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Different Neural Processing of Umami and Salty Taste Determined by Umami Identification Ability Independent of Repeated Umami Exposure

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Abstract—There is a large inter-individual variation for umami taste perception. However the neural mechanism for this variability is not well understood. This study investigated brain responses to umami and salty taste among individuals with different umami identification abilities and the effect of repeated oral umami exposure on umami identification and neural processing of taste perceptions. Fifteen participants with high umami identification ability (''High Tasters, HT) and fifteen with low umami identification ability (''Low Tasters", LT) underwent three weeks of controlled exposure to umami taste (umami training). Prior to and after the training, participants underwent fMRI scans during which the umami taste solution and a control taste (salty) solution were delivered to their mouth using a gustometer. Taste intensity and pleasantness were rated after each scan. Umami taste identification was assessed before and after the umami training using ''Taste Strips" test. Neuroimaging results showed different central processing of umami and salty taste based on umami identification ability, in which the umami LT had stronger activation in the thalamus and hippocampus while the umami HT showed stronger activation in the primary gustatory cortex. In addition, umami identification was significantly improved after umami training for LT. However, it was not reflected in changes in neural activation. The current study shows that attention and association/memory related brain structures play a significant role in the perception of umami taste; and with reference to the results of repeated umami exposure, the presence of very subtle changes regarding the neural processing.

Keywords: functional magnetic resonance imaging (fMRI), taste perception, umami identification, repeated exposure.

INTRODUCTION

Umami is a basic taste (Kurihara, 2009), which stems from a Japanese term meaning ''good taste" or ''delicious" (Chandrashekar et al., 2006; Roper, 2007), and is often used to describe a meaty, savory flavor. In humans the main substance eliciting umami taste is L-glutamate, an amino acid abundantly found in food that often occurs as monosodium glutamate (MSG) (Garcia-Bailo et al., 2009). MSG are found naturally in a wide array of vegetables such as tomatoes, potatoes, mushrooms, carrots, and various seaweeds, as well as fish, seafood, meat, and cheese (Kurihara and Kashiwayanagi, 2000; Kurihara, 2009). Umami taste is highly significant in the palatability of food flavors (Rolls, 2009), and is important for the maintenance of health (Prescott, 2004; Shoji et al., 2016). Regarding the cerebral processing of umami taste, it is well established that the neural representation of umami taste is in the primary and secondary gustatory cortex, including the anterior insula, frontal operculum, and the orbitofrontal cortex (de Araujo et al., 2003; Schoenfeld et al., 2004; McCabe and Rolls, 2007; Nakamura et al., 2011; Singh et al., 2015; Prinster et al., 2017).

There are significant variations for umami taste perception in the general population (Lugaz et al., 2002; Singh et al., 2010). Individual differences in umami taste sensitivity result from genetic variations in taste receptors (Shigemura et al., 2009a,b), or other determinants of taste physiology such as dietary conditions and hormonal levels (Loper et al., 2015). However, much less had been explored regarding the central mechanisms for the perceptual variability regarding umami taste. In addition, umami taste is less familiar as compared to other tastes and is commonly confounded with salty taste (Overberg et al., 2012). There were only 3.8% of people from Germany reporting awareness of the umami taste (Singh et al., 2010). Previous research has shown that the sensitivity to umami taste is largely dependent on the familiarity with that taste (Kobayashi et al., 2006; Singh et al., 2015). Interestingly, brain responses to umami can change

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Abbreviations: fMRI, functional Magnetic Resonance Imaging; MSG, monosodium glutamate.

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following repeated exposure to umami - "umami training" (Singh et al., 2015).

The objectives of the current study were: (1) to investigate the neural mechanism that influence responses oral umami taste stimuli among people with different abilities for umami taste identification; and (2) to investigate the effect of repeated umami taste exposure on umami taste identification.

EXPERIMENTAL PROCEDURES

Participants

Thirty adult participants (age range 20–33 years, mean age years 24.6 years; body mass index BMI 19–30.5, mean 23.6) were recruited for the study including 21 males (age range 20–33 years, mean age 24.8 years; BMI 19–30.5, mean 23.9) and 9 females (age range 21–27 years, mean age 24.2 years; BMI 20.3–27.2, mean 22.9). Participants' gustatory function was screened via taste sprays that consist of supra-threshold concentrations of "sweet" (sucrose), "sour" (citric acid), "salty" (sodium chloride), and "bitter" (quinine hydrochloride) (Welge-Luessen et al., 2013). All participants were able to identify each of the four tastes correctly. In addition, participants received an interview regarding other inclusion criteria. Based on self reports, all participants were non-smoking, non-pregnancy or non-breast feeding (female participants), right-handed and with normal olfactory functions. The study was approved by the Ethics Committee at the Technical Dresden (EK number 366082015) and performed in accordance with the WMA Helsinki declaration. Participants provided written informed consent prior to commencement of the study.

Umami taste identification

To identify people with high and low ability of umami taste identification ("High Tasters, HT" and "Low Tasters, LT"), a modified version of the "Taste Strips" test (Burghart, Wedel, Germany; length of 8 cm, tip area of 2 cm^2, impregnated with tastant) was applied (Landis et al., 2009; Mueller et al., 2011). Filter paper strips were impregnated with MSG or sodium chloride (NaCl) solutions, in four concentrations each (0.016, 0.04, 0.1 and 0.25 g/ml). One strip at a time was placed on the tongue, and the mouth was rinsed with tap water after presentation of each strip. Each test step included a triplet of strips, one with a certain concentration of umami (see above) and two with NaCl in the same concentration as had been applied with the Na – Glutamate strip. After each triplet, subjects were asked to identify the strip with the different taste. The entire test comprised eight repetitive steps, with a random sequence of concentrations and every concentration being applied twice (Landis et al., 2009; Manzi and Hummel, 2014). The total number of correct answers was used as a measure of umami identification.

Umami HT and LT were classified according to the umami identification score, with participants above 50% correct identification of the umami taste (5 or more out of 8) were regarded as umami HT, and participants below 50% correct identification of the umami taste strips (3 or less out of 8) were classified as umami LT.

