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ORIGINAL PAPER

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Co-morbidity of adult attention-deficit/hyperactivity disorder with focus on personality traits and related disorders in a tertiary referral center

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Abstract *Objective* The prevalence and consequences of co-morbid axis-I and axis-II disorders as well as personality traits were examined in a large cohort of adult attention-deficit/hyperactivity disorder (AADHD) at a tertiary referral center. *Methods* In- and outpatients referred for diagnostic assessment of AADHD were screened. 372 affected probands were examined by means of the Structured Clinical Interview of DSM-IV axis-I/II disorders, the Revised NEO Personality Inventory (NEO-PI-R), and the Tridimensional Personality Questionnaire (TPQ). *Results* Lifetime co-morbidity with mood disorders was 57.3%, with anxiety disorders 27.2%, and with substance use disorders 45.0%. The histrionic personality disorder (35.2%) was the most frequent personality disorder. AADHD patients exhibited significantly altered scores on most of the NEO-PI-R and TPQ personality dimensions. The extent of substance abuse and dependence, as well as the presence of antisocial personality disorder alone or the cumulative number of other specific personality disorders was associated with lower psychosocial status ($p < .0001$). *Discussion* In a cohort of patients with AADHD referred to a single tertiary center co-morbidity with axis-I/II disorders was remarkably prevalent. In AADHD co-morbid mood, anxiety, and personality disorders as well as substance abuse/dependence is likely to be predictive of poor outcome.

Key words adult attention deficit hyperactivity disorder · co-morbidity · NEO-PI-R · TPQ

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Introduction

Co-morbidity is thought to be a common phenomenon in attention-deficit/hyperactivity disorder (ADHD). McGough et al. [24] reported that 87% of the unitary affected parents of children with ADHD had at least one and 56% had at least two other psychiatric disorders. While the clinical relevance of psychiatric co-morbidity is acknowledged in children, it has remained controversial in adult ADHD (AADHD). Moreover, understanding of the neurobiological underpinnings of AADHD co-morbidity is rather limited.

Although several longitudinal studies of ADHD children failed to demonstrate greater current or

lifetime prevalence of mood disorders in young adulthood [21, 32, 45], Fischer et al. [12] reported increased rates of major depression. Retrospective studies consistently show that 35–50% of all probands affected with AADHD suffer from one or more depressive episodes during the assessed lifespan [1, 3, 18, 40, 43]. Likewise, several longitudinal studies indicated that ADHD children do not appear to develop increased lifetime or current rates of anxiety disorders in adulthood [12, 21, 32, 45]. Contrary to these findings, retrospective clinical studies demonstrated an increased lifetime prevalence of anxiety disorders with 40–60% of all adults with ADHD [42]. Biederman et al. [3] demonstrated a greater lifetime co-morbidity of generalized anxiety disorder (GAD), agoraphobia, and social phobia in clinic-referred ADHD adults. In another AADHD sample an effect of ADHD on the rate of obsessive-compulsive disorder (OCD), social phobia, GAD, and multiple anxiety disorders was shown [1]. Shekim et al. [40] reported that 51% of adults with ADHD met criteria for GAD, 15% for panic disorder, 13% for OCD, and 8% for phobias.

The findings of Weiss et al. [45] and Rasmussen [32] demonstrated an increased prevalence of substance use disorders in the ADHD group compared to control, that was not observed in all longitudinal studies [12, 13, 21]. Several retrospective studies reported the prevalence of alcohol abuse among adults with ADHD to be increased 2 to 3-fold compared to controls [3, 23, 25, 26]. An elevated lifetime prevalence of alcohol dependence was found in both male and in female AADHD patients [1]. Mannuzza et al. [21] detected an increased prevalence of any current non-alcoholic substance use disorder (including cannabis), other longitudinal studies could not confirm this finding [12, 32]. The prevalence of any current non-alcoholic substance use disorder (including cannabis) was increased in the predominant number of retrospective studies [1, 3, 10, 40].

