Increased intensity perception of aversive taste following right anteromedial temporal lobe removal in humans

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Summary

We used a modified version of the Spatial Taste Test to assess taste intensity perception in patients with either left or right temporal resection from the anteromedial temporal lobe (AMTL), and a group of control subjects. Sweet, sour, salty and bitter solutions were applied onto discrete locations of the tongue to stimulate either left or right fungiform, or left or right foliate papillae. Intensity ratings were assessed with the Labeled Magnitude Scale. Subjects also sipped 5 ml of each solution for whole mouth stimulation. Genetically based determinants of taste sensitivity were assessed with ratings of 6-n-propylthiouracil, and covaried from all analyses. As in previous studies, analysis of covariance indicated that the subjects in the right temporal group rated an aversive bitter taste as more intense than did subjects in the control group. In contrast, there were no group differences for sucrose ratings, suggesting that the AMTL may be involved preferentially in processing aversive compared with hedonic tastes. No group × side, or group × location effects were present. These results confirm that removal of the right AMTL in humans results in increased taste intensity/aversiveness perception. This finding complements existing literature indicating that the AMTL is important for processing aversive taste, and suggests that inhibitory mechanisms may play an important role in such processing.

Keywords: cerebral dominance; temporal lobe; aversion; reward; taste perception

Abbreviations: AMTL = anteromedial temporal lobe; AN(C)OVA = analysis of (co)variance; LMS = Labeled Magnitude Scale; PROP = 6-n-propylthiouracil

Introduction

Although its exact location is still debated, the human primary gustatory area is located within the insula/frontal and/or parietal operculum in heteromodal paralimbic cortex (Kinomura et al., 1994; Petrides and Pandya 1994; Small et al., 1997a, 1999; Zald et al., 1998; Faurion et al., 1999; Francis et al., 1999; Frey et al., 1999; Kobayakawa et al., 1999). The precise location of the secondary gustatory area also remains uncertain, but is likely to be in the orbitofrontal heteromodal paralimbic cortex (Francis et al., 1999; Small et al., 1999). This region is implicated in stimulus reinforcement learning (Rolls, 1996), and is also an area that non-human animals will self-stimulate in order to receive an electric shock (Mora et al., 1980). The location of the cortical gustatory areas within the paralimbic cortex suggests that sensory and affective processing of taste are highly integrated.

Taste-responsive neurones have also been described in the amygdala (Scott et al., 1993; Yan and Scott, 1996), a structure implicated in making hedonic judgements about many different types of sensory stimuli (reviewed in Ledoux, 1992). Amygdalar taste cells show little differential sensitivity to quality of taste stimuli (Scott et al., 1993) but, rather, they are tuned to palatability (hedonic assessment of tastes) and are sensitive to concentration, one of the factor(s) that influences palatability. They are thus thought to impart hedonic meaning to taste stimuli (Nishhiyo et al., 1998; Scott et al., 1993). Projections to the amygdala from both primary (Turner et al., 1980; Mufson et al., 1981) and secondary taste cortices (Amaral and Price, 1984), as well as from the nucleus of the solitary tract taste nucleus (Norgren, 1974; Price, 1981), have been elucidated in monkeys. Additionally, reciprocal connections between the lateral hypothalamus and amygdala have been demonstrated in monkeys (Aggleton
placing the amygdala in a strategic position to integrate information about current internal state with taste and many other sensory and situational variables associated with the context of ingestion.

We have conducted a previous series of studies to elucidate the role of the anteromedial temporal lobe (AMTL), including the amygdala, in human gustation (Small et al., 1997a, b, 1998). The results of these and other studies (Henkin et al., 1977; Zald et al., 1998; Francis et al., 1999) suggest that this region is involved in both hedonic and sensory analysis of taste, which is consistent with the hypothesis that there is a high degree of integration of sensory and affective processing of tastes, and that the AMTL is a key region where this interplay may take place. Neuroimaging studies have confirmed that the amygdala responds to aversive flavours (Small et al., 1997a) and tastes (Zald et al., 1998). The AMTL also responds to less aversive tastes such as 0.023 M citric acid solution (Small et al., 1997b), 0.1 M saline solution and 0.3 M glucose solution (Francis et al., 1999). In studies of patients with surgical removal from the AMTL, including at least 80% resection of the amygdala, we have reported elevated thresholds for recognition, but not detection, of citric acid (Small et al., 1997b), deficits in suprathreshold taste intensity estimation and increased sensitivity to a bitter taste (Small et al., 1998). The current study was designed to investigate further the changes in intensity perception following removal of the AMTL.

