TASTE RESPONSES TO MONOSODIUM GLUTAMATE AFTER ALCOHOL EXPOSURE

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Abstract — Aims: The aim of the present study was to evaluate the effects of acute and chronic exposure to alcohol on taste responses to a prototypic umami substance, monosodium glutamate (MSG). Methods: The rated intensity and pleasantness of MSG taste (0.03–10.0%) was compared in chronic male alcoholics (n = 35) and control subjects (n = 25). In a separate experiment, the effects of acute exposure of the oral mucosa to ethanol rinse (0.5–4.0%) on MSG taste (0.3–3.0%) were studied in 10 social drinkers. Results: The alcoholic and control group did not differ in terms of the rated intensity and pleasantness of MSG taste. Electrogustometric thresholds were significantly (P < 0.01) higher, i.e. worse, in the alcohol-dependent subjects. The difference remained significant after controlling for between-group differences in cigarette smoking and coffee drinking. Rinsing with ethanol did not alter either intensity or pleasantness of MSG taste in social drinkers. Conclusions: The present results suggest that: (i) neither acute nor chronic alcohol exposure modifies taste responses to MSG; (ii) alcohol dependence may be associated with deficit in threshold taste reactivity, as assessed by electrogustometry.

INTRODUCTION

It is often assumed that heavy alcohol (ethanol) consumption may compromise the taste and smell function (Smith, 1972; Bauer and Mott, 1996; Rupp et al., 2003). However, sound evidence supporting this notion is sparse. In many studies, alcohol dependence was not associated with any obvious alteration in smell reactivity (Jones et al., 1975a,b, 1978; Kessler et al., 1991). Effects of heavy alcohol drinking on gustatory function are even less clear. Many years ago, Smith (1972) had shown that alcohol-dependent subjects had higher alteration in smell reactivity (Jones, 1972). Jones et al. (1978) have reported that non-Korsakoff alcoholics did not present any deficits in taste reactivity to suprathreshold salty solutions. In a more recent study, the rated intensity and pleasantness of suprathreshold concentrations of sucrose, quinine, sodium chloride and citric acid, representing the four basic taste categories, did not differ between alcohol-dependent and control subjects (Bogucka-Bonikowska et al., 2001). Although Kampov-Polevoy et al. (1997, 1998) have reported that alcohol-dependent men may show some alteration in pleasantness ratings of sweet solutions (but see also Bogucka-Bonikowska et al., 2001), the intensity ratings and abilities to discriminate various sucrose concentrations did not differ between the alcoholics and controls. Thus, it seems that chronic alcohol consumption may alter the taste threshold to bitter solutions but not the suprathreshold reactivity to sweet, bitter, salty and sour stimuli.

Umami taste is now recognized to be the fifth basic taste category in mammals. It has been suggested that this taste category evolved to enhance detection of amino acids (e.g. glutamate and aspartate) and oligopeptides in foods (for review, see Bellisle, 1999; Brant, 2000; Doty, 2003). Monosodium glutamate (MSG) is a prototypic umami substance that is widely used as a research tool and flavour enhancer (Yamaguchi, 1991; Yamaguchi and Ninomiya, 2000; Kobayashi and Kennedy, 2002; Nelson et al., 2002). Preclinical studies have indicated that MSG solutions may evoke umami taste through interactions with both metabolotropic (mGlur) and ionotropic (iGlur) glutamate receptors expressed by taste receptor cells in a taste bud (Brand, 2000). Two subtypes of mGlur, i.e. mGlur1 (Toyono et al., 2003) and mGlur4 (Chaudhari et al., 2000; Nakashima et al., 2001), as well as the N-methyl-D-aspartate (NMDA) subtype of iGlur (Brand, 2000; Nakashima et al., 2001), are candidate receptors involved in MSG detection by taste receptor cells.