Co-morbidity of ADHD with the entire spectrum of specific personality disorders remains unclear. Fischer et al. [12], showed co-morbidity of childhood ADHD with histrionic, antisocial, passive-aggressive, and borderline personality disorders at follow-up. A small pilot study by Burket et al. [5] (only 10 ADHD patients) found that subjects in the ADHD Group had significantly more personality disorders than those in the No ADHD Group (4.5 vs. 1.6 diagnoses/subject). Paranoid, histrionic, borderline, passive-aggressive, and dependent personality disorders were significantly more frequent in the ADHD group. The only personality disorder that has been studied repeatedly in AHDH is antisocial personality disorder (ASPD). In several prospective studies, childhood ADHD was associated with increased co-morbidity of ASPD (range 12–23% vs. 2–4%) at follow-up compared to controls [12, 21, 32, 46]. Cross-sectional studies confirmed the co-morbidity of AADHD with ASPD. Biederman et al. [3] reported that the co-morbidity of AADHD with ASPD was 12% in a cohort referred for treatment. A gender effect was detected with males being at higher risk than females [1]. In a cohort of patients suffering from primary alcoholism, 51% of the subgroup of alcoholics with AADHD fulfilled criteria of ASPD [16]. In male prison inmates the overall prevalence of AADHD was 45% [37], but the relevance of such findings in very selected samples to general AADHD patients remains to be demonstrated.

Personality traits have also been studied only rarely in ADHD patients. One study compared personality profiles, as assessed by the Revised NEO Personality Inventory (NEO-PI-R) questionnaire, of probands with AADHD without any history of other psychiatric conditions to profiles from a clinical control group of non-psychotic adult outpatients being treated with psychotherapy [30]. The AADHD group obtained significantly higher scores of Neuroticism and significantly lower scores of Conscientiousness than controls. A study in prison inmates fulfilling the diagnostic criteria for AADHD, compared to those without a history of or current ADHD symptoms confirmed higher scores for Neuroticism, and lower scores of Conscientiousness and Agreeableness [34]. Downey and associates [9] reported that three groups, current smokers with AADHD, AADHD never smokers, and current smokers without AADHD, scored more than a standard deviation above the norm on the Tridimensional Personality Questionnaire (TPQ) dimension Novelty Seeking. Current smokers with AADHD scored significantly higher than current smokers without AADHD. In a follow-up study, AADHD patients scored significantly higher than norm in Novelty Seeking and Harm Avoidance [10].

Taken together, scattered data from several studies with predominantly small cohorts suggest that AADHD results in co-morbidity with axis-I and axis-II disorders as well as substantial deviations in personality dimensions. However, some findings are conflicting and derive from divergent populations rendering direct comparison difficult. We have therefore ascertained a large cohort of AADHD patients and examined the presence of axis-I and axis-II disorders to investigate the hypothesis whether AADHD is highly co-morbid with other psychiatric disorders. Additionally, we conducted extensive personality assessment to explore whether AADHD patients feature distinct personality profiles.

Methods

Participants

As part of an ongoing study on AADHD multilevel endophenotyping, in- and outpatients of the Department of Psychiatry and Psychotherapy, University of Wuerzburg, referred for diagnostic

assessment and treatment of AADHD, were examined with the Structured Clinical Interview of DSM-IV axis-I disorders between 2003 and 2005. 372 patients (173 females, 199 males; mean age 33.3 years, SD ± 10.3) were recruited. The Ethics Committee of the University of Wuerzburg approved the study and written informed consent was obtained from all patients after procedures and aims of the study had been fully explained.

Inclusion criteria were AADHD according to the diagnostic criteria of DSM-IV, onset before the age of 7 years via retrospective diagnosis, life-long persistence, and current diagnosis. Age at recruitment was between 18 and 65 years. Probands affected with substance use disorders underwent detoxification in an in-patient setting. Exclusion criteria were: the symptoms occur exclusively during the course of a pervasive developmental disorder, schizophrenia, or other psychotic disorder or symptoms are better accounted for by another mental disorder (criterion E of DSM-IV). Further exclusion criteria were: IQ level below 80 (MWT-B < 13 points), bipolar affective disorder (excluded due to the unsolved problems of differential diagnosis).

Measures

Diagnosis of childhood manifestation of ADHD was retrospectively assessed with the DSM-IV symptom list for ADHD (17 items) that was used as a structured clinical interview and the Wender-Utah-Rating Scale (WURS-K (21 items; males: mean 57.7, SD 14.4; females: mean 55.1, SD 14.3) [44]. Additional information from school report cards/certificates and from parents was included if available but were not obligatory. Adult manifestations were assessed with the DSM-IV symptom lists for ADHD: The ADHS-DC was used to obtain additional information. To ensure diagnostic validity informative input from partners, relatives, and friends was also collected.

