

## COMORBID ANXIETY AND AFFECTIVE DISORDER IN ALCOHOL-DEPENDENT PATIENTS SEEKING TREATMENT: THE FIRST MULTICENTRE STUDY IN GERMANY

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**Abstract** — The goals of this study were to describe demographic variables, drinking history, and the 6-month prevalence of Axis I comorbidity among alcohol-dependent subjects in Germany. The variables: amount of alcohol consumption, age at onset of the first alcohol consumed, age at onset of daily alcohol consumption, age at onset of withdrawal symptoms and number of detoxifications were related to the different comorbid disorders and gender. In this study, 556 patients from 25 alcohol treatment centres were enrolled between 1 January 1999 and 30 April 1999. After a minimum of 10 days of sobriety patients who fulfilled ICD-10 and DSM-IV criteria of alcohol dependence were interviewed for data collection using the Mini-DIPS (German version of the Anxiety Disorders Interview Schedule) and a standardized psychosocial interview. The 6-month prevalence of comorbid Axis I disorders was 53.1%. Among the patients with comorbidity, affective and anxiety disorders were most frequent. Comorbid stress disorder was associated with an early start of drinking, an early beginning of withdrawal symptoms, highest number of detoxifications, and the highest amount of alcohol consumed. Female patients with anxiety disorder consumed more alcohol and started earlier than females without this comorbid disorder. The data do not answer the question of the pathogenesis of comorbid disorders and alcoholism, but indicate that stress disorders in alcoholic patients and anxiety disorders in female alcoholics influence the course and severity of alcoholism.

### INTRODUCTION

While many alcohol treatment units exclusively focus on alcohol problems, psychiatric comorbidity may be underestimated both diagnostically and therapeutically.

Although the impact of co-occurring disorders remains controversial (Schuckit, 1985; Bean-Bayog, 1988) it is reasonably clear that alcohol-dependent individuals who meet diagnostic criteria for one or more comorbid psychiatric disorders differ from those without comorbidity in many clinically relevant ways. Among alcohol-abusing and alcohol-dependent patients, prevalence rates for psychiatric comorbidity of between 57% and 84% have been reported (Powell *et al.*, 1987; Regier *et al.*, 1990; Wittchen *et al.*, 1992). Depressive disorders as well as anxiety disorders were found very frequently (Arolt and Driessen, 1996; Schuckit *et al.*, 1997; Berglund and Ojehagen, 1998; Swendsen *et al.*, 1998; Tondo *et al.*, 1999).

The amount of pure alcohol consumed is higher in Germany than in most other European countries. However, there is a paucity of data concerning psychiatric comorbidity in

alcohol-dependent patients (Driessen *et al.*, 1998). This multicentre study, which is the largest in sample size yet undertaken in Germany, aimed to close that gap. The CART (Classification and Regression Trees) procedure was used for data analysis. Two main issues were addressed by the study: (1) to investigate the current (6 months) prevalence of psychiatric comorbidity in alcohol-dependent patients in 25 treatment centres; (2) to analyse the relation of comorbid disorders and gender on alcohol-related variables.

### SUBJECTS AND METHODS

The Multicentre Study of Psychiatric Comorbidity in Alcoholics (MUPCA) is a retrospective study that enrolled 556 patients from 25 centres between 1 January 1999 and 30 April 1999. These 25 centres cover a population of 7 250 000 inhabitants, representing ~10% of the population of Germany, and they treat annually about 15 285 patients with alcohol-related disorders. Only those patients who fulfilled ICD-10 (World Health Organization, 1992) and DSM-IV (American Psychiatric Association, 1994) criteria of alcohol dependence were included in this study. Patients with additional substance misuse or dependence were excluded.

