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Cerebral Imaging in Taste

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Since Roy and Sherrington (1890) suggested that an increase of the local blood flow may signal an increased neuronal activity, many efforts were developed to map brain tissue and brain activity leading to the first observation of an increased oxygen content in the visual area due to visual stimulation (Le Bihan *et al.*, 1986; Belliveau *et al.*, 1991; Kwong *et al.*, 1992; Ogawa *et al.*, 1992). Neural activity results in an increased blood flow with a relative decrease in deoxyhemoglobin and an increase in oxyhemoglobin. In functional magnetic resonance imaging (fMRI), a relative decrease in deoxyhemoglobin is reflected as an increase of the magnetic resonance signal.

The main advantage of the technique is a high spatial resolution, 1 mm or better depending on the equipment, allowing interpretation of individual brain activity. But, the temporal resolution is limited by the rise-time of the hemodynamic response (between 5 and 8 s) actually recorded.

For a short time resolution, magnetoencephalography (MEG), which directly records the brain electrical activity, is a complementary choice. Magnetic fields are measured using SQUID sensors on the whole scalp. The recorded signal results from the neuronal activity, the localization of which is to be found by resolving the inverse problem. In this calculation, the number of activated foci responsible for the signal and their initial putative localization are first chosen by the experimenter. The great advantage of the technique is that the signal recorded is due to the electrical activity of neurons with a temporal precision of a millisecond.

Associating both techniques enables researchers to look at firing foci in individual brains. Not only similarities but also differences in results may be informative, as both techniques look at physiological events through the filters of different time-windows.

Investigating taste adds the challenge of mastering hydraulic stimulation from a distance towards the mouth of a lying person. Cerf *et al.* (1996a,b) [a/b?] used a continuous flow alternating water and stimulus in an ON–OFF paradigm. Small boluses (50 µl) were sent to the subject's mouth repetitively (with no increase of the volume of fluid in the mouth) every 3 s to minimize adaptation. The time intensity perception was recorded with the finger-span technique and used as a template to correlate with the NMR signal on each voxel. This template allowed the detection of activation better than did the standard fitting of the stimulation paradigm waveform with a 6 s time constant (Cerf *et al.*, 1996a,b; Van de Moortele *et al.*, 1997) and taste areas were localized in the insula and frontal, rolandic, temporal opercula as expected from electrophysiological recordings in the monkey or clinical observations in humans (Cerf, 1998; Faurion *et al.*, 1999; Cerf-Ducastel *et al.*, 2001).

Other regions were found activated for taste in the literature using fMRI. The orbitofrontal cortex (OFC) is thought to be the region dedicated to the reward value of the food. O'Doherty *et al.* (2001) showed, with fMRI, interindividual differences for areas activated by glucose (pleasant) and by salt (slightly unpleasant). By contrast, neither group analysis nor single subject analysis provided any evidence of chemical topography in either insula or opercula. Small *et al.* (2003) showed regions responding to pleasantness in the anterior insula extending to the OFC. O'Doherty *et al.* (2001) showed that the OFC responded to changes in pleasantness associated with eating.

de Araujo *et al.* (2003) showed unimodal activations for taste in the anterior superior insula and frontal operculum. Taste and olfaction seem to converge in the far anterior insula, the caudal OFC and in the ventral forebrain. Taste (sucrose) and olfaction (strawberry odor) synergy was found in the lateral anterior OFC: the activation was more pronounced for the stimulation with the mixture (flavor) than predicted by the sum of the activation to each stimulus separately. In a medial part of the OFC, appeared information relevant to taste and smell subjectively matching together. Finally, only the OFC responded to anticipation of pleasant and unpleasant taste.

The amygdala may in a similar way signal aversive taste and affectively positive taste (O'Doherty *et al.*, 2001) or preferentially aversive taste (Zald *et al.*, 2002). Pleasantness/unpleasantness might be expressed in the amygdala on the basis of match/mismatch association of odor and flavor (Small *et al.*, 2003). The amygdala may be triggered by novelty (Zald *et al.*, 2002), which may result from mismatching flavor. We suggest, now, that activation for striking taste, unpleasant because of novelty aspects, may be more pronounced than for mild pleasant taste and may engage the memory circuits at a higher degree.

Kringelbach *et al.* (2004) described taste activation in the dorsolateral prefrontal cortex, a region already known to be implicated in response selection, working memory, attention, integration, i.e. executive control.

Although fMRI is powerful at spatially localizing taste relevant activation, MEG is the best technique to locate the first temporal activation (so-called 'primary' taste area). Kobayakawa *et al.* (1996, 1999) showed a first activation in the most posterior superior region of insula and rolandic operculum and the onset latencies were <100ms for NaCl and ~120–140ms for saccharin. Simultaneous EEG and MEG recordings also confirmed these findings (Mizoguchi *et al.*, 2002). Yamamoto *et al.* (2003) showed a more anterior insular early projection, using a different electrogustometric stimulation technique (Barry *et al.*, 2001).

Cerf-Ducastel *et al.* (2001) showed, with fMRI, activations in response to pure taste and to somatosensory or trigeminal oral stimuli such as strong acid or potassium aluminate in similar regions. However, an analysis of the co-activation of those areas discriminated different regions such as the rolandic operculum for somatosensory stimuli and the anterior inferior insula for taste. The anterior inferior insular area, which was found activated in the left hemisphere of strongly right-handed subjects and in the right hemisphere of strongly left-handed subjects (Faurion *et al.*, 1999) was also found to co-activate with the left angular gyrus in right-handers (Cerf-Ducastel *et al.*, 2001), a structure that is known to be related to comprehension of language. Furthermore, it was shown with MEG (Kobayakawa *et al*, in preparation) that this very region was the latest one to be activated, between 800 and 1400 ms. These results suggest that the activation of the anterior inferior insular area might

be related to the awareness of the stimulus quality or of the emergence to consciousness of the name of the perceived stimulus.

The activation located in anterior inferior insula, which is near by the frontal operculum and the caudal OFC, might correspond to activations reported in other studies in response to taste (38, 20, –4; –32, 22, 0) by Kringelbach *et al.* (2004), in response to sucrose and strawberry odor (–31, 22, 0) by de Araujo *et al.* (2003), in response to glucose (–33, 17, 2) by O'Doherty *et al.* (2001) and in response to unpleasant taste (–39, 27, –3) by Small *et al.* (2003).

The review of brain activations found in response to taste with fMRI, MEG and PET requires that one keeps in mind that those different techniques do not provide directly comparable data. By contrast with fMRI, PET often requires averaging over subjects and long periods of stimulation (Frey and Petrides, 1999), MEG mostly identifies activations from the fissural cortex. Different results might thus reflect differences in the techniques. However, complementary investigations with those techniques will allow the description and understanding of the sequence of events, i.e. the dynamics of the spatiotemporal pattern of activation in the brain in response to taste stimulation.

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