

# Depressive Mood and Craving During Alcohol Withdrawal: Association and Interaction

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## Abstract

**Background:** Symptoms of both depression and craving for alcohol occur regularly in patients suffering from alcoholism, especially during ethanol withdrawal. In order to test the hypothesis whether both symptoms are associated, reflecting possibly a common basic disturbance, self-rated depression and craving were analysed during an alcohol detoxification program.

**Methods:** A sample of 69 alcoholic inpatients (55 male, 14 female, age 43.3, standard deviation 9.2 years) were included in the study. Craving and depressive symptoms were assessed on the first and the 14th day following admission. Craving was measured with the Obsessive-Compulsive Drinking Scale (OCDS) and depression with the Self-Rating-Depression-Scale (SDS). Correlations and partial correlations of the subscales were analysed with parametric or non-parametric tests.

**Results:** Craving assessed with the OCDS-sum score decreased between day 1 ( $30.9 \pm 8.8$ ) and day 14 ( $24.3 \pm 8.6$ ,  $p < 0.01$ ). The sum score of the Self-Rating-Depression-Scale (SDS) decreased significantly between day 1 ( $47.4 \pm 8.8$ ) and day 14 ( $40.1 \pm 10.1$ ,  $p < 0.01$ ). There was a significant correlation between the SDS- and OCDS-sum scores both at the first and the 14th day after admission ( $r = 0.62 / 0.44$ ;  $p < 0.01$ ). These correlations persisted when the following variables were controlled for by using a partial correlation method: sex, age, years since first alcohol related problems and first physical withdrawal symptoms occurred; numbers of inpatient detoxifications, amount of clomethiazole prescribed and amount of alcohol consumed daily before admission.

**Conclusions:** During alcohol detoxification, increased depressive mood is associated with a higher craving for alcohol. In withdrawal and early abstinence, craving associated with a negative affect seems to be predominant. This might influence the strategies for use of medication and psychotherapy during alcohol withdrawal (German J Psychiatry 2004; 7 (2):6-11).

**Keywords:** alcohol, withdrawal, craving, depression, SDS, OCDS

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## Introduction

Depressive symptoms during alcohol withdrawal are common and have been reported repeatedly (Butterworth, 1971; Dackis et al, 1986; Kiefer & Barocka, 1999; Laine et al, 1999; Schuckit et al, 1997). Secondary depressive symptoms caused by alcohol abuse last up to six weeks after detoxification (Kiefer & Barocka, 1999; Schuckit et al, 1997). A steady decline in the number of symptoms can be found over time individuals abstain from

alcohol (Mayfield, 1985). The relevance of depressive mood disturbances following detoxification has been demonstrated by showing their association with long-term increase in the relapse risk (Glenn Parsons, 1991; Hartka et al, 1991). In addition, craving for alcohol is a psychopathological symptom closely related to relapsing behaviour in patients suffering from alcoholism. Certain studies evaluating longitudinal treatment effects in alcohol dependence demonstrate a positive correlation between craving intensity and relapse severity (O'Malley et al, 1992; Paille et al, 1995; Volpicelli et al, 1992). Moreover, both symptoms, depression and craving, have been considered to be associated with disturbances of two neurotransmitter systems, the dopaminergic system (Laine et al, 1999; Modell et al, 1990) and the serotonergic

system (Heinz et al, 1998; Uzbay et al, 1998), that have been shown to be dysregulated during alcohol withdrawal.

To our knowledge no data have been published examining the relationship between craving for alcohol and depressive mood during ethanol detoxification. The aim of our study was to test the hypothesis whether depression and craving are associated applying two well-validated self-rating instruments, the Self-Rating-Depression-Scale (SDS; (Zung et al, 1965) and the Obsessive-Compulsive-Drinking-Scale (OCDS; (Anton et al, 1996).

