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Screening for adult attention-deficit/hyperactivity disorder in alcohol dependent patients: Underreporting of ADHD symptoms in self-report scales

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ABSTRACT

Background: Attention-deficit/hyperactivity disorder (ADHD) is a common comorbid disorder that is frequently overlooked in adults with alcohol use disorder (AUD). Moreover, identifying ADHD in AUD patients is time-consuming and difficult. The aim of this study was to assess the clinical utility of two self-report screening instruments for adult ADHD in AUD patients.

Methods: 404 adults seeking residential treatment for AUD were screened using the Conners' Adult ADHD Rating Scale Screening Self-Rating (CAARS-S-SR) and the Adult ADHD Rating Scale (ASRS). Results were compared with ADHD diagnosis obtained from a stepped approach: first, a structured interview (Diagnostic Interview for ADHD in adults 2.0.; DIVA) was applied; second, probable ADHD diagnoses had to be confirmed by two expert clinicians.

Results: At the previously reported cut-off values, ASRS and CAARS-S-SR showed low sensitivities of 57.1 and 70.6%. A high number of false negative results (NPV ASRS: 89.5%; CAARS-S-SR: 92.3%) indicates underreporting of ADHD symptoms. Sensitivity improved at lower cut-off (ASRS ≥ 11; CAARS-S-SR ≥60) or with a combination of both instruments at lower cut-offs. Area Under the Curve (AUC) for the combination of ASRS and CAARS-S-SR was superior to the AUCs of the single questionnaires.

Conclusions: Underreporting of ADHD symptoms in ASRS and CAARS-S-SR of AUD patients requires lower cut-off values to detect the majority of ADHD, albeit at the expense of an increased rate of false-positive results. Cut-off values should be adjusted to the clinical setting. Clinicians should take into consideration that a negative screening result does not necessarily imply absence of ADHD.

1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) in childhood increases the risk for later substance use during adolescence and adulthood (Lee et al., 2011; Wilens and Morrison, 2011) and is a risk factor in young adults for continued heavy alcohol and illicit drug use (Vogel et al., 2016). Hence, adult ADHD is highly prevalent in patients with substance use disorder (SUD) (van Emmerik-van Oortmerssen et al., 2012) including alcohol use disorder (AUD) (Johann et al., 2003; Luderer et al., 2018; Roncero et al., 2015).

Recognizing ADHD in SUD patients is of particular concern, since substance treatment outcome and treatment retention is worse (Arias et al., 2008; Carroll and Rounsaville, 1993; Ercan et al., 2003; Levin et al., 2004; Rukstalis et al., 2005; Wilens and Morrison, 2011; Wise et al., 2001), their social functioning is more impaired (Moura et al., 2013), and their mortality risk is increased (Dalsgaard et al., 2015).

Diagnosing ADHD in SUD patients is often complicated and bears the risk of over-diagnosis by mixing ADHD symptoms with symptoms of SUD or other psychiatric disorders (Fatseas et al., 2012). On the other hand, adults with ADHD tend to underreport their current ADHD symptoms (Crunelle et al., 2018; Sibley et al., 2012). However, time-consuming diagnostic interviews for all patients in SUD treatment are not feasible in a typical clinical setting. Therefore, guidelines strongly recommend routine screening for ADHD in SUD treatment facilities

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(Atkinson and Hollis, 2010; Crunelle et al., 2018; Matthys and Crunelle, 2016). To date, only three studies (Daigre et al., 2015; Reyes et al., 2016; van de Glind et al., 2013) have reported screening results for patients with AUD and all of these studies assessed the same screening instrument (Adult ADHD Self-Report Scale; ASRS; Kessler et al., 2005). It is also not clear from these studies how much the duration of abstinence influences the reporting of ADHD symptoms.

We recently reported on a high prevalence rate of ADHD (20.5%) in a large sample of alcohol dependent inpatients (N = 415) (Luderer et al., 2018). In this study, reliable ADHD diagnoses were ensured via an extensive diagnostic procedure including a structured interview (Diagnostic Interview for ADHD in Adults [DIVA] (Kooij, 2012)) in all patients followed by successive diagnostic interviews by two expert clinicians if DIVA results indicated probable childhood or adulthood ADHD. However, administering a fully structured interview in all patients is not feasible in a routine clinical setting. ADHD self-report scales would be advantageous to minimize the effort of diagnosing ADHD if they were able to reliably identify patients with comorbid ADHD. We used the above-mentioned sample of patients with AUD with its thorough verification of ADHD to assess the validity of two adult ADHD self-report scales, the six-item Adult ADHD Self Report Scale v1.1 (ASRS) (Kessler et al., 2005) and the 30-item self-rating screening questionnaire from the Conners' Adult ADHD Rating Scales (CAARS-S-SR) (Conners et al., 1999).

