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One-year abstinence improves ADHD symptoms among patients with polysubstance use disorder



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ABSTRACT

Introduction: Attention-deficit/hyperactivity disorder (ADHD) is a common comorbid disorder in patients suffering from substance use disorder (SUD). Individuals with co-occurring SUD and ADHD are more likely than SUD patients without ADHD to have developed SUD at a younger age, be polysubstance users, and need inpatient treatment more often. The present study investigates whether individuals with polysubstance use disorder who remain abstinent for a year after entering treatment have a more substantial reduction in ADHD symptoms than those who relapsed and controls.

Material and methods: Subjects were SUD patients (N = 115) and healthy controls (N = 34). ADHD symptoms were assessed using the adult ADHD Self-Report Scale (ASRS). Substance use was assessed by self-reports on the Alcohol Use Disorders Identification Test (AUDIT) and the Drug Use Disorders Identification Test (DUDIT). Participants were defined as having relapsed if they had an AUDIT score ≥ 8 or a DUDIT score ≥ 2 for women and ≥ 6 for men.

Results: Patients who remained abstinent for one year reported a substantial reduction of ADHD symptoms compared to patients who relapsed and controls.

Conclusions: Abstinence alleviates ADHD symptoms among patients with polysubstance use disorder. We suggest that confirmation of an ADHD diagnosis should follow a period of abstinence to avoid identification of false-positive cases.

1. Introduction

One of the most common disorders associated with substance use disorder (SUD) is attention-deficit/hyperactivity disorder (ADHD) (Brook, Whiteman, Cohen, Shapiro, & Balka, 1995; Kessler et al., 2006; Wilens & Spencer, 2010). Nearly 25% of the adults between 18 and 44 years old who have been diagnosed with SUD in the United States have also been diagnosed with ADHD (Kessler et al., 2006). Other studies show that 40% of clinical SUD samples in different countries screened positive for ADHD (Glind et al., 2013; van Emmerik-van Oortmerssen et al., 2012).

ADHD has an adverse effect on the course of SUD (McAweeney, Rogers, Huddleston, Moore, & Gentile, 2009; Wilens et al., 2011). Relative to SUD patients without ADHD, SUD patients with ADHD are more likely to have developed SUD at a younger age, become polysubstance users, and need inpatient treatment more often (Arias et al., 2008; Tamm et al., 2013). Also, SUD patients who screen for a concurrent adult ADHD diagnosis have been shown to have more severe and chronic SUD (Young et al., 2015), and a childhood ADHD diagnosis in SUD patients is associated with higher relapse rates after treatment termination (Carroll & Rounsaville, 1993).

ADHD is manifested in childhood, and it persists into adolescence in

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Abbreviations: SUD, substance use disorder; ADHD, attention deficit hyperactivity disorder; ASRS, ADHD Self-Report Scale; AUDIT, Alcohol Use Disorders Identification Test; DUDIT, Drug Use Disorders Identification Test; WASI, Wechsler abbreviated scale of intelligence; GP, general practitioner; REK, Regional Ethical Committee; DSM, Diagnostic and Statistical Manual of Mental Disorders; ANOVA, analysis of variance

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almost 75% of the cases, and into adulthood in close to 50% (Wilens & Spencer, 2010). Most studies have focused on how the onset of ADHD, often in combination with conduct or bipolar disorders, increases the risk of later SUD (Wilens et al., 2011).

Comorbid ADHD place patients with SUD at risk of impaired recovery, with longer duration of substance use and slower remission rate (Wilens, Biederman, & Mick, 1998).

SUD complicates the diagnostic process, particularly for clients identified with ADHD in adulthood and for those with symptoms below the diagnostic threshold (Levin, Evans, & Kleber, 1998). Diagnosing ADHD in adult patients with SUD requires accurate retrospective information, and this is often difficult to obtain because of inadequate anamnestic data (Faraone et al., 2007; Levin et al., 1998). Consequently, there is a group of adults who meet all the criteria for an ADHD diagnosis except age at onset (Faraone et al., 2007). However, studies have found that this group has similar forms of psychiatric comorbidity, neurocognitive impairment, and familial transmission as the group with a confirmed diagnosis, only differing on the childhood onset requirement of the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) (Faraone et al., 2006; Faraone et al., 2006). Furthermore, because SUD often emerges in adolescence, the apparent late onset of ADHD may reflect the onset of SUD rather than ADHD, and although subthreshold ADHD may be a milder form of the disorder (Norén Selinus et al., 2016), it could also reflect nonspecific risk characteristics for SUD rather than symptoms of ADHD (Faraone et al., 2006). Taken together, this means that improvement of SUD symptoms may also lead to an improvement of problems associated with ADHD symptoms.