## Material and Methods

### Subjects

A sample of 69 alcoholic inpatients (55 male, 14 female, age 43.3 years, standard deviation ( $\pm$ ) 9.2 years) admitted consecutively to the detoxification unit of the Department of Psychiatry and Psychotherapy, University Hospital of Hamburg, completing at least two weeks of the standardised detoxification program, were included in the study. Subjects were primary alcoholics according to Schuckit (Schuckit, 1994) without any psychiatric comorbidity or additional illegal substance abuse. Examination was done independently by two physicians, one of them an experienced psychiatrist. The patients fulfilled at least six of nine diagnostic criteria for dependence according to DSM-IV (American Psychiatric Association, 1995) and at least three of six diagnostic criteria for a dependence syndrome according to the research criteria of ICD-10 (World Health Organisation, 1993).

The following data were gathered: years since first alcohol related problems occurred ( $12.4 \pm 9.7$  years), years since first symptoms of physical withdrawal occurred ( $8.2 \pm 8.3$  years), number of inpatient detoxifications ( $4.2 \pm 7.5$ ), amount of alcohol consumed daily ( $326.0 \pm 205.1$  g/d), tobacco use ( $26.1 \pm 16.0$  cigarettes per day), routine laboratory including gamma-GT ( $121 \pm 139.8$  U/l), ASAT ( $33.6 \pm 53.9$  U/l), ALAT ( $34.1 \pm 53.9$  U/l), MCV ( $112.9 \pm 18.8$  fl). Drug screening for opioids, cannabinoids, cocaine and amphetamines was negative in all patients included.

The study protocol was approved by the Local Ethics Board and all subjects gave written informed consent prior to the investigation.

### Assessment

Basic data were obtained with a structured interview. Craving and depressive symptoms were assessed on the first and the 14th day following admission. Two self-rating scales were used to enhance the comparability between both instruments. An additional, observer-rated scale (like the

HAM-D) was not used to minimise influences on the self-rating depression scale.

Craving was measured with the German version of the Obsessive-Compulsive Drinking Scale (OCDS, see Table 2 for details) (Mann Ackermann, 2000) including three 100 mm visual analogue scales (VAS) measuring mean and maximum craving and its frequency. The OCDS-sum score was additionally subdivided in three factors according to (Roberts et al, 1999). The first factor was called "resistance / control impairment" (items 5, 6, 7, 8, 12), the items ask for the ability to stop drinking or to control the drinking behaviour or thoughts related to drinking. The second factor "obsession" (items 1, 2, 4, 11, 13) includes the quantity of obsessive thoughts and behaviour related to alcohol consumption. "Interference" is the third factor (items 3, 9, 10) describing the extent of disturbances in the social or work functioning caused by drinking or thoughts related to drinking. Mean anxiety during last three days was measured with an additional VAS: The patient was asked to rate the extent of anxiety using an VAS between 0 ("inexistent") and 100 ("very high").

For the assessment of depressive symptoms the Self-Rating-Depression-Scale (SDS; (Zung et al, 1965), was applied (see Table 2 for details). (Sakamoto et al, 1998) used principal component analysis to extract three factors interpretable as cognitive (items 11, 12, 14, 16, 17, 18, 20), affective (items 1, 3, 10, 13, 15), and somatic symptoms (items 4, 5, 7, 9). Besides the SDS-sum score we analysed the course for each factor separately.