The gustatory system has been described as the gatekeeper to the internal environment (Scott, 1991). There are two options for action following taste perception: swallow or spit. Taste perception is tuned to identify nutrients, signified by the taste of sweet, sour, salty and savoury, and to identify poisons, signified by bitter taste (Bartoshuk, 1991). Perception of sweet, sour, salty and savoury tastes will probably lead to ingestion, whereas perception of bitter taste, especially if unexpected, will probably result in rejection. In our previous study, increased taste intensity perception following right AMTL removal was specific to the bitter taste. This suggests that there may be separate neural substrates for aversive and hedonic responses to taste perception, with the AMTL playing a larger role in processing aversive tastes. However, in our previous study, we had not controlled for potential underlying group differences in genetically determined taste sensitivity. There are at least three genetically determined normal variations of human taste bud density on the tongue, and the number of taste buds present correlates with taste intensity perception or ‘taster status’ (Bartoshuk et al., 1994). In the present investigation, we used intensity ratings of 6-n-propylthiouracil (PROP) to determine taster status (Bartoshuk et al., 1994), and co-varied taster status from all analyses.

Intensity perception for the four classical tastes (sweet, sour, salty and bitter) was evaluated with a shortened version of the Spatial Taste Test developed by Bartoshuk and colleagues (Prutkin et al., 1999) in subjects with removal from either the left or right AMTL. Tastes were applied individually to the left or right side of the tongue in one of two different locations: the front, to stimulate the fungiform papillae, or the side, to stimulate the foliate papillae. Whole mouth stimulation was also performed with a simple sip and spit test.

Based upon our previous studies, we predicted that subjects with removal from the right AMTL would rate the tastes as more intense than would subjects in the control group, and that this effect would be most pronounced for the aversive taste of bitter (quinine solution) compared with the hedonic taste of sweet (sucrose solution). We further reasoned that if taste information ascends ipsilaterally (Pritchard, 1991), and if the right hemisphere is predominant for taste (Small et al., 1997a, b, 1999; Zald et al., 1998), then the effect should also be more pronounced for tastes applied to the right side of the tongue. Finally, if AMTL plays a greater role in processing aversive rather than hedonic tastes, then there should be larger differences between the groups for bitter (aversive taste) compared with sweet (hedonic taste).

Methods

Subjects

Subjects were 18 patients at the Montreal Neurological Hospital who had undergone unilateral resection from the AMTL (eight from the left and 10 from the right) for the treatment of pharmacologically intractable epilepsy. All patients had epilepsy arising from a single focus, determined by clinical pattern, EEG recordings and MRI scans. According to surgical reports, all patients had had at least four-fifths of the amygdala and uncus removed as well as partial resection of the hippocampus ranging in length from 2 to 4 cm. Varying amounts of the parahippocampal gyrus had also been removed, ranging in length from 0 to 4 cm, as well as varying amounts of dentate gyrus, ranging in length from 2 to 3 cm. In addition, five of the 18 patients had had removal of temporal neocortex (left temporal = 3 of 8, right temporal = 2 of 10). In these patients, the neocortical resections ranged between 4 and 5.5 cm along the first, second and third temporal gyri. Because the amygdala was the structure of interest for this study, the extent of amygdalar resection was evaluated in postoperative MRI scans (examples in Fig. 1). It was confirmed that, in all cases, there had been significant excision of the amygdala comprising at least three-quarters of the total volume. All subjects gave informed consent according to the declaration of Helsinki (BMJ 1991; 302: 1194) to participate in the study, which was approved by the Montreal Neurological Institute’s Research Ethics Committee.