The present study investigates how 12 months of sobriety following the onset of treatment affects the presence of self-reported ADHD symptoms in a clinical sample of polysubstance users. Polysubstance use disorder is frequent in clinical SUD samples (Andrade, Carroll, & Petry, 2013). Comorbid ADHD place patients with SUD at risk of impaired recovery, with longer duration of substance use and slower remission rate (Wilens et al., 1998).

To our knowledge, this is the first study to report changes in self-reported ADHD symptoms in people with polysubstance use disorder during the 12-month period after initiation of treatment. Using a prospective design and a control group, we addressed the following question: Will individuals with polysubstance use disorder who remain abstinent for one-year show a greater improvement in ADHD symptoms compared with those who relapsed and controls?

2. Material and methods

2.1. Participants

One hundred and fifty SUD patients were recruited from 10 outpatient and residential treatment facilities within the Stavanger University Hospital catchment area (Norway) between March 2012 and May 2013. We employed broad inclusion criteria focusing on polysubstance use disorder because it is common in clinical settings Belin, Epstein, Calu, & Shaham, 2011; Pelletier, & Potvin, 2013). The main inclusion criteria at baseline were: (a) evidence of SUD with polysubstance use, operationalized as the use of more than one drug on a single occasion, or a history of abusing multiple drugs; (b) enrolled in a new treatment sequence by the substance use treatment service; and (c) at least 16 years of age. At baseline, 22 patients were excluded because they did not meet the inclusion criteria (four had no substance use addiction and 18 did not report polysubstance use), leaving 128 patients in the study.

The control group (N=38) was a convenience sample recruited by posters exhibited at social welfare and GP offices. Controls and SUD patients were compensated with NOK 400 (\sim USD 50) for the baseline testing. During the one-year follow-up period, 13 SUD patients and four people from the control group withdrew or dropped out of the study.

The final group included 115 SUD patients and 34 controls. The retention rate was 89.8% for patients and 89.5% for controls. This study was reviewed and approved by the Regional Ethical Committee (REK 2011/1877) and conducted according to its guidelines and those of the Helsinki Declaration (1975). Written informed consent was obtained from all participants.

2.2. Procedures

The study is part of a prospective cohort study of a sample of SUD patients in the Stavanger University Hospital catchment area. To minimize contamination from drug withdrawal and the acute neurotoxic effects of psychoactive substances, baseline assessment was performed after two weeks of abstinence (Miller, 1985) by experienced and trained staff. Information on substance use was assessed using the Alcohol Use Disorders Identification Test (AUDIT) (Bohn, Babor, & Kranzler, 1995) and the Drug Use Disorders Identification Test (DUDIT) (Voluse et al., 2012). At the one-year follow-up, patients were defined as relapsing to a significant level of use if they had an AUDIT score \geq 8, or a DUDIT score \geq 2 for women and \geq 6 for men (Bohn et al., 1995; Voluse et al., 2012).

2.3. Adult ADHD self-report scale (ASRS)

The ASRS is a frequently used screening instrument for ADHD (Kessler et al., 2005). It is composed of 18 items that reflect the symptoms used to define ADHD according to the fifth edition of the Diagnostic and statistical manual of mental disorders (DSM-V) (Association, 2013). The results from this scale assess the presence of ADHD symptoms, but on its own, it is not an adequate diagnostic tool.

Symptoms are rated on a 5-point Likert-type scale (0-4 = never, rarely, sometimes, often, and very often), with a range of 0 to 72 for the 18-item instrument. This instrument has previously been validated in SUD populations (Dakwar et al., 2012; Van de Glind et al., 2013).

In the present study, we included a sum score across all the 18 ASRS items, a sum score for the ASRS items that assess inattention (items 1-4 and 7-11), and a sum score for the items that assess hyperactivity/impulsivity (items 5, 6, and 12-18).

