



ADHD symptoms as risk factor for PTSD in inpatients treated for alcohol use disorder

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ABSTRACT

Attention deficit hyperactivity disorder (ADHD) and post-traumatic stress disorder (PTSD) are more common in alcohol use disorder (AUD) patients than in the general population. Still, there is a lack of knowledge about the relationship between the two conditions in these patients. The main objective of this study was to examine the prevalence of ADHD symptoms, and the relationship between ADHD symptoms and PTSD in AUD inpatients in treatment. Data from 85 AUD patients were collected. The Adult ADHD Self-Report Scale (ASRS) was used to measure ADHD symptoms in all patients. Differences between groups split by PTSD diagnosis and by ASRS clinical cut-off were described, and the relationship between ADHD symptom level and PTSD was tested in a multiple regression model. Almost half the patients scored above ASRS cut-off and 14% had PTSD. Of the patients whose score was above cut-off on the ASRS 23% had PTSD, versus 7% among those below cut-off. Higher ASRS score was associated with PTSD even when age, sex and trauma were adjusted for. This study confirms the high level of ADHD symptoms in AUD patients in treatment. Diagnostic evaluation of PTSD is recommended in patients with ADHD attending inpatient treatment programs for AUD.

1. Introduction

Patients with alcohol use disorders (AUD) have high psychiatric comorbidity (Jorgensen et al., 2018; Lai et al., 2015). This includes a higher prevalence of attention deficit and hyperactivity disorder (ADHD) (van de Glind et al., 2014), with up to one in four AUD and other substance use disorder (SUD) patients in treatment meeting the criteria for ADHD (van Emmerik-van Oortmerssen et al., 2012). These patients do worse in treatment (Fiksdal Abel et al., 2017; Kaye et al., 2013). There is also a high degree of co-morbidity between AUD and post-traumatic stress disorder (PTSD), studies indicating that one in ten AUD patients have PTSD, but estimates vary greatly both in treatment-seeking individuals and among those not in treatment (Blanco et al., 2013; Debell et al., 2014). The increased prevalence is commonly understood to be due to PTSD patients self-medicating with alcohol or drugs (Chilcoat and Breslau, 1998; McFarlane, 1998), but there is also growing evidence that the co-morbidity may be explained by common underlying causes, possibly neurobiological (Enman et al., 2014; Gilpin and Weiner, 2017).

Patients with AUD report more traumatic experiences than the general population (Dube et al., 2002; Mills et al., 2006). Trauma is a risk factor for the development of AUD (Dube et al., 2002; Kisely et al., 2020; Mills et al., 2006). Frightening or distressing events such as assault, abuse or serious accidents, or a prolonged traumatic experience may give rise to PTSD (Khoury et al., 2010). PTSD is more prevalent among patients with AUD than in the general population (Smith and Cottler, 2018). It could be that the increased prevalence is purely due to a higher incidence of traumatic experiences in AUD patients, but it could also be because AUD patients are more vulnerable. The relationship between AUD, traumatic experiences and PTSD is a complex one (Breslau et al., 2003; Brunetti et al., 2017). Could it be that features such as co-morbidity are important for the development of PTSD in AUD patients?

ADHD has been identified as a risk factor for PTSD (Adler et al., 2004; Ford and Connor, 2006; Spencer et al., 2016; Wozniak et al., 1999). It has been questioned whether ADHD and PTSD really represent two separate phenomena (Szymanski et al., 2011), but it has been concluded that even if the maladies share risk factors (Antshel et al.,

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2013) they must be considered two distinct disorders (Ford and Connor, 2006). Having one aggravates the other (Antshel et al., 2013; Biederman et al., 2013).

Despite the high prevalence of both PTSD and ADHD in AUD patients the relationship between the two disorders has been little studied. In this study, we aimed to examine the relationship between PTSD diagnosis and ADHD symptom score in patients in long-term inpatient treatment for AUD. We hypothesized that PTSD is more common among traumatized patients with high level of ADHD symptoms as measured by the Adult ADHD self-report scale (ASRS).

