Diagnosing ADHD during active substance use: Feasible or flawed?

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ABSTRACT

Background: Attention Deficit Hyperactivity Disorder (ADHD) is highly prevalent in patients with a substance use disorder (SUD). Because of possible problems with validity, diagnostic assessment of ADHD is usually postponed until after a period of abstinence, which may jeopardize adequate and timely treatment. The aim of this study is to investigate how a diagnostic assessment of ADHD in patients who are actively using substances compares to the results of a second assessment after a period of full or partial abstinence.

Methods: Prospective test-retest study in a SUD treatment center among 127 treatment seeking adult SUD patients with a comorbid diagnosis of adult ADHD. Conners’ Adult ADHD Diagnostic Interview for DSM-IV was administered at intake and after four SUD treatment sessions.

Results: The mean time interval between intake and retest assessment was 78 days (SD = 32; range 31–248). At the second ADHD assessment, substance use had decreased to about 50% of baseline consumption. Of the 127 patients with an initial diagnosis of ADHD, 121 patients (95.3%) still fulfilled DSM-IV adult ADHD criteria at re-diagnosis. Subtyping of ADHD was less stable (Cohen’s Kappa = 0.53). Agreement on the number of childhood and adult ADHD symptoms between both assessments was good (intraclass correlation coefficient of 0.69 and 0.65, respectively). Sensitivity analyses in subgroups of patients who were fully abstinent during the second assessment yielded very similar results.

Conclusions: These findings strongly suggest that a pragmatic approach, in which patients are evaluated for ADHD even when they are not (yet) abstinent, is feasible and justifiable.

1. Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is highly prevalent in treatment seeking patients with a substance use disorder (SUD). A meta-analysis estimated the mean prevalence of ADHD in treatment seeking SUD patients at 23.1% (van Emmerik-van Oortmerssen et al., 2012). An international multi-center study among 3558 treatment seeking SUD patients found that ADHD prevalence was associated with country and type of substance, with a higher ADHD prevalence in subjects using drugs compared to alcohol (Van de Glind et al., 2014). In general, SUD patients with ADHD constitute a subgroup with more serious problems; e.g., they use more substances and are more frequently hospitalized (Arias et al., 2008). ADHD in SUD patients is also related to other comorbidities, such as borderline personality disorder, antisocial personality disorder and mood disorders (van Emmerik-van Oortmerssen et al., 2014; Wilens et al., 2005) and childhood trauma (Konstenius et al., 2017).

Since common genetic (Arcos-Burgos et al., 2012) and neurobiological (Frodl, 2010) characteristics may be at the root of both SUD and ADHD, one could argue that treatments of both disorders could be combined. This is especially important because symptoms of untreated ADHD such as poor concentration and impulsivity interfere with substance treatment engagement and may lead to poorer substance treatment outcomes (Ercan et al., 2003). Similar to integrated treatments for other comorbidities (e.g., Seeking Safety (Najavits and Hien, 2013) or COPE (Back, 2010) for integrated treatment of SUD and PTSD), an integrated CBT treatment for patients with co-occurring ADHD and SUD has recently been developed (van Emmerik-van Oortmerssen et al., 2013).

When patients are to be allocated to integrated treatments, a practical problem emerges. In SUD patients, the diagnostic assessment of ADHD is complicated by the effects of drug intoxication or withdrawal
which may either cause or suppress ADHD symptoms such as agitation, impulsive behaviors, concentration difficulties or restlessness (Fatseas et al., 2012). This is why some authors advise to perform an ADHD assessment only after a period of abstinence (Milin et al., 1997). Others argue that prolonged abstinence is often not feasible and advocate a careful examination of symptoms during past periods of abstinence or prior to the onset of the substance use (Mariani and Levin, 2007). There are studies suggesting that psychiatric symptoms in general and ADHD symptoms more specifically may vary as a function of substance use, with evidence of both increases and decreases of symptoms during reduced substance use. In a study monitoring psychiatric symptoms during SUD treatment, 13% of the patients reported a worsening of psychiatric symptoms during re- treatment and the special integrated treatment of SUD and ADHD was only started if the ADHD diagnosis was confirmed during retest. Of the 184 patients who were diagnosed with SUD and ADHD at intake and started SUD treatment (July 2011–January 2016), 129 patients (70.1%) completed the four SUD therapy sessions and were successfully contacted for the retest. The other patients dropped out of the trial and also of the current study. The patients who dropped out had a lower educational level, had alcohol use problems instead of drug use disorder more often, and reported less substance use (van Emmerik-van Oortmerssen et al., 2017). Due to missing data of two patients, the total number of patients who participated in this study was 127.

