Sweet Liking, Novelty Seeking, and Gender Predict Alcoholic Status

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Background: The relationship between a hedonic response to sweet taste and a propensity to excessive alcohol drinking is supported by both animal and human studies. There is evidence indicating that the tendency to rate more concentrated sweet solutions as the most pleasurable (i.e., sweet liking) is associated with the genetic vulnerability to alcoholism. However, sweet liking by itself is insufficient to predict the alcoholic status of the individual. Our previous study indicated that alcoholic status can be predicted by a combination of hedonic response to sweet taste and personality profile as measured by the Tridimensional Personality Questionnaire (TPQ). This study was designed to further test this hypothesis.

Methods: Participants were 165 patients admitted to a residential treatment program for the treatment of alcoholism, drug dependence, and/or interpersonal problems secondary to substance-abusing family members. In addition to a routine medical examination, on the 24th day after admission, patients completed the TPQ, the standard sweet taste test was conducted, and paternal family history of alcoholism was evaluated.

Results: Sweet liking was strongly associated with a paternal history of alcoholism. The odds of receiving an alcohol dependence diagnosis were shown to increase, on the average, by 11% for every one-point increase in the TPQ novelty-seeking score in sweet-liking but not in sweet-disliking subjects. Gender contributed independently to the probability of alcohol dependence, with males exhibiting higher rates of alcoholism than females.

Conclusions: These findings support the hypothesis that a hedonic response to sweet taste is associated with a genetic risk for alcoholism. Alcoholic status may be predicted by a combination of sweet liking, the TPQ novelty-seeking score, and gender in a mixed group of alcoholic, polysubstance-dependent, and psychiatric patients.

Key Words: Sweet Liking, Novelty Seeking, Alcoholism, Genetic Risk.
liking is associated with a genetic risk of alcoholism, as measured by a paternal history of alcoholism, rather than by the alcoholic status of an individual (Kampov-Polevoy et al., 2003a,b). One study (Kampov-Polevoy et al., 2001) indicates that both factors (i.e., paternal history of alcoholism and alcoholic status) may contribute to the likelihood of being a sweet liker. At least two reported studies (Kran- zler et al., 2001; Scinska et al., 2001) failed to replicate these findings, most likely due to the differences in methods used for evaluation of sweet-liking status (for discussion, see Kampov-Polevoy et al., 2003a).

There are also indications that although sweet liking is associated with the genetic risk of alcoholism, this trait by itself is insufficient to predict the alcoholic status of an individual. Only a combination of sweet-liking status and personality profile as measured by the Tridimensional Personality Questionnaire (TPQ) is sufficient to make such prediction (Kampov-Polevoy et al., 1998). The goal of this study was to further test the hypothesis that the predictive value of a hedonic response to sweet taste regarding the risk of alcoholism may be enhanced if used in combination with the TPQ personality profile. The materials presented in this article are a secondary analysis of the data collected in our earlier study (Kampov-Polevoy et al., 2003b).

METHODS

Subjects

Subjects were patients admitted to a private residential treatment program for substance abuse and psychiatric disorders (Pavillon International, Mill Spring, NC). The treatment program used a closed-session format and emphasized 12-step facilitation and relapse-prevention principles. Individuals with psychosis or medical conditions requiring constant medical care were excluded from the treatment program. Patients were admitted to the treatment program who had substance use disorders and/or interpersonal problems secondary to substance-abusing family members. At admission, a routine medical examination was conducted.

The patients’ psychiatric as well as alcohol and drug abuse/dependence status was evaluated by a state-licensed psychiatrist by using DSM-IV criteria. After the medical and psychiatric examination, a complete description of the study was offered to all subjects who were not excluded due to clinical and/or historical evidence of diabetes mellitus, hepatitis, pancreatitis, or other serious medical disorders. Written informed consent was obtained from all participants. Out of 180 approached eligible patients, 15 either declined to participate in the study or were discharged early and, therefore, did not complete the sweet taste test and the TPQ.

The total study group consisted of 165 subjects [age, 37.7 ± 9.0 years (mean ± SEM); males, 48.3%; Caucasians, 94%]. A total of 77% of the patients met DSM-IV criteria for substance dependence: 25% for alcohol dependence only, 30% for alcohol and drug (i.e., cocaine, heroin, mari-juana, and prescription drugs) dependence, and 22% for drug (i.e., cocaine, heroin, marijuana, and prescription drugs) dependence only. Sixty percent of subjects were cigarette smokers. Forty-eight percent of subjects were diagnosed with lifetime psychiatric disorders: anxiety disorder (22%), bipolar disorder (12%), or depression (39%).