All patients had a Full Scale IQ rating (Wechsler, 1981) of at least 75, and were left-hemisphere dominant for language function. Subjects with known atypical hemispheric language representation were excluded. Left hemisphere language lateralization was established via intracarotid amobarbital
Fig. 1 MRI scans illustrating representative resections. Top row: slices from the postoperative MRI of a patient from the right AMTL group whose surgery included temporal neocortex. From left to right for all rows: horizontal, sagittal and coronal sections. Second row: slices from the postoperative MRI of a patient from the left AMTL group, whose surgery included temporal neocortex. Third row: slices from the postoperative MRI of a patient from the right AMTL group, whose surgery included minimal removal of temporal neocortex. Bottom row: slices from the postoperative MRI of a patient from the left AMTL group, whose surgery included minimal removal of temporal neocortex. Slices were selected to provide the optimal view of amygdalar removal. The resections presented here are representative of all patients in this study and are typical of surgeries performed at the Montreal Neurological Institute for the relief of intractable temporal lobe epilepsy.

testing (Wada and Rasmussen, 1960), or it was presumed based upon right-handedness, right ear advantage on dichotic listening tests, and concordance between neuropsychological test profile and side of EEG or MRI abnormality. Thirteen healthy control subjects matched to the patient group for age, sex and smoking habits constituted the control group.
Aversive taste perception following right AMTL removal

Table 1 Subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Sex (F:M)</th>
<th>Mean age in years (range)</th>
<th>Mean PROP (range)</th>
<th>Mean education in years (range)</th>
<th>Mean IQ (range)</th>
<th>Smokers (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LT</td>
<td>8</td>
<td>(5,3)</td>
<td>38 (23–52)</td>
<td>42 (4–88)</td>
<td>15 (10–21)</td>
<td>102 (86–122)</td>
<td>15</td>
</tr>
<tr>
<td>RT</td>
<td>10</td>
<td>(6,4)</td>
<td>33 (18–41)</td>
<td>63 (33–99)</td>
<td>15 (12–17)</td>
<td>93 (76–124)</td>
<td>2</td>
</tr>
<tr>
<td>C</td>
<td>12</td>
<td>(8,4)</td>
<td>31 (22–41)</td>
<td>41 (15–85)</td>
<td>16 (11–23)</td>
<td>NA</td>
<td>4</td>
</tr>
</tbody>
</table>

LT = left temporal; RT = right temporal; C = control; F = female; M = male; NA = not available.

(Table 1). All patients had not eaten for at least 1.5 h prior to testing.

Taste solutions

According to the procedure for the Spatial Taste Test (Prutkin et al., 1999), we used the following solutions: 1.0 M sucrose, 1.0 M NaCl, 0.001 M quinine hydrochloride and 0.032 M citric acid. The solutions were made with USP (United States Pharmacopoeia) grade tastes mixed with double-distilled deionized water. Long-handled Q-tips were used to apply the solutions onto the tongue to achieve discrete locus stimulation. For whole mouth stimulation, solutions were presented as 5 ml of liquid in a 30 ml plastic cup. A 150 ml plastic tumbler filled with double-distilled deionized water was available for rinsing between trials.

Labeled Magnitude Scale (LMS)

Taste intensity perception was assessed via ratings made on the LMS, a semantic scale of perceptual intensity characterized by quasi-logarithmic spacing of its verbal labels (Green et al., 1996) (Fig. 2). A laminated photocopy of the LMS was placed in front of the subjects so that they could make their rating by crossing the scale with a mark made with a water-soluble marker. The LMS has been shown to yield ratio-level data comparable with those produced by magnitude estimation (Green et al., 1996). The scale was also translated into French because many of the subjects were francophone (strongest imaginable sensation = la plus forte sensation imaginable, very strong = très forte, strong = forte, moderate = modéré, weak = faible, and barely detectable = à peine détectible). A transparency was made of the LMS with a ruler that divides the scale into 100 units. This numerical scale was superimposed on the laminated scale after each trial to ascertain the numerical value associated with the point marked by the subjects.

6-n-Propylthiouracil (PROP) papers

PROP papers were made according to the procedure outlined by Bartoshuk and colleagues (Bartoshuk et al., 1994). Five grams of PROP was added to 500 ml of boiling tap water to make a saturated solution. Circles (3 cm in diameter) were cut from Whatman 1 filter paper and dipped into the solution until they were completely soaked. The papers were allowed to dry and then packaged in wax paper envelopes.

