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Human taste cortical areas studied with functional magnetic resonance imaging: evidence of functional lateralization related to handedness

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Abstract

Whole-brain functional magnetic resonance imaging was used to detect local hemodynamic changes reflecting cortical activation in five left handed and five right handed human subjects during bilateral stimulation of the tongue with various tastes. Activation was found bilaterally in the insula and the perisylvian region. These regions correspond to the primary taste cortical areas identified with electrophysiological recordings in monkeys and suggested from former clinical observations in human subjects. Moreover, a unilateral projection was described for the first time in the inferior part of the insula of the dominant hemisphere, according to the subject's handedness. © 1999 Elsevier Science Ireland Ltd. All rights reserved.

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In monkeys, the cortical representation of taste has been localized in the insula, the adjacent frontal operculum, the base of pre and post-central operculum (or Rolandic operculum), and in the supratemporal plane [1,3,17,19]. Insula [15,18] and parietal cortex [5,10] were previously suggested as potential candidates for primary cortical taste projection in humans. Recent progress in non-invasive brain imaging with functional magnetic resonance imaging (fMRI) allows the functional topography of the taste system to be studied with a high spatial resolution in healthy subjects.

The study was approved by an Institutional Ethics Committee, and included 10 healthy subjects, 21–25-years-old, who signed an informed consent. Five subjects were right-handed and five were left-handed according to the Dellatolas test [8]. Each subject participated in one fMRI session. In each session, three gustatory stimuli were tested (three experiments) and a water control was performed (one experiment), all in blind conditions. The stimulation paradigm included a first 60 s water rinse,

followed by two ON – OFF periods of 30 s gustatory stimulation ended by a 90 s water rinse. Water and sapid solutions were continuously delivered into the subject's mouth as boli of 50 μl manually pushed every 3 s through silicone and polyethylene tubes connected to glass microsyringes. Stimuli were sodium chloride 85 mM (salty), aspartame 2 mM (sweet), quinine hydrochloride 1 mM (bitter), glycyrrhizic acid 0.5 mM (liquorice), 5′guanosine mono phosphate 1 mM (umami) and D-threonine 250 mM (no semantic description).

As shown by psychophysical experiments, and electrophysiological recordings in animals, the taste perception or the neural taste response is often delayed with respect to the onset of stimulation. The response also lasts longer than the stimulus presentation. Furthermore, significant interindividual differences do not allow any prediction from one subject's sensitivity to another one's [9]. In order to take into account this particularity of the sense of taste, the perception time course was recorded for each subject during each experiment with the finger span technique [4] and used to extract fMRI cortical activation [7,22].

Experiments were performed on a 3T whole-body MR

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scanner (Bruker, Germany). The subject's head was fixed by foam cushions and bands to avoid motion artifacts. For functional MRI, twelve axial contiguous 6-mm thick slices were scanned using a gradient-echo EPI sequence. High-resolution anatomical images were acquired using an inversion-recovery sequence. The observed volume consisted in 8 slices centered on the Sylvian fissure. Experiments were processed individually using a custom software written under IDL (Interactive Data Language, Research System Inc., Boulder, CO). Activation maps were calculated on a pixel-by-pixel basis, using the correlation coefficient between the MR signal time course and the perception profile [2,7,22]. Clusters including at least two contiguous pixels (correlation threshold: 0.4) were considered as significantly activated (Fig. 1).

Results were gathered from 15 experiments with left-handers and from 18 experiments with right-handers (one subject participated in two fMRI sessions). Activated regions included several clusters. The occipital region was not analyzed because of the presence of ghosting artifacts due to echo planar imaging [6].

Among a total of 303 activation occurrences observed, 82 were located in insular lobe (27%), 37 in Rolandic operculum (12.2%), 33 in temporal operculum (10.9%), 27 in frontal operculum (9%). Other areas were occasionally activated such as the anterior cingulate gyrus (7.6%), the dorso medial thalamus (1.3%), the temporal lobe (9.9%) as well as the frontal lobe (4.9%), the prefrontal cortex (8.2%), the parietal lobe (9%).

These observations agree well with previous anatomical and electrophysiological studies in monkeys describing insula and frontal operculum as the primary gustatory areas [1,3]. Along the same lines of evidence, in human subjects, gustatory perceptions were elicited by electrical stimulation of the superior part of the insula [18]. Moreover, taste disorders due to tumors or infarcts in the anterior part of the insula [15] were reported. An insular activation in response to gustatory stimulation was also found, in humans, with PET (positron emission tomography) [12] and with MEG (magnetoencephalography) [13,16].