It has been shown repeatedly that the glutamatergic system in the brain is involved in the mediation of the neurobehavioural effects of ethanol. For example, a large body of evidence indicates that NMDA receptors are particularly sensitive to clinically relevant ethanol concentrations (for review, see Løvring, 1997; Spanagel and Bienkowski, 2002). While acute ethanol inhibits NMDA receptors, chronic ethanol administration leads to enhancement of the NMDA receptor function (Danysz et al., 1992; Hoffman, 1995). Another line of research has also indicated that mGlurRs, including mGlur1 and mGlur5, are modulated by both acute and chronic alcohol administration (Minami et al., 1998; Spanagel and Bienkowski, 2002). Given the role played by peripheral iGlurRs and mGlurRs in detection of umami substances, one may hypothesize that acute and/or chronic alcohol exposure alters sensitivity to MSG taste. Thus, in the present study, we decided to evaluate taste responses to MSG in chronic alcoholics and non-alcoholic controls. In order to evaluate the basic taste sensitivity of the two groups, detection thresholds were assessed by means of electrogustometry (Experiment 1). The effects of acute exposure of the oral mucosa to ethanol solutions on reactivity to MSG taste were assessed in social drinkers (Experiment 2).
MATERIALS AND METHODS

Experiment 1

Subjects. Thirty-five abstinent male alcoholics were recruited from inpatients at the Department of Psychiatry, The Ludwik Rydygier Medical University, Bydgoszcz, and the Department of Prevention and Treatment of Addictions, Institute of Psychiatry and Neurology, Warsaw. All alcoholics met the ICD-10 criteria for alcohol dependence. Potential participants were excluded if they had a psychotic disorder or another substance use disorder other than nicotine and/or caffeine dependence. Subjects with active liver disease were also eliminated. However, mild elevation of baseline transaminase levels was accepted. The mean ± SEM duration of alcohol abuse and dependence was 15.4 ± 1.4 years (range: 3–37) and 11.3 ± 1.1 years (range: 1–26), respectively. The mean duration of last abstinence was 13.4 ± 6.1 weeks (range: 1–216). The alcoholic subjects consumed 30.4 ± 1.8 standard drinks/day in the last week before admission (range: 7.5–52.5).

Twenty-five male volunteers without a history of psychiatric disorder and consuming =1 standard drink/day served as controls. Only subjects with Alcohol Use Disorders Identification Test (AUDIT; Babor and Grant, 1989) scores <8 were included in the study. The controls were recruited from families of staff members, through the institutions involved in the study.

The subjects in both groups were Caucasians, aged 19–59 years (see Table 1 for details), in good medical health and had no recent history of acute conditions known to alter gustatory or olfactory function (Cullen and Leopold, 1999). Blood alcohol levels were not assessed before a taste test.

The whole study was carried out in accordance with the ‘Declaration of Helsinki’ of the World Medical Association. The protocol for the study was reviewed and approved by a local Ethics Committee on Human Studies (protocol no. IPiN/1/2002). Each participant read and signed an informed consent form after the study procedures had been fully explained.

Preparation of MSG samples. Six MSG solutions (0.03, 0.1, 0.3, 1.0, 3.0, 10.0% w/w; Sigma, Poznan, Poland) were prepared using sterile deionized water (Polfa, Lublin, Poland). The range of MSG concentrations was selected on the basis of previous reports (Yamaguchi, 1991; Kobayashi and Kennedy, 2002). Deionized water served as a control stimulus and thus each participant received and rated seven different gustatory stimuli. Rows of 1-ml single-use syringes were filled with the MSG solutions (syringe 1 = water, syringe 2 = 0.03% MSG, syringe 3 = 0.1% MSG, syringe 4 = 0.3% MSG, etc.) and stored at −4°C until use.

Electrogustometer. The electrogustometer (TR-06, Rion Co., Ltd, Tokyo, Japan) used in the study is a commercially available device that is used for assessing the human taste function (Kuga et al., 1999; Miller et al., 2002; Sienkiewicz-Jarosz et al., 2005). The apparatus allows the delivery of anodal currents of low intensity (from −6 to 34 dB, in 2-dB steps; 4–400 µA) at known durations. In the present study, the stimulus duration was kept at 0.5 s (Ajdukovic, 1984; Kuga et al., 1999). The electrogustometer was equipped with a stainless steel, flat, circular stimulus rod (5 mm in diameter) and a larger indifferent electrode (a neck band). During the test, the stimulus probe was placed on the tongue tip (Miller et al., 2002), while the indifferent electrode was attached to the subject’s neck. The participant signalled any new taste sensation on the tongue with the help of a response button connected to a small buzzer.

Procedure. A single taste test was conducted between 10 AM and 2 PM in quiet, well-ventilated rooms. The subjects were asked to refrain from eating, drinking and smoking for at least 1 h prior to the test session. Before the start of the session, each participant was familiarized with rating scales and questioned regarding drinking coffee and tea, and smoking cigarettes. The Fagerström Test for Nicotine Dependence (FTND) was used to assess nicotine dependence in current smokers (Fagerström et al., 1996).