Co-morbidity was assessed with the structured clinical interviews of axis I (SCID I) and axis II (SCID II) disorders. SCID II was performed in combination with self-ratings and corresponding interviews strictly according to the guidelines by a single experienced psychiatrist (CJ). Personality traits were assessed with the NEO-PI-R [8] and TPQ [7]. For comparison of personality traits, a sample was recruited from students of the University of Dresden (338 females and 116 males; mean age 22.28 years, SD ± 5.11). Because of limited comparability of the patient and control samples with regard to gender ratio and age, the reference values of the German manual of the NEO-PI-R were used as additional controls [30].

Psychosocial status was assessed on the basis of a standardized biographical history of each patient. The following conditions were rated with one point each (mean 1.72, SD 1.42) (rates determined in this cohort in % are in parenthesis). Family status: divorced (6.2%), or separated (3.5%), or two or more times married (7.0%). Education: discontinued (6.7%), two ore more classes repeated (12.1%). Occupational qualification: unskilled (12.6%), unemployed (16.7%). Additional factors were psychiatric in-patient treatment (25.0%), delinquency (28.0%), suicidal behavior (26.4%), and aggressive behavior (23.9%). This results in a psychosocial status scale (0–9), where low scores indicate a higher psychosocial status. In our sample, the psychosocial status was not age-dependent. The intellectual functioning was assessed with MWT-B (IQ mean 111, SD 13.9).

Following evaluation of the frequency of specific axis-I and axis-II disorders according to DSM-IV the following a priori hypotheses were examined: (1) the co-morbidity of AADHD with axis-I disorders is highly prevalent, especially with mood disorders and substance use-related disorders [12, 22, 32, 46], (2) the co-morbidity of AADHD with personality disorders is prevalent, especially with antisocial personality disorders, (3) presence of an increased number of axis-I disorders, and substance-related disorders alone are highly predictive of lower psychosocial status [27]. (4) Presence of an increased number of co-morbid personality disorders, and antisocial personality disorder alone are highly predictive of lower psychosocial status. Regarding personality dimensions, the following hypotheses were tested: (5) NEO-PI-R Neuroticism scores are increased, and Conscientiousness scores are reduced in AADHD [30, 34], (6) TPQ Novelty Seeking and Harm Avoidance scores are significantly higher in AADHD patients.

Statistical analyses

Frequencies of co-morbid axis-I and axis-II disorders were calculated for the entire AADHD sample and the subtype samples. Differences in the gender distribution and frequency of co-morbid disorders between the AADHD subtypes were tested by χ^2 or Fisher's exact test. Differences in psychosocial status between patients with and without specific co-morbid disorders (ASPD or substance use disorders) were tested by ANOVA. The relationship between the number of co-morbid disorders and psychosocial status was investigated by linear regression. Personality traits (as measured by NEO-PI-R and TPQ) were compared using General Linear Models (GLM), see table footnotes for details. All reported p-values are nominal, uncorrected and should be evaluated against appropriate levels of significance to account for multiple testing of several hypotheses.

Results

Subtypes

In our cohort the combined type (C-Type, 51.3%) was the most prevalent subtype of AADHD followed by the predominantly inattentive type (I-Type, 27.7%) and the predominantly hyperactive-impulsive type (H-Type, 21.0%). The distribution of the subtypes was similar in both sexes (I-Type; f = 24.3%, m = 30.7%), (H-Type; f = 20.8%, m = 21.1%) (C-Type; f = 54.9%, m = 48.2%) with slightly more males being inattentive (p = 0.33, χ^2 test).