Repeated umami taste exposure

The umami taste repeated exposure followed a three weeks training period during which subjects were provided with samples of umami taste solution in 30-ml spray bottles, along with written instructions and documentation forms. They were asked to apply the training solution twice daily, after rinsing the mouth with water, with approximately 6–8 h between applications, and to document their sensations in a journal (Singh et al., 2015). To ensure compliance, participants were required to return to the lab and have their training bottles exchanged every week. The umami identification test was performed before and after the training period. A schematic of the study design is depicted in Fig. 1.

functional Magnetic Resonance Imaging (fMRI) experimental design

Umami taste was represented by MSG. As a control stimulus, salty taste (NaCl) was used. A gustometer (Burghart GU002; Burghart, Wedel, Germany) was utilized for taste stimulation during the fMRI scanning procedure (Iannilli et al., 2012; Seo et al., 2013; Singh et al., 2015). Umami and salty solutions (0.25 g/ml each) were applied onto the tongue using Teflon™ tubing and a plastic mouthpiece. Teflon® tubing carrying the stimulation and rinsing liquids was fed through the wall. From the mouthpiece held between subjects' lips, droplets of stimuli, rinse or water were delivered onto the tongue.

Participants underwent two fMRI sessions: one prior to (PRE), and one after (POST) the training phase of umami taste. In both sessions, identical functional scanning procedures were performed, following the scheme of a block design with 20 s (eight scans) period of stimulation (ON condition), rinsing, and rest (OFF condition) constituting one block. The block designed acquisition scheme yielded 48 scans per tastant in each participant during the PRE and POST session, respectively, and as many control scans with water as stimulant (Iannilli et al., 2012).

During ON periods, one of the tastants was delivered, while during OFF periods water (Evian®, Danone Waters, Frankfurt, Germany) was applied to the tongue. Synthetic saliva (KCl [25 mM] plus $NaHCO_3$ [0.25 mM]) was used to rinse the mouth after taste stimulation. Blocks were repeated three times within one run, with alternating sequences of umami and salt stimulation, and four runs were performed with short breaks in between, each stimulant thus being repeated six times. After each fMRI run, subjects verbally rated the intensity and pleasantness of both tastants via intercom, on a rating scale (range for intensity: from 0 = no sensation to 10 = maximum intensity; for pleasantness: from −5 = very unpleasant to 5 = very pleasant). The duration of an entire functional MRI session was approximately 15 min. The design is depicted in Fig. 2.

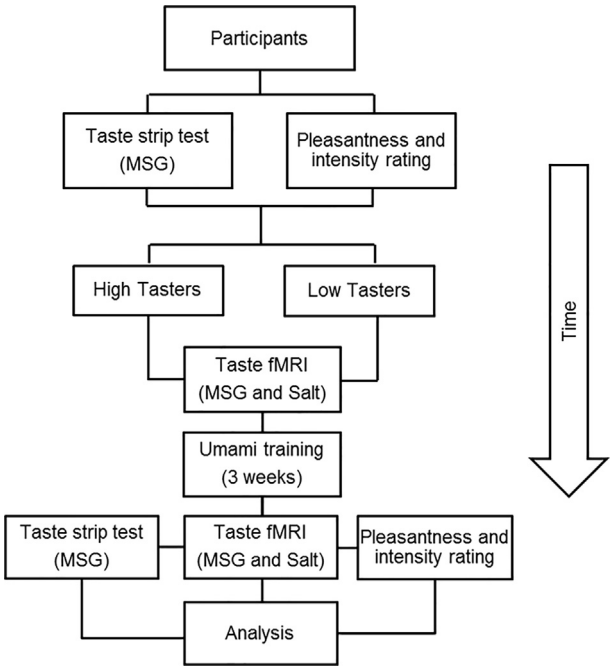

Fig. 1. Diagram for the experimental design.

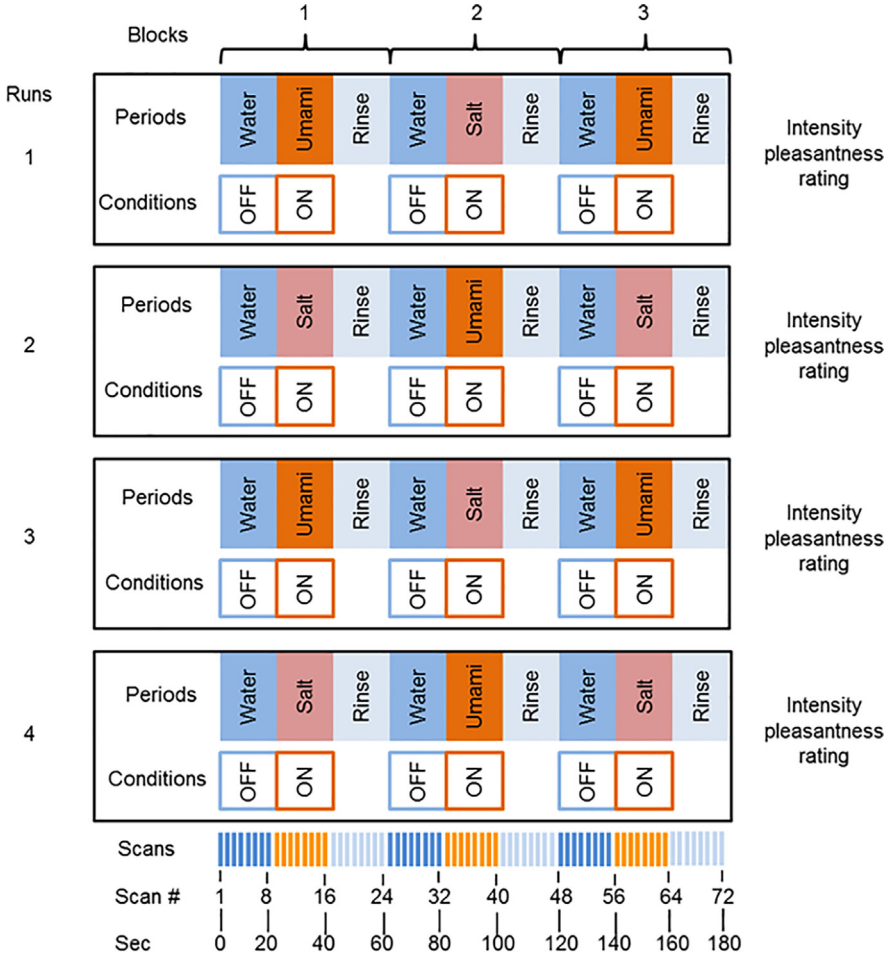

Fig. 2. Schematic drawing of the block designed fMRI procedure, performed twice, prior to and after umami training.