In order to highlight the severity of individual items in the ASRS, we dichotomized responses to the ASRS items into "severe/not severe" according to recommendations by Kessler et al. (Kessler et al., 2005). Lastly, we used the "severe/not severe" dichotomized items to identify clinically significant ASRS profiles. The ASRS profile was dichotomized as "clinically significant" if ≥ 9 items were dichotomized as "severe", and "not clinically significant if < 9 items were dichotomized as severe". This method is commonly used in clinical practice, and in line with the original recommendations by Kessler et al. (Kessler et al., 2005).

2.4. Statistical analyses

All analyses were performed using IBM SPSS v24 for Mac. Two-tailed p-values < 0.05 were considered statistically significant. Data were assessed for normality with histograms, Q–Q plots, Kolmogorov–Smirnov tests, and Shapiro-Wilk tests. Visual inspection of histograms and Q-Q-plots revealed that ASRS-scores at baseline and 1 year follow up did not deviate from normality. This was also evident from the Kolmogorov-Smirnov test ($D_{(149)}=0.05$, p=0.200; and 1 year $D_{(149)}=0.06$, p=0.200, respectively) and Shapiro-Wilk test (baseline $w_{(149)}=0.99$, p=0.651; and 1 year $w_{(149)}=0.99$, p=0.327). Sub-analysis of normality for each participant group yielded similar results (data not shown). As the data was normally distributed, parametric statistics were used throughout. The statistical procedures of the demographic variables have been published in a previous paper (Hagen et al., 2017).

Mixed ANOVA was used to compare changes in abstainers,

relapsers, and controls from baseline to the one-year follow-up. Variables for which one group's responses differed from those of the other two groups were expected to show a significant interaction. To determine the cause of interaction effects, a paired samples t-test was used to evaluate mean change from baseline to one-year within each group. Effect sizes were calculated as Cohen's d for paired samples and parametric data, where 0.5 was considered a medium effect and 0.8 was considered a large effect (Cohen, 1988). Main effects were not interpreted in the presence of a statistically significant interaction (Bordens & Abbott, 2002).

Lastly, the frequency of individual items dichotomized as severe was estimated for each group (i.e., abstinent, relapsed, and control), and changes in frequency during the one-year follow-up were investigated for each item using a repeated measures ANOVA. As multiple comparisons were made, Bonferroni adjusted P-values (0.05/18 = 0.003) were used to establish statistical significance.

3. Results

3.1. Group characteristics

We presented data for the clinical and demographic variables for patients who remained abstinent for a year (N = 51), patients who relapsed (N = 64), and controls (N = 34) in a previous paper (Hagen et al., 2017). In short, patients and controls did not differ in age, but controls were more often female (44% vs. 33%) and had a higher mean level of education (14.2 vs. 11.8 years) and a higher mean IQ score (105.5 vs. 98.2) at baseline. Three patients and five controls were < 18 years of age at the time of inclusion. Although there were no differences in baseline demographic variables between the two SUD groups, the abstinent group obtained a higher mean WASI IQ score (100.7 vs. 95.8). As measured by the mean AUDIT/DUDIT score, baseline levels of substance abuse did not differ between the two SUD groups.

3.2. ASRS total score

At baseline, there was a significant difference (t = 6.4, p < 0.001) in ASRS total score between patients (m = 34.7, SD = 10.7) and controls (m = 21.2, SD = 11.4). At baseline, patients who relapsed during the follow-up period had a higher ASRS total score than patients who remained abstinent, but this difference was not statistically significant (Table 1). Repeated measures ANOVA showed a significant effect of group [F(2146) = 18.0, P < 0.001] and time [F(1146) = 25.7, P < 0.001], and a significant group × time interaction [F(2146)

Table 1
ASRS scores at baseline and one-year follow-up.

	Abstinent group (N = 51)		Relapse group (N = 64)		Control group (N = 34)	
	Baseline	1 year ^a	Baseline	1 year ^a	Baseline	1 year ^a
ASRS Part 1: inattention	18.5	12.4	18.7	16.8	10.6	10.6
	(6.8)	(8.0)***	(6.3)	(6.0)*	(6.1)	(6.2)
ASRS Part 2: hyperac- tivity	15.5	10.8	16.5	14.7	10.8	10.3
	(6.5)*	(7.4)***	(5.5)	(5.8)*	(5.2)	(5.3)
ASRS Total score ^b	34.0 (11.8)	23.3 (14.4)	35.6 (9.6)	31.6 (9.6)	21.2 (11.4)	21.0 (9.3)
	[18]	[9]***	[25]	[19]*	[3]	[2]

All data are means (SD).