Hypothesis 1: co-morbid axis-I disorders

AADHD patients who completed SCID I (N = 349) were used to determine the prevalence of co-morbid axis-I disorders according to DSM-IV criteria (Table 1). These disorders form five groups: mood, anxiety, somatoform, eating, and substance disorders. The most prevalent co-morbid disorders were mood disorders, of which major depression had a lifetime co-morbidity of 44.7%. These were followed by substance use disorder, especially cannabis dependence (17.8%), cannabis abuse (15.2%), and alcohol abuse (12.3%). Social phobia was the most common anxiety disorder with 9.5% lifetime and 8.3% current co-morbidity. Eating disorders (8.6% lifetime, 2.6% current) and somatoform disorders (3.7% current) showed low rates. Taken together, 83.7% of the patients suffered from at least one co-morbid axis-I disorder and 78.5% from at least one personality disorder (axis-II disorders, Fig. 1). More than 45% of the patients had two or more co-morbid personality disorders and nearly 60% had two or more axis-I disorders.

Table 1 Current and lifetime prevalence of axis-I disorders (according to DSM IV, SCID I) in 349 AADHD patients

	Lifetime N (%)	Current N (%)
Mood disorders	200 (57.3)	102 (29.2)
Major Depression	156 (44.7)	38 (10.9)
Dysthymic Disorder	–	41 (11.8)
Depression NOS	62 (17.8)	38 (10.9)
Anxiety disorders	95 (27.2)	75 (21.5)
Panic disorder	23 (6.6)	20 (5.7)
Agoraphobia	16 (4.6)	13 (3.7)
Social phobia	33 (9.5)	29 (8.3)
Specific phobia	19 (5.4)	17 (4.9)
Obsessive Compulsive disorder	10 (2.9)	8 (2.3)
Posttraumatic stress disorder	16 (4.6)	13 (3.7)
Somatoform disorders		13 (3.7)
Somatization disorder	–	3 (0.9)
Pain disorder	–	2 (0.6)
Undifferentiated somatoform disorder	–	4 (1.2)
Hypochondria	–	6 (1.7)
Eating disorders	30 (8.6)	9 (2.6)
Anorexia Nervosa	16 (4.6)	2 (0.6)
Bulimia Nervosa	20 (5.7)	7 (2.0)
Substance use disorders	157 (45.0)	58 (16.6)
Alcohol abuse	43 (12.3)	5 (1.4)
Alcohol dependence	37 (10.6)	15 (4.3)
Sedative abuse	12 (3.4)	1 (0.3)
Sedative dependence	8 (2.3)	2 (0.6)
Cannabis abuse	53 (15.2)	11 (3.2)
Cannabis dependence	62 (17.8)	27 (7.7)
Amphetamine abuse	30 (8.6)	0
Amphetamine dependence	15 (4.3)	2 (0.6)
Opiate abuse	13 (3.7)	0
Opiate dependence	9 (2.6)	1 (0.3)
Cocaine abuse	22 (6.3)	2 (0.6)
Cocaine dependence	8 (2.3)	0
Hallucinogen abuse	27 (7.7)	0
Hallucinogen dependence	5 (1.4)	1 (0.3)
Polysubstance abuse	14 (4.0)	0
Polysubstance dependence	17 (4.9)	0
Other substances abuse	1 (0.3)	0
Other substances dependence	2 (0.6)	0

The diagnostic procedures of ADHD and AADHD were performed by two residents in psychiatry (JR and MH), supervised in every case by an experienced psychiatrist (CPJ), who evaluated the co-morbid axis-I disorders by the Structural Clinical Interview of axis-I disorders of DSM-IV (SCID I). Definition of "lifetime" includes former and current diagnoses. Additional information of childhood ADHD was gained by Wender Utah Rating Scale (WURS)
–: there is no other information for this disorder than the current one

Hypothesis 2: co-morbid axis-II disorders

Personality disorders form three clusters, which all display high co-morbidity with AADHD (Table 2). The most frequent in each cluster were paranoid (12.0%, cluster (A), histrionic (35.2%, cluster (B), and avoidant personality disorder (18.3%, cluster (C). Special focus was on differences in the co-morbidity of specific personality disorders and clusters among the subtypes of AADHD. No significant differences were detected for obsessive-compulsive ($p = 0.07$) and antisocial ($p = 0.36$) personality disorders among subtypes. The H-Type showed higher co-morbidity with narcissistic personality disorder ($p = 0.02$), but lower co-morbidity with cluster B personality disorders ($p = 0.007$). The I-Type showed higher co-morbidity with cluster C personality disorders ($p = 0.0003$).