Our observations of activation in the Rolandic operculum also agree with previous studies. In the monkey, Benjamin and Burton [3] showed that the Rolandic operculum receives a direct gustatory thalamic projection through branched neurons simultaneously projecting onto the ipsilateral insula [17]. In human beings, a lesion in the Rolandic operculum could induce gustatory deficits [5] and, in epileptic patients, the ablation of this area could suppress gustatory hallucinations [10].

According to the literature, the gustatory thalamus does not project directly towards the temporal operculum. However, a lesion of this cortical area, in the monkey, increases taste deficits induced by simultaneous ablation of insula and Rolandic operculum [1]. In addition, the same region is also activated by taste stimulation in a PET study [12].

In the present study using a whole tongue stimulation, all areas, except the inferior insula, appeared bilaterally activated. Two regions in the insula were distinguished in this fMRI study (Table 1). In the superior part, the activation
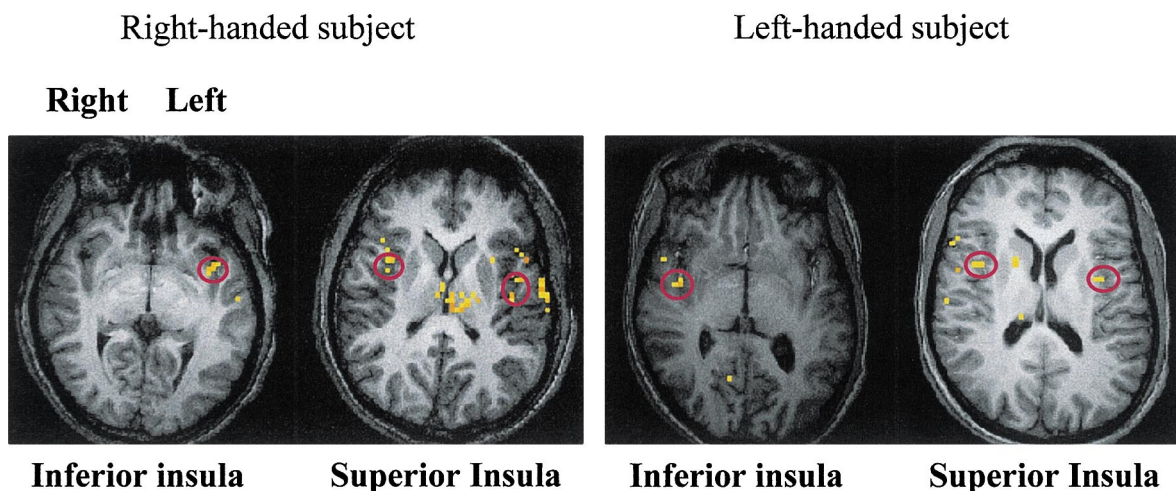
Right-handed subject   Left-handed subject

Right   Left

Inferior insula   Superior Insula   Inferior insula   Superior Insula

Fig. 1. Activation in superior and inferior parts of insula: axial fMRI images (repetition time (RT): 6 s; echo time (TE): 40 ms; flip angle: 90°; 64×64 pixels, field of view (FOV): 20 cm) were superimposed to corresponding axial anatomical images (inversion time (TI): 800 ms; TR: 3 s; TE: 8 ms; flip angle: 90°; 256×256 pixels, FOV: 20 cm) for a right-handed subject stimulated with quinine (left) and for a left-handed subject stimulated with NaCl (right). Activated pixels were extracted by correlation to the perception profile. (The right-hand side of the subject appears on the left-hand side of the image; the insular activation foci are circled). In the superior part of insula, activation was found in both hemispheres for the right and for the left-handed subject; the Pearson r calculated between the perception profile and the averaged temporal MR profile were $r = 0.71$ in the right insula and $r = 0.83$ in the left insula for the right-handed subject, $r = 0.70$ and $r = 0.74$, respectively, for the left-handed subject. In the inferior part of insula, activation was found only in the left hemisphere of the right-handed subject ($r = 0.84$) and in the right hemisphere of the left-handed subject ($r = 0.74$). Activation could also be observed in the frontal operculum, the Rolandic operculum and the temporal operculum of the dominant hemisphere of each subject.