2. Materials and methods

2.1. Study participants

The study was approved by the Norwegian Regional Ethics Committee before data collection commenced (ID no: 21505/2017/1314).

Data were collected in three rehabilitation clinics in the Eastern region of Norway. These clinics offer long-term residential treatment stays (>30 days) for patients with various substance use problems, mainly AUD. Entry into long-term treatment is based on diagnosis of alcohol/substance use disorder according to ICD-10, and an impaired functioning level. Altogether 366 patients were admitted to treatment in the clinics during our inclusion period, of whom 224 (61%) were considered eligible for participation in the current study. Inclusion criteria was current AUD. Eligibility was considered by the clinics on the basis of the somatic and mental condition of the patient at inclusion and the patient's ability, at the time, to perform the interview and fill out the questionnaire. Thus, exclusion criteria were severe somatic illness, psychosis and cognitive impairment. In addition, patients who did not speak a Scandinavian language were excluded. The eligible patients were provided with information about the study and 114 (51%) patients signed written consent. Of the 110 patients (49%) who declined, 76 were men (69%; mean age 48.7 (standard deviation (SD) 11.6)) and 34 were women (31%; mean age 46.3 (SD 11.5)). Of the patients enrolled in the study 29 (25%) did not return a valid ASRS form and were excluded from the data analysis. Thus, 85 patients were included in the current study.

2.2. Measures

2.2.1. Mini international neuropsychiatric interview (M.I.N.I.)

During an interview conducted by trained staff M.I.N.I. was used to diagnose AUD and SUD, PTSD, current anxiety, lifetime depression and antisocial personality disorder (ASPD). Anxiety included panic disorder, agoraphobia, social phobia and generalized anxiety disorder. All other information was collected using self-report forms. The interview and self-report forms were administered at the clinics where the patients were staying.

2.2.2. Measure of harmful alcohol use

The extent of harmful drinking of alcohol was measured using the Alcohol Use Disorders Identification test (AUDIT), a 10-question instrument dealing with relationship to alcohol during the preceding year (Saunders et al., 1993). The responses range from 0 to 4 and add up to a total score between 0 and 40 where a higher score indicates more problematic alcohol use. Internal consistency as measured by Cronbach's α was 0.76 for the AUDIT scale in our sample.

2.2.3. The Adult ADHD Self-Report Scale

In this study we are not utilizing ADHD diagnoses, but measure the level of ADHD symptoms in a clinical sample of AUD patients. To collect information about ADHD symptoms we used the Adult ADHD Self-Report Scale (ASRS) (Kessler et al., 2005). The full version of this questionnaire consists of 18 items addressing inattentive or hyperactive-impulsive symptoms with five ordered response

alternatives *Never* (0), *Seldom* (1), *Sometimes* (2), *Often* (3) and *Very often* (4). A six-item screening version of the ASRS has demonstrated good specificity and sensitivity (Kessler et al., 2005). We calculated the total score of these six items, using a cut-off point of ≥ 14 (Kessler et al., 2007). This cut-off has previously been examined in a study of clinical utility of ASRS in an AUD population, where it performed with sensitivity of 87% and specificity of 66% (Daigre et al., 2015). Another report using this threshold found low sensitivity (57%) and suggested a lowered cut-off of ≥ 11 in order to avoid under-reporting (Ludrer et al., 2018). With the lowered cut-off negative predictive value was 96%, but the number of false positives was high with a positive predictive value of 61%. As our purpose was not detection of clinical cases at the cost of increased number of false positives, we chose to use the established cut-off of ≥ 14 to achieve the assumed most balanced identification of cases and to be able to compare our results with previous findings. The cut-off variable was used to stratify the sample for descriptive statistics. In the regression analysis we employed the full version ASRS score. To calculate the full version score we employed a scoring regime put forward by Kessler et al., 2005, where the response scale is dichotomized and the distinction between 0 and 1 for each item is balanced regarding false positives vs false negatives based on dichotomous clinical ratings (Kessler et al., 2005). In our sample, internal consistency for the 18 item ASRS scale was $\alpha = 0.90$.