2. Methods

2.1. Study design and participants

We have previously reported on the design of this study (Luderer et al., 2018). In brief, prior to diagnostic assessment of ADHD, two ADHD self-report questionnaires were administered to alcohol dependent patients undergoing a long-term residential rehabilitation treatment in the addiction center MEDIAN Klinik Wilhelmsheim, Germany.

The study had no external funding and was approved by the local ethics committee beforehand. Main inclusion criteria were written informed consent and a diagnosis of alcohol dependence according to ICD-10 (World Health Organization, 1993). Exclusion criteria were serious cognitive deficits.

All newly admitted patients with a diagnosis of alcohol dependence were informed about the study in a group setting during the second week of their treatment. Participants received no allowances. Individuals were informed that their treatment would not be affected by their decision to volunteer for the study.

We included 78.2% (N = 488) of all alcohol dependent patients that were in treatment at the site during the study period (January to October 2016). 85.0% (N = 415) of those included received the entire diagnostic assessment as described below.

Mean age of the participants was 47.6 years (± 10.7) and 72.0% were male. 38.1% of study patients were abstinent during the last 30 days before admission and 88% were abstinent on admission. DIVA was conducted at 4–5 weeks after admission. Mean time between DIVA and the final expert`s interview was 24.7 (± 16.4) days. This means that a minimal abstinence duration of at least four weeks during inpatient treatment was ensured prior to initiation of the diagnostic assessment.

2.2. ADHD diagnosis

After completing self-report screening instruments, a structured interview (DIVA; Kooij, 2012) was administered to all patients at weeks 4–5 after admission as previously described (Luderer et al., 2018). DIVA is a structured, clinician-administered, paper and pencil interview that assesses the DSM-IV ADHD criteria for childhood and adulthood. Each ADHD symptom is explained using different examples. DIVA is free of charge and available in many different languages including German. The interview takes 45–90 min and was conducted by two medical doctors previously trained in its application. Four or more symptoms in at least one cluster (inattention/hyperactivity-impulsivity) during adulthood or five or more symptoms in at least one cluster during childhood led to consecutive clinical interviews conducted by two expert clinicians to assure maximum diagnostic reliability. Hence, a diagnosis of ADHD required a DIVA interview suggestive of ADHD and two consecutive assessments by expert clinicians confirming adult ADHD. The expert clinicians' interview was a free-form exploration of DSM-5 criteria accompanied by extensive additional information from clinical staff (clinical observations, staff checklist for diagnostic criteria), informants' ratings of adulthood symptoms, parents' ratings of childhood symptoms and school records. Expert 1 would see all patients with suspicious DIVA results. If expert 1 rejected ADHD diagnosis, expert 2 would not additionally interview these patients. If experts' opinions did not match, cases were discussed. If a unanimous decision could not be made, ADHD was not diagnosed ("suspected ADHD"). Since a negative rating from expert 1 was not reassessed by expert 2, analysis of inter-rater agreement could not be conducted.

The previously reported per protocol analysis comprised 415 patients. Eleven patients had to be excluded from this analysis since adult ADHD was only suspected in these patients but not confirmed, resulting in N = 404 for our analyses. For each questionnaire, a number of patients had to be excluded due to missing items in the questionnaires (see Statistical Methods).

2.3. ADHD screening instruments

2.3.1. Adult ADHD Self Report Scale v1.1 (ASRS)

The Adult ADHD Self Report Scale v1.1 (ASRS) was developed by the World Health Organization (WHO)

The screening consists of six items with a five-stepped Likert scale (0 = never … 4 = very often) and is based on DSM-IV criteria for ADHD (Kessler et al., 2005). The ASRS showed, after dichotomizing answers (positive rating for items 1-3: ≥ 2; for items 4-6: ≥3) and with a cut-off of ≥ 4, a sensitivity of 68.7% and a specificity of 99.5% in a population-based sample (Kessler et al., 2005). A more recent publication suggested an alternative scoring algorithm with a simple sum score, resulting in a minimum score of 0 and a maximum score of 24 (Kessler et al., 2007). At the proposed cut-off of ≥ 14, sensitivity was 64.9%, specificity 94.0%, positive predictive value (PPV) 49.9%, and negative predictive value (NPV) 96.7% in the general population.