Table 1
Activation occurrences observed in superior and inferior parts of insula in five right and five left-handed subjects in response to taste stimulation[a]

Right-handed subjects						Left-handed subjects					
		Inferior insula		Superior insula				Inferior insula		Superior insula	
Subject	Stim	Left	Right	Left	Right	Subject	Stim	Left	Right	Left	Right
BRO	NaCl			X	X						
BRO	Asp	X	X	X	X						
BRO	Qui	X									
VIT	NaCl	X				BOU	D-thr			X	
VIT	Asp	X				BOU	Gly				X
VIT	Qui	X		X		BOU	Gmp		X	X	X
RIN	NaCl			X		VIN	NaCl		X	X	X
RIN	Asp	X		X	X	VIN	Asp		X		
RIN	Qui	X		X	X	VIN	Qui		X	X	X
RIN	D-thr		X	X	X	FRI	NaCl	X	X	X	X
RIN	Gly			X	X	FRI	Asp		X	X	X
RIN	Gmp			X	X	FRI	Qui	X	X	X	X
BOUR	D-thr	X		X	X	MAR	NaCl		X	X	X
BOUR	Gly			X	X	MAR	Asp	X	X	X	X
BOUR	Gmp	X		X	X	MAR	Qui	X	X	X	X
FAV	D-thr			X		GIG	NaCl			X	X
FAV	Gly			X	X	GIG	Asp		X	X	X
FAV	Gmp	X		X	X	GIG	Qui		X	X	X
Total		10	2	15	12	Total		4	12	13	13

[a] In the superior insula, activation was found bilaterally, for right and left-handed subjects. In addition, right-handed subjects exhibited mainly unilateral activation in left inferior insula and left-handed subjects in right inferior insula ($P = 0.002$, χ^2).

was found mainly bilateral (with 15 occurrences in the left hemisphere and 12 in the right hemisphere in right-handers, 13 in both hemispheres in left-handers). Conversely, in the inferior part of insula, the activation was found mainly unilateral, in the dominant hemisphere of the subject (with 10 occurrences in the left hemisphere vs. two in the right one in right handers and 12 occurrences in the right hemisphere vs. four in the left one in left handers). This lateralization effect was significant ($P = 0.002$, χ^2).

The early activation of the superior part of insula (between 120 and 250 ms) found in MEG experiments in human subjects [13,16], and the short (6.5 ms) electrophysiological delays measured in the monkey [3], characterize a direct projection from the gustatory thalamic relay. By comparison, the unilateral activation observed in the inferior part of insula may be interpreted as a second order gustatory area. A PET study already reported a left insular activation in response to gustatory stimulation for right-handers [12], but could not discriminate two levels of activation, and missed the upper right insular activation. The lack of activation of the upper insula would have resulted from: (i) the low spatial resolution of PET; and (ii) the inter-subject averaging, which cancels inter-individual differences, encompassing the inferior and superior activation. In a MEG study performed on right-handed subjects, a late response component at 430 ms has been reported in response to olfactory stimulation in the left insula after a first response in the superior temporal plane or the parietal

cortex [11]. We may thus hypothesize the existence of a lateralized integration between gustatory and olfactory information, in the inferior part of insula.

The present study is the first one, to our knowledge, to investigate the cortical organization of taste chemoreception activation for left-handed subjects. Cerebral lateralization is still not ascertained in left-handers. Several studies tend to show that cognitive function is less lateralized in left-handers than in right-handers [14]. However, our sample of five left-handers was selected on the basis of a high degree of handedness and we observed a clear lateralization. Along these lines, studies have shown that the level of handedness increases the cerebral lateralization of visual processing [21].

The involvement of temporal operculum suggests that second order processes in the lower part of insula might be related to semantic processing [20], which, itself, might be a prerequisite for taste cognition. Although mere hypotheses, these ideas are worth noting for further experimental design.

In conclusion, our results may resolve a literature controversy about the human taste cortical representation. The taste activation we observed both in the operculo-insular area and in the foot of the pre- and postcentral gyri confirms both earlier contradictory electrophysiological and clinical findings. The unilateral lower insular activation described in this study should probably be related to a secondary processing; MEG studies are needed to check the latency of this

activation and compare it with the second olfactory dipole already described in literature [11]. Our findings furthermore add an argument to the hypothesis of a generalized hemispheric specialization of second order processes for sensory perceptions.

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