The RCT from which the data of this study were drawn, has been reviewed and approved by the ethics committee of the Academic Medical Centre in Amsterdam. All participants signed informed consent.

2.2. Measures

The Conners’ Adult ADHD Diagnostic Interview for DSM-IV (CAADID) (Epstein et al., 2000) was used for the ADHD diagnostic assessment at intake and at retest. This instrument was administered by a psychologist or a medical doctor specially trained in the administration of the CAADID; in each patient, the intake and retest assessments were performed by different interviewers. In the CAADID, information regarding all DSM-IV criteria for ADHD is systematically collected. In evaluating the criterion whether symptoms are better explained by another disorder, no additional formal questionnaires were used, but a clinical judgment was made. At both assessments, special attention was paid to examining ADHD symptoms in periods of no substance use, if possible, in order to distinguish between substance-induced symptoms and ADHD. Although guidelines on ADHD assessment (National Institute for Health and Care Excellence, 2008) emphasize the importance of collecting collateral information of a parent or other inform- ant, we did not systematically include this information in the current study. This was mainly for practical reasons as many SUD patients have troubled, infrequent or non-existing relationships with their families. The Time Line Follow Back method (TLFB) (Sobell and Sobell, 2012) was used to collect information on substance use in the two months before intake and retest. From this instrument, we composed a variable ‘Excessive substance use’, defined as four or more standard drinks per day (women) or at least six standard drinks per day (men) in the case of alcohol, more than 1 joint per day in the case of cannabis, and/or any use of illicit drugs other than cannabis. In this way, we aimed to create a pragmatic variable which could be used for different substances at the same time. To avoid that e.g., using one standard drink of alcohol rendered the same value in this variable as using one whole gram of cocaine, we set different thresholds for defining ex- cessive alcohol, cannabis, or other drug use according to severity.

2.3. Data analysis

The significance of the difference between substance use at intake and at retest was calculated using the non-parametric Wilcoxon signed-rank test. The percentage of confirmed ADHD cases at retest was used as a measure of stability of the ADHD diagnosis at intake. An intraclass correlation coefficient (ICC) was calculated to compare the total number of ADHD symptoms at intake and at retest. Finally, Cohen’s kappa (κ) was used as a measure for the stability of ADHD subtypes.

All statistical analyses were conducted with SPSS v22.

3. Results

Of the 127 participants, the majority were male (85.0%), employed (71.7%) and single (62.2%), with a mean age at intake of 34.7 years (SD 8.8). The mean time interval between intake and retest assessment was 78 days (SD = 32, range 31–248). Only 11 patients (8.7%) used any ADHD medication at intake because they had received an ADH

Table 1
Substance use at intake and retest (N = 127).

<table>
<thead>
<tr>
<th>Substance use in past 60 days (mean number of days, SD)</th>
<th>At intake</th>
<th>At retest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>36.9 (21.1)</td>
<td>20.5 (18.3)</td>
</tr>
<tr>
<td>Cannabis</td>
<td>31.4 (21.8)</td>
<td>15.5 (17.0)</td>
</tr>
<tr>
<td>Stimulants</td>
<td>2.9 (2.7)</td>
<td>0.9 (1.7)</td>
</tr>
</tbody>
</table>

Data are given for primary substance only.

a Excessive use: For alcohol: at least four standard drinking units per day (women) or at least six standard drinking units per day (men). In the case of cannabis: more than 1 joint per day. In the case of other drugs: any use.

b p < 0.001, Wilcoxon signed-rank test for non-parametric data, comparing substance use at intake and at retest.

diagnosis earlier in their history and had started medication elsewhere; this medication situation was unchanged between intake and retest except for one patient who started medication.