2.3.2. Conners' Adult ADHD Rating Scales

Conners' Adult ADHD Rating Scales (CAARS) are a set of self-report and observer rating instruments (Conners et al., 1999). We used the 30 items screening self-rating version (CAARS-S-SR) that is based on DSM-IV criteria in the German version (Lidzba et al., 2013). The results for each item are converted into normalized t-values, adjusted for age and gender. The main scale of the CAARS-S-SR is the ADHD-Index, where a score ≥60 would indicate a probable ADHD and a score ≥70 is considered highly suspicious of ADHD. In non-SUD patients, the ADHD-Index (cut-off ≥65) showed a sensitivity of 82%, a specificity of 87%, a NPV of 83%, a PPV of 87%, and Cohen's kappa was 0.67 (Taylor et al., 2011). The German version showed slightly different results in a non-SUD sample (sensitivity 71%, specificity 75%, NPV 72%, PPV 74%, Cohen's kappa 0.458).

2.4. Statistical methods

The gold standard for ADHD diagnosis consisted of a DIVA interview indicative of ADHD and unanimous clinical confirmation of ADHD by two experts in the field of ADHD and SUD (ML, TW). Rejection of ADHD diagnosis resulted from either a. negative DIVA results, b. expert 1 rejecting ADHD diagnosis, or c. expert 2 rejecting ADHD diagnosis and agreement with expert 1 after discussing the case. Eleven patients with positive DIVA but no definite confirmation of ADHD in the experts'

interviews (termed “suspected ADHD”) were excluded from analysis.

Only fully completed questionnaires or those with only one missing item were analyzed. Missing items were not imputed or estimated but counted as “0”. Results of the screening instruments were assessed for the two groups (ADHD vs. No ADHD) at different cut-off values for the main scale of each questionnaire, and sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were calculated. As an overall estimation of the performance of the instruments, Cohen’s Kappa was calculated. Values between 0.6 and 0.79 are considered moderate levels of agreement (McHugh, 2012). The same analyses were applied for a combination of both questionnaires.

Receiver operating characteristic (ROC) analyses were used to examine the screening efficacy. In order to assess and compare the ROC curves for the diagnostic instruments, we used predicted probabilities derived from logistic regression with ADHD diagnosis as dependent variable and the scores of the corresponding questionnaires as covariates. For the statistical comparison we calculated the Area Under the Curve (AUC) for each screening questionnaire and performed a test according to DeLong et al. (1988).

3. Results

Performance of the screening questionnaires varied depending on the specific instrument and the cut-off values used (Kappa 0.469 – 0.705; see Table 1). In general, lower cut-off values showed better performance, but the levels of agreement between screening results and ADHD diagnoses remained moderate.

The CAARS-S-SR showed the best Kappa value (0.675) and best sensitivity when using the ADHD index with the lowest threshold of ≥60. With this cut-off, we found 114 positive screening results, which identified 75 of 85 ADHD cases correctly (sensitivity: 87.7%) albeit at the expense of a high proportion of false positive CAARS-S-SR (34.2%, PPV: 65.8%). Increasing the cut-off to ≥65 or even ≥70 decreased the rate of false positive CAARS-S-SR to 24.1%, (PPV 75.9%) and 20.1% (PPV: 79%), respectively, but increased the number of false negative CAARS-S-SR and thus reduced sensitivity.

Using the established cut-off values for the ASRS, we found a low sensitivity but good results for specificity and positive predictive value (Table 1). The reason for this is the low rate of positive ASRS in this study when applying the established cut-offs (71 ASRS + for ≥4 positive answers and 57 ASRS + for sum score ≥14). This goes along with a high rate of false negative ASRS. 35.7% of ADHD patients would have been missed with ≥4 positive answers and 42.9% with a sum score of ≥14 in the ASRS. In contrast, the rate of false positive ASRS is fairly low. When the cut-off for the ASRS was lowered to ≥11, only 11.9% of ADHD cases were missed (sensitivity 88.1%), but ADHD diagnosis could not be confirmed in 38.8% of positive ASRS screening results.

The best results regarding sensitivity and NPV were achieved with a combination of either positive ASRS (≥11) or positive CAARS-S-SR (≥60) that led to a 100% detection rate of ADHD (sensitivity 100%) but was accompanied by a high number of false-positive self-report results leading to a low specificity (78.1%) and low PPV (54.9%).

