMRI study, if repetitive applications of stimuli with short duration were used.

Besides, the present authors also presented four concentrations of NaCl (30 mM, 100 mM, 300 mM and 1 M) to six healthy volunteers under the same stimulus and recording condition as previously. Participants were asked to rate the perceived intensity with fingers (from 0 to 5), a few seconds after the taste detection. They found significant differences in the ECD amplitudes in area G across concentrations [$F(3,15) = 8.99$, $P < 0.001$, one-way ANOVA], but non-significant difference in the latency [$F(3,15) = 0.60$, n.s.], as shown in the onset latency of GEMfs (Saito *et al.*, 1998). They also observed significant differences in the perceived intensities across concentrations [$F(3,15) = 10.7$, $P < 0.001$]. When the value was plotted against log concentration, the linearity was, however, better with the ECD amplitude ($R^2 = 0.976$) than with perceived intensity ($R^2 = 0.878$).

In this paper, we have demonstrated that the transition area between the posterior insula and parietal operculum and the CS was the most likely candidate for the PGA in humans and that the activation latency differs among tastants and amplitudes reflect concentrations.

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