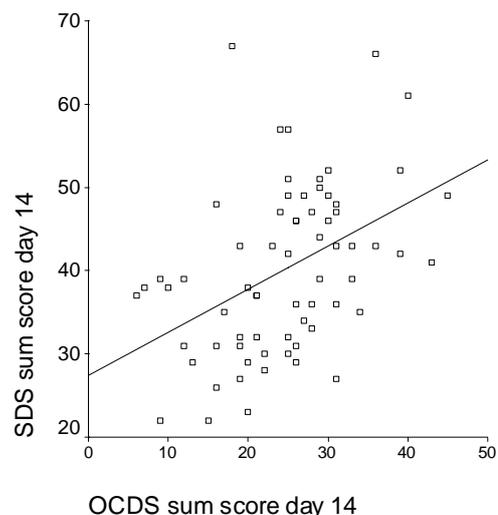
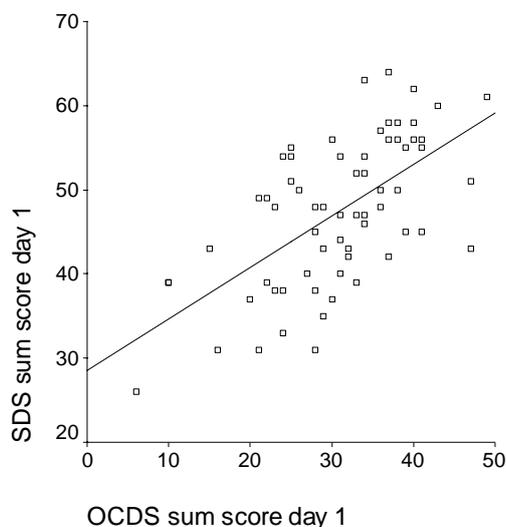
### Data Analysis

All data were expressed as mean  $\pm$  SD. Normal distribution of each variable was tested with the Kolmogoroff-Smirnow test. To test for significant differences between day 1 and day 14, *t*-tests for paired samples were applied for normal distributed data. Correlation were calculated using Pearson's correlation coefficient. Partial correlations were used to assess the impact of possibly confounding variables. In general, the null hypothesis was rejected if a *p*-value less than 0.05 was obtained (comparisonwise error rate). According to (Bender Lange, 2001) a correction to account for the experimentwise error rate was not performed because of the explorative character of the study. All data were analysed using SPSS 11.0 (SPSS inc, Chicago, USA).

## Results

Craving assessed with the OCDS sum score decreased from day 1 ( $30.9 \pm 8.8$ ) to day 14 ( $24.3 \pm 8.6$ ,  $p < 0.01$ ). Self-rated average craving for alcohol on a 100 mm visual analogue scale decreased significantly from day 1 ( $53.1 \pm 32.4$ ) to day 14 ( $21.7 \pm 27.6$ ,  $p < 0.01$ ), maximal craving from  $65.9 \pm 31.7$  to  $32.4 \pm 34.0$  ( $p < 0.01$ ), craving frequency from  $53.6 \pm 36.4$  to  $21.2 \pm 28.3$  ( $p < 0.01$ ). Self rated anxiety on the VAS was

**Figure 1. Correlation of OCDS (Obsessive-compulsive-drinking-scale) and SDS (Self-rating-depression-scale) sum scores at day 1 and day 14 ( $r=0.61$  resp.  $r=0.44$ ,  $p<0.01$ ). Each marker represents the sum scores of one patient.**



$47.8 \pm 32.5$  at day 1 and  $26.9 \pm 24.5$  at day 14 ( $p<0.01$ ). The sum score of the Self-Rating-Depression-Scale (SDS) decreased significantly between day 1 ( $47.4 \pm 8.8$ ) and day 14 ( $40.1 \pm 10.1$ ,  $p<0.01$ ).

According to prior factor-analyses of both the SDS- and the OCDS sum scores (Roberts et al, 1999; Sakamoto et al, 1998) we analysed three sub-factors. Each of the factors of the OCDS ("obsession", "interference", "resistance/control impairment") decreased during both measure points (obsession factor:  $9.2 \pm 3.6$  to  $6.4 \pm 3.5$ , interference factor:  $6.3 \pm 3.0$  to  $5.4 \pm 2.8$ , resistance/control impairment factor:  $15.4 \pm 3.4$  to  $12.5 \pm 4.3$ ;  $p<0.01$ ). Additionally, the SDS-factors affect, cognition, and a somatisation were analysed. All decreased significantly from day 1 to day 14 (affective factor:  $11.3 \pm 2.9$  to  $9.7 \pm 3.2$ ,  $p<0.01$ ; cognitive factor:  $18.6 \pm 5.1$  to  $15.3 \pm 5.0$ ,  $p<0.01$ ; somatic factor:  $9.5 \pm 2.2$  to  $7.6 \pm 2.2$ ,  $p<0.01$ ).