Tests

Sweet Taste Test. The sweet-taste test was conducted by a trained nurse in the morning at least 1.5 hr after breakfast (8:30–9:00 AM) and 1 hr after smoking and tooth brushing. Each of 5 concentrations of sucrose solution (0.05, 0.10, 0.21, 0.42, and 0.83 M) was presented 5 times in a pseudoran-
alcoholic, polysubstance-dependent, and psychiatric patients. For this analysis, subjects with alcoholism only and subjects addicted to several substances including alcohol were designated to the alcoholic group, and subjects without any substance abuse/dependence and subjects addicted to substances other than alcohol were designated to the nonalcoholic group. Hedonic response to the sweet taste was presented as a dichotomous categorical variable (presence or absence) instead of using five ordinal categorical variables corresponding to hedonic ratings of sugar solutions of different concentrations. This decision was made for the following reasons: (1) originally, the difference between sweet-liking and sweet-disliking individuals was described in terms of their hedonic response to sucrose concentrations that are equal to or exceed 0.6 M (Thompson et al., 1976). Most publications that focus on the hedonic response to sweet taste operate with the same or similar categories (e.g., Cabanac, 1979; Janowsky et al., 2003; Kranzler et al., 2001; Looy et al., 1992; Looy and Weingarten, 1991; Pangborn, 1970; Thompson et al., 1976). Therefore, expressing the hedonic response to sweets as a dichotomous categorical variable allows comparing our data with the results reported in literature. (2) Hedonic response to sweet taste expressed as a dichotomous categorical variable (sweet liking/sweet disliking) in previous studies was shown to have sufficient power to discriminate FH⁺ versus FH⁻ status (Kampov-Polevoy et al., 2001, 2003a,b).

Table 1 presents the distribution of the prevalence of sweet-liking status, drug abuse, smoking, TPQ scores, and psychiatric disorders in different subgroups. It shows the general trend for a higher prevalence of sweet likers in FH⁺ group compared with the FH⁻ group, although in nonalcoholic males this trend did not reach statistical significance. FH⁺ nonalcoholic subjects were also more likely to have drug abuse or dependence than their FH⁻ counterparts, but this trend reached statistical significance only in females. The only statistically significant differences in TPQ scores between the FH⁺ and FH⁻ groups were found in the novelty-seeking and reward-dependence scales of alcoholic females.

In the overall sample, hedonic response to sweet taste was significantly linked with FH⁺ subjects. The estimated odds of being FH⁺ for sweet likers were 4.95 times the estimated odds for sweet dislikers (95% confidence interval, 2.44–10.38). However, sweet liking by itself was insufficient to predict either the alcoholic or drug-dependent status of an individual (p > 0.05; Pearson’s χ² test of independence for a 2 × 2 table).

However, novelty seeking, which was shown to be independent from the family history status (p > 0.05; two-sample t test), was significantly associated with drug dependence (p = 0.0001; two-sample t test) but not with alcoholic status (p > 0.05; two-sample t test).

We then estimated a predictive value of various traits regarding the alcoholic status of individuals by using logistic regression models fitted for a binary response variable of diagnosis of alcohol dependence (presence/absence) and for the following explanatory variables: family history of alcoholism (FH+/FH⁻), TPQ novelty-seeking score (continuous variable), TPQ harm-avoidance variable (continuous variable), TPQ reward-dependence score (continuous variable), and hedonic response to sweet taste (sweet liking/sweet disliking). The following covariables were controlled for possible confounding effects: age (years), gender (male/female), drug abuse/dependence (presence/absence), and cigarette smoking (presence/absence). The method of backward elimination was used to obtain a model with the fewest parameters that would fit the data. The goodness of fit for each model was obtained; then, the

