

## NICOTINE AND ALCOHOL DEPENDENCE IN PATIENTS WITH COMORBID ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD)

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**Abstract — Aims:** Several studies have shown that attention-deficit/hyperactivity disorder (ADHD) represents a significant risk factor for the onset and development of an addiction. Thirty-five per cent of adult ADHD patients are known to be addicted to alcohol. Many ADHD patients also have an increased nicotine consumption, which typically, leads to an improvement of attention, ability to concentrate and control of impulses. There may be pathophysiological connections here. On the other hand, it can also be assumed that there is a high prevalence of addicted patients with undiagnosed ADHD. **Methods:** Ninety-one adult alcohol-dependent patients were examined for ADHD in this study, using the Wender Utah Rating Scale (WURS-k), Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) symptom check-list for ADHD and the Conners' Adult ADHD Rating Scales (CAARS, Long Version). The patients were divided into diagnostic sub-groups according to DSM-IV (inattentive type, impulsive type, combined type). Nicotine consumption was investigated using the Fagerström Test of Nicotine Dependence (FTND) and then graded as 'minimal', 'average' or 'high' nicotine dependence. **Results:** There were 20.9% (WURS-k) or 23.1% (DSM-IV diagnostic criteria) of the patients addicted to alcohol, who showed evidence of ADHD in childhood. With the help of CAARS, it could be demonstrated that 33.3% of the patients who fulfilled the diagnostic criteria of ADHD, according to DSM-IV, had persisting ADHD in adulthood. The FTND showed a statistically significant difference in nicotine dependence between alcohol-dependent patients with and without ADHD in childhood. Patients numbering 76.2% with ADHD, demonstrated an 'average to high' level of nicotine dependence compared to 45.7% of those patients without ADHD. Furthermore, the number of patients not addicted to nicotine (19%) was significantly lower than among those without ADHD (36.6%) ( $P = 0.029$ ). **Conclusions:** The results of this investigation reveal that a large number of ADHD patients suffer from alcohol dependence, and an even greater number from excessive nicotine dependence. The outcome indicates that there are most likely pathophysiological connections with alcohol and nicotine dependence, and that this substance abuse is probably a form of 'self-medication'. The results clearly underline the great importance of early and adequate diagnosis and therapy of ADHD, in order to prevent exacerbation of addictive illness.

### INTRODUCTION

Several studies have already demonstrated that attention-deficit/hyperactivity disorder (ADHD) indeed represents a risk factor for the exacerbation of addictive illnesses. A comorbidity of ADHD and substance abuse has been described in approximately 71% of patients (Wilens *et al.*, 1997). Jacob *et al.* (2007) found in a large cohort study a lifetime prevalence of 45% for substance use disorder in adults with ADHD. Patients with ADHD and drug addiction showed a tendency to commence early and to experiment more freely with substance abuse than those addicted patients without ADHD (Biederman *et al.*, 1998; Ohlmeier *et al.*, 2005). Around 35% of adult ADHD patients are known to be addicted to alcohol (Shekim *et al.*, 1990). Similarly, reviews of adult studies (Wilens, 2004) indicate that the overlap between substance use disorders (SUD) and ADHD is actually greater than expected. Studies of subjects with alcohol and drug use disorders show that around 15–25% of adults referred for SUD are also affected by ADHD (Carroll and Rounsaville, 1993; Levin *et al.*, 1998a; Schubiner *et al.*, 2000; Wilens, 2004). Other authors are of the opinion that ADHD combined with a

comorbid disorder (disturbed personality, depression, anxiety, etc.) additionally increases the risk of addiction (Biederman *et al.*, 1995).

There is also a greater likelihood of adolescents with ADHD developing an addiction to cigarettes compared to adolescents without ADHD (Pomerleau *et al.*, 1995; Milberger *et al.*, 1997; Wilens, 2004). Current estimates of regular tobacco use by adolescents with ADHD are twice as high compared to unaffected adolescents (Lambert and Hartsough, 1998). The higher risk of cigarette smoking in patients with ADHD has been observed to be equal in both genders. Significant differences in cigarette addiction persist in ADHD, with a higher frequency in young adults, even in those without personality disorders (Lambert and Hartsough, 1998; Wilens, 2004).