fMRI data acquisition and analyses

Brain images were obtained using a 3 T scanner (Verio; Siemens, Erlangen, Germany). Functional data were recorded with TR = 2.5 s, slice thickness = 3 mm, and slice spacing = 3 mm. T1 anatomical images of the brain were acquired after the functional runs in the PRE session with the following parameters: TR = 1.89 s, slice thickness = 1 mm, slice gap = 0.fMRI data were analyzed using SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK) implemented in MATLAB 2013a (MathWorks, Natick, MA, USA). Preprocessing included motion correction, co-registration of functional with anatomical images, segmentation into compartments of white and gray matter and cerebrospinal fluid, normalization with respect to standardized brain images, and smoothing. On an individual level, ON and OFF conditions were compared, yielding contrasts for each taste quality (umami or salt) during the PRE and POST part separately. On the group level, the overall brain responses to taste perception was assessed by a conjunction analyses for salt and umami tastes with the whole sample (n = 30 including both HT and LT) during the PRE session. The threshold for this analysis was set at cluster-level $FWE_{corrected}$ p < 0.05 and cluster size k > 30 voxels across the whole brain. Next, a three-way ANOVA with umami taster status (HT and LT), taste quality (umami and salt) and training (PRE and POST) was built. No significant interactive effect from taster status × taste quality × training, taste quality × training, or taste quality × taster status was observed. Therefore, the subsequent analyses were performed for salt and umami taste separately. First, a two-way ANOVA (training: PRE and POST; taster status: HT and LT) was modeled to investigate the effect of umami taster status and training on brain responses. In addition, a conjunction analyses with a conjunction null hypothesis to identify regions of overlapping responses to both umami and salt taste between HT and LT. This conjunction analyses identifies voxels that are significantly activated in each of the individual contrasts included in the conjunction (Nichols et al., 2005). The F- and T-map contrasts threshold was set at $p_{uncorrected} \leq 0.005$ and a minimum of eight voxels per cluster. For identification of activated areas in general, the Automated Anatomical Labeling (AAL) tool in the SPM12 framework was used, with at least 5% of a cluster required to be represented in a certain region.

Other statistical analyses

Statistical analyses were performed using the SPSS software package (SPSS 21, SPSS Inc., Chicago, IL, USA). Two-way ANOVA (training: PRE and POST; taster status: HT and LT) was applied to test the effect of umami taster status and training on psychophysical measurements including umami taste identification, taste intensity and hedonics. The level of significance was set to $p < 0.05$.

RESULTS

Participants' characteristics

Fifteen umami HT (four female, mean age 23.8 years, mean BMI 22.8; 11 males, mean age 25.3 years, mean BMI 24.3), and 15 umami LT (five female, mean age 24.6 years, mean BMI 22.9; 10 males, mean age 24.3 years, mean BMI 23.5) were included in the study. The HT and LT groups were not significantly different regarding age ($t_{28} = -0.46$, $p = 0.65$), sex distribution ($\chi^2 = 0.16$, $p = 0.69$), or body mass index ($t_{28} = -0.52$, $p = 0.61$).

Psychophysical ratings for umami taste

Before umami training, the umami identification score was significantly higher for HT as compared to LT (HT mean = 5.9, SD = 1.3; LT mean = 2.3, SD = 1.1; $t_{28} = -8.21$, $p < 0.001$). There was a significant umami taster status × training interactive effect on umami identification ($F_{1,56} = 15.16$, $p < 0.001$), indicating that the umami training had different effect for HT or LT. In other words, the increased umami identification score from PRE to POST session was mainly driven by the increased umami identification among LT (PRE mean = 2.3, SD = 1.1; POST mean = 5.7, SD = 1.7; $t_{14} = -5.7$, $p < 0.001$) but not HT (PRE mean = 5.9, SD = 1.3; POST mean = 6.7, SD = 1.1; $t_{14} = -2.1$, $p = 0.052$) (Fig. 3). In addition, the difference of the umami identification between HT and LT was diminished to a nonsignificant amount after training ($t_{28} = -1.93$, $p = 0.064$) (Fig. 3). There was no effect of umami taster status or training on intensity ($F_{1,56} = 0.05$, $p = 0.82$ for umami taster status; $F_{1,56} < 0.01$, $p = 0.99$ for training) or pleasantness ($F_{1,56} = 0.14$, $p = 0.71$ for umami taster status; $F_{1,56} = 0.96$, $p = 0.33$ for training) for umami taste.

Psychophysical ratings for salty taste

After umami training, salt intensity was significantly increased ($F_{1,56} = 7.44$, $p = 0.008$), while the pleasantness of salty taste significantly decreased ($F_{1,56} = 7.37$, $p = 0.009$). There was no interactive effect between umami taster status and training ($F_{1,56} = 1.77$, $p = 0.19$) or umami taster alone ($F_{1,56} = 1.03$, $p = 0.32$) on the intensity of salt taste. Similarly, no interactive effect between umami taster status and training ($F_{1,56} = 0.14$, $p = 0.71$) or umami taster status ($F_{1,56} = 0.25$, $p = 0.62$) was found for salt pleasantness. In both the PRE and POST sessions, the umami taste was perceived as less intense

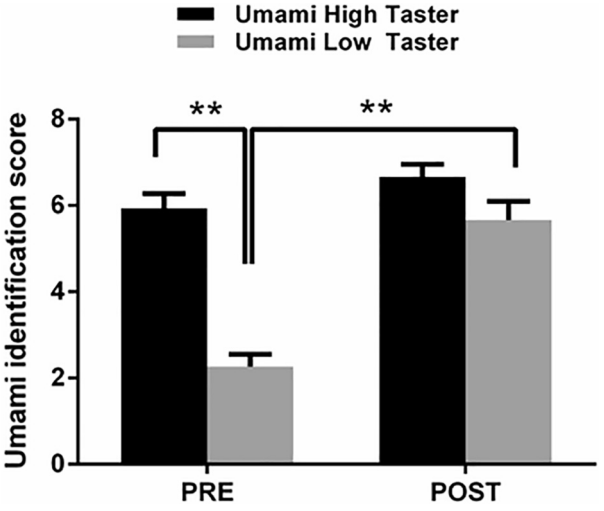

Fig. 3. Umami identification score (means, SEM) in umami high tasters (HT) and low taster (LT) groups prior to (PRE) and after (POST) the umami taste training. $^{**}p < 0.01$.