2.2.4. Traumatic experiences

Exposure to trauma was measured using a structured self-report form with five questions. These questions have previously been used in a study of psychiatric inpatients (Toft et al., 2018). The first three questions asked whether the person had experienced the following in his or her childhood: sexual assaults (1), physical abuse (2) and other traumatic event that has subsequently caused significant problems (3). The last two questions dealt with experiences in adulthood: sexual assault or physical abuse (4) and other traumatic event that has subsequently caused significant problems (5). For each item the response alternatives were: *No* (0), *Yes, once* (1) or *Yes, several times* (2). Variables denoting the severity of traumatic experience were constructed by calculating the total of scores for questions dealing with history of trauma in childhood and adulthood, respectively. The maximum severity scores were 6 for childhood trauma and 4 for adulthood trauma.

2.2.5. Mental distress

The Hopkins Symptom Checklist 10 question version (HSCL-10) was used to measure mental distress (Derogatis et al., 1974). This is a widely used self-report tool that covers common symptoms of anxiety and depression experienced during the preceding week. There are four response categories for all items: *Not at all* (1), *A little* (2), *Quite a bit* (3) and *Extremely* (4). The average score for each individual was calculated yielding a score between 1 and 4 where higher score corresponded to more mental distress. Internal consistency for HSCL-10 in our sample was $\alpha = 0.90$.

2.3. Statistical analyses

Statistical analyses were performed using STATA version 15. One person had one missing item in the ASRS, and that person's mean was imputed for the missing item. Similarly, for one person with one missing item on the HSCL-10 and another person with one missing item on the AUDIT, the persons' means were imputed.

Chi square and Student's t-tests were used to test for differences between groups as stratified by ASRS cut-off and PTSD.

Logistic regression models were used to investigate the relationship between ADHD symptom scores and PTSD diagnosis, corrected for severity of and adulthood trauma experience, age and sex. Another logistic regression model was built to test the association between PTSD and ASPD, adjusted for adulthood trauma experience, age and sex. All statistical tests were two-tailed with a significance level of $\alpha = 0.05$.

3. Results

Of the 85 patients included in the study 25% percent were women and the mean age was 52.3 (SD 10.2). Twenty percent of the participants had SUD related to other substances in addition to AUD. The patients had been staying at the clinic for a median of 7 (Interquartile range (25th-75 percentiles (IQR) 5-12) days before the baseline measure. They reported the latest alcohol-containing drink to have been consumed median 18 (IQR 12-30) days prior to baseline measure.

Forty-six percent of the sample had ASRS scores above cut-off (Table 1). Gender and SUD diagnoses were equally distributed between the ASRS groups, while there was a trend towards patients above ASRS cut-off being slightly younger ($p = 0.053$). The patients scoring above ASRS cut-off had less education, more symptoms of mental distress (HSCL-10) and more severe alcohol problems (AUDIT). Anxiety disorders and ASPD were more common among those who scored above ASRS cut-off. There were more patients with history of childhood trauma, but not adulthood trauma in the ASRS positive group. PTSD was more common among the ASRS positive patients.

Fourteen percent of the total sample and 20% of the participants with adulthood trauma were diagnosed with PTSD. The descriptive statistics for the sample stratified by PTSD diagnosis are shown in Table 2. While there was no gender difference between the two groups, the patients with PTSD were younger. Patients with PTSD reported more symptoms of mental distress and more severe alcohol problems. Lifetime depression and ASPD was more common among the patients with PTSD. There were more patients with PTSD that scored above ASRS clinical cut-off and the PTSD patients had higher ASRS score.

Bivariate analyses with PTSD diagnosis as outcome variable showed significant increased odds ratios (OR) for ASRS score, severity of adulthood trauma, ASPD and decreased OR for age (Table 3). There was no association between PTSD and gender. ASRS score was associated with PTSD diagnosis when adjusted for age, sex and adulthood trauma severity in a multiple logistic regression model. As the comorbidity of ASPD and ADHD is known to be high, a similar adjusted model with

Table 1

Sociodemographic variables and clinical characteristics of patients above or below ASRS cut-off.

