NeuroImage 119 (2015) 210–220

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Functional specialization of the male insula during taste perception

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ARTICLE INFO

Article history:
Received 2 February 2015
Accepted 22 June 2015
Available online 30 June 2015

Keywords:
Cortical mapping
Functional magnetic resonance imaging (fMRI)
Insula
Lateralization
Taste

ABSTRACT

The primary gustatory area is located in the insular cortex. Although the insular cortex has been the topic of multiple parcellation studies, its functional specialization regarding taste processing received relatively little attention. Studies investigating the brain response to taste suggested that the insular cortex is involved in processing multiple characteristics of a taste stimulus, such as its quality, intensity, and pleasantness. In the current functional magnetic resonance study, younger and older adult male subjects were exposed to four basic tastes in five increasing concentrations. We applied a data-driven analysis to obtain insular response maps, which showed that the insular cortex processes the presence of taste, its corresponding pleasantness, as well as its concentration. More specifically, the left and right insular cortices are differentially engaged in processing the aforementioned taste characteristics: representations of the presence of a taste stimulus as well as its corresponding pleasantness dominate in the left insular cortex, whereas taste concentration processing dominates in the right insular cortex. These results were similar across both age groups. Our results fit well within previous cytoarchitectural studies and show insular lateralization in processing different aspects of taste stimuli in men.

Introduction

Information from the senses of vision, hearing, and touch is unimodally represented in distinct areas of the cerebral cortex, termed primary sensory areas. For taste, most researchers agree that the primary gustatory area resides in the insular cortex (see e.g. Small (2010) for a review). The insular cortex is characterized by its widespread anatomical connections and its heterogeneous cytoarchitecture. To better understand the function of the insula, multiple studies have investigated the subdivision of the insular cortex based on its anatomical structure, functional connectivity, and task-evoked activity. Cytoarchitectonically, the insula shows a smooth gradual change in its grey matter structure from agranular to granular in the anteroventral to posterodorsal direction (see e.g. Mesulam and Mufson (1982)). Correspondingly, diffusion weighted imaging studies have shown an anterior–posterior transition in white-matter connectivity variation within the insula (Cerliani et al., 2012; Nanetti et al., 2009). Studies investigating the functional connectivity of the insula have indicated that the anterior insula can be subdivided into two areas: the anterodorsal insula and anteroventral insula (Chang et al., 2013; Deen et al., 2011; Kelly et al., 2012). Kurth et al. (2010b) investigated the task-evoked subdivision of the insula. Their large meta-study indicates that the insula functionally divides into areas associated with sensorimotor, cognitive, chemical sensory (i.e. olfactory and gustatory), and social–emotional domains. Furthermore, Kelly et al. (2012) found that results from clustering methods correspond remarkably well across the three different modalities (task-evoked co-activation, functional connectivity during rest, and gray matter structural covariance), indicating a strong resemblance between anatomical and functional properties within the insular cortex.

Although the parcellation studies described above indicate that the insula divides into multiple subareas with distinct properties, the exact location of the primary gustatory area is still under debate. Experimental studies in non-human primates have suggested that this area is located in either the anteroventral or anterodorsal insula (Mesulam and Mufson, 1982; Yaxley et al., 1990). However, a growing body of neuroimaging studies has indicated that the anteroventral insula processes taste in humans (Bender et al., 2009; Rudenga et al., 2010; Small, 2012; Small et al., 2001). Meta-analyses of Kurth et al. (2010b) and Veldhuizen et al. (2011) have shown that the anteroventral part of the insula is most associated with processing taste. Although Kurth et al. (2010b) demonstrated a right insula dominance for gustatory processing, Veldhuizen et al. (2011) did not find any proof of laterality.

There are several factors that complicate investigating the functional organization of the insula during taste perception. First, taste stimuli are always accompanied by somatosensory information. Therefore, brain activation may be evoked by somatosensory stimulation instead of

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http://dx.doi.org/10.1016/j.neuroimage.2015.06.062

taste or in addition to taste. To overcome this, several researchers contrasted the taste stimulus with a baseline stimulus, such as water or a tasteless solution containing artificial saliva. However, both water and tasteless artificial saliva still activate the primary gustatory area (de Araujo et al., 2003; Veldhuizen et al., 2007). Therefore, contrasting with such baseline stimuli reduces sensitivity.

A second complication resides in the fact that several subregions of the insular cortex have been reported to process different aspects of taste (e.g. pleasantness, intensity or presence). Selective attention to these different aspects seems to enhance brain activity in different parts of the insular cortex, although direct comparisons between these attention tasks have not yet been conclusive (Bender et al., 2009; Nitschke et al., 2006; Veldhuizen et al., 2007). Studies that tried to investigate the brain response while manipulating stimulus intensity, specifically, suggest that changes in intensity are associated with changes in activity in the middle insular cortex (Small et al., 2003; Spetter et al., 2010; Veldhuizen et al., 2010). Although many studies have focused on the orbital frontal cortex with respect to pleasantness, several have indicated that the insula also codes taste pleasantness (Bender et al., 2009; Cerf-Ducastel et al., 2012; Nitschke et al., 2006; Small et al., 2001). Since pleasantness and intensity highly correlate in many cases (Pfaffmann, 1980), it is hard to disambiguate the two, especially when both are not measured and/or manipulated within the same paradigm. Therefore, it is unclear whether the resulting insular responses represent either pleasantness or intensity coding.