($F_{1,56} = 16.79$, $p < 0.001$ for PRE session; $F_{1,56} = 57.74$, $p < 0.001$ for POST session), but more pleasant ($F_{1,56} = 17.59$, $p < 0.001$ for PRE session; $F_{1,56} = 83.64$, $p < 0.001$ for POST session) as compared to salt taste. There was no effect of umami taster status on the pleasantness or intensity of either taste qualities.

Brain activation to taste perception

During the PRE session and among the whole sample of participants, brain activation to both umami and salt tastes was observed in the primary gustatory regions, including the insula, operculum, pre- and post-central gyrus. In addition, taste-induced brain activation was found in multiple other regions such as the thalamus, orbitofrontal cortex, middle cingulate cortex, inferior parietal lobule, supplementary motor area, middle frontal cortex, and inferior frontal triangular gyrus ($FWE_{corrected}$ $p \leq 0.05$ and cluster size >30 voxels) (Table 1 and Fig. 4).

Brain activation to umami taste

Umami HT, as compared to LT, had stronger activation in the primary gustatory cortex, including the frontal operculum, postcentral gyrus, as well as secondary gustatory area such as the orbitofrontal cortex. On the contrary, umami LT showed larger activation in the thalamus, hippocampus and posterior insula (Table 2, Fig. 5A). There was neither significant effect of umami t aster × training interaction nor effect of umami training alone on brain activation to umami taste.

Brain activation to salty taste

Like the results for umami taste, umami HT showed larger brain responses to salty taste in the primary gustatory areas and the supplementary motor area (Table 3, Fig. 5B). The contrast umami LT > umami HT showed

Table 1. Overall brain activation to conjunctive umami and salty taste perception

p-FWE	*k*	*T*	*x*	*y*	*z*	Region
< 0.001	976	7.60	46	−46	54	Inferior Parietal Lobule R
		6.12	40	−60	52	
		5.94	38	−56	42	
< 0.001	1643	7.56	−4	22	44	Supplementary Motor Area L
		7.42	4	24	42	
		7.07	4	16	50	
< 0.001	1358	6.91	−50	8	44	Precentral Gyrus/Frontal Operculum L
		6.80	−48	20	40	
		6.29	−42	12	44	
< 0.001	579	6.79	−46	−48	54	Inferior Parietal Lobule L
		6.08	−36	−54	44	
< 0.001	270	6.64	−2	−26	32	Middle Cingulate Cortex L
		5.11	−4	−10	32	
< 0.001	283	6.58	40	24	2	Insula/Inferior Orbitofrontal Cortex R
		5.44	52	24	−6	
< 0.001	369	6.04	58	−4	34	Rolandic Operculum/Postcentral Gyrus R
0.005	41	5.95	44	52	12	Middle Frontal Cortex R
		5.21	38	56	16	
< 0.001	202	5.77	−38	18	0	Insula/Superior Temporal Pole L
		5.60	−52	16	−6	
< 0.001	269	5.73	44	20	44	Frontal Inferior Triangular Gyrus R
		5.24	44	28	34	
		5.21	42	34	22	
0.005	40	5.56	8	−14	8	Thalamus R
0.003	58	5.55	−8	−16	10	Thalamus L
		5.02	−10	−16	0	

Whole-brain analyses thresholded at *p*-FWE corrected ≤0.05 (cluster level) and a minimum cluster size of 30 voxels; FWE, family wise corrected; HT, umami high tasters; LT, umami low tasters; R, right hemisphere; L, left hemisphere; *k*, cluster size in voxels; *xyz*, MNI space peak coordinates.

significant activation of the hippocampus, thalamus, caudate, posterior cingulate cortex in response to salty taste. There was neither significant effect of umami tast er × training interaction nor effect of umami training alone on brain activation to salty taste.

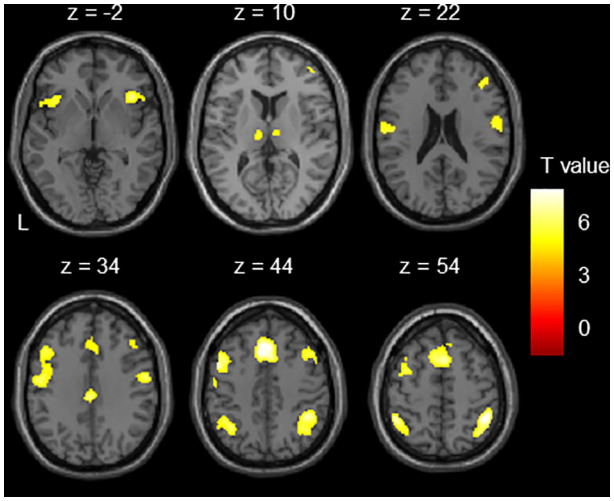

Fig. 4. Conjunction analyses showing brain activation to umami and salty taste in all participants (n = 30 including umami high and low tasters). Reported activations were significant at $pFWE_{corrected} \leq 0.05$ (30 voxels) and were shown on the axial slices with z – MNI coordinate. The color scale indicates statistical T values; L, left hemisphere.

Conjunction analyses results

Conjunction analysis of brain response to umami and salty tastes was performed for the (HT vs LT) contrast and vice versa. For the HT vs LT, stronger activation in the left inferior frontal operculum, left middle frontal cortex, right middle temporal gyrus, and the left superior parietal lobule was observed. For LT vs HT, the right hippocampus, postcentral gyrus, right lingual cortex and the thalamus was found with larger activations (Table 4, Fig. 6). A less stringent conjunction analysis with uncorrected $p < 0.01$ (based on the global null hypothesis) shows larger cluster of the thalamus activation (peak at MNI coordinates 2 −24, $T = 2.88$, cluster size = 35 voxels).

DISCUSSION

In the whole sample of participants, overall taste-induced (umami and salty tastes) brain activations were observed in the anterior insular cortex, frontal operculum, the pre- and post-central gyrus, middle cingulate cortex and thalamus. These brain regions showed large overlap to the gustatory cortex for basic taste processing, as suggested by previous meta-analysis of human fMRI studies (Veldhuizen et al., 2011; Yeung et al., 2017). Therefore, the conjunction analyses of umami and salty taste suggested the effectiveness of the taste stimulation paradigm and the fMRI experimental design to study brain activation in response to oral taste perception.