		ASRS < cut-off n=46 (54%)	ASRS > cut-off n=39 (46%)	p value
<i>Socio-demographics</i>				
Sex (female)	n (%)	12 (26)	9 (23)	0.748
Age	Mean (SD)	54.2 (9.7)	50.0 (10.3)	0.053
Upper secondary school	n (%)	36 (86)	24 (63)	0.020
Part or full time work	n (%)	15 (33)	6 (15)	0.067
<i>Mental health</i>				
HSCL-10 score	Mean (SD)	1.9 (0.6)	2.3 (0.7)	0.006
Major depression, lifetime	n (%)	31 (67)	29 (76)	0.367
Anxiety disorder, current	n (%)	20 (44)	29 (74)	0.006
ASPD	n (%)	3 (7)	9 (24)	0.025
PTSD	n (%)	3 (7)	9 (23)	0.029
<i>Traumatic experience</i>				
Childhood (yes/no)	n (%)	27 (60)	33 (85)	0.013
Adulthood (yes/no)	n (%)	28 (62)	26 (67)	0.672
<i>Substance use</i>				
AUDIT score	Mean (SD)	26.8 (6.4)	30.5 (6.9)	0.011
Other SUD	n (%)	6 (13)	11 (28)	0.082

ASRS=Adult ADHD self-report scale. HSCL-10=Hopkins symptoms checklist 10. ASPD=Antisocial personality disorder AUDIT=Alcohol Use Disorder Identification Test. Differences were tested for significance with Chi-square tests for dichotomous variables and Student's t-tests for continuous variables.

Table 2

Sociodemographic variables and clinical characteristics of patients with or without PTSD.

		No PTSD n=73 (86%)	PTSD n=12 (14%)	p value
<i>Socio-demographics</i>				
Sex (female)	n (%)	18 (27)	3 (25)	1.000 ^a
Age (years)	Mean (SD)	53.2 (9.6)	46.7 (12.3)	0.039
Upper secondary school	n (%)	53 (77)	7 (64)	0.454 ^a
Part or full time work	n (%)	21 (29)	0 (0)	0.033 ^a
<i>Mental health</i>				
HSCL-10 score	Mean (SD)	2.0 (0.6)	2.7 (0.6)	<0.001
Major depression, lifetime	n (%)	48 (67)	12 (100)	0.016 ^a
Anxiety disorder, current	n (%)	39 (54)	10 (83)	0.058
ASPD	n (%)	8 (11)	4 (36)	0.047 ^a
<i>ASRS</i>				
Above cut-off	n (%)	33 (41)	11 (73)	0.020
Total score	Mean (SD)	7.0 (4.5)	10.8 (3.9)	0.003
<i>Substance use</i>				
AUDIT score	Mean (SD)	27.8 (0.8)	32.4 (1.4)	0.032
Other SUD	n (%)	13 (18)	4 (33)	0.247 ^a

HSCL-10=Hopkins symptom checklist 10. ASPD=Antisocial personality disorder. ASRS=Adult ADHD self-report scale. AUDIT: Alcohol Use Disorder Identification Test. Student's t-tests and Chi square tests were used as appropriate, where not otherwise specified. ^aFisher's exact test.

ASPD as explanatory variable was built in order to account for the effect of ASPD on PTSD. ASPD was not associated with PTSD when adjusted for age, sex and adulthood trauma severity.

4. Discussion

In this investigation of inpatients in treatment for AUD we found that a diagnosis of PTSD was more common among patients with a higher level of ADHD symptoms. PTSD was related to ADHD symptom level even after adjusting for age, sex and severity of trauma.