Clinical observations have revealed that ADHD patients with nicotine addiction often demonstrate an improvement of attention, concentration ability and control of impulses. One of the more intriguing possibilities is that the nicotine released when smoking cigarettes remediates or partially relieves the symptoms of ADHD, including inattention and impulsivity (Levin *et al.*, 1996). It still remains a question of debate whether or not smoking can be considered as a form of self-medication for ADHD patients (Conners *et al.*, 1996).

Various investigators (Henningfield *et al.*, 1990, 1991) have noted that tobacco dependence is not only a significant addiction in its own right, but also leads to the development of several other forms of drug dependence (Fleming *et al.*,

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1989; Torabi *et al.*, 1993). Studies based on the increase of drug use very often demonstrate that the majority of people who use illegal drugs have previously smoked cigarettes or indulged in alcohol (Kandel, 1980; Kandel *et al.*, 1992), whereas those who have never smoked before, only rarely abuse illicit substances. Tobacco, therefore, is considered as a gateway drug ('gateway hypothesis') to the development of other dependences (Kandel and Logan, 1984).

The aim of this study was to investigate, retrospectively, the number of alcohol-dependent patients who showed symptoms of ADHD in childhood, and whether or not these symptoms persisted into adulthood. Furthermore, the question remains as to whether nicotine dependence and the extent of consumption have any connection with the symptoms of ADHD.

## PATIENTS AND METHODS

Adult patients numbering 91, with alcohol dependence, gave their consent to participate in this study as in-patients for a period of 6 months in the Department for Addiction at a psychiatric institution (Klinikum Wahrendorff). The European Addiction Severity Index (EuropASI) (Gsellhofer *et al.*, 1999) was used for evaluation of the addiction case history. At a clinical interview, all 91 patients (59 males and 32 females) met the diagnostic criteria required for alcohol-dependent syndrome according to ICD-10 and Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), and were permitted to participate in this investigation. The examination was performed only after a 10-day detoxification therapy as it was imperative that the patients were no longer suffering from any withdrawal symptoms. Exclusion criteria included psychoses stemming from schizophrenic symptoms and other illnesses. The authorized German translation of the Wender Utah Rating Scale (WURS-k) (Retz-Junginger *et al.*, 2002) and the DSM-IV symptom checklist for ADHD (American Psychiatric Association, 1994) served as investigating instruments for the retrospective assessment of the presence of ADHD in childhood. Additionally, the DSM-IV criteria were used to divide the patients into diagnostic sub-groups (inattentive type, impulsive type, combined type). The Conners' Adult ADHD Rating Scales (CAARS, Long Version) (Conners *et al.*, 1999) were used to assess persisting ADHD symptoms in adulthood. Nicotine consumption was tested using the Fagerström Test of Nicotine Dependence (Fagerström and Schneider, 1989) and then graded as 'minimal', 'average' or

'high' nicotine dependence. Approval for this study was given by the Ethics Committee of Hannover Medical School.

## STATISTICAL ANALYSIS

The  $\chi^2$ -test was performed for comparison of proportions. The Linear Trend Test was applied to test for a trend in ordinal categories. The unpaired *t*-test was used to compare means between two groups.

## RESULTS

Ninety-one patients fulfilled the required diagnostic criteria for alcohol dependence according to ICD-10 and DSM-IV. The group was composed of 59 male and 32 female patients with an average age of  $46.8 \pm 9.8$  years. The socio-demographic data are presented in Table 1. Nineteen (20.9%) of the 91 patients achieved the cut-off of  $\geq 30$  in the WURS-k and, therefore, fulfilled the criteria for ADHD symptoms in childhood. The DSM-IV symptom checklist confirmed retrospectively the ADHD diagnosis in childhood in 21 patients (23.1%). In 7 (33.3%) of these 21 alcohol-dependent patients who were affected by ADHD in childhood, the CAARS gave evidence of persisting ADHD also in adulthood. Additionally, the diagnostic differentiation of ADHD subtypes was undertaken according to DSM-IV. This revealed that 13 patients (14.3%) were categorized as 'inattentive type', 2 patients (2.2%) as 'hyperactive type' and 6 patients (6.6%) as 'combined type' of ADHD. The results of WURS-k, DSM-IV symptom checklist and CAARS are presented in Table 2.