A combination of both positive ASRS and CAARS-S-SR at same cut-offs showed the best Kappa value (0.717) with a low number of false positive screening results (PPV: 79.0%, specificity: 94.6%) and good sensitivity (76.2%). As could be predicted, sensitivity was lower than with the single instruments at the same cut-offs (ASRS: 88.1%; CAARS-S-SR: 88.2%), but specificity (94.6%) and PPV (79.0%) were much improved and NPV (93.7%) virtually unchanged.

This is also reflected in the ROC curves where the combination of both questionnaires showed a favorable progression (see Fig. 1). Comparing the ROC curves statistically by calculating the AUCs, we found a significant main effect between the four modalities ($CHI2(3) = 51.5$, $p < .0001$). The combination of ASRS and CAARS-S-SR was superior to all three single questionnaires (ASRS dichotomized $p = .0286$, ASRS sum score $p = 0.0009$, CAARS-S-SR $p = 0.0043$).

4. Discussion

To our knowledge, this is the largest study on the validity of the ASRS in AUD inpatients and the first study to assess the validity of the CAARS-S-SR and a combination of both questionnaires in these patients.

International guidelines strongly recommend screening for ADHD in SUD patients (Atkinson and Hollis, 2010; Crunelle et al., 2018; Matthys and Crunelle, 2016). However, only three studies have yet investigated the clinical utility of ADHD screening instruments in this population (Table 2, Daigre et al., 2015; Reyes et al., 2016; van de Glind et al., 2013) despite the fact that AUD is one of the most frequent SUD (Grant et al., 2015; Rehm et al., 2015; Wittchen et al., 2011) and ADHD occurs in up to every fifth patient with alcohol dependence (Daigre et al., 2015; Johann et al., 2003; Luderer et al., 2018).

All of the previous studies on ADHD screening instruments in AUD patients have investigated the self-report scale ASRS (Daigre et al., 2015; Reyes et al., 2016; van de Glind et al., 2013). Daigre et al. (2015) found an ADHD prevalence rate of 21.1% in 355 alcohol dependent outpatients. A sum score of ≥14 in the ASRS showed a sensitivity of 86.7%, a specificity of 66.1%, a PPV of 40.6%, and an NPV of 94.9%. The International ADHD in Substance use disorders Prevalence (IASP) study investigated 640 in- and outpatients with alcohol as the main substance of abuse (van de Glind et al., 2013). An ADHD prevalence rate of 8% was reported. When a cut-off of ≥4 for the dichotomized ASRS was used, a sensitivity of 80%, a specificity of 76%, a PPV of 23%, and an NPV of 98% was calculated (van de Glind et al., 2013). The third study (Reyes et al., 2016) performed an analysis of the ASRS in 379 alcohol dependent in- and outpatients using a cut-off of ≥4 for the dichotomized ASRS (van de Glind et al., 2013). They reported a sensitivity of 79.3%, a specificity of 70.3%, a PPV of 18.1% and an NPV of 97.6%.

Of note, the ADHD prevalence in two of these studies was the lowest reported so far in AUD patients (7.7% and 8%), potentially indicating differences related to the study population or the diagnostic process assessing adult ADHD (Reyes et al., 2016; van de Glind et al., 2013). Since PPV and NPV are influenced by disease prevalence, we adjusted the PPV and NPV of these two studies to our ADHD prevalence of 21.0% in order to facilitate comparison between study results. After adjustment for our higher ADHD prevalence, the PPV was calculated at 41.5% (for (Reyes et al., 2016)) and 46.5% (for (van de Glind et al., 2013)) whereas the NPV was calculated at 93.0% and 93.8%, respectively.

Taken together, the findings of the three studies differ substantially from our results (Table 2). The comparative studies found a high total number of positive ASRS together with a high rate of false positive ASRS indicating over-reporting of ADHD symptoms in their study populations. In our study, we only found few patients with a positive ASRS in general and few with a false positive ASRS at the established cut-offs. However, false negative results occurred rather frequently, which indicates under-reporting of ADHD symptoms.