Table 2. Different brain activation to umami taste in umami high tasters and low tasters

	k	*T* value	*x*	*y*	*z*	Regions
HT > LT	200	5.74	−52	−50	−2	Inferior Temporal Gyrus L
	210	4.72	−58	8	26	Inferior Frontal Operculum L
		3.61	−56	2	34	
		3.02	−50	−8	36	
	171	4.56	60	10	28	Inferior Frontal Operculum R
		2.95	64	0	22	
	154	3.98	−18	−56	72	Superior Parietal Lobule L
	195	3.80	−52	−28	46	SupraMarginal L
		2.93	−60	−20	38	
	119	3.73	−4	−62	58	Precuneus R L
	34	3.59	−16	0	70	Supplementary Motor Area L
	81	3.58	38	−46	56	Inferior Parietal Lobule R
	41	3.56	−32	−40	32	Inferior Parietal Lobule L
	23	3.56	−48	−50	18	Middle Temporal Gyrus L
	163	3.37	54	−52	14	Inferior Temporal Gyrus R
		3.28	50	−48	−4	
	26	3.28	−28	−38	48	Postcentral Gyrus L
	14	3.28	−32	36	46	Middle Frontal Cortex L
	21	3.04	30	42	−4	Orbitofrontal Cortex R
	12	3.03	38	52	24	Middle Frontal Cortex R
	17	2.99	40	40	36	Middle Frontal Cortex R
	12	2.87	2	−30	48	Middle Cingulate Cortex R
	9	2.85	54	−30	54	Inferior Parietal Lobule R
LT > HT	185	4.77	4	−16	24	Middle Cingulate Cortex R
		4.04	14	−8	30	
		2.78	−8	−8	30	
	36	3.70	44	−8	60	Precentral gyrus R
	29	3.43	−56	4	−28	Middle Temporal Gyrus L
	32	3.37	0	−36	2	Lingual gyrus R
	32	3.32	−20	−24	14	Thalamus L
		3.17	−12	−26	10	
	22	3.27	18	−28	−8	Hippocampus R
	20	3.21	50	−58	26	Angular Gyrus R
	10	3.13	−36	−16	24	Insula L
	13	3.03	−6	−26	18	Thalamus L
	9	3.03	−22	−12	20	Caudate L
	8	3.01	22	−8	18	Caudate R
	13	2.96	−18	−16	−14	Hippocampus L
	10	2.90	−4	−38	32	Posterior Cingulate Cortex L
	9	2.86	4	−4	2	Thalamus R
	12	2.86	−4	54	−2	Anterior Cingulate Cortex L

Whole-brain analyses thresholded at uncorrected $p \leq 0.005$ and a minimum cluster size of eight voxels; HT, umami high tasters; LT, umami low tasters; R, right hemisphere; L, left hemisphere; *k*, cluster size in voxels; *xyz*, MNI space peak coordinates.

Effect of umami tasters

There was a significant effect of umami taster status on brain responses to taste perception, with very similar activations observed for umami and salty tastes. These findings may suggest a common central system involved in processing the two taste qualities, which had been suggested previously (Nakamura et al., 2011). On the one hand, the umami HT had larger activation in the frontal operculum compared to umami LT. The frontal operculum is regarded as part of the human primary gustatory cortex (Lundstrom et al., 2011; Veldhuizen et al., 2011). It has been shown that PROP (6-*n*-Propylthiouracil) tasters had significantly larger brain activation of the somatosensory and the gustatory area with oral perception of fat (Eldeghaidy et al., 2011). Therefore, superior umami taste identification might be correlated with an increased density of mechanosensitive trigeminal nerves, leading to a higher spatial tactile acuity. On the other hand, stronger activation in the hippocampus and thalamus were observed for umami LT as compared to HT, indicating that memory-related brain regions were involved. It is known that the thalamus is a gateway through which peripheral neural signals pass to reach the cortex. In fact, studies in other primates suggest an obligatory relay from the nucleus of the solitary tract by the taste thalamus to the taste cortex (Pritchard et al., 1986; Rolls, 1989). Besides, the thalamus plays a significant role in chemosensory attention (Plailly et al., 2008). For example, the state of hunger increases brain activation to umami taste in the thalamus and substantia nigra (Haase et al., 2009). The hippocampus was suggested to be involved in taste processing (Yeung et al., 2017), and associative learning (DelParigi et al., 2004) and the recall of taste stimuli (Haase et al., 2009). In addition, stronger activation of the anterior and posterior cingulate