### Table 1. Patient Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>FH⁻</th>
<th>FH⁺</th>
<th>FH⁻</th>
<th>FH⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>23</td>
<td>15</td>
<td>32</td>
<td>15</td>
</tr>
<tr>
<td>Age</td>
<td>40 ± 1.9</td>
<td>38 ± 2.5</td>
<td>39 ± 2.2</td>
<td>33 ± 2.7</td>
</tr>
<tr>
<td>Sweet likers (%)</td>
<td>9%</td>
<td>38%*</td>
<td>22%</td>
<td>54%*</td>
</tr>
<tr>
<td>Drug abuse/dependence (%)</td>
<td>30%</td>
<td>47%</td>
<td>22%</td>
<td>67%*</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>65%</td>
<td>80%</td>
<td>44%</td>
<td>67%</td>
</tr>
<tr>
<td>Patients with psychiatric problems</td>
<td>52%</td>
<td>47%</td>
<td>84%</td>
<td>60%</td>
</tr>
<tr>
<td>Novelty seeking</td>
<td>16.6 ± 1.4</td>
<td>22.5 ± 0.9**</td>
<td>19.7 ± 1.2</td>
<td>20.3 ± 1.4</td>
</tr>
<tr>
<td>Harm avoidance</td>
<td>18.3 ± 1.6</td>
<td>18.6 ± 0.9</td>
<td>16.9 ± 1.5</td>
<td>20.3 ± 2.3</td>
</tr>
<tr>
<td>Reward dependence</td>
<td>18.9 ± 0.7</td>
<td>22.0 ± 0.9**</td>
<td>19.4 ± 0.9</td>
<td>19.9 ± 0.7</td>
</tr>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>34</td>
<td>21</td>
<td>18</td>
<td>7</td>
</tr>
<tr>
<td>Age</td>
<td>39 ± 2.2</td>
<td>38 ± 2.3</td>
<td>37 ± 3.0</td>
<td>36 ± 4.2</td>
</tr>
<tr>
<td>Sweet likers (%)</td>
<td>23%</td>
<td>67%*</td>
<td>19%</td>
<td>57%</td>
</tr>
<tr>
<td>Drug abuse/dependence (%)</td>
<td>54%</td>
<td>59%</td>
<td>44%</td>
<td>71%</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>66%</td>
<td>74%</td>
<td>44%</td>
<td>29%</td>
</tr>
<tr>
<td>Patients with psychiatric problems</td>
<td>46%</td>
<td>41%</td>
<td>59%</td>
<td>71%</td>
</tr>
<tr>
<td>Novelty seeking</td>
<td>20.6 ± 1.1</td>
<td>20.0 ± 1.5</td>
<td>17.8 ± 1.9</td>
<td>20.4 ± 2.4</td>
</tr>
<tr>
<td>Harm avoidance</td>
<td>15.2 ± 1.5</td>
<td>13.7 ± 1.4</td>
<td>14.3 ± 2.1</td>
<td>16.7 ± 3.7</td>
</tr>
<tr>
<td>Reward dependence</td>
<td>16.7 ± 1.2</td>
<td>17.8 ± 1.2</td>
<td>17.8 ± 1.2</td>
<td>21.1 ± 1.2</td>
</tr>
</tbody>
</table>

* Difference between FH⁻ and FH⁺ groups was significant with Pearson’s χ² test of independence for 2 × 2 contingency table (p < 0.05).

** Difference between FH⁻ and FH⁺ groups was significant with two-sample t test (p < 0.05).
predictors that, when dropped from the model, resulted in a significant increase in deviance \((p < 0.05)\) were retained. Predictors not producing a significant increase in the goodness of fit were dropped from the model. We started the backward-elimination procedure with all-term interactions, including the three-way interactions, and arrived at the model with the interaction of novelty-seeking score \(\times\) sweet liking being significant in predicting alcoholism in our sample \((p = 0.031)\), whereas paternal history of alcoholism, harm avoidance (HA), and reward dependence (RD) were not significant factors in the prediction of alcoholism. Figure 1 illustrates the fitted model showing the conditional odds of alcoholism calculated on the basis of the novelty-seeking score and sweet-liking status interaction \([\text{odds were calculated as } p/(1-p), \text{ where } p \text{ is an estimated probability}]\) for males and females. The figure illustrates that for both males and females in the sweet-liking group, the estimated odds of being an alcoholic, on the average, increase by 11% as the novelty-seeking score increases by one point. In the sweet-disliking group, such an effect is minimal (i.e., the estimated conditional odds of alcoholism, on average, decrease by only 1% per one-point increase in the novelty-seeking score). Also, the model suggests that although the novelty-seeking scores and sweet-liking factor interaction effect is similar for males and females, the probability of having alcoholism in two individuals with similar novelty-seeking scores and sweet liking is significantly higher in males compared with females. On the average, the estimated conditional odds for alcoholism are 1.78 times greater in males than in females (95% confidence interval, 1.52–2.21).