Procedure

The Spatial Taste Test (Prutkin et al., 1999) was conducted first. Solutions were applied individually to each location...
and side. However, each solution was applied to the left and right sides of a location (front or side of the tongue) to facilitate comparison, before application to the second location. Ratings were made before the tongue was retracted into the mouth to ensure that the rating was based only upon the area intended to be stimulated. Subjects used a water-soluble marker to indicate their rating on the laminated LMS, which was wiped clean after recording each rating. Subjects rinsed with double-distilled deionized water after every taste pair. Each taste was applied to both sides and both locations before beginning stimulation with the next taste. The locus of presentation (fungiform or foliate papillae), side of presentation and order of taste presentation were counterbalanced across subjects, with the exception that the bitter solution was always presented last. This was to reduce the effects of the lingering after taste of bitter on the evaluation of the other tastes. To stimulate the fungiform papillae, subjects simply stuck out their tongue as far as was comfortable and then the taste was applied to the tongue. To stimulate the foliate papillae, subjects were given a piece of gauze to facilitate holding their tongue, and then asked to pull out their tongue as far as was comfortable. With their other hand, they were asked to hold open the side of their mouth that was being stimulated. After stimulation, they were told to keep holding their tongue, but were allowed to release hold on their mouth so that they could use the pen to make their rating on the LMS. The circumvallate and palate papillae were not stimulated due to time constraints. Foliate and fungiform papillae were chosen because they were found to be the easiest to stimulate in pilot testing.

After completion of the discrete locus stimulation, subjects were presented the four tastes as 5 ml solutions in 30 ml plastic cups. Again, order of presentation was counterbalanced across subjects, with the exception that the bitter solution was always presented last. Subjects were asked to sip the entire solution, hold it in their mouths for several seconds, and then expectorate. Ratings were made immediately following expectoration. Subjects then rinsed twice before tasting the next solution.

After the Spatial Taste Test and the whole mouth taste test quinine, PROP taster status. Subjects into non-, medium- and super-tasters was made according to the criteria of Bartoshuk (personal communication). A score of >71 corresponded to super-taster, 15–71 to medium-taster and <15 to non-taster (Fig. 2).

**Statistical analysis**

Two repeated measures analyses of covariance (ANCOVA) were carried out. In each, age and PROP taster status served as covariates. The first analysis evaluated estimates made in response to discrete locus stimulation. Taste, loci and side of the tongue were the within-subject variables and group membership was the between-subjects variable. The second analysis evaluated estimates made in response to the whole mouth presentation of the tastes. Taste was the within-subject variable and group the between-subject variable.

**Results**

Analysis of the discrete locus data revealed an effect of taste [F(3,31) = 3.4, P = 0.02], but no effect of either loci [F(3,31) = 1.4, P = 0.24] or side [F(3, 31) = 0.01, P = 0.92] of presentation. There were also no interactions between the within-subject variables. Pairwise comparison with Bonferroni correction for multiple comparisons indicated that the effect of taste arose because subjects in all groups tended to rate the sucrose as less intense than all other tastes (when compared with citric acid, P = 0.02; NaCl, P =0.002; quinine, P < 0.000) (Fig. 3).

A main effect of group [F(2,25) = 3.55, P = 0.05] was present. Pairwise comparison with Bonferroni adjustment for multiple comparisons showed that subjects in the right temporal group rated the tastes as significantly more intense than did subjects in the control group (P = 0.05) (Fig. 4). There was no significant difference between the left temporal and control (P = 0.30) or right temporal groups (P = 0.9) (Fig. 4). Thus, although only the right temporal group differed significantly from the control group, the left temporal and right temporal groups performed in a manner similar to each other. An effect of PROP taster status was also present [F(2,25) = 15.5, P = 0.001], but was covaried out. A one-way ANOVA was performed to assess potential group differences in PROP taster status; none was present [F(3,29) = 1.9, P = 1.8]. Figure 5 displays individual PROP ratings across the three groups.

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**Fig. 3** Mean intensity ratings summed across groups. Error bars represent the standard error of the mean.
In the analysis of whole mouth stimulation ratings, there was no effect of taste, and the predicted effect of group only approached significance \( F(2,25) = 3.1, P = 0.06 \). Pairwise comparison again showed that the nature of the difference was similar to that seen in the discrete stimulation, with subjects in the right temporal group tending to rate the tastes as more intense than subjects in the control group (Fig. 4), although the difference was not significant \( P = 0.07 \).