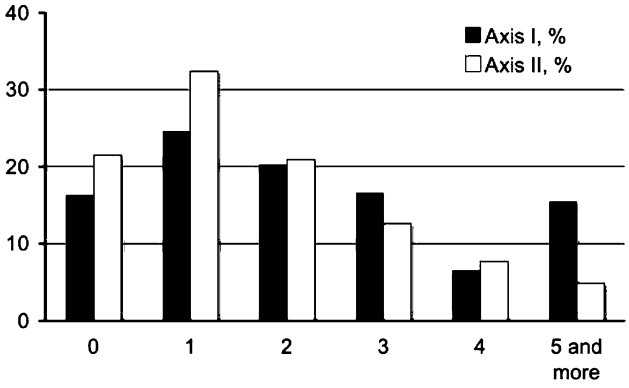

Fig. 1 Frequency of co-morbid axis-I and II disorders of 349 patients based on SCID I and II

Hypotheses 3 and 4: psychosocial level

High rates of co-morbid axis-I disorders or personality disorders were associated with significantly lower psychosocial level ($p < .0001$). An increase in the number of co-morbid axis-I or personality disorders by one resulted in a mean increase of the psychosocial score by 0.22. Particularly, AADHD patients with co-morbid substance abuse/dependence or ASPD had a significantly lower psychosocial status ($p < .0001$). Patients affected with co-morbid ASPD scored an average of 3.1 psychosocial problems, compared to 1.7 in non-affected AADHD patients. There were no differences between the psychosocial status of patients affected with Cluster B or C personality disorder.

Hypothesis 5: personality traits assessed with NEO-PI-R

AADHD patients had significantly higher Neuroticism scores than the published German reference values and the control sample ($p < 0.0001$, respectively). For comparison with the control sample we had restricted inclusion of patients to those younger than 36 years. Extraversion, Openness to experience and Conscientiousness of AADHD patients were significantly lower than those of the reference values and the control group (for details see Table 3).

In the age-restricted sample, we also found significant differences between the sexes for Neuroticism ($p < 0.0001$), Extraversion ($p = 0.01$) and Openness to experience ($p = 0.04$). In all cases the scores of females were higher than those of males. For Conscientiousness there was no gender effect ($p = 0.55$), but the interaction of gender and group was significant ($p = 0.0002$), i.e., in the control group, females

Table 2 Frequency of specific personality disorders in the overall AADHD sample (N = 349) and in AADHD subtypes (100 I-Type, 180 C-Type, 69 H-Type)

Personality disorder	All AADHD N (%)	I-Type N (%)	C-Type N (%)	H-Type N (%)
Cluster A				
Paranoid PD	42 (12.0)	11 (11.0)	21 (11.7)	10 (14.5)
Schizoid PD	3 (0.9)	0	1 (0.6)	2 (2.9)
Schizotypal PD	0	0	0	0
Cluster B				
Antisocial PD	20 (5.7)	3 (3.0)	12 (6.7)	5 (7.3)
Borderline PD	95 (27.2)	17 (17.0)	56 (31.1)	22 (31.9)
Histrionic PD	123 (35.2)	24 (24.0)	74 (41.1)	25 (36.2)
Narcissistic PD	104 (29.8)	21 (21.0)	55 (30.6)	28 (40.6)
Cluster C				
Avoidant PD	64 (18.3)	24 (24.0)	30 (16.7)	10 (14.5)
Dependent PD	10 (2.9)	2 (2.0)	7 (3.9)	1 (1.5)
Obsessive-compulsive PD	59 (16.9)	19 (19.0)	23 (12.8)	17 (24.6)
Passive-aggressive PD	49 (14.0)	8 (8.0)	29 (16.1)	12 (17.4)
Depressive PD	28 (8.0)	7 (7.0)	14 (7.8)	7 (10.1)

Co-morbid axis-II disorders were evaluated by the Structural Clinical Interview of personality disorders of DSM-IV (SCID II). The analyses were performed separately for the specific personality disorders and Clusters A, B, and C

Table 3 Mean NEO-PI-R Scores of AADHD and two different control samples with the corresponding standard deviation in parentheses and the p-value, respectively