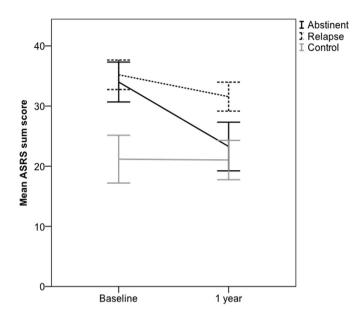


Fig. 1. Mean ASRS sum score for each group at baseline and one-year follow up. Footnote: Changes in mean ASRS sum score from baseline to one-year for each group. Standard deviation indicated by error bars.

= 10.2, p < 0.001] (illustrated in Fig. 1). Follow-up analyses showed that the interaction could be attributed to the significant alleviation of ADHD symptoms in the abstinent group (t = 5.5, p < 0.001), with a large effect size (d=0.82), and significant symptom improvement in the relapse group (t = 2.4, p = 0.017), with a moderate effect size (d=0.37). In the control group, the ASRS total score did not change from baseline to one year later (m = 21.2, SD = 11.4 vs. m = 21.0, SD = 9.4). At both time-points, the total score in the control group was slightly lower than that at follow-up in the SUD patients who were abstinent (m = 23.3, SD = 14.4), and considerably lower compared with those who relapsed (m = 31.6, SD = 9.6).

3.3. Inattention symptoms

At baseline, there was a significant difference (t = 6.4, p < 0.001) in inattention symptoms between patients (m = 18.6, SD = 6.4) and controls (m = 10.6, SD = 6.1). The patient groups (abstained and relapsed) did not differ at baseline on the ASRS inattention subscale. Repeated measures ANOVA showed significant main effects of group [F (2146) = 18.0, p < 0.001] and time [F(1146) = 21.1, P < 0.001], and a significant group × time interaction [F(2146) = 10.2, p < 0.001]. Follow-up analyses showed that the interaction could be attributed to the significant improvement in the abstinent group (t = 5.5, p < 0.001), with a medium to large effect size (d = 0.82), and a significant improvement in the relapse group (t = 2.3, p = 0.025), with a small effect size (d = 0.31). The ASRS inattention score in the control group did not change over time.

3.4. Hyperactivity-impulsivity symptoms

At baseline, there was a significant mean difference (t = 6.4, p < 0.001) between patients (m = 16.1, SD = 5.9) and controls (m = 10.6, SD = 6.2) on the ASRS hyperactivity/impulsivity subscale. The patient groups did not differ on this score at baseline, but the repeated measures ANOVA showed significant main effects for group [F (2145) = 10.8, p < 0.001] and time [F(1145) = 17.9, p < 0.001], and a significant group \times time interaction [F(2145) = 5.4, p = 0.006]. Follow-up analyses showed that the interaction could be attributed to significant improvement in the abstinent group (t = 4.5, p < 0.001), with a moderate effect size (d = 0.66), and significant improvement in

^a Results of paired samples *t*-test. This measures improvement in mean score from baseline to one-year later within the group.

^b Number with clinical score is indicated by [N].

p < 0.05.

^{***} p < 0.001.

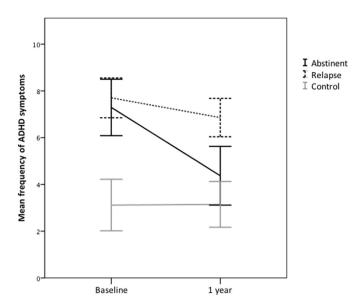


Fig. 2. Mean frequency of severe ADHD symptoms (in total) for each group. Footnote: Changes in frequency of severe ADHD symptoms from baseline to one-year for each group.

the relapse group (t = 2.4, p = 0.021), with a small effect size (d = 0.31). The change in the hyperactivity-impulsivity subscale was not statistically significant for the control group.

3.5. ASRS scores indicating severe ADHD symptoms

The frequencies of number of severe ADHD symptoms (in total) for each group are presented in Fig. 2. Overall, patients reported a significantly higher number of severe symptoms than controls at baseline (t = 6.1, p < 0.001). The frequency of severe symptoms did not differ between the two patient groups at baseline (t = 0.6, p = 0.570). The abstinent group demonstrated a significant decrease (t = 4.4, p < 0.001) in severe symptoms from baseline (m = 7.3, SD = 4.3) to 1 year (m = 4.3, SD = 4.5), whereas the changes in the relapse group (t = 2.0, p = 0.054) and the control group (t = -0.1, p = 0.937) were not statistically significant.