At intake, alcohol was the most frequent primary substance of abuse (46.5%) followed by cannabis (26.8%), stimulants (23.6%) and other illicit drugs (3.1%). Table 1 presents information on substance use at intake and retest. At retest, days of excessive substance use in the last 60 days had decreased by about 50% and the mean number of days of excessive substance use in the past week had dropped from 2.9 at intake to 0.9 at retest. The differences between substance use at intake and at retest were statistically significant (p < 0.001). At retest, 72 patients (56.7%) reported being abstinent from their primary substance of abuse for at least one week; three of them had already been abstinent from their primary substance of abuse at intake as well, the remaining 69 patients (54.3%) were considered active substance users at intake and abstinent at retest and were analyzed separately in one of the four sensitivity analyses looking at ADHD stability. As 81.1% of the patients used more than one substance at intake, it is important to take any other substances into consideration as well. At retest, 40 patients (31.5%) reported being abstinent from all substances over the last week; they all reported active substance use at intake and were used in the second sensitivity analysis. 25 patients (19.7%) reported zero days of excessive use of the main substance of abuse in the past 60 days; 23 of them (18.1%) reported active use of their primary substance at intake and were analyzed in a third sensitivity analysis. Only 14 patients (11.0%) reported zero days of excessive use of any substance in the past 60 days. They all reported active use of at least one substance at intake, and were also analyzed in a sensitivity analysis.

Of the 127 SUD patients with adult ADHD at intake, 121 (95.3%) still fulfilled criteria of adult ADHD at retest. Of the six patients who did not meet ADHD criteria at retest, three patients did not endorse sufficient symptoms in childhood, one patient did not endorse sufficient symptoms in adulthood, one did not reach symptom threshold in childhood and adulthood, and for one patient, ADHD symptoms were better explained by the presence of another disorder. Intraclass correlation coefficients (ICCs) for the total number of ADHD symptoms between intake and retest assessment were 0.69 for adult ADHD and 0.65 for childhood ADHD symptoms, indicating good agreement over time. However, ADHD subtypes were less stable over time (see Table 2): in 33 of the 121 patients (27.3%) with a diagnosis of adult ADHD at intake and at retest, the adult subtype changed between intake and retest assessment resulting in a κ of 0.53, indicating moderate stability over time. For the childhood ADHD subtype, stability was very similar with a κ of 0.51.

Sensitivity analyses were conducted in four subgroups of patients who had become abstinent between intake and retest. Although we aimed for all patients to become abstinent, in practice only a minority achieved this goal. Of the 69 patients who had become abstinent for their primary substance for at least one week, three did no longer meet ADHD criteria (95.7% diagnostic stability). The subtype of ADHD in adulthood changed in 27.3% of these patients between intake and retest (κ = 0.51). Of the 40 patients who had become abstinent for all substances for at least one week, only one did no longer meet ADHD criteria (97.5% diagnostic stability). The subtype of ADHD in adulthood changed in 18.0% of these patients between intake and retest (κ = 0.66). Of the 23 patients who had become abstinent for their primary substance for 60 days, two did no longer meet ADHD criteria (91.3% diagnostic stability). The subtype of ADHD in adulthood changed in 23.8% of these patients between intake and retest (κ = 0.58). Of the 14 patients who had been abstinent for all substances for 60 days, all 14 still met ADHD diagnostic criteria at retest. The ADHD subtype in adulthood changed in 21.4% of these patients (κ = 0.63). Stability of ADHD symptoms in these subgroups, as reflected by the ICC, was very similar to those in the total study population (Table 3).