NEO-PI-R	All AADHD (N = 350)	Reference values	p-value[a]	Control sample (N = 446)	p-value[b]
Neuroticism	116.6 (26.0)	91.1 (23.6)	<.0001	94.8 (24.1)	<.0001
Extraversion	103.2 (22.2)	110.5 (19.9)	0.005	113.7 (19.5)	.0006
Openness to experience	114.0 (19.7)	123.8 (19.4)	<.0001	131.8 (16.5)	<.0001
Agreeableness	112.0 (17.0)	112.6 (17.0)	1.0	111.8 (16.4)	0.85
Conscientious-ness	91.3 (20.7)	113.9 (20.1)	<.0001	111.6 (20.4)	<.0001

Personality traits were evaluated by the Revised NEO Personality Inventory (NEO-PI- R). For comparison a control sample was recruited from students of the University of Dresden (334 females and 112 males; mean age 22.28, years, SD ± 5.11). Because of limited comparability of the patient and control sample with regard to gender ratio and age, the reference values of the German manual of the NEO-PI-R were used as additional, internal controls. Comparison of NEO-PI-R scores between AADHD cases and controls was performed by using a general linear model with case/control status and sex (and a sex by group interaction where appropriate) as independent variables. Since the control group consisted of students we restricted our AADHD patients to those younger than 36 years. For this comparison, we therefore used 183 AADHD patients for NEO-PI-R. Comparison of the above mentioned scores with published reference values was performed by standardizing each patient's score with the appropriate age- and gender-specific population mean and standard deviation and comparing the resulting standardized scores to zero by the sign test

[a] Comparison of all AADHD with reference values of the German NEO-PI-R manual [REF]

[b] Comparison of all AADHD patients younger than 36 years (N = 183) with control sample (all younger than 36 years)

had higher scores than males (mean 113.1 vs. 107.2), while in the AADHD group females had lower scores (mean 83.5 vs. 91.6). In the German reference values, males and females had similar Conscientiousness scores.

Hypothesis 6: personality traits assessed with TPQ

Novelty Seeking and Harm Avoidance scores of AADHD patients were significantly higher than that of the published German reference values [47] and the control group ($p < 0.0001$, respectively) (Table 4). Furthermore, patients not affected with substance abuse or dependence showed significantly lower scores of Novelty Seeking ($p < 0.0001$). Reward Dependence scores of AADHD patients were significantly lower than the reference values ($p = 0.002$), and lower than those of the control sample; however, this difference was not significant due to the restricted sample size ($p = 0.2$). There were no gender effects on Reward Dependence ($p = 0.25$), modest effects on Novelty seeking ($p = 0.045$), but significant effects on Harm Avoidance ($p < 0.0001$) of which the score of females exceeded those of males.

Discussion

Concerning prevalence and consequences of axis-I and axis-II disorders in AADHD the present study is among the most extensive. The results reveal that co-morbidity of AADHD with both axis-I and axis-II disorders is remarkably frequent and the balanced gender ratio in AADHD and its subtypes confirms previous findings [2, 3]. The rate of co-morbidity with axis-I disorders is in accordance with the report by McGough et al. [24]. The lifetime prevalence of any axis I disorder is 46.4% in the National Co-morbidity Survey Replication (NCS-R) [18], which is much

Table 4 Mean TPQ Scores of AADHD and two different control samples with the corresponding standard deviation in parentheses and the p-value, respectively

TPQ	All AADHD (N = 360)	Reference values	p-value[a]	Control sample (N = 446)	p-value[b]
Novelty seeking	19.8 (5.7)	17.1 (5.3)	<.0001	17.1 (5.3)	<.0001
Harm avoidance	19.4 (7.1)	14.7 (6.2)	<.0001	15.4 (6.4)	<.0001
Reward dependence	17.6 (4.4)	18.6 (3.9)	0.0002	19.3 (4.0)	0.2

Personality traits were evaluated by the Tridimensional Personality Questionnaire (TPQ). Statistical methods as described in the footnote to Table 3.
[a] Comparison of all AADHD with German norm [47]
[b] Comparison of all AADHD patients younger than 36 years (N = 191) with control sample (all younger than 36 years)

lower than the 83.7% in AADHD patients in the current study.