Although none of the group by within-subject variable interactions were significant, the interaction between taste and group approached significance \( F(6,75) = 1.9, P = 0.10 \) in the discrete locus data analysis (Fig. 6).

Since we had predicted that the right temporal group would rate the quinine as more intense than would the control group, especially if it was applied to the right side of the tongue, we conducted a planned comparison to look specifically for this effect. Thus, a grand mean for the ratings of quinine for each side of the tongue was computed.

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**Fig. 4** Mean intensity ratings made by each group, summed over tastes. Error bars represent the standard error of the mean. LT = left temporal; RT = right temporal; C = control.

**Fig. 5** PROP intensity ratings by individual subjects. Some circles represent more than one subject (C, three subjects gave a rating of 50; RT, three subjects gave a rating of 33; LT, two subjects gave a rating of 26). LT = left temporal; RT = right temporal; C = control.

**Fig. 6** Mean intensity ratings made by each group for each taste. Note that ratings for sucrose (sweet) are similar for all three groups, whereas there is a trend for the patient groups to rate the other three tastes as more intense. Error bars represent the standard error of the mean. LT = left temporal; RT = right temporal; C = control.

**Fig. 7** Mean intensity ratings for the quinine solution on the left versus right side of the tongue. Error bars represent the standard error of the mean. LT = left temporal; RT = right temporal; C = control.
planned comparison test of simple main effects was then conducted, again using PROP taster status and age as covariates. Although side was again not significant \( F(2,25) = 0.2, P = 0.66 \), there was a main effect for group \( F(2,25) = 4.0, P = 0.03 \). Bonferroni-adjusted \( t \) tests indicated that the difference was as predicted, with the right temporal group’s ratings of the quinine being significantly more intense than that of the control group \( P = 0.03 \). The left temporal group rating did not differ from that of the control \( P = 0.6 \) or right temporal \( P = 0.9 \) groups (Fig. 7).

The same procedure was followed for the sucrose ratings as was used for the quinine ratings. We had predicted that if the AMTL was involved preferentially in processing aversive tastes, then AMTL lesions should have an effect upon quinine (aversive taste) ratings but not on sucrose (hedonic taste) ratings. A planned comparison test of simple main effects confirmed that there were no group differences for sucrose ratings \( F(2,25) = 0.1, P = 0.9 \) (Fig. 6). There was also no effect of side \( F(1,25) = 0.4, P = 0.84 \) or group \( \times \) side \( F(1,25) = 0.72, P = 0.5 \).

Additionally, even though the group by taste interaction only approached significance, in the depiction of the data presented in Fig. 6 both left temporal and right temporal groups appear to rate all tastes except sucrose as more intense than did the control group. Thus, although the difference is clearest for the taste of quinine in the right temporal group in both the current study and our previous experiment (Small et al., 1998), the effect does not appear to be specific to quinine. Rather, this effect seems to be present, but to a lesser degree, for the tastes of sour and salty as well. Interestingly, like the bitter solution, both sour and salty solutions are generally rated as unpleasant, whereas sucrose is consistently given pleasant ratings (unpublished observations).

**Discussion**

As predicted, and in accordance with our previous results (Small et al., 1998), we report increased taste intensity perception following removal from the right AMTL. In the current study, the effect was significant for discrete locus stimulation and approached significance for whole mouth stimulation. Patients in the right temporal group also had insignificantly higher PROP ratings than did subjects in the other groups (Fig. 5). This higher PROP rating may have resulted from differences in genetically determined taster status. Conversely, it may be a manifestation of increased taste sensitivity following removal from the AMTL. However, even with PROP ratings covaried out of the equation, the right temporal group gave significantly greater taste intensity estimates than the other groups. We also observed a trend for a group \( \times \) taste interaction. A planned comparison confirmed our prediction that intensity ratings for quinine would be higher for the right temporal group than the left temporal and control groups. A second planned comparison indicated that there was no group difference for the sucrose ratings, suggesting that AMTL is involved predominantly with processing aversive rather than hedonic tastes.