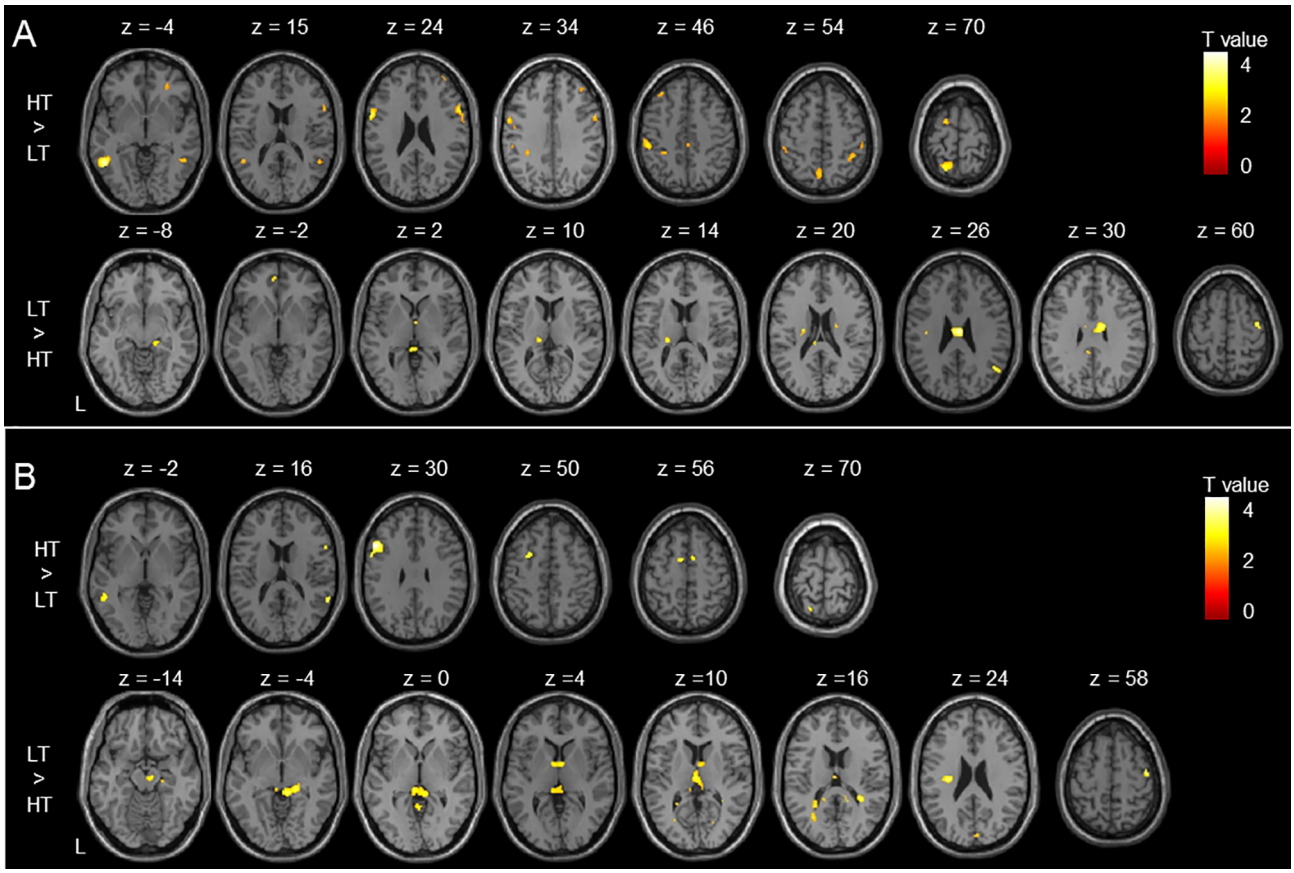

Fig. 5. Different brain activation among umami high tasters (HT) and umami low tasters (LT) in response to: (A) umami taste; (B) salty taste. All reported activations were significant at $p_{uncorrected} \leq 0.005$ (eight voxels) and were shown on the axial slices with z – MNI coordinate. The color scale indicates statistical T values; L, left hemisphere.

cortex was found for LT as compared to HT when umami and salt taste was analyzed separately, and these areas have been shown to be associated with attention to taste perception (Veldhuizen et al., 2007). In fact, studies of the neuronal mechanisms of attention show that the modulatory effects of the top-down pathways during chemosensory perceptions (e.g. associative learning or attention) are most evident when the bottom-up input is weak or ambiguous, for otherwise the bottom-up input then dominates the system and there is little or no attentional or cognitive modulation that can be observed (Deco and Rolls, 2005; Rolls, 2011). Results from the present study seems to fit well into this theory: activation in the thalamus and hippocampus among LT as compared to HT may suggest that LT had weaker bottom-up input into the gustatory system, but an enhanced attentional and top-down modulation during taste processing. In addition, LT subjects had stronger activation than HT subjects in associative areas, indicating that the perception of umami was novel and unusual (compare (Woollett et al., 2009)).

Taken together, those results suggested that the processing of umami and salty taste qualities converge in the central nervous system and processed within common neural areas depending on individual variability for umami taste identification. However, whether this is true for other taste qualities requires future investigation.

Effect of repeated exposure to umami taste

In the present study, the umami identification score for LT was significantly increased after training. However, brain imaging failed to show changes of brain responses to taste perception from PRE to POST sessions.

The umami identification in the current study was assessed using the ‘‘Taste Strips” test. This test is a quasi-threshold measurement for taste perception with both correct detection and recognition of the target taste is required. Therefore, one possible cause for the improved umami identification score among LT may be the increased experience and familiarity for umami (Kobayashi and Kennedy, 2002). Moreover, there was a significant decline of the umami taste identification ability ten days after stopping MSG exposure, suggesting a short-lived plasticity of umami taste perception (Kobayashi et al., 2006). For the current study, the discrepancy between psychophysical and neural imaging results regarding the effect of repeated umami exposure on taste perceptions further supports the idea that the improvement of umami identification is experience-dependent. The enhanced umami identification ability in our present and previous studies appears to be due to mechanisms that could not be identified with the currently employed techniques.

Table 3. Different brain activation to salty taste in umami high tasters and low tasters

	k	*T* value	*x*	*y*	*z*	Regions
HT > LT	317	4.30	−52	18	30	Inferior Frontal Operculum L
		2.97	−34	20	40	
	30	3.29	62	−50	18	Middle Temporal Gyrus R
	26	3.25	−26	6	50	Middle Temporal Gyrus L
	24	3.13	8	6	58	Supplementary Motor Area R
	8	3.12	−18	−58	70	Superior Parietal Lobule L
	18	3.08	−8	2	56	Supplementary Motor Area L
	49	3.07	−52	−46	−2	Middle Temporal Gyrus L
	9	2.96	60	16	16	Inferior Frontal Operculum R
LT > HT	479	4.88	20	−30	−8	Hippocampus R
		3.96	10	−34	−4	
		3.63	0	−16	10	Thalamus L
	76	4.20	−32	−18	24	Insula L
	33	4.02	48	−10	58	Postcentral Gyrus R
	47	3.85	32	−40	16	Superior Temporal Gyrus R
	17	3.55	−34	−10	66	Precentral gyrus L
	89	3.51	6	0	6	Caudate L
		3.31	−4	0	4	Caudate R
	27	3.51	8	−16	−14	Ventral Tegmental Area R
	49	3.36	−24	−50	14	Precuneus L
	27	3.35	0	−50	0	Cerebellum L
	32	3.22	−28	−64	16	Calcarine L
	24	3.13	−18	−42	20	Posterior Cingulate Cortex L
	10	3.01	16	−44	18	Posterior Cingulate Cortex R
	18	2.98	24	−74	8	Calcarine R
	12	2.87	6	−86	26	Cuneus R

Whole-brain analyses thresholded at uncorrected $p \leq 0.005$ and a minimum cluster size of eight voxels; HT, umami high tasters; LT, umami low tasters; R, right hemisphere; L, left hemisphere; *k*, cluster size in voxels; *xyz*, MNI space peak coordinates.