A modified version of the initially ascending, single-staircase detection threshold procedure was used to assess electrogustometric thresholds (Sienkiewicz-Jarosz et al., 2005). The subject was asked to signal any new taste sensation on the tongue by pressing the response button. The current intensity was increased if no response occurred within 3 s. The current intensity was decreased (‘reversal’) if the subject signalled detection of the stimulus. The reported threshold (in µA) was an average of the last four out of eight reversals. For technical reasons, only 19 alcoholics could be tested by electrogustometry. Baseline characteristics of these subjects did not differ from that reported for the whole alcoholic group.

Table 1. Baseline characteristics of subjects recruited for Experiment 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls (n = 25)</th>
<th>Alcoholics (n = 35)</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>38.4 ± 2.5</td>
<td>42.1 ± 1.6</td>
<td>P &gt; 0.05; t-test</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79.6 ± 1.9</td>
<td>74.6 ± 2.1</td>
<td>P &gt; 0.05; t-test</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>176.1 ± 0.8</td>
<td>177.4 ± 1.1</td>
<td>P &gt; 0.05; t-test</td>
</tr>
<tr>
<td>University degree (%)</td>
<td>36.0</td>
<td>20.0</td>
<td>P &gt; 0.05; Fisher exact test</td>
</tr>
<tr>
<td>Presently employed (%)</td>
<td>80.0</td>
<td>54.3</td>
<td>P &gt; 0.05; Fisher exact test</td>
</tr>
<tr>
<td>Married (%)</td>
<td>64.0</td>
<td>57.1</td>
<td>P &gt; 0.05; Fisher exact test</td>
</tr>
<tr>
<td>Current smokers (%)</td>
<td>44.0</td>
<td>80.0</td>
<td>P &lt; 0.01*; Fisher exact test</td>
</tr>
<tr>
<td>FTND score</td>
<td>1.7 ± 0.4</td>
<td>5.1 ± 0.5</td>
<td>P &lt; 0.01*; Mann–Whitney U-test</td>
</tr>
<tr>
<td>Tea drinking (cups/day)</td>
<td>2.8 ± 0.3</td>
<td>2.8 ± 0.4</td>
<td>P &gt; 0.05; Mann–Whitney U-test</td>
</tr>
<tr>
<td>Coffee drinking (cups/day)</td>
<td>1.1 ± 0.2</td>
<td>2.1 ± 0.3</td>
<td>P &lt; 0.05*; Mann–Whitney U-test</td>
</tr>
</tbody>
</table>

*Means ± SEM.

bFTND, the Fagerström Test for Nicotine Dependence (calculated only for smokers).

*Significant difference.
The MSG samples were administered 5 min after completion of electrogustometry. The subjects received an additional 1 ml sample of deionized water on an unblinded basis as a neutral reference point. Then, increasing concentrations of MSG (0.0–10.0%) were administered in a volume of 1 ml on the anterior tongue from the single-use syringes. The participants were asked to thoroughly taste each sample within the entire oral cavity, and to rate intensity and pleasantness on 100-mm lines labelled at the ends for intensity ‘not at all’ and ‘extremely’ (scored 0–100) and for pleasantness ‘extremely unpleasant’ and ‘extremely pleasant’ (scored −50 to 50) (Scinska et al., 2000, 2001). The testing of each sample was separated by a duration of 60 s during which the subjects filled the response forms, rinsed their mouths with deionized water and waited for the next sample. The subjects were instructed to spit out the solutions. The test was performed by an experimenter who was blinded to the actual content of the syringes, and no feedback was given to the participant as to the correctness of his taste responses.

Experiment 2

Subjects. Ten social drinkers (six males and four non-pregnant females) were recruited from families of staff members, through the institutions involved in the study. Subjects with AUDIT scores <8 points and consuming ≤1 standard drink/day were included. Six participants were current smokers. The subjects were Caucasians, aged 19–30 years, in good medical health and had no recent history of conditions known to alter gustatory function (Cullen and Leopold, 1999). Their mean (±SEM) age, weight and height was 23.5 ± 1.0 years, 74.7 ± 5.7 kg and 177.0 ± 3.0 cm.

