VOLUME INTAKE AND CRAVING IN ALCOHOL WITHDRAWAL

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Abstract — Aims: It has been shown that beer consumption is associated with alcohol craving, in contrast to wine or spirits consumption. The present study was undertaken to evaluate whether the daily volume intake of alcoholic beverages is associated with craving in patients undergoing alcohol withdrawal. Methods: A total of 158 male patients were assessed using the obsessive compulsive drinking scale (OCDS) at admission. The daily volume intake of alcoholic beverages was calculated by adding the volume of all regularly consumed alcoholic beverages, disregarding their alcohol percentage. Lesch’s typology was used to classify patients for subgroup analysis. Results: The daily volume intake of alcoholic beverages correlated significantly with the extent of the OCDS at admission. The daily volume intake of alcoholic beverages was calculated by adding the volume of all regularly consumed alcoholic beverages, disregarding their alcohol percentage. Lesch’s typology was used to classify patients for subgroup analysis. With general linear models, we found a significant association of the calculated daily volume intake of all alcoholic beverages with craving (F = 6.426; P = 0.012), but not for the daily ethanol intake. Differentiating the patients according to Lesch’s typology a significant association was particularly found in Lesch Type 2 (model of anxiety) patients (F = 11.31; P = 0.001). Conclusion: Our results support the hypothesis that volume intake is associated with craving and suggest a role of pathophysiological changes in volume regulating mechanisms (such as vasopressin or ANP) in the neurobiology of alcohol craving, particularly in male patients of Lesch’s Type 2 undergoing alcohol withdrawal.

INTRODUCTION

The role of craving in alcohol dependency and its relation to relapse has been the subject of various studies (Geerlings and Lesch, 1999; Flannery et al., 2003; Bottlender and Soyka, 2004). While there are different concepts about craving, one of the most common concept describes craving as obsessive thoughts and compulsive behaviour (Modell et al., 1992). Changes in volume regulation during alcohol intoxication and withdrawal are well known and have been the focus of various studies (Eisenhofer et al., 1985; Trabert et al., 1992; Taivainen et al., 1995; Kiefer et al., 2002a). Furthermore, these alterations have been described to persist after detoxification in long-term abstinent alcoholics (Döring et al., 2003; Jahn et al., 2004). An association between craving and changes in volume regulation has been postulated (van Ree et al., 1994; Döring et al., 2003), but has not been studied in detail until recently. In a previous study, we demonstrated that craving is not associated with alcohol intake alone. Instead, it also depends on the type of alcoholic beverage consumed. In this recent study, we found that beer consumption, in contrast to wine or spirits consumption, is associated with higher alcohol craving (Hillemacher et al., 2005a). Furthermore, craving for alcohol shares pathophysiological similarities with craving for other substances, especially food craving (Pelchat, 2002).

The aim of this study was to analyse whether the volume intake of alcoholic beverages in total is associated with craving in alcohol withdrawal. The results may help to clarify whether or not volume regulating mechanisms play a role in the pathophysiology of craving.

METHODS

The study was part of the FARS (Franconian Alcoholism Research Studies) (Hillemacher et al., 2004; Bayerlein et al., 2005; Bleich et al., 2005). As in the prior study the association between type of beverage consumption and craving was found only in male patients (Hillemacher et al., 2005a) and because of the small number of female patients we included only male patients in the analysis. Written informed consent was obtained from all the included 158 patients. The procedures were in accordance with the ethical standards of the responsible regional committee on human experimentation (Ethics Committee of the Medical Faculty, University of Erlangen-Nuremberg, Germany) and with the Declaration of Helsinki of 1975, as revised in 1983. All participants suffered from alcohol dependency according to ICD-10 and were included in the study on the day they were admitted to the closed detoxification unit.

All patients were detoxified using clomethiazole and carbamazepine as an individual symptom-triggered treatment. Other detoxification medication was not used apart from vitamins, potassium, or magnesium. Patients with known psychiatric illnesses other than substance abuse of alcohol and nicotine in the medical history at admission (according to ICD-10) were excluded from the study.

The extent of craving was assessed after admission using the obsessive compulsive drinking scale (OCDS) (Anton et al., 1995, 1996), distinguishing between the total score (OCDS-T) and the obsessive (OCDS-O) and compulsive (OCDS-C) subscale of the OCDS.