Table 4. Conjunction analyses showing different brain activation between umami high tasters and low tasters in response to both umami and salty tastes

	k	*T* value	*x*	*y*	*z*	Regions
HT > LT	110	3.94	−56	12	26	Inferior Frontal Operculum L
	41	3.42	−52	−46	−2	Middle Temporal Gyrus L
	13	3.18	−18	−58	70	Superior Parietal Lobule L
	16	2.80	58	−52	10	Middle Temporal Gyrus R
LT > HT	25	3.62	18	−28	−8	Hippocampus R
	18	3.46	44	−10	60	Precentral Gyrus R
	22	3.03	2	−34	2	Lingual Cortex R
	9	2.93	2	−2	4	Thalamus R

Whole-brain analyses thresholded at uncorrected $p \leq 0.005$ and a minimum cluster size of eight voxels; HT, umami high tasters; LT, umami low tasters; R, right hemisphere; L, left hemisphere; *k*, cluster size in voxels; *xyz*, MNI space peak coordinates.

Comparing the present study to previous work is difficult, because the previous work focused only on changes of familiarity-based brain responses induced by umami training in a relatively small sample (Singh et al., 2015). Still the work by Singh et al. (2015) demonstrated activation in the parahippocampal region following training with umami indicating recruitment of associative/memory-related brain areas. While obtained under different circumstances, the current work also emphasized the role of association and attention in the processing of taste.

Moreover, variability of umami taste perception (e.g. the umami sensitivity) is suggested to be determined by a combination of biological and environmental factors (Chen et al., 2009; Raliou et al., 2009). Umami taste indicates the rich content of protein in food (van Dongen et al., 2012; Lease et al., 2016), and sensitivity to umami taste is positively correlated with the preference and presumably greater intake of high-protein food (Luscombe-Marsh et al., 2008). Since no dietary record or information regarding nutrient status was collected in the current study, it is not known whether the differences observed in umami taste perceptual abilities also relate to differences in protein intake.

In summary, the current study demonstrated a central regulation of oral processing of umami and salty tastes, in which the umami HT showed stronger activation in the primary taste cortex, while umami LT had stronger

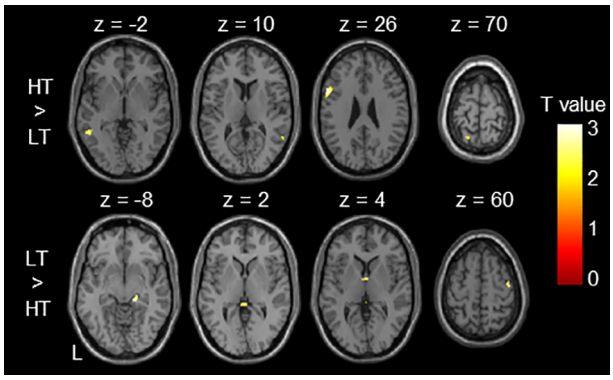

Fig. 6. Conjunction analyses showing overlapping brain activation in response to umami and salty tastes between umami high taster (HT) and low tasters (LT). All reported activations were significant at $p_{uncorrected} \leq 0.005$ (eight voxels) and were shown on the axial slices with *z* – MNI coordinate. The color scale indicates statistical *T* values; L, left hemisphere.

activation of the hippocampus and thalamus. In addition, although psychophysical results suggested the effectiveness of repeated umami exposure on improving umami "Taste Strips" test scores among LT, it was not reflected in changes of neural activation. This suggests the presence of very subtle mechanisms in regulating taste perception that could not be identified with the currently employed techniques.

REFERENCES

Chandrashekar J, Hoon MA, Ryba NJ, Zuker CS (2006) The receptors and cells for mammalian taste. Nature 444:288–294.

Chen QY, Alarcon S, Tharp A, Ahmed OM, Estrella NL, Greene TA, Rucker J, Breslin PA (2009) Perceptual variation in umami taste and polymorphisms in TAS1R taste receptor genes. Am J Clin Nutr 90:770S–779S.

de Araujo IE, Kringelbach ML, Rolls ET, Hobden P (2003) Representation of umami taste in the human brain. J Neurophysiol 90:313–319.

Deco G, Rolls ET (2005) Attention, short-term memory, and action selection: a unifying theory. Prog Neurobiol 76:236–256.

DelParigi A, Chen K, Salbe AD, Hill JO, Wing RR, Reiman EM, Tataranni PA (2004) Persistence of abnormal neural responses to a meal in postobese individuals. Int J Obes 28:370–377.

Eldeghaidy S, Marciani L, McGlone F, Hollowood T, Hort J, Head K, Taylor AJ, Busch J, Spiller RC, Gowland PA, Francis ST (2011) The cortical response to the oral perception of fat emulsions and the effect of taster status. J Neurophysiol 105:2572–2581.

Garcia-Bailo B, Toguri C, Eny KM, El-Sohemy A (2009) Genetic variation in taste and its influence on food selection. OMICS 13:69–80.

Haase L, Cerf-Ducastel B, Murphy C (2009) Cortical activation in response to pure taste stimuli during the physiological states of hunger and satiety. NeuroImage 44:1008–1021.

Iannilli E, Singh PB, Schuster B, Gerber J, Hummel T (2012) Taste laterality studied by means of umami and salt stimuli: an fMRI study. NeuroImage 60:426–435.

Kobayashi C, Kennedy LM (2002) Experience-induced changes in taste identification of monosodium glutamate. Physiol Behav 75:57–63.

Kobayashi C, Kennedy LM, Halpern BP (2006) Experience-induced changes in taste identification of monosodium glutamate (MSG) are reversible. Chem Senses 31:301–306.

Kurihara K (2009) Glutamate: from discovery as a food flavor to role as a basic taste (umami). Am J Clin Nutr 90:719S–722S.

Kurihara K, Kashiwayanagi M (2000) Physiological studies on umami taste. J Nutr 130:931S–934S.

Landis BN, Welge-Luessen A, Bramerson A, Bende M, Mueller CA, Nordin S, Hummel T (2009) "Taste Strips" – a rapid, lateralized, gustatory bedside identification test based on impregnated filter papers. J Neurol 256:242–248.

Lease H, Hendrie GA, Poelman AAM, Delahunty C, Cox DN (2016) A sensory-diet database: a tool to characterise the sensory qualities of diets. Food Qual Prefer 49:20–32.