Taste-responsive cells have been identified in the amygdala of non-human primates (Scott et al., 1993; Yan and Scott, 1996; Karadi et al., 1998). In all our cases (Small et al., 1997a, 1998; this study), the AMTL lesions included at least 80% resection of the amygdala. Taste-responsive cells in the monkey amygdala are sensitive to concentration (Scott et al., 1993). Moreover, to our knowledge, there are no reports in the literature of taste-responsive cells in any of the other structures that were included in our patients’ surgical resections (e.g. hippocampus or parahippocampal gyrus). It is therefore plausible that the changes in taste intensity perception associated with AMTL lesions are due to disruption of functioning of amygdalar taste neurones, which are sensitive to taste concentration. A similar effect has been observed in rats (Touzani et al., 1997). Touzani and colleagues reported lower preference (determined by a two-bottle choice test) for saccharin and increased aversion to a high concentration of saccharin and quinine solutions following bilateral ibotenic acid lesions of the central amygdalar nucleus. These authors suggest that the central nucleus of the amygdala plays an important role in the normal response to exteroceptive food stimuli via modulation of the aversive value of taste stimuli (Touzani et al., 1997). While the patients in our studies had much larger lesions, which were unilateral rather than bilateral, the similarity in behavioural effects is striking. Additionally, the effect of increased taste intensity perception that we have observed in humans seems to be greatest for aversive solutions (especially quinine, see also Small et al., 1998) compared with the hedonic sucrose ratings. Therefore, although this issue currently cannot be resolved, it is possible that the increased intensity ratings reflect a potentiation in aversive value as opposed to, or in addition to, an increased intensity perception. A greater involvement of the AMTL in processing aversive, when compared with hedonic, tastes and smells has also been observed in neuroimaging studies (Small et al., 1997b; Zald et al., 1997, 1998).

Taste stimulus concentration is related to both intensity perception and palatability. For example, Kocher and Fisher reported that tastes perceived as unpleasant tended to receive higher ratings of intensity (Kocher and Fisher, 1969). Conversely, motivational factors such as satiety can influence intensity perception. For example, Giza and Scott showed that injection of a glucose load reduces perceived sweetness intensity in rats (Giza and Scott, 1987). Thus, it is difficult to dissociate intensity perception from motivational factors such as perceived aversiveness. It is interesting that in the current study, the greatest similarity between intensity ratings for the groups were with sucrose, the only pleasant-tasting stimulus used (Fig. 6). In fact, in accordance with Kocher and Fisher (Kocher and Fisher, 1967), subjects in all groups rated the sucrose as less intense than other tastes. This dissociation of ratings between the most and least pleasant tastes suggests that the effect of increased taste intensity is
specific to aversive taste. It also indicates that the difference in quinine intensity ratings was not due simply to differential use of the scale by the three groups. However, given the apparent difficulty in separating the perception of intensity versus aversiveness, we cannot know within the context of this paradigm if it is the intensity, aversiveness or some interaction between these two perceptual experiences that gives rise to the increase in intensity ratings observed here.

In addition to disentangling intensity from aversiveness, questions that remain are why and how should disruption of gustatory processing in the amygdala lead to increased aversiveness or intensity perception? One explanation is that the AMTL lesion results in disinhibition of cortical taste cells sensitive to concentration or palatability. Berridge has made a similar proposal to account for the potentiation of aversion to a taste observed in decerebrate rats (Grill and Norgren, 1978) and in rats with bilateral lesions to the ventral pallidum (Berridge, 1996). He suggested that the function of the ventral pallidal neurones might be to amplify hedonic evaluations rather than to mediate aversion. The enhanced aversion produced by its removal could then be interpreted as a disinhibition effect. Berridge did not speculate as to the site of disinhibition.