The lifetime prevalence of major depression in this study is in line with other retrospective studies of AADHD and clearly higher than the lifetime prevalence of mood disorders in the National Co-morbidity Survey Replication (NCS-R) of 20.8%. The lifetime prevalence of anxiety disorders (27.2%) in the current study is confirmed by other retrospective clinical studies. There is not a considerable difference to the lifetime prevalence of anxiety disorders in the NCS-R (28.8%). The strikingly increased co-morbidity of lifetime substance use disorders in our study (45.0%) is in agreement with other retrospective studies and markedly higher than the lifetime prevalence of substance use disorders (14.6%) in the NCS-R.

Our findings indicate high co-morbidity of AADHD with almost all specific personality disorders. Most frequent was the co-morbidity with histrionic personality disorder which differs markedly to the prevalence in a general population assessed by the ECA survey (2.1%) [28]. Besides our comprehensive study, there is only very limited data of co-morbidity of the entire spectrum of personality disorders in patients affected with ADHD assessed with a Structured Interview for Personality Disorders. The pilot study Burket et al. [5] assessed a limited number of 37 adolescent females for ADHD using the Diagnostic Interview for Children and Adolescents and assigned to groups based on the presence or absence of ADHD (ADHD Group, n = 10; No ADHD Group, n = 27).

Co-morbidity of AADHD with ASPD was relatively rare (5.7%) in the current study and was not much different to the prevalence of the ECA (rural 3.9%, urban 3.4%) [41], although several prospective follow-up and cross-sectional studies had provided evidence that this co-morbidity is distinctly increased in AADHD [2, 37]. The findings of a relatively low co-morbidity of antisocial personality disorders and low rate of C-Type are therefore largely confirmatory. Adults affected with C-Type were more likely than those affected with I-Type to have had oppositional defiant disorder (ODD) in their past, to experience interpersonal hostility and paranoia, to have attempted suicide, and to have been arrested [27]. Particularly, increased impulsivity associated with C-Type was predicted to predispose to antisocial behavior. According to Faraone and associates [11], C-Type patients have a more severe disorder than the other DSM-IV subtypes. However, in our study the prevalence of ASPD was very similar among subtypes and even the rates observed for C-Type and H-Type (6.7% and 7.3%) are lower than in other studies [3, 12, 21, 32, 46].

AADHD and personality disorders are chronic conditions with a variable course. Several competing hypotheses have been proposed to account for the co-morbidity of AADHD with personality disorders [23, 39]. None of these disorders are precursors of each other, and all are defined by early onset. As converging lines of evidence indicate that co-morbidity of AADHD with ASPD represents a clinical subtype, our results demonstrate that the psychosocial status of patients affected with this co-morbidity is significantly impaired, while the co-morbidity of AADHD with Cluster B personality disorders in general does not influence the psychosocial status. Adults with ADHD having the least favorable outcome possibly are among those who are detained in prison [31]. The presence of a personality disorder has adverse effects on treatment outcome for a wide range of axis I disorders and is also associated with chronic symptoms and functional impairment [33].

The extent of substance use disorders, as well as the cumulative number of other specific personality disorders may be additionally relevant factor for poor outcome. While we did not conduct a longitudinal study with follow-up investigations of patients to assess the course of illness and development of their psychosocial status, we clearly demonstrated that the current psychosocial status of patients with axis I disorders is significantly worse than that of patients without such co-morbidities. There is an obvious dosage effect, with a linear inverse relationship between the number of co-morbid disorders and the current psychosocial status.

With NEO-PI-R and TPQ representing sensitive instruments for the assessment of personality traits, and underlying basic neurobiological dispositions [14, 15], significant differences in NEO-PI-R and TPQ scores in the present AADHD cohort corroborate a report by Rosler et al. [38] in which high Neuroticism scores, alongside with high scores on disorganization

and attention difficulties, were the best predictors of ADHD diagnosis. Analyses of personality profiles detect differences in structure and not only in the magnitude of these traits that may complete the diagnosis of AADHD. In our large sample, we find highly significant differences in AADHD patients compared to published norms and a non-clinical control sample for most personality traits, which remain significant after correction for multiple testing.