The SDS and OCDS sum scores, as well as all sub factors were normally distributed.

A significant correlation between the SDS- and OCDS-sum

scores was detected at both measure points ( $r=0.61 / 0.44$ ;  $p<0.01$ ; Figure 1). These correlations persisted when controlling for sex, age, years since first alcohol related problems and first physical withdrawal symptoms occurred, numbers of inpatient detoxification, amount of clomethiazole prescribed and amount of alcohol consumed daily before admission by partial correlation. No correlation appeared between the self-rated anxiety and the OCDS sum score; and only a marginal correlation with the SDS sum score at day 14 ( $r=0.26$ ;  $p<0.05$ ).

Additionally, correlation coefficients were calculated for each of the OCDS- and SDS sub factors and the sum score of SDS or OCDS, respectively. All tests were statistically significant ( $p<0.05$ , Table 1).

The analysis of interactions of OCDS-sum score and alcohol history revealed a correlation between craving at day 1 and the amount of alcohol consumed daily ( $r=0.36$ ,  $p<0.01$ ). No other statistical significant associations was detectable. However, significant associations between alcohol history and the SDS-sum score were detectable at day 1 (years since occur-

**Table 1. Correlation of OCDS- and SDS-sub factors with SDS- and OCDS-sum scores**

		OCDS day 1				OCDC day 14				
		sum	rci	obs	int	sum	rci	obs	int	
	sum	$r=0.61^{**}$	$r=0.33^{**}$	$r=0.39^{**}$	$r=0.42^{**}$	sum	$r=0.44^{**}$	0.20*	0.29**	0.34**
SDS	cogn	$r=0.36^{**}$				SDS	cogn	$r=0.29^{**}$		
Day 1	aff	$r=0.35^{**}$				Day 14	aff	$r=0.33^{**}$		
	som	$r=0.35^{**}$					som	$r=0.24^{**}$		

\* $p<0.05$ , \*\* $p<0.01$ ,  $r$ =correlation coefficient (Pearson or Spearman), OCDS=Obsessive-Compulsive Drinking Scale, SDS=Self-Rating-Depression-Scale, sum=sum score, rci=factor "resistance/control impairment", obs=factor "obsession", int=factor "interference", cogn=cognitive factor, aff=affective factor, som=somatic factor.

**Table 2. Content of SDS and OCDS Items**

SDS	OCDS
1. Depressed affect	1. Time occupied by ideas or thoughts related to drinking
2. Diurnal symptom variation	2. Frequency of thoughts related to drinking
3. Crying spells	3. Social interference of ideas or thoughts related to drinking
4. Sleep disturbance	4. Disturbance due to thoughts related to drinking during abstinence
5. Decreased appetite	5. Effort to resist thoughts related to drinking during abstinence
6. Decreased libido	6. Success in stopping thoughts related to drinking during abstinence
7. Weight loss	7. Drinks per day
8. Constipation	8. Drinking days per week
9. Tachycardia	9. Interference of work due to drinking
10. Increased fatigue	10. Social interference due to drinking
11. Confusion	11. Anxiety or confusion when prevented from drinking alcohol
12. Psychomotor retardation	12. Effort to resist consumption of alcohol
13. Psychomotor agitation	13. Drive to consume alcohol
14. Hopelessness	14. Control over the drinking
15. Irritability	
16. Indecisiveness	
17. Personal devaluation	
18. Emptiness	
19. Suicidal tendencies	
20. Dissatisfaction	

rence of first alcohol related problems,  $r=0.29$ ,  $p<0.05$ ; years since occurrence of first physical withdrawal symptoms,  $r=0.44$ ,  $p<0.01$ ; amount of alcohol consumed daily,  $r=0.27$ ,  $p<0.05$ ).

## Discussion

During alcohol withdrawal, a significant association between symptoms of depression and craving for alcohol was detected in subjects suffering from chronic alcoholism. Both at the first day of detoxification and after 14 days, a highly significant and positive correlation between mean values of OCDS and SDS were detectable.