To compare different types of alcohol dependency we used the questionnaire for Lesch’s typology (Lesch, 1985; Lesch et al., 1990; Lesch and Walter, 1996). This well-established classification has been used in various investigations (Sperling et al., 2000; Lesch et al., 2001; Bleich et al., 2004) and differentiates four types of alcohol dependence. Type 1 patients (model of allergy) suffer from heavy alcohol

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withdrawals and tend to use alcohol to weaken withdrawal symptoms. Type 2 patients (model of anxiety or conflict) use alcohol as self-medication because of its anxiolytic effects. An underlying affective disorder is the main characteristic of Type 3 patients. Type 4 patients (alcohol as adaptation) show pre-morbid cerebral defects and a high social burden.

Furthermore, sociodemographic and personal data, such as daily ethanol intake in grams, the period of drinking (in years), and the type of consumed alcoholic beverages in litres, were taken in a standardized self-structured interview according to Wetterling et al. (1999). All patients were interviewed by the same trained observer (K.B.). The consumption of alcohol was documented as volume and percentage of alcohol content of the consumed beverages, so that the daily ethanol intake (in grams) and the daily volume intake (the sum of all consumed alcoholic beverages, in litres, independently of their ethanol percentage) could be calculated (mean daily ethanol intake 253.6 g/day, SD 200.2; mean daily volume intake 3.78 l/day, SD 2.46).

None of the utilized variables was normally distributed (using the Kolmogorov–Smirnov test). Hence, we used non-parametric methods (such as Spearman’s rho and Mann–Whitney U-test) for statistical analysis. We used general linear models to test for confounding variables and to clarify the impact of both variables (daily ethanol intake and daily volume intake) on craving. For receiver operating curves (ROC) analysis we established two groups labelled ‘high’ and ‘low’ craving alcoholics. Therefore we applied the OCDS total score scale as a dependent variable, using a previously described median split division (Ingaldsson et al., 2003), because no validated ranking of the OCDS items had been published at the time of the analysis. Also we used a median split division of the daily volume intake, comparing high versus low volume intake.

All statistical tests were two-sided, and a significance level of \( \alpha = 0.05 \) was used. The data were analysed using SPSS for Windows 11.5 (SPSS Inc., Chicago, IL).

**RESULTS**

Descriptive statistics of the study population are presented in Table 1. As shown in Fig. 1, patients with ‘high craving’ \( (N = 74) \) had a significantly higher daily volume intake than patients with ‘low craving’ \( (N = 84) \) (Mann–Whitney \( U \)-test: \( U = 1941, W = 5511, Z = -4.07, P < 0.001 \)). Also patients with ‘high volume intake’ \( (N = 89) \) suffered from significantly higher craving scores than patients with ‘low volume intake’ \( (N = 69) \) (Mann–Whitney \( U \)-test; OCDS total: \( U = 1882, W = 4297, Z = -4.17, P < 0.001 \); Fig. 2).

Using Spearman correlation analysis, we found significant results for the correlation of the daily ethanol intake (OCDS-T: \( r = 0.38, P < 0.001 \); OCDS compulsive subscale: \( r = 0.42, P < 0.001 \); OCDS-O: \( r = 0.26, P = 0.001 \); \( N = 158 \)) and daily volume intake of alcoholic beverages (OCDS-T: \( r = 0.33, P < 0.001 \); OCDS-C: \( r = 0.32, P < 0.001 \); OCDS-O: \( r = 0.27, P = 0.001 \); \( N = 158 \)).

As daily volume intake and daily ethanol intake were significantly correlated \( (r = 0.50, P < 0.001, N = 158) \) we performed general linear models for variance analysis. The OCDS-T was used as a dependent variable. First we included the following variables in the analysis: daily ethanol intake, age, and years of drinking. For none of these variables a significant association could be found. A significant trend was found for daily ethanol intake \( (F = 3.58, P = 0.060, r^2 = 0.05, r^2 \text{ corrected} = 0.03) \). When adding the daily volume intake of alcoholic beverages to the same model we found a significant