4.1. Prevalence of ADHD symptoms

Forty-six percent of the participants in this study scored above the ASRS cut-off level. This is in line with the International ADHD in Substance Use Disorder Prevalence Study (IASP) that included seven European countries reporting an average of 40% above cut-off in a SUD population where 55% had AUD (van de Glind et al., 2014). Earlier studies from Norway using ASRS have reported higher figures (van de Glind et al., 2014), but our results confirm lower rates found in a recent study (Fiksdal Abel et al., 2017), indicating that Norwegian prevalence rates are comparable to other European countries. The ASRS is a widely used instrument screening for ADHD symptoms during the preceding six months, and has demonstrated good validity in the general population (Kessler et al., 2005; Kessler et al., 2007) and in various psychiatric and substance use populations (van de Glind et al., 2013), but, importantly, it cannot be used to diagnose ADHD. The prevalence of diagnosable ADHD may be lower due to the high sensitivity, but rather low specificity of ASRS in SUD populations (van de Glind et al., 2013).

4.2. Prevalence of PTSD

In our study, 14% of the total sample and 20% of those exposed to traumatic event in adulthood had PTSD. This fits well with previous reports estimating that more than 10% of those with AUD have comorbid PTSD, although figures range from 2%–63% (Debell et al., 2014). We found that the patients with PTSD had more severe alcohol use problems and also more symptoms of mental distress. In addition, more of the PTSD patients had ASPD and a history of depression than the non-PTSD patients. Depression commonly co-occur with PTSD, and there is symptom overlap between the disorders. Comorbid ASPD has also been found, maybe because such personality traits may be

Table 3
Bivariate and multiple logistic regression analyses with PTSD diagnosis as dependent variable.

Variable	Unadjusted OR	95% CI		p	Adjusted OR	95% CI		pp
		Lower bound	Upper bound			Lower bound	Upper bound	
Sex (ref.: Male)	1.02	0.25	4.18	0.980	0.47	0.09	2.35	0.358 ^a
Age	0.94	0.89	1.00	0.046	0.94	0.88	1.01	0.086 ^a
Adulthood trauma severity	1.94	1.14	3.28	0.014	2.38	1.20	4.73	0.013 ^a
ASRS score	1.23	1.06	1.43	0.006	1.21	1.01	1.44	0.037 ^a
ASPD (ref.: no)	4.64	1.11	19.4	0.036	1.50	0.24	9.37	0.718 ^b

OR=Odds ratio. CI=Confidence intervals. ASRS=Adult ADHD self-report scale. ^aModel fitted with sex, age, adulthood trauma severity and ASRS score. ^bModel fitted with antisocial personality disorder (ASPD) as explanatory variable adjusted for sex, age and adulthood trauma severity.

associated with impulsivity that increase the risk of traumatic events to occur (Sareen et al., 2004). In the general population women are more than twice as likely to develop PTSD as men, although men seem to experience more traumatic events (Tolin and Foa, 2006). This is in contrast to our study where PTSD is equally common among both genders, but self-reported adulthood trauma is almost twice as common among women. One possible explanation for this could be that woman may be more inclined to seek psychiatric treatment than AUD treatment due to stigma, whereas the opposite could be the case for men, possibly leading to a shifted ratio as compared to the general population. Further studies are needed to explore the gender differences for these associations among AUD inpatients.

4.3. Relationship between PTSD and ADHD symptoms

ADHD symptom level was related to PTSD diagnosis in a regression model adjusted for age, sex and adulthood trauma severity. Previous research has established an association between ADHD and PTSD in the general population, but few studies have investigated this relationship in clinical samples of AUD inpatients – a population known to have an increased prevalence of both ADHD and PTSD (Smith and Cottler, 2018; van Emmerik-van Oortmerssen et al., 2012). A previous report showed that severity of ADHD symptoms predicts severity of PTSD symptoms in male inpatients with AUD when controlling for trauma severity (Evren et al., 2016). This latter report controlled for childhood trauma but had no information about adulthood trauma, which is expected to be more strongly associated with adult PTSD. Our findings are in line with these results also when controlling for adulthood trauma. A meta-analysis that included 22 studies in children and adults with both healthy and traumatized control groups reported a pooled relative risk (RR) of 2.9 for PTSD in ADHD and a pooled RR of 1.7 for ADHD in PTSD (Spencer et al., 2016). Although a reciprocal increase in risk of comorbidity is established, the causal mechanisms behind the relationship are still unknown. Our and previous studies show that AUD patients with a high level of ADHD symptoms have experienced more trauma during childhood (Konstenius et al., 2017). Studies in child samples have found associations between maltreatment and ADHD (Stern et al., 2018), and one could speculate that childhood trauma creates a vulnerability for adulthood PTSD through an increased risk of ADHD. The mechanism through which ADHD increases the risk of PTSD is not known. One study found that childhood ADHD with comorbid conduct disorder predicted exposure to abuse or neglect in adolescence, indicating long-lasting effects of disruptive behaviors that negatively affect the interaction with surroundings and possibly lead to traumatic experiences (Stern et al., 2018). Adult individuals with ADHD might also be more likely to engage in behaviors that would expose them to higher risk of traumatic events and therefore they would be at higher risk of developing PTSD. But studies show that the ratio of PTSD is higher for patients with ADHD than without ADHD, even when the control subjects have a history of trauma (Spencer et al., 2016). In our study, patients who score above ASRS cut-off do not have a history of adulthood trauma more often than the others, suggesting that higher exposure to traumatic events caused by ADHD-typical behavior in adulthood is not the only reason for the