The percentages of severe symptoms are presented for each group on each ASRS item in Table 2. The control group had no statistically significant change from baseline on any items of the ASRS. The relapse group had significant change on two symptoms, but these did not withstand Bonferroni correction for multiple comparisons. For the abstinent group, eight items demonstrated a significant improvement from baseline to the one-year follow-up, but only three items were considered statistically significant following Bonferroni correction: Item 8: sustained attention (F[1, 50] = 14.8, p < 0.001), Item 9: concentration when listening (F[1, 50] = 24.3, p < 0.001), and Item 13: Restlessness (F[1, 50] < 27.3, p < 0.001).

4. Discussion

This study compared patients with polysubstance use disorder who remained abstinent, patients who relapsed, and healthy controls on changes in self-reported ADHD symptoms from baseline to follow-up assessment one year later. The abstinent group showed a substantial reduction of ADHD symptoms compared with the relapse and control groups. In fact, the scores of the abstinent group at follow-up were only slightly higher than those of the healthy controls, who were in the normal range for ADHD symptoms at both baseline and follow-up. The improvements in the abstinence group were particularly prominent on the ASRS items that reflect problems related to sustained attention, concentration, and restlessness.

4.1. Improvement of self-reported ADHD symptoms

SUD complicates diagnostic procedures and accuracy for patients with comorbid ADHD symptoms of hyperactivity, impulsivity, and inattention. These symptoms are, however, not restricted to individuals with an ADHD diagnosis. Patients with SUD can develop impulsivity and hyperactivity, and have difficulty with attention as a result of the neurotoxic effects of the drugs that they use and the lifestyle associated with SUD (Yuan et al., 2009). Impulsivity and executive dysfunctions have been associated with almost all stages of SUD (Stevens et al., 2014), as individuals with these characteristics have an increased probability of starting to use drugs, more destructive intensification of use, and more relapses after treatment (Jentsch, 2009; Robbins, Gillan, Smith, de Wit, & Ersche, 2012; Winstanley, Olausson, Taylor, & Jentsch, 2010).

Systematic use of screening tools to identify ADHD in childhood is rare, which creates a risk of leaving cases undetected (Wilens et al., 2011). If these individuals later develop SUD, their attentional and impulsivity problems may be addressed for the first time as part of the initial diagnostic work in the SUD. Our findings suggest that active SUD and the associated lifestyle could account for some of the problems related to sustained attention, concentration, and restlessness, as these ADHD symptoms were substantially reduced in our clinical sample after one year of abstinence. The clinical importance of this result is strengthened by previous studies with the same cohort that have demonstrated improved executive functions, increased satisfaction with life, and reduced psychological distress (Hagen et al., 2017). Thus, our findings support the recommendation from previous research that there should be a "treatment hierarchy" that begins with treatment of the most prominent SUD symptoms and stabilization of the drug addiction (Wilens, 2004).

The reduction in ADHD symptoms in the two polysubstance use disorder groups in this study was compelling. The abstinence group showed a more profound reduction in severe ADHD symptoms, but the relapse group also showed some improvements. It is possible that, on average, SUD treatment improves ADHD symptomatology because it introduces a period of stability and reduces substance use. Several psychosocial treatments are recommended for SUD and comorbid mental disorders, including motivational interviewing, cognitive-behavioral therapy, contingency management, relapse prevention, case management, and social skills training (Horsfall, Hunt, & Walter, 2009). To make behavioral changes, these treatments for SUD require cognitive processing and learning abilities (Roehrich & Goldman, 1993). This could involve learning about program rules, treatment philosophy, and the negative effects of different drugs (Grohman & Fals-Stewart, 2003), all of which represent a substantial learning requirement at the onset of therapy. However, the present results suggest that a slow, careful, stepwise approach to learning requirements should be adopted in treatment, one that initially focuses on stabilizing the patient, providing structure, and supporting abstinence from substance use.

Diagnosing ADHD with active SUD is challenging. The risk of false-positive ADHD diagnoses in patients assessed by ASRS has been reported (Lugoboni et al., 2017; Roncero et al., 2015). Thus, our finding is a reminder that a period of abstinence, preferably evident by urine tests or other means of substance monitoring, should be in place before providing conclusions regarding an ADHD diagnosis.