The number of average to heavy smokers among the total random samples of alcohol-dependent patients was found to be 52.7%. With a view to nicotine dependence according to Fagerström and Schneider, 1989, among the alcohol-dependent patients there was a statistically significant difference between the patients with and without ADHD ( $P = 0.003$ ). At 76.2%, patients with ADHD showed a marked tendency towards an 'average to high' nicotine dependence when compared to those patients without ADHD (45.7%) ( $P = 0.029$ ). On the other side, the rate of alcohol-dependent patients with ADHD, with 'no' or 'very low' nicotine dependence (19%) was definitely lower than in the group of patients without ADHD (38.6%) (Table 3).

Table 1. Characteristics of patients

	Alcohol dependence with ADHD (DSM-IV)	Alcohol dependence without ADHD (DSM-IV)	Total group— alcohol dependence	<i>p</i> -value
Number of patients, <i>n</i> (%)	21 (23.1)	70 (76.9)	91 (100)	
Males/females, <i>n</i>	15/6	44/26	59/32	$P = 0.471$
Age ( <i>y</i> ), Mean $\pm$ SD	43.85 $\pm$ 9.32	47.80 $\pm$ 9.87	46.89 $\pm$ 9.84	$P = 0.108$
Final examinations, <i>n</i> (%)	0 (0)	9 (12.9)	9 (12.9)	$P = 0.083$
Graduation, <i>n</i> (%)	2 (9.5)	6 (8.6)	8 (8.8)	$P = 0.892$
Employed, <i>n</i> (%)	9 (45)	22 (31.4)	31 (34.4)	$P = 0.260$
Married, <i>n</i> (%)	4 (19.0)	25 (37.7)	29 (31.9)	$P = 0.151$
Divorced, <i>n</i> (%)	6 (28.6)	14 (20.0)	20 (22.0)	$P = 0.405$

Table 2. Attention deficit hyperactivity disorder diagnosed with Wender Utah Rating Scale (WURS-k\*), DSM-IV symptom check-list for ADHD and Conners' Adult ADHD Rating Scales (CAARS)

	Alcohol-dependent patients (n = 91) with ADHD
DSM-IV**, n (%)	21 (23.1)
Inattentive type, n (%)	13 (14.3)
hyperactive-impulsive type, n (%)	2 (2.2)
combined type, n (%)	6 (6.6)
WURS, n (%)	19 (20.9)
CAARS***, n (%), (DSM-IV pos, n = 21)	7 (33.3)

\* WURS = The authorized German translation of the Wender Utah Rating Scale (WURS-k) indicates ADHD with a score of more than 30.

\*\* CAARS = Conners' Adult ADHD Rating Scales (the analysis is conducted separately with respect to sex and age and gives an indication of the subject's current state).

\*\*\* DSM-IV = Diagnostic and Statistical Manual of Mental Disorders (a score higher than six in the first nine items indicates attentional problems; a score higher than six in the last nine items indicates hyperactivity).

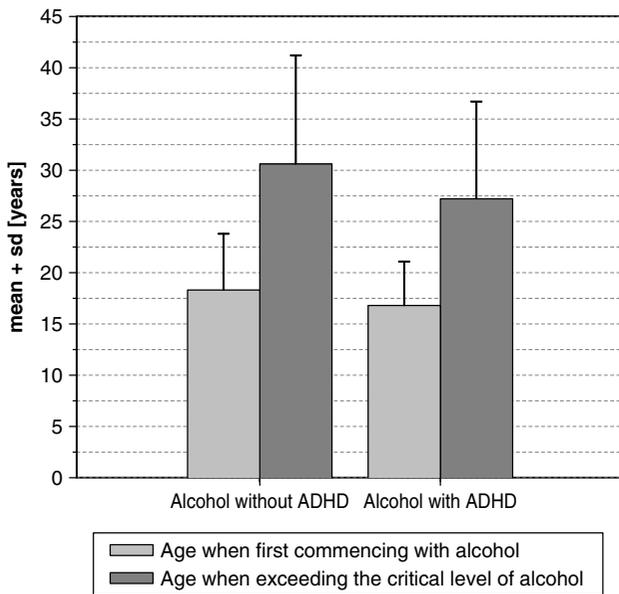


Fig. 1. Age when first commencing with alcohol and first experience exceeding the critical level of alcohol consumption in alcohol-dependent patients (n = 91) with and without comorbid ADHD.

Furthermore, alcohol addiction started at an earlier age in patients with comorbid ADHD (exceeding the critical level of alcohol consumption at 27.2 years (±9.52) with existing ADHD versus 30.6 years (±10.6), however, this result was not significant. Figure 1 presents the age of first alcohol abuse with and without comorbid illness.