4. Discussion

The current study shows that a diagnosis of adult ADHD made at intake in treatment seeking SUD patients who are actively using substances, is a valid indicator for the presence of ADHD at a second diagnostic interview performed after an extended period of reduced substance use or abstinence. We found high diagnostic stability (95.3%) and high symptom stability (ICC > 0.65) over time but ADHD subtypes were less stable across assessments in this population.

These findings should be evaluated against the background of previous findings on the stability of ADHD and the design of the current study. Unfortunately, there is only one study, in a non-SUD adult population, that has looked at the interrater reliability of the CAADDI. Epstein and Kollins (2006) investigated the test-retest reliability in 30 ADHD patients who were assessed by two different trained interviewers with a time interval of three to four weeks and found acceptable agreement for childhood and adult ADHD (κ = 0.69 and κ = 0.67, respectively) with a higher agreement for adulthood ADHD if criterion B (age of onset) was excluded (κ = 0.80). It should be noted, however, that in the Epstein and Kollins study only 15 of the 30 patients initially met diagnostic criteria for adulthood ADHD and that in the current study retest interviewers knew that all patients had a diagnosis of adulthood ADHD at intake. Therefore, it is of interest to also look in more detail at the test-retest reliability of the number of ADHD symptoms in the current study, which was also good in our study. In our opinion, this is an important second indicator of stability of diagnosis over time.

The stability of the ADHD diagnosis over time and across substance use that we found implicates that there is no need to postpone the ADHD assessment in substance abusing patients. The advantage of assessing ADHD in an early phase of SUD treatment is that the treatment of ADHD can start earlier as well, which is important because patients might drop out along the way and miss the opportunity of ADHD treatment if it is withheld until a later stage of SUD treatment.

Despite the fact that different ADHD subtypes are defined in the DSM-IV, the validity of these subtypes in childhood and adulthood is controversial. In DSM-5, subtypes were removed and presentation styles have been included instead. Future studies should pay special attention to the stability of these presentation styles. Although there is some evidence supporting the validity of a distinction between the inattentive and combined subtypes (Adams et al., 2008; Woo and Rey, 2005), other studies claim that there is no compelling evidence that ADHD subtypes are different with regard to their neuropsychological profiles (Bernfeld, 2012). Willcutt et al. (2012) performed a meta-analytic review of 546 studies in samples of children, adolescents and adults to assess DSM-IV symptom dimensions and subtypes, and
 concluded that there is only weak evidence for the validity of the hyperactive/impulsive subtype after first grade. They also found minimal support for the distinction between the inattentive and combined subtypes in studies of etiological influences, academic and cognitive functioning and treatment response. However, none of the included studies reported test-retest reliability estimates for the ADHD subtypes over periods of less than one year. Data on the stability in time of ADHD subtypes are scarce and have focused on the transition from childhood to adulthood; in general, they show marked longitudinal instability of ADHD subtypes (Willcutt et al., 2012) (based on five studies in the meta-analysis, with follow-ups from five to nine years) with a greater persistence of inattentive than hyperactive/impulsive childhood symptoms of ADHD in adulthood (Kessler et al., 2010). In a study by Srbnecki et al. (2013) on a six-year follow up of 101 children with ADHD, a considerable change in subtype was also observed.

Considering these literature findings, our finding that the ADHD subtype changed between intake and retest in 27% of the patients, may therefore not necessarily reflect an actual change of ADHD-like symptoms caused by (changes in) substance use, but can also be accounted for by inter-rater differences or by instability of the ADHD subtypes per se, both of which have been reported in non-SUD populations. This hypothesis is corroborated by the fact that sensitivity analyses in an abstinence subgroup provided similar test-retest results.