Finally, a third complication stems from a methodological problem: researchers often used high taste concentrations because neuroimaging methods are rather insensitive to neuronal responses near detection threshold. Yet, high taste concentrations are often accompanied by disgust responses and may therefore elicit confounding mechanisms.

To investigate functional specialization of the insula during taste perception, while trying to overcome the above-mentioned difficulties, we analyzed data from male subjects, who were exposed to basic tastes in increasing concentrations. We included both young and older adult males to obtain results on insular taste processing across age groups. For data analysis, we used a data-driven multivariate blind source separation approach that enabled us to disassociate insular activity related to multiple characteristics of the taste stimuli.

Materials and methods

Participants

In this study, we acquired data of 21 healthy young males (mean age 23.9, SD = 2.81, range 19–30 years) and 19 healthy older males (mean age 65.8, SD = 4.3, range 60–72 years). Participants were enrolled in the study on the basis of written informed consent. Participation was in accordance with the requirements of the medical ethical committee at the University Medical Center Groningen.

Participants were included when they reported no history of taste, smell, neurological, or psychological disorders. They were right handed, non-smoker for at least 3 months, and had normal or corrected to normal vision with MR-compatible lenses. Participants using any form of medication that possibly affected taste perception (i.e. gastrointestinal complaints, dry mouth, nausea, and taste disturbance) were not included in the study. Participants received a monetary compensation for participation.

One participant from the young male group was removed from the study after aborting the paradigm prematurely due to technical difficulties with the gustometer. Furthermore, one participant from the older males group was removed due to an unforeseen claustrophobic response.

Because food intake as well as brain responses to food images vary across the menstrual cycle (see e.g. Bryant et al., 2006; Frank et al., 2010; van Vugt, 2009), we anticipated that inclusion of female participants within the study would introduce extra undesired variation, negatively affecting the data-driven analysis. We therefore only included male participants exclusively.

Taste stimuli and delivery

Stock solutions of sweet (560 mM sucrose), salty (180 mM NaCl), sour (10 mM citric acid), and bitter (1 mM quinine HCl) were created, matching taste stimuli used in previous studies (e.g. Bender et al., 2009; Jabbi et al., 2008; Rolls, 2011). These stock solutions were diluted with sterilized water to form series of 0%, 12.5%, 25%, 50%, and 100% of the original stock concentrations. The 0% solution was also used for rinsing. Stimuli were delivered in the form of a 2-ml bolus, using an in-house designed MR-compatible gustometer, consisting of 30 10-ml syringes manually operated by an experimenter. Syringes were held firmly in place within the gustometer, and five removable stops were placed between the plunger and barrel to ensure 2-ml bolus deliveries. The syringes were attached to tubes (inner diameter 3 mm; outer diameter: 4.1 mm). Tubes containing water were connected together using stopcocks, such that only one tube ending provided a water stimulus. All tubes ended in a tight bundle of 17 tubes (one for water and 16 for tastants), which were held together in a central mouthpiece (a cut-off pacifier). The mouthpiece was secured to the headcoil and rested above the teeth of the participant, such that the participant was able to close his lips around the ending of the bundle (bundle diameter: ~14 mm). The half-closed tubing system combined with the small tube diameter countered spontaneous leaking while at the same impeding the participant to easily suck liquid from the tubes. Participants were instructed to try and keep their head as still as possible during tasting and swallowing. We did not specifically instruct them to limit tongue movement to minimize the risk of choking. Stimuli were administered manually by pushing the plunger to the next mechanical stop and administration lasted for approximately 1 s. Auditory countdown trough headphones guaranteed timely stimulus administration.

Experimental design

The experiment was divided in two sessions. In the first 1-hour screening session, which was scheduled between 9:00 and 12:00 AM, inclusion and exclusion criteria were checked, saliva samples were collected (results will be reported elsewhere), a hypogeusia-screening was performed using taste strips (Mueller et al., 2003; Steinbach et al., 2009), and participants were familiarized with the experimental procedure. The second session took place within 7 days after the first session and contained a functional magnetic resonance imaging (fMRI) scan between 9:00 and 12:00 AM or between 4:00 and 7:00 PM. Participants were instructed not to eat or drink during a 2-hour period prior to the scanning session.

Hypogeusia screening

Taste function was assessed using spoon-shaped filter paper strips, which were impregnated with four basic tastes in four different concentrations (Mueller et al., 2003; Steinbach et al., 2009). Two tasteless strips were included. During each taste trial, participants were instructed to first rinse their mouth with water followed by placing a taste strip on the middle anterior third of the tongue. Subsequently, participants were instructed to identify the taste by choosing one out of five answers: sweet, sour, salty, bitter, and neutral (multiple forced choice). The order of the taste stimuli was randomized at each concentration, and stimulus presentation was in ascending (i.e. low to high) order of concentrations. The hypogeusia screening required approximately 10 minutes. Identifying hypogeusia was based on total number of correctly identified stimuli; participants scoring below 8 were excluded. We identified no hypogeusia in any of the recruited participants.