Reasons for these contradictory results are diverse. One of the previous studies included only outpatients (Daigre et al., 2013) and two studies a mix of in- and outpatients (Reyes et al., 2016; van de Glind et al., 2013) whereas our study assessed patients during long-term residential treatment of 8–16 weeks. Even though all comparative studies appeared to have excluded acute intoxication or withdrawal symptoms (Daigre et al., 2015; Reyes et al., 2016; van de Glind et al., 2013), it is very likely that our study patients showed longer abstinence durations prior to diagnostic assessment (≥4 weeks). Two of the three studies (Reyes et al., 2016; van de Glind et al., 2013) found low ADHD prevalence rates of 7.7% and 8%, respectively, in patients with AUD, potentially indicating a selection bias compared to our study. Also, a high dropout rate could potentially influence study results but only one study reported on their dropout rate (van de Glind et al., 2013). The authors found a high dropout rate of almost half of all included patients before diagnostics could be completed and a larger proportion of

Table 1
Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, and κ of Each Self-Report Screening Test Versus ADHD Diagnosis.

A) ASRS

	ASRS + / ADHD + (N)	ASRS + / ADHD- (N)	ASRS-/ ADHD- (N)	ASRS-/ ADHD + (N)	Sensitivity (95 % CI)	Specificity (95 % CI)	PPV	NPV	Kappa	N
Sum score ≥11	74	47	269	10	74/84 88.1 % (81.2-95.0)	269/316 85.1 % (81.2-89.0)	74/1216 1.2 %	269/279 96.4 %	0.630	400
Sum score ≥12	62	24	292	22	62/84 73.8 % (64.4-83.2)	292/316 92.4 % (89.5-95.3)	62/86 72.1 %	292/3149 3.0 %	0.656	400
Sum score ≥13	56	19	297	28	56/84 66.7 % (56.6-76.7)	297/316 94.0 % (91.4-96.6)	56/75 74.7 %	297/325 91.4 %	0.631	400
Sum score ≥14	48	9	307	36	48/84 57.1 % (46.6-67.7)	307/316 97.2 % (95.3-99.0)	48/57 84.2 %	307/3438 9.5 %	0.616	400
Old scoring method (≥4 positive answers) *	54	17	299	30	54/84 64.3% (54.0-74.5)	299/316 94.6 % (92.1-97.1)	54/71 76.1 %	299/3299 0.9 %	0.625	400

B) CAARS-S-SR

	CAARS-S-SR + / ADHD + (N)	CAARS-S-SR + / ADHD- (N)	CAARS-S-SR-/ ADHD- (N)	CAARS-S-SR-/ ADHD + (N)	Sensitivity (95 % CI)	Specificity (95 % CI)	PPV	NPV	Kappa	N
ADHD Index ≥60	75	39	279	10	75/85 88.2 % (81.4-95.1)	279/318 87.7 % (84.1-91.3)	75/114 65.8 %	279/289 96.5 %	0.675	403
ADHD Index ≥65	60	19	299	25	60/85 70.6 % (60.9-80.3)	299/318 94.0 % (91.4-96.6)	60/79 75.9 %	299/324 92.3 %	0.663	403
ADHD Index ≥70	49	13	305	36	49/85 57.6 % (47.1-68.2)	305/318 95.9 % (93.7-98.1)	49/62 79.0 %	305/341 89.4 %	0.595	403

C) Combination

	ASRS + or CAARS-S-SR + / ADHD + (N)	ASRS + or CAARS-S-SR + / ADHD- (N)	ASRS- and CAARS-S-SR- / ADHD- (N)	ASRS- and CAARS-S-SR- / ADHD + (N)	Sensitivity (95 % CI)	Specificity (95 % CI)	PPV	NPV	Kappa	N
ASRS sum ≥11 OR CAARS-S-SR ADHD Index ≥60	84	69	246	0	84/84 100% (100.0-100.0)	246/315 78.1% (73.5 – 82.7)	84/153 54.9%	246/246 100.0 %	0.600	399
ASRS sum score ≥11 AND CAARS-S-SR ADHD Index ≥60	64	17	298	20	64/84 76.2 % (67.1 – 85.3)	298/315 94.6% (92.1 – 97.1)	64/81 79.0%	298/318 93.7%	0.717	399

Results of the screening instruments at different cut-off values in comparison with ADHD diagnosis.
PPV = Positive Predictive Value. NPV = Negative Predictive Value. Kappa = Cohen's Kappa. CI = Confidence interval.
ASRS = Adult ADHD Self Report Scale v1.1. CAARS-S-SR = Conners' Adult ADHD Rating Scale – Screening Self Rating.
ASRS + /- = positive/negative screening result for ASRS at the respective cut-off.
CAARS-S-SR + /- = positive/negative screening result for CAARS at the respective cut-off.
ADHD + /- = ADHD diagnosis present/not present.
A) * positive rating for items 1-3: ≥ 2; positive rating for items 4-6: ≥3.

negative ASRS screening results in those patients who dropped out. Since treatment retention is worse for patients with ADHD (Levin et al., 2004), it is conceivable that more ADHD patients with false negative ASRS results dropped out of treatment. As a consequence, this could have led to a higher sensitivity and higher NPV. Since our drop-out rate was considerably lower (14.3%) (Luderer et al., 2018) we probably had a higher chance of successfully assessing those patients with ADHD but false negative ASRS results.