The next analysis was performed to compare the present results with those of a similar study conducted in male subjects with and without alcohol dependence (Kampov-Polevoy et al., 1998). That study showed that a combination of sweet liking and TPQ scores was sufficient to predict an alcoholic versus nonalcoholic status at 65% sensitivity and 94% specificity, with correct classification in 63% (104 of 165) of subjects.

**DISCUSSION**

This study extends previous research exploring the relationship between a hedonic (pleasurable) response to sweet taste and excessive alcohol intake. Since Ramirez and Sprott (1978) and Forgac et al. (1988) demonstrated a relationship between sweet intake and alcohol intake in mice, a number of studies have confirmed these findings in mice (Bachmanov et al., 1996; Belknap et al., 1993), in rats (Bell et al., 1994; Dess et al., 1998; Gahtan et al., 1996; Gosnell and Krahn, 1992; Kampov-Polevoy et al., 1990, 1994, 1995; Koros et al., 1998; Overstreet et al., 1993, 1997; Sinclair et al., 1992), and in monkeys (Higley and Bennett, 1999). In addition to a high intake of sweet solutions, rats genetically selected for high alcohol intake were shown to prefer stronger concentrations of sweets compared with alcohol-avoiding rats (Sinclair et al., 1992). Similar patterns of hedonic response to sweet taste were also described in human subjects. For example, Thompson et al. (1976) showed that most individuals can be classified into one of two categories: sweet likers, reporting an increasing pleasurable response to increasing concentrations of sucrose across the range of 0.0 to 2.0 M, and sweet dislikers, who may show an increasing pleasurable response only up to a 0.2 M concentration and then show decreasing pleasurable responses as sucrose concentrations increase to 0.6 M. These patterns of the hedonic response to sweet taste were described in a number of studies (Cabanac, 1979; Looy et al., 1992; Looy and Weingarten, 1991; Pangborn, 1970; Thompson et al., 1976). Similar to animal data (Sinclair et al., 1992), in humans, sweet liking has been shown to be associated with excessive alcohol intake; the prevalence of sweet likers is higher among alcoholics than among nonalcoholic control subjects (Kampov-Polevoy et al., 1997, 1998, 2001; but see Bogucka-Bonikowska et al., 2002; for discussion, see Kampov-Polevoy et al., 2003a). Further studies provided evidence that sweet liking is linked to genetic vulnerability for alcoholism as measured by the paternal history of alcoholism (Kampov-Polevoy et al., 2001, 2003a,b; for conflicting evidence, see Kranzler et al.,...
These findings are consistent with the results of our previous study, which showed that a combination of sweet liking and TPQ personality profile is sufficient to predict alcoholic status (Kampov-Polevoy et al., 1998). Therefore, despite significant differences in study samples (e.g., alcoholic and nonalcoholic males without comorbid psychiatric disorders and drug abuse in the previous sample and males and females with alcoholism, polysubstance abuse, and/or psychiatric disorders in this sample), the results of the analysis were quite similar, suggesting potential generalization of these findings.