Loper HB, La Sala M, Dotson C, Steinle N (2015) Taste perception, associated hormonal modulation, and nutrient intake. Nutr Rev 73:83–91.

Lugaz O, Pillias AM, Faurion A (2002) A new specific ageusia: some humans cannot taste L-glutamate. Chem Senses 27:105–115.

Lundstrom JN, Boesveldt S, Albrecht J (2011) Central processing of the chemical senses: an overview. ACS Chem Neurosci 2:5–16.

Luscombe-Marsh ND, Smeets AJ, Westerterp-Plantenga MS (2008) Taste sensitivity for monosodium glutamate and an increased liking of dietary protein. Br J Nutr 99:904–908.

Manzi B, Hummel T (2014) Intensity of regionally applied tastes in relation to administration method: an investigation based on the "taste strips" test. Eur Arch Otorhinolaryngol 271:411–415.

McCabe C, Rolls ET (2007) Umami: a delicious flavor formed by convergence of taste and olfactory pathways in the human brain. Eur J Neurosci 25:1855–1864.

Mueller CA, Pintscher K, Renner B (2011) Clinical test of gustatory function including umami taste. Ann Otol Rhinol Laryngol 120:358–362.

Nakamura Y, Goto TK, Tokumori K, Yoshiura T, Kobayashi K, Nakamura Y, Honda H, Ninomiya Y, Yoshiura K (2011) Localization of brain activation by umami taste in humans. Brain Res 1406:18–29.

Nichols T, Brett M, Andersson J, Wager T, Poline JB (2005) Valid conjunction inference with the minimum statistic. NeuroImage 25:653–660.

Overberg J, Hummel T, Krude H, Wiegand S (2012) Differences in taste sensitivity between obese and non-obese children and adolescents. Arch Dis Child 97:1048–1052.

Plailly J, Howard JD, Gitelman DR, Gottfried JA (2008) Attention to odor modulates thalamocortical connectivity in the human brain. J Neurosci 28:5257–5267.

Prescott J (2004) Effects of added glutamate on liking for novel food flavors. Appetite 42:143–150.

Prinster A, Cantone E, Verlezza V, Magliulo M, Sarnelli G, Iengo M, Cuomo R, Di Salle F, Esposito F (2017) Cortical representation of different taste modalities on the gustatory cortex: A pilot study. PLoS ONE 12:e0190164.

Pritchard TC, Hamilton RB, Morse JR, Norgren R (1986) Projections of thalamic gustatory and lingual areas in the monkey, *Macaca fascicularis*. J Comp Neurol 244:213–228.

Raliou M, Wiencis A, Pillias AM, Planchais A, Eloit C, Boucher Y, Trotier D, Montmayeur JP, Faurion A (2009) Nonsynonymous single nucleotide polymorphisms in human tas1r1, tas1r3, and mGluR1 and individual taste sensitivity to glutamate. Am J Clin Nutr 90:789S–799S.

Rolls ET (1989) Information processing in the taste system of primates. J Exp Biol 146:141–164.

Rolls ET (2009) Functional neuroimaging of umami taste: what makes umami pleasant? Am J Clin Nutr 90:804S–813S.

Rolls ET (2011) Chemosensory learning in the cortex. Front Syst Neurosci 5:78.

Roper SD (2007) Signal transduction and information processing in mammalian taste buds. Pflugers Arch 454:759–776.

Schoenfeld MA, Neuer G, Tempelmann C, Schussler K, Noesselt T, Hopf JM, Heinze HJ (2004) Functional magnetic resonance tomography correlates of taste perception in the human primary taste cortex. Neuroscience 127:347–353.

Seo HS, Iannilli E, Hummel C, Okazaki Y, Buschhuter D, Gerber J, Krammer GE, van Lengerich B, Hummel T (2013) A salty-congruent odor enhances saltiness: functional magnetic resonance imaging study. Hum Brain Mapp 34:62–76.

Shigemura N, Shirosaki S, Ohkuri T, Sanematsu K, Islam AA, Ogiwara Y, Kawai M, Yoshida R, Ninomiya Y (2009a) Variation in umami perception and in candidate genes for the umami receptor in mice and humans. Am J Clin Nutr 90:764S–769S.

Shigemura N, Shirosaki S, Sanematsu K, Yoshida R, Ninomiya Y (2009b) Genetic and molecular basis of individual differences in human umami taste perception. PLoS ONE 4:e6717.

Shoji N, Satoh-Ku Riwada S, Sasano T (2016) Clinical significance of umami taste and umami-related gene expression analysis for the objective assessment of umami taste loss. Curr Pharm Des 22:2238–2244.

Singh PB, Schuster B, Seo HS (2010) Variation in umami taste perception in the German and Norwegian population. Eur J Clin Nutr 64:1248–1250.

Singh PB, Hummel T, Gerber JC, Landis BN, Iannilli E (2015) Cerebral processing of umami: a pilot study on the effects of familiarity. Brain Res 1614:67–74.

van Dongen MV, van den Berg MC, Vink N, Kok FJ, de Graaf C (2012) Taste-nutrient relationships in commonly consumed foods. Br J Nutr 108:140–147.

Veldhuizen MG, Bender G, Constable RT, Small DM (2007) Trying to detect taste in a tasteless solution: modulation of early gustatory cortex by attention to taste. Chem Senses 32:569–581.

Veldhuizen MG, Albrecht J, Zelano C, Boesveldt S, Breslin P, Lundstrom JN (2011) Identification of human gustatory cortex by activation likelihood estimation. Hum Brain Mapp 32:2256–2266.

Welge-Luessen A, Leopold DA, Miwa T (2013) Smell and taste disorders-diagnostic and clinical work-up. In: Welge-Luessen A, Hummel T, editors. Management of smell and taste disorders-a practical guide for clinicians. Stuttgart: Thieme. p. 49–57.

Woollett K, Spiers HJ, Maguire EA (2009) Talent in the taxi: a model system for exploring expertise. Philos Trans R Soc Lond B Biol Sci 364:1407–1416.

Yeung AWK, Goto TK, Leung WK (2017) Basic taste processing recruits bilateral anteroventral and middle dorsal insulae: An activation likelihood estimation meta-analysis of fMRI studies. Brain Behav 7:e00655.

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