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The patients were interviewed face to face after a minimum of 10 days and a maximum of 28 days of sobriety and when withdrawal symptoms could no longer be observed by clinical means. The patients were selected consecutively. The Mini-DIPS (Markgraf, 1994) and a standardized psychosocial interview were applied. The DIPS represents the German version of the Anxiety Disorders Interview Schedule (Di Nardo and Barlow, 1988). The Mini-DIPS is the short form of this structured interview according to DSM-IV and ICD-10 criteria for current (6 months) comorbidity and covers the following disorders: anxiety, affective, somatization, obsessive-compulsive, post-traumatic stress, acute stress, dissociative, and eating disorders (F30–F50). Furthermore, it allows the exclusion of patients with schizophrenic psychoses. The Mini-DIPS distinguishes between primary and additional diagnoses. Primary diagnoses are those that are clinically most significant and severe in each patient; additional diagnoses are defined when other disorders with a lower degree of severity are present. However, the Mini-DIPS does not cover personality disorders (Axis II diagnoses). The additional interview systematically obtained information about sociodemographic characteristics and alcohol-related history. Twenty-three interviewers from the participating centres were trained in the use of the Mini-DIPS, but test–retest reliability and inter-rater reliability were not determined in this study.

#### Data analysis

The following statistical analyses were performed: main group comparisons used  $\chi^2$ -test or Fisher's exact test for categorical variables, and the *t*-test for continuous variables. For these analyses, SPSS 8.0 for Windows was used.

To investigate the relationship between comorbid disorders and alcohol-related variables, the method using the CART software (Breiman *et al.*, 1984; see also Steinberg and Colla, 1997) was applied. Since in this study the target variables are continuous, regression tree analyses were performed. The goal in a regression tree is to partition the data into relatively homogeneous (low standard deviation) terminal nodes; e.g. the study patients are partitioned into relatively homogeneous subgroups with the different target variables such as 'amount of consumed alcohol' through the predictor variables 'comorbid disorders'. The results are presented in the form of decision trees; a 10-fold cross-validation was used to assess the tree accuracy. To compare the resulting subgroups respective to the alcohol-related variables, one-way analysis of variance was performed. The differences in the nodes were all statistically significant at  $P < 0.05$ .

## RESULTS

The sociodemographic data of the patients are described in Table 1 and the alcohol history/alcohol-related behavioural consequences in Table 2. About 91% of the patients experienced alcohol-related social consequences, such as fines or loss of driver's licence in their history. Only 11.5% of all patients were motivated by their medical conditions. However, 76.4% decided on their own to begin the current treatment. In 7.7% of the patients, pressure from the employer was the cause for the admission. Details of the 6-month prevalence of comorbid psychiatric Axis I disorders (collectively  $n = 292$ ;

Table 1. Sociodemographic characteristics of 556 alcohol-dependent patients

Characteristic	Total sample ( $n = 556$ )	%
Sex		
Male	463	83.3
Female	92	16.5
Missing data	1	0.2
Age (mean $\pm$ SD, years)	43.7 $\pm$ 9.05 (min: 18; max: 80; $n = 555$ )	
Highest education level		
Without secondary school	36	6.3
Secondary school	421	77.9
High school	48	8.4
University	42	7.4
Employment status		
Employed	188	33.8
Unemployed	269	48.3
Retired	67	12.1
Students/schoolchildren	3	0.5
Houseman/wife	17	3.1
Soldiers	1	0.2
No data	11	2.0
Marital status		
Single	202	36.4
Married	128	23
Widowed	18	3.2
Divorced	208	37.4
Main source of income		
Job	169	30.2
Illegal jobs	2	0.4
Unemployment insurance	179	32.2
Health insurance	17	3.1
Welfare work	80	14.4
Support from partner	20	3.6
Pension	65	11.7
No data	24	4.4

53.1%) are presented in Table 3. In 42.3% of all patients, anxiety disorders ( $n = 235$ ), in 24.3% affective disorders ( $n = 135$ ), and in 6.1% ( $n = 34$ ) post-traumatic stress disorder (PTSD) were diagnosed. Overall, the anxiety disorders and among them the phobic disorders (Table 3) account for the most frequent diagnoses.

As our aim was to investigate the relationship between comorbidity and alcohol-related variables, CART was applied to partition the group of patients into homogeneous subgroups (with low SD) with reference to the alcohol-related variables.