4.2. Strengths and limitations

Many studies in this field have used cross-sectional designs (van Holst & Schilt, 2011), and thus they were unable to track longitudinal changes. We used a prospective design for the patient and control groups, which allowed us to monitor possible training effects through repeated testing and reports on the same questionnaires (Schulte et al., 2014). However, there was a significant difference in years of

 Table 2

 Percentage of severe scores on ASRS items at the one-year follow-up.

ASRS items		Abstinent group $(N = 51)$		Relapse group $(N = 64)$		Control group $(N = 34)$	
		Baseline % ^a	1 year %	Baseline % ^a	1 year %	Baseline % ^a	1 year %
Part 1 In	attention						
1	Finishing	33.3	21.6	37.5	34.4	5.9	8.8
2	Organization	25.5	13.7	29.7*	14.1	2.9	2.9
3	Remembering	52.9*	33.3	54.7	59.4	8.8	17.6
4	Initiation	70.6*	51.0	76.6	71.9	26.5	38.2
7	Careless	33.3*	13.7	29.7	21.9	11.8	14.7
8	Attention	52.9***,b	21.6	53.1	42.2	23.5	11.8
9	Listening	70.6***,b	31.4	64.1	62.5	23.5	20.6
10	Finding things	21.6	17.6	23.4	25.0	2.9	2.9
11	Easily distracted	68.6**	45.1	76.6	67.2	38.2	47.1
Part 2 H	yperactivity						
5	Fidgets	76.5	62.7	89.1*	75.0	61.8	58.8
6	Overactive	29.4	21.6	28.1	26.6	26.5	11.8
12	Staying seated	3.9	0.0	10.9	4.7	0.0	0.0
13	Restless	58.8***,b	23.5	59.4	53.1	14.7	8.8
14	Relaxing	35.3	27.5	34.4	35.9	11.8	11.8
15	Talks excessively	21.6**	5.9	23.4	23.4	11.8	14.7
16	Blurts out answers	45.1	41.2	46.9	48.4	32.4	35.3
17	Waiting turn	17.6	9.8	21.9	14.1	2.9	8.8
18	Interrupts	11.8	5.9	10.9	6.25	2.9	2.9

^{% =} percentage of participants with self-reported severe symptoms within this group. ASRS, Adult ADHD Self-Report Scale.

education, gender, and work experience between the patients and controls. Regarding education, all Norwegian citizens receive compulsory education from 5 to 16 years of age. Hence, it was difficult to recruit age-matched participants with fewer than 10 years of education who did not use drugs.

The present study has several other limitations. First, the patients in the relapse and abstinence groups were self-selected (based on their self-reports), and time-sensitive variables that we did not assess may have influenced our outcome variables. Thus, we cannot conclude that the differences in the outcomes observed at 12 months were only caused by changes in substance use status. Furthermore, we only assessed ADHD symptoms at baseline and one-year follow-up; therefore, we cannot determine when the abstinence group's improvements in ADHD symptoms occurred during the follow-up period. In addition, the assessment of ADHD symptoms with ASRS does not constitute a full diagnostic procedure. Without historical anamnestic data in our study, it is difficult to suggest whether the alleviation of symptoms only applies to a subthreshold group of patients or if it is also associated with late-onset ADHD diagnosis.

Future research should include longitudinal prospective cohort studies with repeated measures of the trajectories of ADHD symptomatology in SUD patients. The presence or absence of ADHD should be assessed at baseline or collected from hospital journal data whenever possible. Cohort studies assessing ADHD in childhood, focusing on the participants developing SUD later in the trajectory, could provide valuable information and possibly explain the mechanism behind the findings presented here.

5. Conclusions

To our knowledge, this is the first study to report improvement of ADHD symptoms for people with polysubstance use disorder during a 12-month treatment sequence. Our data suggest that there is a clinically (as well as a statistically) significant reduction in self-reported ADHD symptoms for SUD patients following one year of abstinence. This is useful knowledge for patients suffering from comorbid SUD and ADHD,

as well as for clinicians. Our finding is a reminder that the assessment of ADHD should follow a period of abstinence to avoid false-positive ADHD diagnoses. Instead of focusing on ADHD as a persistent disorder, treatment should focus on how supporting stable abstinence may reduce ADHD-like symptoms.

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^a Comparison between baseline and one-year follow-up.

^b Significant after Bonferroni correction.

p < 0.05

^{**} p < 0.01.

^{***} p < 0.001.

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