The current study has both strengths and limitations. The most important strengths are the relatively large sample size and the careful assessment of ADHD in this representative population of treatment seeking SUD patients in regular SUD care. The study also has limitations. First, most patients were not fully abstinent at retest. However, in a series of sensitivity analyses we found that test-retest findings were very similar for patients who were and those who were not fully abstinent of the primary substance of abuse or even of all substances. Second, in some patients, despite the mean interval of 78 days between the intake and retest assessment, there was some overlap between the last 60 days before retest and the last 60 days before intake that were used to assess substance use. This applies to 42 patients, who had their retest assessment within 60 days after intake, which resulted in some overlap of the two assessments ranging from one day to a maximum of 29 days. However, there generally was a substantial change in substance use between intake and retest, and the current stability data clearly indicate that an ADHD diagnosis can reliably be made during a period of active substance abuse. Furthermore, it also illustrates that full abstinence is not easily reached, also in treatment seeking SUD patients which underlines the clinical relevance of our findings. Third, no informant data were available due to practical reasons. This is an important limitation since self-report can be unreliable. For example, a study by Sibley et al. (2012) demonstrated that young adults without ADHD tended to overreport current symptoms while young adults with ADHD tended to underreport their symptoms. It is unclear to what extent this may have affected our test-retest reliability results, but our conclusions should be viewed with caution. Fourth, as mentioned in the methods section, DSM-IV criteria were used for diagnosing ADHD. However, in DSM-5 some important changes were introduced: (1) the age of onset criterion was changed from ‘prior to the age of 7 years’ to ‘prior to the age of 12 years old’; and (2) the threshold for the number of symptoms in adulthood was changed from 6 to 5. It cannot be excluded that these changes have affected our results. However, in a previous paper we have shown that the prevalence of DSM-IV and DSM-5 ADHD in treatment-seeking SUD patients was very similar (Van de Glind et al., 2014). Finally, in the current study only the stability of the presence, not the absence, of ADHD at intake was examined and therefore no conclusions can be drawn on the stability of the absence of ADHD in actively substance abusing SUD patients. However, in a recent study, it was shown that screening for ADHD in SUD treatment-seeking patients with the ASRS-v1 (the screener that was also used in our recruitment procedure) two weeks before and at the time of the diagnostic assessment of ADHD with the CAADID, resulted in very similar sensitivities of the ASRS-v1 (0.84 and 0.88, respectively) with only 3.4% false negatives of the screener two weeks before the diagnostic assessment with the CAADID (Van de Glind et al., 2013). Although no information was provided about the changes in substance use between both time points and although it is not clear how many patients had become abstinent, these results suggest that the risk of missing an ADHD diagnosis due to the suppression of ADHD symptoms during substance use is probably very small. We therefore think that our data are a good approximation of the real diagnostic stability of ADHD in treatment-seeking SUD patients. It is unclear, however, whether these data are generalizable to non-treatment-seeking SUD patients. However, in the earlier mentioned meta-analysis (van Emmerik-van Oortmerssen et al., 2012) ADHD prevalence was not affected by treatment-seeking status and we have no clear indications that the process of diagnostic assessment would be different in a community sample. In fact, it is likely that none-treatment seeking people with a SUD are generally less severely afflicted and that change in substance use over time is less pronounced than in treatment seeking SUD patients. Therefore, we expect that test-retest reliability of the ADHD diagnosis in this population might even be higher than in our treatment seeking study population.

Further research on this topic could include a similar design but
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The data presented here were collected within the framework of a randomized controlled trial (RCT) to test the efficacy of the integrated treatment for adult treatment seeking SUD patients with comorbid ADHD. The RCT was supported by Fonds NutsOhra, project number 1001-036. The funding body had no role in study design, in the collection, analysis and interpretation of the data, in the writing of the report, and in the decision to submit the article for publication.

Contributors
KVE, RS, WvDB and EV designed the study. KVE and FK managed data collection. Analyses were performed by KVE and MK. KVE, RS and WvDB led the drafting of the manuscript. EV and FK revised the manuscript. All authors contributed to and approved of the final version of this manuscript.

Conflict of interest
No conflict declared.

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