All the patients ( $n = 538$ ) consumed an average ( $\pm$  SD) of 345  $\pm$  218 g of pure alcohol/day. There was a sex difference: males ( $n = 451$ ) with 357  $\pm$  220 and females ( $n = 87$ ) with 285  $\pm$  198) g of pure alcohol/day ( $P = 0.0001$ ). Those patients with a PTSD drank more alcohol ( $n = 34$ ; 447  $\pm$  230 g/day) than those without ( $n = 503$ ; 338  $\pm$  215 g/day) ( $P = 0.0037$ ). Of those without a PTSD disorder, male patients consumed more alcohol ( $n = 424$ ; 351  $\pm$  216 g/day) than female patients ( $n = 79$ ; 273  $\pm$  197 g/day) ( $P = 0.0029$ ). Among the female patients, those with an anxiety disorder ( $n = 28$ ; 318  $\pm$  230 g/day) drank more than those without ( $n = 41$ ; 232  $\pm$  148 g/day) ( $n = 0.062$ ).

The age of onset of first alcohol consumption was 15.4  $\pm$  4.7 years. Males started with 15.2  $\pm$  4.8 years, females with 16.5  $\pm$  4.1 years ( $P = 0.0172$ ). Males with an obsessive-compulsive disorder started earlier to consume alcohol than those without (12.2  $\pm$  2.8 vs 15.3  $\pm$  4.8 years;  $P = 0.0336$ ).

Table 2. Drinking history and alcohol-related behaviours/consequences

Drinking history	<i>n</i>	Mean $\pm$ SD	Minimum	Maximum
Age at first drink (years)	539	15.4 $\pm$ 4.74	3	59
Age at first intoxication	525	17.82 $\pm$ 6.17	3	66
Age at daily alcohol consumption	525	23.13 $\pm$ 8.49	3	65
Gram of pure alcohol/day	538	345.53 $\pm$ 218.21	24	1400
Alcohol-related behaviours/consequences:				
	<i>n</i>	% of all patients		
Social consequences (fines, loss of driver's licence, imprisonment)	505	90.83		
Admission to the current treatment because of:				
	<i>n</i>	% of all patients		
Decision by the patient	425	76.4		
Pressure from the employer	43	7.7		
Medical conditions	64	11.5		
Accidents	2	0.4		
Others	21	4.0		

Table 3. Psychiatric comorbidity (Axis I) of 556 alcohol-dependent patients

Disorder	No. of patients without disorder	No. of patients with disorder <sup>a</sup>	% of patients with disorder <sup>a</sup>
Anxiety disorder (F41.XX)	321	235	42.3
General anxiety disorder (F41.1)	484	72	12.9
Phobia (F40)			
Agoraphobia <sup>b</sup> (F40.0X)	483	73	13.1
Social phobia (F40.1)	479	76	13.7
Panic disorder (F41.0)	527	29	5.2
Specific phobia (F40.2)	452	103	18.5
Affective disorder (F3X.X)	421	135	24.3
Major depression episode (F32)	537	19	3.4
Major depression recurrent (F33)	495	61	11.0
Bipolar affective disorder (F31)			
Dysthymia (F34.1)	507	49	8.8
Obsessive-compulsive disorder (F42)	544	12	2.2
Stress disorder	521	35	6.3
Post-traumatic stress disorder (F43.1)	522	34	6.1
Acute stress disorder (F43.0)	555	1	0.2
Somatization disorder	537	19	3.4

<sup>a</sup>Includes patients with more than one diagnosis.

<sup>b</sup>Includes agoraphobia with panic disorder.

Females with anxiety disorders started drinking earlier than those without anxiety disorders (15.5  $\pm$  4.1 vs 17.6  $\pm$  3.8;  $P = 0.014$ ).

On average, males started a regular drinking style at the age of 22.2  $\pm$  7.9 years, females some years later (28.3  $\pm$  9.6 years;  $P = 0.0001$ ). Those females with an anxiety disorder started earlier than those without (24.7  $\pm$  6.9 vs 31.9  $\pm$  10.5 years) ( $P = 0.0003$ ).