DISCUSSION

The results of this study confirm that a high percentage of the alcohol-dependent patients admitted to a large addiction-medical psychiatric department fulfilled the diagnostic criteria of DSM-IV for the presence of ADHD. Retrospectively, a

high percentage of these patients could be diagnosed as having had ADHD in childhood, which, in some cases, persisted into adulthood. 23.1% of the alcohol-dependent patients investigated in this study showed the diagnostic criteria for the presence of ADHD in childhood, and 33.3% (CAARS) of those for persisting ADHD in adulthood.

Our data provide evidence that a high percentage of alcohol-dependent patients had ADHD in childhood (23.1%), many of whom also had ADHD persisting in adulthood (33.3%). On the other side, Kessler *et al.* (2006) found quite a high prevalence of ADHD in adults of 4.4%, so that our study found a rather moderate rate of persisting ADHD in the entire examined group of alcohol-dependent patients. However, according to our data concerning the prevalence in childhood, ADHD can represent a considerable risk factor for the onset and development of alcohol dependence. Furthermore, those patients with ADHD were much more likely to commence with alcohol at an early age, so ADHD can be considered to be a risk factor for 'early introduction' to alcohol.

With regard to nicotine consumption, it could be verified that high nicotine dependence was significantly more frequent in alcohol-dependent patients with comorbid ADHD. Patients numbering 76.2% with comorbid ADHD were found to have high nicotine dependence, versus 45.7% of patients without ADHD. The results lead to the supposition that there are pathophysiological connections with alcohol and nicotine dependence in patients with ADHD, and that substance abuse is taken up as a form of 'self-medication'.

Opinions differ as to why cigarette smoking in ADHD is predictive of SUD. Exposure to peers who smoke and use other licit (alcohol) and illicit substances serves to draw attention to the possible link (Kandel and Logan, 1984). Alternatively, pre-clinical investigators (Fung and Lau, 1989) hypothesized that early exposure to nicotine may result in neuronal sensitization and initiation, pre-disposing to later behaviours linked to SUD. From a preventive standpoint, reducing the manifest psychiatric symptoms, such as in ADHD, may result in a decrease in cigarette consumption. It was recently shown in a prospective trial of almost 6 years, that stimulant pharmacotherapy of ADHD may significantly hinder the onset of cigarette smoking in adolescents (Monuteaux *et al.*, 2004). It is also of interest to note that nicotine and nicotine agonists have proved effective in the treatment of ADHD (Conners *et al.*, 1996). Findings also indicate that ADHD accelerates the transition from substance abuse to substance dependence (Biederman *et al.*, 1998). There is also evidence that ADHD increases the risk of drug use disorders in those individuals with alcohol abuse or dependence (Biederman *et al.*, 1998). ADHD is also known to affect remission from SUD. A study was carried out with 130 adults with ADHD and SUD and 71 non-ADHD adults with SUD, and the results showed that the average time to SUD remission was more than twice as long in ADHD patients than in the control subjects (144 vs 60 months, respectively) (Wilens *et al.*, 1998). Studies performed on ADHD patients suggest that persisting ADHD can lead to continued misuse and abuse of substances following dependence, a longer duration of SUD and a lower rate of remission (Biederman *et al.*, 1998; Wilens *et al.*, 1998). Similarly, adults with ADHD seeking treatment for substance abuse have been shown to display a more chronic and severe form of SUD along with

Table 3. Nicotine and alcohol dependence with and without comorbid ADHD

	Alcohol dependence with ADHD (DSM-IV) <i>n</i> = 21	Alcohol dependence without ADHD (DSM-IV) <i>n</i> = 68*	<i>P</i> -value
Number of cigarettes smoked daily			
upto 10, <i>n</i> (%)	4 (19.0)	23 (33.8)	<i>P</i> = 0.051**
11–20, <i>n</i> (%)	4 (19.0)	17 (25.0)	
21–30, <i>n</i> (%)	7 (33.3)	20 (29.4)	
31 and more, <i>n</i> (%)	6 (28.6)	8 (11.8)	
Fagerström Test of Nicotine Dependence (FTND)	<i>n</i> = 21	<i>n</i> = 70	
No/very low nicotine dependence, <i>n</i> (%)	4 (19.0)	27 (38.6)	<i>P</i> = 0.029**
Minimal nicotine dependence, <i>n</i> (%)	1 (4.8)	11 (15.7)	
Average to high nicotine dependence, <i>n</i> (%)	16 (76.2)	32 (45.7)	
Total score	5.71 ± 3.30 <i>n</i> = 21	3.47 ± 2.78 <i>n</i> = 70	<i>P</i> = 0.003***