As reported previously, we have found a higher AUD severity and an earlier onset of AUD in patients with ADHD (Luderer et al., 2018). Age of onset and severity of AUD have not been reported in studies assessing ADHD screening instruments in AUD patients (Daigre et al., 2015; Reyes et al., 2016; van de Glind et al., 2013). Therefore, it could be that we examined a more severely affected group of patients contributing to the high ADHD prevalence rates we have found in our sample. However, in patients with ADHD, increased SUD severity (Huntley et al., 2012) and early onset of SUD (Biederman et al., 2006) have both been described before, which would support the "generalizability" of our high prevalence rate.

Due to low self-perception and self-awareness (Manor et al., 2012) and lower ability to link ADHD symptoms to actual impairments (Morstedt et al., 2015), patients with ADHD tend to underreport their current ADHD symptoms (Owens et al., 2007; Sibley et al., 2012). This appears to be even more pronounced in patients with decades of substance abuse (Pineiro-Dieguez et al., 2016). Therefore, a high rate of false negative screening results in self-report scales seems more plausible and is in line with the results of our study. Hence, patients with AUD and comorbid ADHD seem to under-report their symptoms to a larger extent than it was known from previous studies.

For the CAARS-S-SR, there are no data available in AUD patients. However, one study investigated the ASRS and CAARS in cocaine dependent outpatients (Dakwar et al., 2012). In 102 patients (24.5% with ADHD), the CAARS showed a sensitivity of 80%, a specificity of 90.5%, a PPV of 74.1% and an NPV of 93.1%. In our study, we found a lower sensitivity, a higher specificity, and virtually identical numbers for the PPV and NPV at the established cut-off for the CAARS-S-SR (ADHD index ≥ 65). However, comparing the two studies is complicated as the authors investigated cocaine-dependent outpatients and used a CAARS with only 18 items and a different scoring method (Dakwar et al., 2012).

The lower sensitivity compared to all previous studies on alcohol-dependent patients led us to decrease the cut-off for the ASRS and

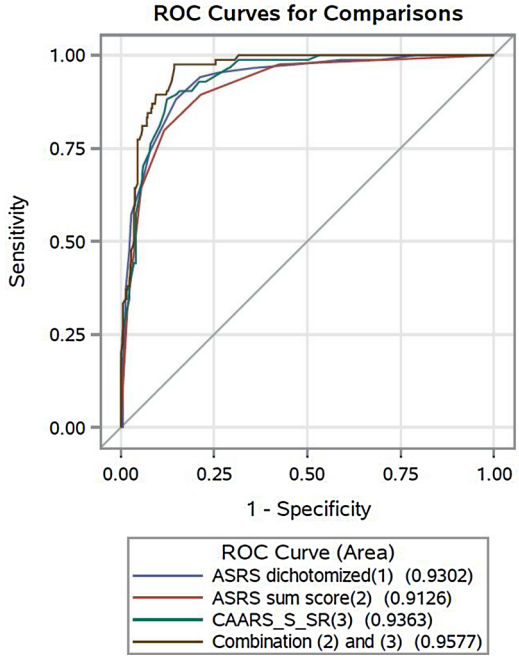

Fig. 1. Area Under the Curve (AUC) for ASRS dichotomized, ASRS sum score, CAARS-S-SR and a combination of ASRS sum-score and CAARS-S-SR.

CAARS-S-SR. At a cut-off of ≥11, the ASRS now correctly detected 88.1% of all ADHD patients and was accompanied by a low false negative rate (NPV 96.4%). This compares well with the previous ASRS studies albeit at a better specificity and PPV. The same applies to the CAARS-S-SR at a lower ADHD Index of ≥60 as it now showed a high sensitivity of 88.2% together with a low false negative rate (NPV 96.5%) but with superior specificity (87.7%) and PPV (65.8%) compared to the AUD studies using the ASRS. In a study on individuals with SUD in a correctional setting the authors also lowered the cut-off for the ASRS (to ≥12) to achieve a better sensitivity, summarizing "that the cut off of the screener may need to be adjusted depending on the circumstances within which it is used" (Bastiaens and Galus, 2017).