Withdrawal symptoms first occurred at a mean age of 34.2  $\pm$  9.8 years for all patients. Those patients with a PTSD disorder usually suffered earlier from withdrawal symptoms (29.3  $\pm$  8.1 vs 34.5  $\pm$  9.9 years;  $P = 0.0036$ ) and underwent more detoxifications than those without (4.0  $\pm$  6.7 vs 7.8  $\pm$  9.1;  $P = 0.0016$ ). Of patients with no PTSD, females had a higher age of onset of withdrawal symptoms than males (37.5  $\pm$  9.9 vs 24.7  $\pm$  6.9 years;  $P = 0.0001$ ). A higher age of onset of withdrawal symptoms was also observed in females without PTSD but with anxiety disorders, compared with those

without anxiety disorders (46.9  $\pm$  10.3 vs 34.0  $\pm$  7.9 years;  $P = 0.0022$ ).

## DISCUSSION

Although we studied treatment-seeking alcohol-dependent subjects, who are known for higher comorbidity rates than non-treated subjects (Berkson bias), the 6-month prevalence of Axis I disorders in our sample was lower (53.1%) than in previous studies of treated alcoholics (Hesselbrock *et al.*, 1985; Ross *et al.*, 1988). Our result is comparable with prevalence rates in previously treated alcoholics in the general US population (Regier *et al.*, 1990; Kessler *et al.*, 1997) and with alcoholics in general hospitals (Arolt and Driessen, 1996). Which factors might contribute to these findings? Only alcohol-dependent patients were investigated and patients with an additional substance misuse were excluded. Most of the

other published investigations included multiple substance-disordered alcoholics. Additionally, many groups used the National Institute of Mental Health Diagnostic Interview Schedule (DIS), whereas we applied the Mini-DIPS. Agreement data for both tests are not available. On the one hand, it cannot be excluded that the Mini-DIPS results in smaller prevalence rates, in comparison to DIS. On the other hand, Driessen *et al.* (1998) used the CIDI interview in a monocentre study and found prevalence rates in the same range for Axis I as in our multicentre study. Furthermore, cultural differences as well as differences in the health insurance system might influence the admission rate of different parts of the population to psychiatric hospitals.

One shortcoming of this study is that the minimum delay between starting sobriety and assessment was short (10 days). In Germany, acute inpatient detoxification of alcoholics is carried out by health insurance funds, but, in most cases, it is limited to 10 days. In a very few cases the health insurance funds agreed to pay for further in-patient treatment programmes (duration about 3 weeks) that have been established in some psychiatric hospitals. Since many hospitals participating in this study are limited to a treatment programme of 10 days each, patients were included after a minimum of 10 days of sobriety. Knowing that prolonged withdrawal symptoms could bias the evaluation of psychiatric comorbidity, patients with continuing withdrawal symptoms were excluded.

Withdrawal symptoms were measured by clinical means. Patients with prolonged symptoms, such as sweating, tremor, agitation, nausea, headache, clouding of sensorium, auditory, visual or tactile disturbances, hypertension, tachycardia, etc. were excluded. Assuming that many patients with prolonged withdrawal symptoms have been included as comorbid, a higher rate of comorbidity than in other studies might be inferred; in this study, the comorbidity rates were not higher than in other studies. However, there are no strong reasons to suspect that prolonged withdrawal symptoms considerably biased the results of this study.

Another, more general shortcoming of the present study is that the prevalence of comorbid disorders was evaluated retrospectively. A longitudinal study and a greater delay between starting sobriety and assessment would reduce the bias of prolonged withdrawal symptoms. Therefore the results of this study should be interpreted cautiously.