increased risk among AUD patients for developing PTSD. One reason for the increased PTSD comorbidity could be impaired cognitive and emotional processing that accompanies ADHD in most patients (Shaw et al., 2014; Silva et al., 2013). Poor pre-trauma cognitive performance have been associated with increased rates of PTSD (Marx et al., 2009; Parslow and Jorm, 2007). In line with previous literature we find high prevalence of anxiety and ASPD in patients with high level of ADHD symptoms (Matthies and Philipsen, 2016; Reimherr et al., 2017). One could argue that the association between PTSD and ASRS score seen in our study could be explained by increased prevalence of ASPD in patients that score above ASRS cut-off. However, we did not find a significant effect of ASPD on PTSD in an adjusted regression analysis, as we did for ASRS score. Finally, some have proposed that the high comorbidity rates could be caused by overlapping symptomatology and diagnosis criteria between ADHD and PTSD (Szymanski et al., 2011), but this has been contradicted (Ford and Connor, 2006). The comorbid clinical condition is more severe and research has shown that there is a familial coaggregation of the two disorders, indicating overlapping genetic factors (Antshel et al., 2013; Biederman et al., 2013). Preclinical, neuroimaging and genetic studies find similar biological aberrations in the two disorders possibly suggesting a shared vulnerability (Spencer et al., 2016). More research including longitudinal designs are needed to understand the connection between these disorders.

5. Limitations

The limitations to this study include potential symptom overlap between PTSD and ADHD, such as concentration problems which could influence the comorbidity figures. Further, even though the patients reported abstinence for 18 days on average preceding the baseline measure, we cannot be sure that withdrawal symptoms were not influencing the ASRS scores. The ASRS does not yield a formal ADHD diagnoses, but it did allow us to investigate the effect of ADHD symptom levels. Having data about adulthood trauma and not only childhood trauma was a strength, but we might have missed important information without questions that specifically target psychological/emotional abuse and neglect and a questionnaire with known reliability and validity. Some subjects did not return a valid ASRS questionnaire and were not included, potentially introducing a bias towards higher functioning patients in our sample. Finally, a larger sample size would have reduced the risk of false negatives.

6. Conclusions

This study suggests that a high level of ADHD symptoms is related to PTSD in AUD inpatients, even after controlling for age, sex and severity of trauma background. Thus, we show that the association between PTSD and ADHD symptoms, previously found in non-AUD populations, exists in AUD patients. With almost half the patients scoring above ASRS cut-off, this warrants careful attention to trauma background and PTSD symptoms for these patients. Future longitudinal studies are needed to investigate how this influences the course and outcome of AUD treatment.

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Authors' contribution

I.B., J.G.B. and L.L. conceptualized and designed the study and wrote the protocol. I.B. was responsible for data curation and project administration. J.G.B. and L.L. did the funding acquisition. I.B. and J.G.B. conducted the statistical analyses, and wrote the original draft of the manuscript. All three authors have reviewed and edited the manuscript and approved the final version.

Declaration of Competing Interest

The authors declare no conflicting interests.

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