\* two missings,

\*\* Linear Trend Test,

\*\*\* *t*-Test.

a slower recovery from cigarette dependence and SUD (Carroll and Rounsaville, 1993; Pomerleau *et al.*, 1995; Schubiner *et al.*, 2000). In summary, these findings indicate that ADHD influences the initiation, transition and recovery from SUD.

The high prevalence of nicotine dependence in ADHD patients can be explained pathophysiologically, in that nicotine stimulates the release of neurotransmitters (acetylcholine, dopamine and serotonin) and, in this way, increases the attention span. Nicotine appears to have an effect on the nucleus accumbens similar to that of the amphetamine derivatives (Pontieri *et al.*, 1996). Several SPECT studies have shown evidence of a comparable effect of nicotine on the dopamine transporter (DAT), known also with methylphenidate (Dougherty *et al.*, 1999). With nicotine-dependent ADHD patients a marked decrease of striatal DAT was observed (Krause *et al.*, 2002). It is of particular interest to note that various dopaminergically and noradrenergically effective drugs, such as bupropione, nortriptylene and moclobemide, are effective and beneficial in both the treatment of nicotine dependence and in ADHD (Riggs *et al.*, 1998).

Clinical observations have provided evidence that nicotine significantly reduces ADHD symptoms and, therefore, has been discussed as a possible form of therapeutic agent (Conners *et al.*, 1996; Levin *et al.*, 1996; Krause *et al.*, 2002). A double-blind cross-over study served to demonstrate the positive effect of nicotine plasters on ADHD symptoms (Conners *et al.*, 1996). Those individuals dependent on nicotine showed an improvement in attention and concentration and a decrease in hyperactivity. Alcohol-dependent individuals reported diminished 'inner unrest' and 'compulsive drive'. It should be noted that the investigation findings presented here may be the result of a marked increase of nicotine and alcohol dependence in the ADHD group.

The high coincidence of ADHD and addiction illnesses may also be due to a number of other causes. In particular, ADHD patients suffering from hyperactivity and disturbed control impulses and patients of the 'combined type' are known to derive a higher level of pleasure from 'experimentation and risk-taking' concerning drugs and alcohol. It was found that hyperactive ADHD patients with nicotine dependence were more likely to have an additional cocaine addiction compared

to those patients with just attention disorders (Saules *et al.*, 2003). In this connection, it is interesting to observe that ADHD patients have a markedly higher prevalence (35%) of cocaine dependence, and that the use of cocaine in this group is more dominant and starts at an earlier age compared to the non-ADHD individuals addicted to cocaine (Carroll and Rounsaville, 1993). Furthermore, it has been reported that ADHD patients with cocaine abuse have been successfully treated with methylphenidate to reduce the 'cocaine craving', and also to improve the condition of ADHD symptoms (Levin *et al.*, 1998b; Schubiner *et al.*, 2002). This may well be due to the pathophysiological connections between amphetamines, nicotine and cocaine.

Clinical experience reveals that patients with nicotine and alcohol dependence show signs of improvement of ADHD symptoms with this form of 'self-medication'. This appears significant also for the sub-types of ADHD. Our investigations showed significantly high values for the 'inattentive' and the 'combined' types. The isolated 'hyperactive type' was, in comparison, under-represented. It would appear that the over-representation of the 'combined type' in this group—included in the criteria as inattentive and hyperactive—reflects those individuals willing to take on a higher risk. Patients categorized under the 'inattentive type' most likely use the substance primarily for stimulation.

## CONCLUSION

In summary, it may be confirmed that ADHD represents a risk factor for substance abuse and that many patients suffering from an addictive illness may also have comorbid ADHD. ADHD patients with a high degree of nicotine consumption may be abusing large quantities as a form of 'self-medication' and as a 'gateway drug', thus posing a markedly greater risk for the development of other addictions. In conclusion, the results of our study indicate the importance of an early diagnosis and treatment of ADHD, i.e. a 'multimodal therapy' using pharmacological and psychotherapeutic concepts, which may help in reducing the onset and exacerbation of other addictions.

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