Preparation of MSG samples and ethanol rinses. Samples of MSG (0.0, 0.3, 1.0, 3.0% w/w) were prepared in the 1 ml syringes as described above (syringe 1 = water, syringe 2 = 0.3% MSG, syringe 3 = 1.0% MSG, syringe 4 = 3.0% MSG). The syringes were stored at −4°C until use.

Ethanol concentrations (0.5, 1.0, 2.0, 4.0% v/v) were prepared from commercially available rectified spirit (95% v/v; Polmos, Zielona Gora, Poland). Deionized water served as a control solution (0.0% ethanol). The solutions were stored at 4°C in tightly sealed sterilized bottles. The bottles were kept at room temperature for 2–3 h prior to use. Identical 25 ml samples of the five solutions were prepared immediately prior to use in small plastic cups.

The range of ethanol concentrations was selected based on our previous studies. Higher ethanol concentrations produced bitter taste sensation and local irritation (Scinska et al., 2000; Bienkowski et al., unpublished).

Procedure. A single test session was conducted between 10 AM and 2 PM in a quiet, well-ventilated room. The subjects were asked to refrain from eating, drinking and smoking for at least 1 h prior to the test session. The basic aspects of the procedure used in Experiment 2 were identical to those described above for Experiment 1. However, the delivery of each MSG sample was preceded by two rinses. The standard deionized water rinse was followed by the ethanol rinse. The participants were instructed to sip the entire 25 ml sample of ethanol solution, to swish the solution in their mouth for 10 s and to spit it out. Afterwards, the MSG solution was administered in a volume of 1 ml on the anterior tongue. The participants were asked to thoroughly taste each sample within the entire oral cavity and to rate its intensity and pleasantness.

RESULTS

Experiment 1

Table 1 presents the baseline characteristics of the control and alcoholic subjects. There was no significant difference between the controls and alcoholics in terms of age, weight, height, university education, employment, marital status and tea drinking. The percentage of cigarette smokers was significantly higher in the alcoholic group. Moreover, FTND scores were higher in the alcoholic than in the non-alcoholic smokers. The alcoholics consumed significantly more coffee.

Electrogustometric thresholds were significantly higher in the alcoholics (135.9 ± 28.8 μA) than in the controls [58.4 ± 11.2 μA; F(1,42) = 7.58, P < 0.01]. The difference remained significant (P < 0.05) when age, smoking status and coffee drinking were used as covariances, and when subjects with abnormal liver function tests (six alcoholics) were excluded from the analysis. Electrogustometric thresholds did not correlate with duration of alcohol abuse or dependence, alcohol consumption before admission and abstinence duration (Ps > 0.05).

Figure 1 shows intensity (Fig. 1A) and pleasantness (Fig. 1B) ratings of the MSG samples. The two-way ANOVA (group × MSG concentration) revealed that intensity ratings of MSG increased with concentration [F(6,348) = 58.63, P < 0.0001]. Neither a group effect [F(1,58) = 0.68, P = 0.41] nor a group × MSG concentration interaction [F(6,348) = 0.98, P = 0.43] was significant. The ANOVA revealed that...
pleasantness ratings of MSG varied with concentration \( F(6,348) = 6.73, P < 0.001 \). Neither a group effect \( F(1.58) = 1.76, P = 0.18 \) nor a group/MSG concentration interaction \( F(6,348) = 0.54, P = 0.77 \) was significant.

Elimination of the subjects with abnormal liver tests did not change the results of the ANOVA (Ps > 0.3 for group effects and Group/MSG concentration interactions).

Taste responses to MSG in the alcohol-dependent men did not correlate with duration of alcohol abuse or dependence, alcohol consumption before admission and duration of the last abstinence (Ps > 0.05).

Experiment 2
Repeated rinsing did not alter the basic taste reactivity to MSG. The ANOVA did not show any difference \( F(1,36) = 0.62, P = 0.43 \) for intensity, \( F(1,36) = 0.40, P = 0.52 \) for pleasantness] between responses to the first and last series of the MSG samples (i.e. the samples administered after the control water rinses). Thus, the control data were averaged across the two series.

The two-way ANOVA (ethanol concentration × MSG concentration) revealed that pleasantness did not change with MSG concentration \( F(3,36) = 0.40, P = 0.75 \). Similarly, neither an ethanol concentration effect \( F(4,144) = 0.24, P = 0.90 \) nor an MSG concentration × ethanol concentration interaction \( F(12,144) = 0.52, P = 0.89 \) was significant (Fig. 2B).