Two major aspects of the construct craving have been proposed: The first is characterised by positive affects, enhancement motives and enhancement expectancies for drinking ("reward craving"), the second is accompanied by

negative affects (like depressive mood, anxiety, or tension) with the purpose to reduce them ("relief craving"). Hence, one might speculate that some aspects of craving are related to depressive disturbance (relief craving) whether others were not (reward craving).

The Obsessive Compulsive Drinking Scale was designed to measure obsessive thoughts on alcohol use and compulsive behaviour towards drinking, based on the observation that some aspects of alcohol craving have a phenomenological overlap with an obsessive-compulsive syndrome (Modell et al, 1992). Items of the OCDS do not contain specific depressive symptoms; hence a construction bias towards measuring a mood status rather than craving can be excluded.

Moreover, it seems unlikely that the extent of the withdrawal syndrome is solely responsible for the observed correlation between craving and depression, because the correlation remained after controlling for withdrawal intensity.

The SDS is a commonly used and well-validated instrument to assess depressive mood (Sakamoto et al, 1998; Zung et al, 1965; Faravelli et al, 1986). However, depression rating during alcohol withdrawal is problematic as signs of physical withdrawal (e.g. disturbed sleep, nervousness, tachycardia) influence the score due to the inclusion of physical items into the SDS. However, following Sakamoto *et. al.* we extracted three factors of the SDS (cognitive, affective and somatic symptoms), and found that each of these factors correlated with the OCDS-sum score at both time points. Since both cognitive and affective subfactors do not contain physical items, it is unlikely that the association of depression and craving is highly influenced by a somatic withdrawal syndrome – especially after 14 days of continued abstinence.

One might speculate whether a third and independent factor exists influencing both depression and craving. Some of the neurobiological systems that are dysregulated during alcohol withdrawal are known to affect both the dopaminergic and serotonergic systems. In particular, the findings that a central hypodopaminergic state is associated with depressed mood during ethanol withdrawal (Miller et al, 1986) and that a reduced central dopamine transporter availability is correlated with depressive symptoms (Laine et al, 1999) implicates the role of the dopaminergic system in mood regulation.

Also craving has been thought to be caused by a dysregulated dopaminergic system (Verheul et al, 1999; Grace, 2000). Additionally the central nervous serotonergic and endorphinergic system are known to be involved in the development of craving (Ciccocioppo, 1999; Petrakis et al, 1999) and depressive symptoms (Meltzer, 1989). The finding of a correlation between the SDS sum score at both measuring points and the duration of alcohol dependence on one side, and the OCDS factor "Interference" (dealing with social consequences of drinking behaviour) on the other side can be explained in two ways: First, this observation may result from symptoms of chronic dysthymia due to the severe social and personal consequences of long lasting alcohol dependence. Second, chronic alcohol consumption results in social disturbances on the one hand and in heavy dysregulation in some functional systems on the other. Supporting the latter is that chronic alcoholism has shown to be associated with long-lasting malfunction of the dopaminergic (Marchesi

et al, 1997; Wiesbeck et al, 1998), serotonergic (Ballenger et al, 1979) and endorphinergic system (del Arbol et al, 1995) that have also been associated with depression. Interestingly, there is no association between the length of alcohol dependence and OCDS sum score – this finding supports the clinical experience of craving as a symptom occurring in all stages of alcohol addiction and also after long-time of abstinence.

Anxiety has been reported to be a risk factor for relapse (Lucht et al, 2002). The observed, missing correlation between self rated anxiety and craving in our study points out that anxiety may appear independently from addiction related syndromes like craving. It should be remarked that the significance of our finding may be limited due to the use of VAS as the only psychometric instrument for measuring anxiety.

Taken together, depressive mood and craving during alcohol withdrawal were highly related. A systematic bias due to overlapping elements in the rating scales was ruled out, as was the bias due to a general physical disability induced by the withdrawal syndrome. Our findings implicate that it may be of advantage to differentiate between patients with "negative" and "positive" craving. Especially the first group may profit from a combined medical and/or psychotherapeutic treatment focused on both depression and craving.

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