![Fig. 1. Boxplot: difference in daily volume intake between patients with high and low craving. OCDS total score dichotomized by the median, differentiates patients with ‘low craving’ \( (N = 84) \) and patients with ‘high craving’ \( (N = 74) \). Mann–Whitney \( U \)-test: \( Z = -4.07, P < 0.001 \). Details are summarized in the Results section.](image-url)

**Table 1. Descriptive statistics**

<table>
<thead>
<tr>
<th>Lesch’s typology</th>
<th>All patients ( (N = 158) )</th>
<th>Type 1 ( (N = 35) )</th>
<th>Type 2 ( (N = 72) )</th>
<th>Type 3 ( (N = 27) )</th>
<th>Type 4 ( (N = 19) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCDS-T</td>
<td>20.5 ± 7.5</td>
<td>17.6 ± 7.2</td>
<td>21.0 ± 7.3</td>
<td>19.7 ± 7.8</td>
<td>23.6 ± 7.2</td>
</tr>
<tr>
<td>OCDS-O</td>
<td>8.4 ± 4.8</td>
<td>7.0 ± 4.5</td>
<td>8.9 ± 4.6</td>
<td>7.9 ± 5.2</td>
<td>9.3 ± 5.6</td>
</tr>
<tr>
<td>OCDS-C*</td>
<td>12.0 ± 3.7</td>
<td>10.7 ± 3.7</td>
<td>12.1 ± 3.7</td>
<td>11.7 ± 3.2</td>
<td>14.4 ± 3.5</td>
</tr>
<tr>
<td>Age (years)</td>
<td>43.2 ± 8.9</td>
<td>42.9 ± 8.6</td>
<td>44.0 ± 9.1</td>
<td>43.9 ± 8.3</td>
<td>41.1 ± 8.2</td>
</tr>
<tr>
<td>Years of drinking</td>
<td>19.5 ± 10.0</td>
<td>18.0 ± 10.1</td>
<td>18.8 ± 10.0</td>
<td>22.2 ± 9.8</td>
<td>20.9 ± 9.9</td>
</tr>
<tr>
<td>Daily volume intake (l)</td>
<td>3.78 ± 2.46</td>
<td>3.45 ± 2.15</td>
<td>3.85 ± 2.24</td>
<td>4.06 ± 3.33</td>
<td>3.83 ± 2.72</td>
</tr>
<tr>
<td>Daily ethanol intake (g)</td>
<td>253.6 ± 200.2</td>
<td>216.9 ± 126.7</td>
<td>277.9 ± 244.2</td>
<td>265.4 ± 209.1</td>
<td>232.7 ± 116.3</td>
</tr>
</tbody>
</table>

Mean ± SD; five patients could not be classified in one of the subgroups because of missing necessary data.

*Significant differences between the different types of Lesch’s typology tested with Kruskal–Wallis test for independent samples \( (OCDS-C: \chi^2 = 11.7; P = 0.008) \).
association with daily volume intake and craving \((F = 6.4, P = 0.012; r^2 = 0.09, r^2 \text{ corrected} = 0.06)\). For the daily ethanol intake, we did not even find a trend after adding the daily volume intake to the model \((F = 0.51, P = 0.474; \text{ Table 2})\). When using the daily volume intake as dependent variable we found a significant association with the OCDS-T in the whole patients’ group and in Lesch’s Type 2 patients. An association with the daily intake of ethanol was found for all patients, Lesch’s Type 1 patients, and Lesch’s Type 3 patients (Table 3).

With ROC, the association between the daily volume intake of alcoholic beverages could be demonstrated (Area under the curve, AUC = 0.69 (0.60–0.77), \(P < 0.001\); Fig. 3).

**DISCUSSION**

The present results demonstrate that the volume of consumed alcoholic beverages is significantly associated with obsessive and compulsive craving in male patients. Furthermore, results of the variance analysis suggest that daily ethanol intake may act as a confounding variable. This does not mean that ethanol consumption is not involved in craving but points towards an additional influence of volume intake. The present findings are limited because of the lack of obtaining craving dimensions other than obsession and compulsion (Lesch et al., 1997; Geerlings and Lesch, 1999) that might be insufficiently measured by the OCDS (Potgieter et al., 1999). This should be taken into account in further studies.