DISCUSSION

Taste responses to MSG were not influenced by either chronic (Experiment 1) or acute (Experiment 2) alcohol pre-exposure. Thus, it seems that receptor mechanisms involved in detection of MSG taste are not sensitive to alcohol. Our results add to a growing body of evidence (Jones et al., 1978; Kampov-Polevoy et al., 1998; Bogucka-Bonikowska et al., 2001) which indicates that alcohol dependence is not associated with any obvious deficit in reactivity to suprathreshold gustatory cues.

In contrast, electrogustometric thresholds were significantly higher in the alcoholic group. Hence, it seems that alcohol dependence may be related to poorer detection of weak gustatory stimuli. Our findings support the results of Smith (1972) who found that alcoholics had higher taste thresholds to quinine than non-alcoholic controls. The two groups in the latter study did not differ in terms of their smoking habits. Jones et al. (1978) have reported higher thresholds for sodium.
chloride in the group of long-term non-Korsakoff alcoholics when compared with normal controls. However, the difference between the alcoholics and controls was not much and did not reach significance ($P > 0.1$). The non-Korsakoff alcoholics in this latter study did not show any abnormalities in terms of reactivity to higher sodium chloride concentrations and thresholds or suprathreshold olfactory cues. On the other hand, both olfactory and gustatory responses were severely impaired in Korsakoff alcoholics (Jones et al., 1978).

Higher taste thresholds in alcoholics may be a consequence of central and/or peripheral effects of chronic alcohol consumption. Notably, several brain structures (e.g. the striatum and orbitofrontal cortex) and neurotransmitter systems (e.g. dopaminergic and serotonergic transmission) are involved both in taste processing and development of alcohol dependence (Diamond and Gordon, 1997; Yamamoto et al., 1998; Goldstein et al., 2001; Small et al., 2003; Kringlebach and Rolls, 2004; Myrick et al., 2004). It is also possible that the toxic effects of alcohol on the oral mucosa (Maier et al., 1994; Maito et al., 2003) lead to suppression of threshold electrogustometric responses while leaving whole-mouth responses to suprathreshold stimuli largely unaffected (Bogucka-Bonikowska et al., 2001; this study).

Higher thresholds in alcohol-dependent subjects may be an indirect consequence of vitamin and/or mineral deficiencies characteristic of this population (Russell, 1980). However, the lack of correlations between the basic clinical parameters and the electrogustometric thresholds (this study) suggest that the elevated taste threshold is a trait rather than a state marker for alcoholism. This hypothesis needs validation in further studies on children of alcoholics and larger samples of alcohol-dependent subjects.

The groups recruited for Experiment 1 differed in their smoking behaviour and coffee intake. In line with previous reports (e.g. Gurling et al., 1985; Swan et al., 1997), the alcoholics consumed more coffee and were more likely to be smokers. Moreover, the mean FTND score was significantly higher in the alcoholic group, indicating that the alcohol-dependent smokers smoked more heavily than the non-alcoholic smokers. Importantly, the above findings could not be solely responsible for the higher electrogustometric thresholds in the alcoholic group as this latter difference remained significant after controlling for cigarette smoking and coffee drinking.

Limitations of the present study include its relatively small sample size. In addition, it is possible that the alcoholics recruited for Experiment 1 did not represent the whole population of alcoholics. For example, men with more severe forms of alcohol dependence, like those with more antisocial behaviours, are less likely to seek professional help and to enter a treatment programme. One should also bear in mind that the method used in the study, including the concentrations and volumes of the MSG (Experiments 1 and 2) and ethanol solutions (Experiment 2), may not reflect all aspects of gustatory responses in real-life conditions. Given the well-known effects of alcohol on oral biology (Dutta et al., 1992; Maier et al., 1994; Maito et al., 2003), further studies will be necessary to fully evaluate the effects of chronic alcohol consumption on taste reactivity in humans.

In conclusion, the present results suggest that: (i) neither acute nor chronic alcohol exposure modifies taste responses to MSG in humans; (ii) alcohol dependence is associated with higher electrogustometric thresholds. Our results add to a growing body of evidence which indicates that the reactivity of alcohol-dependent subjects to suprathreshold taste stimuli remains largely unaffected. On the other hand, alcohol dependence may be associated with deficit(s) in detection of perithreshold gustatory stimuli.

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REFERENCES