In the aforementioned study on cocaine-addicted patients (Dakwar et al., 2012), the authors also calculated a combination of either positive ASRS or positive CAARS. However, this combination was not found to substantially increase sensitivity compared to the CAARS alone but reduced specificity and PPV. A combination of both positive ASRS and CAARS reduced the rate of false-positive results but at the expense of a low sensitivity (Dakwar et al., 2012). In contrast, our combination of the same screening instruments in residential AUD patients showed promising results. Evaluating a combination of either a positive ASRS (cut-off ≥11) or a positive CAARS-S-SR (≥60) led to a 100% sensitivity, albeit at the expense of many false-positive screening results. The combination of positive ASRS and positive CAARS-S-SR achieved an acceptable sensitivity (76.1%) together with a low number of false-positive and false-negative results.

A high sensitivity would be beneficial for a screening tool to allow identification of most ADHD cases in AUD patients, in particular as this disorder is frequent in AUD (Luderer et al., 2018) and is associated with worse addiction treatment outcomes (Arias et al., 2008; Carroll and Rounsaville, 1993; Crunelle et al., 2018; Ercan et al., 2003; Moura et al., 2013; Wilens and Morrison, 2011). Which instrument or combination of instruments at which cut-offs are useful for clinical practice depends on many aspects. In a clinical setting in which human and time resources are scarce, a screening instrument is expected to exhibit only few false positive results as this reduces unnecessary diagnostic clarification. According to our results, in such a setting it would be recommendable to apply the established higher cut-offs for the ASRS and

Table 2
Previous studies on ADHD screening (ASRS) in patients with alcohol use disorder in comparison to the main results of this study.

Authors	Instrument (cut-off)	N	ADHD prevalence (N)	ASRS+ (N)	ASRS+/ ADHD+ (N)	ASRS+/ ADHD- (N)	ASRS-/ ADHD+ (N)	Sens.	Spec.	PPV	NPV	Gold Standard	Setting
Reyes et al., 2016	ASRS (6 items: ≥ 4) *	379	29 (7.7 %)	127 (33.5 %)	23	104	6	23/29 (79.3%)	246/350 (70.3%)	23/127 (18.1%)	246/252 (97.6%)	PRISM	In- and outpatient
Van de Glind et al. 2013	ASRS (6 items: ≥4) *	640	51 (8 %)	182 (37.3 %)	41	141	10	41/51 (80.4%)	448/589 (76.1%)	41/182 (22.5%)	448/458 (97.8%)	CAADID	In- and outpatient
Daigre et al., 2015	ASRS (6 items: ≥14) **	355	75 (21.1 %)	160 (45.1 %)	65	95	10	65/75 (86.7%)	185/280 (66.1%)	65/160 (40.6%)	185/195 (94.9%)	CAADID	Outpatient
this study	ASRS (6 items: ≥ 4) *	400	84 (21.0 %)	71 (17.8 %)	54	17	30	54/84 (64.3%)	299/316 (94.6 %)	54/71 (76.1 %)	299/329 (90.9 %)	DIVA, followed by two expert interviews	Inpatient
	ASRS (6 items: ≥14) **	400	84 (21.0 %)	57 (14.3 %)	48	9	36	48/84 (57.1 %)	307/316 (97.2 %)	48/57 (84.2 %)	307/343 (89.5 %)	DIVA, followed by two expert interviews	Inpatient
	ASRS (6 items: ≥ 11) **	400	84 (21.0 %)	121 (30.3 %)	74	47	10	74/84 (88.1%)	269/316 (85.1 %)	74/121 (61.2 %)	269/279 (96.4 %)	DIVA, followed by two expert interviews	Inpatient

Sens. = Sensitivity. Spec. = Specificity. PPV = Positive Predictive Value. NPV = Negative Predictive Value. Kappa = Cohen's Kappa.
ASRS = Adult ADHD Self Report Scale v1.1. CAARS = Conners' Adult ADHD Rating Scale – Screening Self Rating.
PRISM = Psychiatric Research Interview for Substance and Mental Disorders. CAADID = Conners' Adult ADHD Diagnostic Interview for DSM-IV.
* positive rating for items 1-3: ≥ 2; positive rating for items 4-6: ≥3. ** sum score (each item rated 0 to 4). *** 12 items from the ADHD index were transposed to gender- and age-adjusted t-values, before calculating a sum score.