In agreement with previous studies (Regier *et al.*, 1990; Kessler *et al.*, 1997) anxiety and affective disorders were most frequent among Axis I comorbidity. Phobias were the most frequent comorbid diagnoses among alcoholic patients with anxiety disorders. Although there were only a few patients in the sample with a PTSD disorder the daily alcohol consumption in this group was the highest. Additionally, this group of patients underwent detoxifications very often, and suffered from withdrawal symptoms at an earlier age. In a study of civilians, Helzer *et al.* (1987) used Epidemiologic Catchment Area survey data to estimate the lifetime prevalence of PTSD among adults, which was found to be 1% for both sexes combined (0.5% for males and 1.3% for females). In a study by Deykin and Stephen (1997) the current prevalence of PTSD was found to be 19.2%. In our study, it was 6.1% of the study population (PTSD = 34). These discrepancies among the studies are unlikely to be due only to methodological differences (both Helzer and Deykin used the DIS); the sample population

was also different. Deykin and Stephen (1997) investigated chemically dependent adolescents, whereas Helzer *et al.* (1987) studied a community sample.

Several causal pathways may explain the co-occurrence of PTSD and alcoholism (Pihl and Stewart, 1991). Alcohol misuse might increase anxiety and arousal levels through psychological processes, such as stressful life events, causing heavy drinking (Kushner *et al.*, 1990). These effects could serve to induce a hyper-arousal state in which the individual may be more vulnerable to develop stress disorder following a traumatic event. Some patients might begin or continue abusing alcohol in order to reduce or control their stress symptoms. This notion of self-medication of drug misuse suggests that individuals who are susceptible to certain aversive states are at a high risk of abusing drugs in order to reduce these aversive states (Khantzian, 1985). The consistent finding of an association between trauma exposure and alcoholism suggests that clinicians working with individuals who abuse alcohol should look carefully for a history of traumatic life events. In patients with comorbid diagnoses of PTSD disorder and alcoholism, treatment needs to address both disorders. Unfortunately, many physicians who are specialized in the treatment of people exposed to trauma regard alcoholism as secondary to the PTSD disorder and thus assume that drinking will normalize following alleviation of PTSD symptoms (Hurley, 1991). There are several problems inherent to this point of view. Independent of aetiological factors, once abusive drinking has begun, the alcohol disorder may follow its own course (Pihl and Stewart, 1991). On the one hand, it seems difficult for individuals to discontinue drinking after PTSD symptom management. On the other hand, if the PTSD symptoms are not treated, the patient may experience a re-emergence or intensification of the PTSD symptoms following sobriety and may again turn to alcohol for a temporary symptom relief. Therefore, both problems should be treated simultaneously.

Among the group of female patients, alcohol consumption was highest in the group of patients with comorbid anxiety disorders. Our study also suggests that female patients with an anxiety disorder experienced onset of drinking, regular drinking, and first occurrence of withdrawal symptoms earlier than females without anxiety disorders. Hesselbrock *et al.* (1985) reported more panic disorders and phobia among hospitalized female, than male, alcoholics. Possibilities include: having an anxiety disorder may promote the development of an alcohol disorder (alcohol as self-medication); having an alcohol disorder may promote the development of an anxiety disorder; a third variable (e.g. genetic factor) may promote the development of both an alcohol use disorder and an anxiety disorder (Nunes *et al.*, 1988; Pohorecky, 1991). The extent to which one disorder promotes the other or whether the influence of other variables actually accounts for some or all of these associations remains speculative (Schuckit and Hesselbrock, 1996; Kushner *et al.*, 1999). Schuckit and Hesselbrock (1994) argued that the interaction is very complex and the available data do not prove a close relationship. These authors hypothesized that the high rate of comorbidity reflects a mixture of true anxiety disorders among alcoholics at a rate equal to or slightly higher than that of the general population, along with temporary, but at times, severe substance-induced anxiety syndromes. Kushner *et al.* (1999) concluded that both alcohol and anxiety disorders demonstrate



a reciprocal causal relationship over time, with anxiety disorders leading to alcohol dependence and vice versa. The debate over the impact of anxiety and stress disorders in the pathogenesis of alcoholism continues. Our data are not qualified to contribute to this debate with regard to pathogenesis, but indicate that PTSD in alcoholic patients and anxiety disorder in female alcoholic patients are substantially associated with the course and severity of alcoholism.

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