Neuroendocrinological changes in alcohol dependency have been described in recent studies (Kiefer and Wiedemann, 2004). We suppose that higher volume intake may lead to higher craving via changes in the vasopressin and atrial natriuretic peptide (ANP) metabolism. Changes in these pathophysiological pathways in alcohol intoxication and withdrawal have been described recently (Eisenhofer et al., 1985; Taivainen et al., 1995; Kiefer et al., 2002a). Taking into account that volume regulating peptides (i.e. ANPs) are involved in anxiety behaviour future investigations should analyse these peptides and their possible association with craving. In alcohol craving a role of the vasopressin metabolism and an involvement of the hypothalamic–pituitary–adrenal (HPA) axis have been proposed (Kiefer et al., 2002b; Döring et al., 2003; Hillemacher et al., 2005b). The present results suggest that our prior findings about the

### Table 2. General linear model on craving

<table>
<thead>
<tr>
<th>Lesch’s typology</th>
<th>All patients ((N = 158))</th>
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<th>Type 2 ((N = 72))</th>
<th>Type 3 ((N = 27))</th>
<th>Type 4 ((N = 19))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>2.53/0.114</td>
<td>1.90/0.178</td>
<td>0.000/0.963</td>
<td>0.52/0.479</td>
<td>0.35/0.564</td>
</tr>
<tr>
<td>Years of drinking</td>
<td>1.00/0.299</td>
<td>0.68/0.415</td>
<td>0.11/0.738</td>
<td>0.40/0.535</td>
<td>0.14/0.711</td>
</tr>
<tr>
<td>Daily volume intake (l)</td>
<td>6.43/0.012*</td>
<td>0.85/0.364</td>
<td>11.31/0.001*</td>
<td>0.22/0.646</td>
<td>0.05/0.829</td>
</tr>
<tr>
<td>Daily ethanol intake (g)</td>
<td>0.51/0.474</td>
<td>3.18/0.085</td>
<td>0.16/0.693</td>
<td>0.16/0.693</td>
<td>0.12/0.731</td>
</tr>
</tbody>
</table>

Results shown as \(F/P\)-value; *Significant results; dependent variable: OCDS-T.

### Table 3. General linear model on daily volume intake

<table>
<thead>
<tr>
<th>Lesch’s typology</th>
<th>All patients ((N = 158))</th>
<th>Type 1 ((N = 35))</th>
<th>Type 2 ((N = 72))</th>
<th>Type 3 ((N = 27))</th>
<th>Type 4 ((N = 19))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.670/0.414</td>
<td>0.22/0.642</td>
<td>2.95/0.090</td>
<td>1.57/0.224</td>
<td>2.65/0.126</td>
</tr>
<tr>
<td>Years of drinking</td>
<td>0.001/0.980</td>
<td>0.62/0.437</td>
<td>0.04/0.841</td>
<td>2.89/0.104</td>
<td>1.88/0.192</td>
</tr>
<tr>
<td>Daily volume intake (l)</td>
<td>6.43/0.012*</td>
<td>0.85/0.364</td>
<td>11.31/0.001*</td>
<td>0.22/0.646</td>
<td>0.05/0.829</td>
</tr>
<tr>
<td>Daily ethanol intake (g)</td>
<td>26.95/0.001*</td>
<td>6.53/0.016*</td>
<td>3.08/0.084</td>
<td>37.46/0.001*</td>
<td>4.56/0.051</td>
</tr>
</tbody>
</table>

Results shown as \(F/P\)-value; *Significant results; dependent variable: daily volume intake.
association of beer consumption with craving (Hillemacher et al., 2005a) may be explained by a volume effect, as beer consumption is associated with higher volume intake than wine or spirits consumption.

Referring to Lesch’s typology we found a significant association between daily volume intake and craving, particularly in Lesch Type 2 patients. These results are limited because of the smaller number of patients in the other subgroups of Lesch’s typology. However, if proposing a dysregulation of vasopressin and ANP as explanation for the present results it is notable that ANP has been discussed to have an anxiolytic activity (Bhattacharya et al., 1996; Wiedemann et al., 2001; Herrmann-Lingen et al., 2003). Animal studies have proposed an involvement of ANP in fear-motivated learning processes (Bidzseranova et al., 1992). Further studies are required to elucidate the pathophysiologically pathways of volume regulating mechanisms in the neurobiology of craving and anxiety during alcohol withdrawal.

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