CAARS-S-SR or, at best, to further assess only patients who have scored both positive in the ASRS and CAARS-S-SR at the lower cut-offs indicated in Table 1. If such a strategy is used, one has to keep in mind that many patients with ADHD will be missed due to false negative results. Vice versa, in a clinical setting in which the time-consuming diagnostic follow-up of positive self-report scales can be provided, lower cut-offs in the ASRS and CAARS-S-SR are recommendable. If an either-or-combination of both scales is used (ASRS or CAARS-S-SR positive), our results suggest that a sensitivity close to 100% without false-negative results might be achieved. Hence virtually all patients with ADHD will be identified with this screening strategy albeit at the expense of a high rate of false positive test results leading to extensive further diagnostics.

4.1. Limitations

It is of importance to use a highly accurate and reliable gold standard for ADHD diagnosis in order to validate ADHD screening instruments. In our study, a structured ADHD interview (DIVA 2.0) that was followed by non-formalized interviews by two expert clinicians served as the gold standard for ADHD diagnosis. However, negative DIVA results were not confirmed or falsified by the two experts but directly led to the final diagnosis of “no ADHD”. In addition, if expert 1 rejected ADHD diagnosis patients were not further assessed by expert 2. Hence, under-diagnosis of ADHD could theoretically be possible and inter-rater reliability could not be calculated. In that sense, we could have potentially increased our diagnostic accuracy if we had performed two expert interviews in every patient independent of DIVA results. On the other hand, all previous studies on ADHD self-report scales in AUD patients only used a single structured ADHD interview as the diagnostic gold standard (Reyes et al., 2016; van de Glind et al., 2013; Daigre et al., 2015). Furthermore, none of the previous studies reported on additional sources of information such as school records and parents’ ratings which we regularly used to complement our diagnostic workup.

In our opinion, the main limitation of the study is the fact that it was conducted at a single rehabilitation facility. The prerequisite for an elective residential long-term treatment over 8–16 weeks in Germany is abstinence on admission and a preceding lengthy and time-consuming application process that needs to be approved by the German pension fund. This particular form of treatment might have led to a selection bias for a subgroup of patients with characteristics unlike the general population of alcohol dependent patients. One could speculate that such a high-threshold program selects for a healthier group of alcohol dependent patients capable of pursuing such a laborious process prior to elective admission.

However, within the limitations of a mono-centric approach, we managed to keep the risk for an internal selection bias as low as possible: almost two thirds of all admitted alcohol dependent patients during the time of the study completed the full diagnostic procedure as per protocol and the drop-out rate from the study was very low (Luderer et al., 2018).

Furthermore, we diagnostically assessed alcohol dependent patients with prolonged and controlled abstinence durations compared to previous reports. Albeit we regard this as an advantage of this study, this approach potentially contrasts with the daily routine of screening ADHD in alcohol dependent patients in other clinical settings either during consumption or with only short durations of sobriety. Hence, this study specifically reports on the psychometric properties of ADHD self-report scales in alcohol dependent patients with prolonged alcohol abstinence.

5. Conclusions

ADHD is highly prevalent but underdiagnosed in alcohol dependent patients (Johann et al., 2003; Luderer et al., 2018; Roncero et al., 2015; van de Glind et al., 2014). Hence, screening for ADHD would be highly recommendable (Crunelle et al., 2018) if screening instruments displayed satisfactory psychometric properties. This study assessed two screening instruments in a large population of abstinent alcohol dependent patients in a very stable residential setting with highly reliable ADHD diagnoses.

Given the results of our study, we can recommend both the ASRS and CAARS-S-SR for ADHD screening. Both self-report scales performed at comparable levels. However, using lower cut-off values for both questionnaires is advisable to increase sensitivity (ASRS ≥ 11; CAARS-S-SR ≥ 60). If feasible, combining both instruments using the same lowered cut-offs can be recommended as this improves psychometric properties.

Our findings indicate that patients with alcohol dependence and ADHD appear to under-report their symptoms in self-rating questionnaires to a larger extent than it was previously known (Daigre et al., 2015; Reyes et al., 2016; van de Glind et al., 2013).

Conflict of interest

The authors report no financial or other relationship relevant to the subject of this article.

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Contributors

ML and TW initiated, designed and coordinated the study, acted as expert investigators who made final ADHD diagnoses, were involved in the data management and data analyses, and wrote the final version of the manuscript together with IR, FK and NKW. NKW collected the data and conducted structured interviews, AR coordinated the data collection. IR supervised data management and data analyses and commented on the manuscript. All authors contributed to interpretation of the data, commented on the manuscript and approved the final version.

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