Rolls has suggested that gustatory processing in the primary gustatory area is not influenced by motivation, because taste cells in this region respond in a similar manner regardless of the level of satiety (Rolls, 1996). However, single-cell recording studies in monkeys have demonstrated that primary gustatory area taste-responsive cells are sensitive to both concentration and quality of taste stimuli, both of which are factors determining palatability (Scott et al., 1986; Yaxley et al., 1990). Additionally, both in rats (Rosenblum et al., 1997) and humans (Faurion, 2001), the insular cortex has been shown to be sensitive to the novelty of tastes. There are reciprocal connections between the amygdala and insular cortex (Turner, 1980; Mufson et al., 1981). We are unaware of any study of the effects of amygdalar inputs on processing of cells in the insular cortex. However, it is possible that amygdalar input to the primary gustatory area results in inhibition of taste cells sensitive to concentration or palatability. There is some evidence that suggests that the saliency of a taste stimulus increases the activity of inhibitory interneurones in the insula (Rosenblum et al., 1997). Rosenblum and colleagues have reported that tasting a novel substance results in tyrosine phosphorylation of the NR2B phosphoprotein, which is concentrated on interneurones in the insular cortex (Rosenblum et al., 1995, 1997). The amount of phosphorylation increases in a dose-dependent manner with stimulus concentration and decreases with familiarization. Determining whether or not this effect is driven by amygdalar inputs, and thus the viability of our speculation, must await future electrophysiological experiments. However, it is also possible that the disinhibition effect, which we propose to account for our result, occurs in other brain regions in addition to or instead of the primary gustatory area. For example, other candidate regions may include the basal forebrain, which has been shown to be sensitive to the affective value of taste (Small et al., 1997a), or the contralateral amygdala.

Contrary to our prediction, the side of the tongue on which the taste was applied did not interact with the side of surgical resection. We had speculated that since the human gustatory system is probably organized in a largely ipsilateral fashion (Pritchard, 1991) and since the right hemisphere (at least at the level of the AMTL) seems to be predominant in at least some aspects of taste perception (Small et al., 1997a, b, 1999; Zald et al., 1998; Francis et al., 1999), tastes applied to the right side of the tongue of patients in the right temporal group would be rated as especially intense. There are several possible reasons why we did not observe this effect, or any other effect of side upon taste intensity perception in patients with unilateral AMTL resection. First, it could be that gustatory information ascends bilaterally in humans. There is general agreement that a lesion in the brainstem up to the pons will lead to decreased sensitivity on the ipsilateral side of the tongue (Goto et al., 1983; Nakajima et al., 1983; Lee et al., 1998; Uesaka et al., 1998; Onoda and Ikeda, 1999), supporting ipsilateral ascension of taste fibres. Gustatory disturbance following lesions to the pons are also predominantly ipsilateral (Uesaka et al., 1998; Onodo and Ikeda, 1999), but bilateral (Uesaka et al., 1998) and contralateral (Onoda and Ikeda, 1999) deficits have been reported. Additionally, contralateral, ipsilateral and bilateral taste deficits have been reported following lesions to higher levels of the gustatory neuraxis including the thalamus and the primary gustatory area (Bornstein, 1940a, b; Motta, 1959; Onoda and Ikeda, 1999; Pritchard et al., 1999). It is therefore possible that taste fibres proceed ipsilaterally to the nucleus of the solitary tract, which in turns sends out projections that ascend ipsilaterally until the pons, at which point at least some fibres decussate, finally culminating in bilateral projections to the thalamus and primary gustatory area. Secondly, it is possible that taste intensity perception constitutes a higher order gustatory function that is only lateralized at higher levels of the neuroaxis, such as the AMTL. This would be analogous to sound perception, which occurs bilaterally, and comprehension of speech, which is usually lateralized to the left hemisphere in right-handed people. However, in the current study, it is important to note that, although the difference between the left temporal and control groups was not significant, the left temporal groups’ ratings were similar to the right temporal groups’ ratings (Figs 5 and 6).

In summary, we report increased taste intensity perception following resection from the right but not the left AMTL. This effect was not influenced by side or locus of stimulation. The effect was also more pronounced for aversive taste, especially bitter (see also Small et al., 1998), compared with sweet, a hedonic taste. This suggests that the increased ratings may reflect a potentiation of aversiveness, manifested by increased intensity perception, and indicates that the right AMTL may be involved preferentially with processing aversive tastes, which is consistent with results from
neuroimaging studies of taste and smell (Small et al., 1997b; Zald et al., 1997, 1998). Moreover, these data corroborate and extend our previous findings suggesting that right AMTL resections may lead to changes in both affective and sensory processing of tastes, supporting our proposal that sensory and affective processing of taste is highly integrated.

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