When considering the mechanisms by which a combination of high novelty seeking and sweet liking may contribute to the risk of developing alcoholism, one has to consider that these are independent traits, and both are believed to be at least partially determined by genetic mechanisms (Cloninger, 1987a; Reed et al., 2001). Over the last 60 years, a number of hypotheses have been suggested to explain a link between a hedonic response to sweet taste and alcohol intake in animals and humans (for review, see Kampov-Polevoy et al., 1999, 2003a; Levine et al., 2003). A better understanding of this association came from the finding that the rewarding effect of both alcohol and sweet taste is mediated by the same brain mechanisms, particularly by the brain opioid system (BOS). The involvement of the BOS in mediating the pleasurable effects of alcohol (for review, see Froehlich and Li, 1993, 1994; Gianoulakis, 2001) and sweet substances (for review, see Levine et al., 2003) has been well documented. This common mechanism may explain why morphine sensitization (Hoshaw and Lewis, 2001) and stimulation of the μ-opioid receptors in the nucleus accumbens (Zhang and Kelley, 1997) can promote a long-lasting increase in both alcohol intake and consumption of sweet solutions in rats. It is of interest for this study that FH− individuals have been shown to have a heritable BOS dysfunction that manifests itself with comparatively low baseline concentrations of plasma β-endorphins and a more pronounced increase in pituitary β-endorphin release after ingestion of moderate doses of alcohol (Froehlich et al., 2000; Gianoulakis et al., 1989, 1996; for review, see Gianoulakis, 2001). This dysfunction is believed to cause the abnormal reinforcement after ingestion of alcohol noted in FH− subjects that contributes to an increased risk of developing alcoholism in such individuals (Levenson et al., 1987; Schuckit, 1980). This dysfunction may also explain the high prevalence of sweet liking in FH− subjects (Kampov-Polevoy et al., 2001, 2003a,b), because the BOS is known to regulate the pleasantness of sweet foods (Drewnowski et al., 1992; Yeomans and Gray, 1996; Yeomans and Wright, 1991). Activation of this system shifts the preference/aversions curve for sweets to the left, toward the preference for weaker sweet solutions (Calcagnetti and Reid, 1983), whereas blockade of this system with the opiate antagonist naloxone produces the opposite effect (Leventhal et al., 1995). These findings make a hedonic response to sweet taste a simple and valuable instrument for evaluation of BOS activity.

The other trait that was consistently associated alcoholism is a personality dimension that has been variously
termed (e.g., behavioral disinhibition, behavioral undercontrol, and deviance proneness) (Allen et al., 1998; Gorenstein and Newman, 1980; Howard et al., 1997; Liraud and Verdoux, 2000; Martin and Sher, 1994; McGue et al., 1999; Scourfield et al., 1996) and that causes early experimentation with alcohol and, as a result, a higher lifetime rate of heavy drinking, alcohol abuse, and alcohol dependence (Castellani and Rugle, 1985; Cloninger et al., 1988; Dewit et al., 2000; Finn et al., 2000; Grant and Dawson, 1997; Masse and Tremblay, 1997; Muthen and Muthen, 2000; Wills et al., 1994). It is of interest that despite the close link between behavioral disinhibition and familial forms of alcoholism, this personality dimension was shown to be independent of FH– status (Basiaux et al., 2001; Schuckit et al., 1990; Zaninelli et al., 1992). Such seemingly conflicting findings are consistent with the view that the risk of alcoholism may relate to the effects of multiple genes (i.e., a polygenic inheritance; for discussion, see Schuckit, 1991), when only a combination of several heritable traits leads to development of the disorder. Therefore, it is conceivable that only a combination of two independent traits—(1) BOS dysfunction inherited from an alcoholic father that manifests itself with increased sensitivity to the reinforcing effect of alcohol and (2) a high degree of behavioral undercontrol that leads to early experimentation with alcohol—can predict the risk of alcoholism in an individual, whereas each of these traits by itself is insufficient to make such prediction.

In this context, we would like to note that in this sample, drug-dependence status could be predicted by a single predictor: high novelty seeking. If confirmed by further studies, this finding may indicate the existence of different mechanisms predisposing individuals for alcoholism and drug addiction.

The third factor contributing to the prediction of alcoholic status was gender, with estimated odds for alcoholics that were approximately 2 times higher in males than in females. This finding is consistent with the view that both genetic and environmental factors associated with gender can modulate the genetic liability to alcoholism (for discussion, see Prescott et al., 1999).

This study has several limitations. First, the severity of co-occurring psychiatric conditions was not properly monitored; therefore, psychiatric diagnoses were not included in the statistical analysis. Behavioral undercontrol was evaluated only with the TPQ novelty-seeking scores, which may not be sufficient. Finally, prediction of alcohol dependence was made in an adult population that already did or did not have alcohol dependence. Therefore, the reported results cannot directly answer whether a combination of a hedonic response to sweet taste and personality profile may predict the risk of developing alcohol dependence. Only a prospective longitudinal study may give a direct answer to this question.

In summary, the results of this study provide further support to the hypothesis that a hedonic response to sweet taste is associated with a genetic risk for alcoholism but, by itself, is insufficient to predict the alcoholic status of an individual. This may be predicted by a combination of sweet liking, the TPQ novelty-seeking score, and gender.

REFERENCES