Various reasons including methodological differences may contribute to some contrasting findings. The reported prevalence of co-morbid conditions among adults with ADHD varies considerably depending upon whether a prospective or retrospective design was used [23]. The longitudinal studies applied earlier diagnostic nomenclatures which lacked clear operational criteria or inclusion criteria based on parents' or teachers' complaints. From the inclusion criterion of prospective longitudinal studies, specifically the diagnosis of childhood ADHD, valuable information about co-morbidity in adulthood has been derived. The persistence of ADHD into adolescence and adulthood represents a risk factor for co-morbid conditions. Vice versa, co-morbid disorders in childhood relate to the persistence of ADHD [20, 24]. Co-morbidity patterns expressed in adulthood (e.g., depression and/or anxiety) may represent a response to ADHD. Since data on persistence of ADHD into adulthood in prospective longitudinal studies are divergent (5–44%), modest proportions of AADHD in longitudinal studies may give unreliable estimates on rates of co-morbid disorders.

This is contrasted by retrospective studies which evaluated a subgroup of childhood ADHD with persistent symptoms. Important advantages of such retrospective studies are the large possible sample sizes, the short time frame and resource efficiency and the avoidance of bias caused by non-random loss to follow-up. On the other hand, retrospective studies usually have no reliable documentation of onset of co-morbid disorders, co-morbidity in childhood, and temporal relationships.

Various sampling biases may also distort the estimation of co-morbidity. Patients with more severe and co-morbid conditions are more likely to participate in treatment studies [23]. However, the significant lifetime psychiatric co-morbidity was not explained by referral bias in a study by McGough et al. [24]. Furthermore, several study populations (e.g., prison inmates) do not reflect the standard clinical setting and findings from these cannot be generalized for all AADHD patients. Our study of 372 patients with AADHD was performed in a tertiary referral center which increases the likelihood of a diagnosis of typical AADHD.

Cohort sizes may also distort the estimation of co-morbidity especially for relatively rare conditions. The number of included probands was between 61 and 147 in longitudinal studies. 59–99% of the probands were re-evaluated for ADHD during adulthood. The persistence rate of ADHD was 5–44% resulting in a low prevalence of AADHD. In a series of longitudinal studies Biederman et al. [1–4] investigated between 84 and 219 affected adults. In the study by McGough et al. [24], persistent ADHD was diagnosed in 79 (52%) of the 152 subjects with lifetime ADHD.

Mean age of patients is also a relevant factor in the assessment of co-morbidity. Most studies specify the co-morbidity of AADHD during the assessed lifespan. There are age-dependent modifications of AADHD with a decline of hyperactivity and, to variable extent, impulsivity. Only limited data is available on the stability of AADHD subtypes during the entire period of adulthood. Consistent with the pattern observed for ADHD, the incidence of antisocial behavior decreases considerably across adolescence and adulthood [19]. In longitudinal studies the average age was between 20.8 and 25.1 at the time of follow-up, while in the study by McGough et al. [24] the mean age of all participants was 43.2 years, whereas in our study mean age of AADHD patients was 33.3 years.

Gender-related differences of AADHD are another arguable aspect. ASPD and co-morbidity of AADHD with ASPD vary as a function of gender and might be more prevalent, or more likely diagnosed in males [3, 36]. While male patients seem more likely to be affected with Cluster personality disorders, females are more likely to have Cluster C personality disorders [35]. Moreover, many studies have shown different treatment seeking behavior in man and women. Biederman et al. [4], however, showed that gender differences in ADHD reported in clinical settings are likely to be caused by referral biases.

Finally, the influence of the ascertainment method of co-morbid disorders is controversial. Likewise, comparability of prevalence rates of substance use disorder in various studies is restricted, because some fail to differentiate between abuse and dependence. Contrary to other studies, we excluded probands affected with co-morbid bipolar affective disorders due to the unsolved concern of differential diagnosis. This may cause a limited study bias, since the 5.3% patients actually diagnosed as having bipolar disorder and AADHD does not exceed significantly the prevalence rate in the general population of about 3.9% in NCS-R [17, 42].

Conclusion

Co-morbidity of AADHD with axis-I/II disorders is a common phenomenon in cohorts of patients referred to a tertiary center. Co-morbid mood and anxiety disorders, as well as the extent of substance abuse/dependence, and presence of ASPD alone or a cumulative number of other specific personality disorders are associated with lower psychosocial status,

and therefore likely to be predictive of poor outcome. The assessment of axis-I/II disorders and personality profiles are essential for clinical and research purposes in AADHD.

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