Autism Spectrum Disorder and Co-occurring Substance Use Disorder – A Systematic Review

Espen Ajo Arnevik[1,2] and Sissel Berge Helverschou[3]

[1]National Advisory Unit on SUD Treatment, Oslo University Hospital, Oslo, Norway. [2]Institute of Psychology, University of Oslo, Oslo, Norway. [3]NevSom – Norwegian Centre of Expertise for Neurodevelopmental Disorders and Hypersomnias, Oslo University Hospital, Oslo, Norway.

ABSTRACT

OBJECTIVE: Patients with co-occurring autism spectrum disorders (ASD) and substance use disorder (SUD) require special attention from clinical services. Screening for this co-occurrence is not generally an integral part of routine clinical assessments, and failure to identify and understand this group of patients may contribute to a worsening of their symptoms and/or an increase in drug abuse. Thus, there is a need to review the evidence base on patients with co-occurring ASD and SUD in order to enhance clinical practice and future research.

METHODS: We reviewed all identified papers on patients with co-occurring ASD and SUD. The focus of the review was on epidemiology, patient characteristics, function of drug use, and the effect of current interventions.

RESULTS: A total of 18 papers were included in the analysis. Eleven papers were based on epidemiological studies, although only one study reported the prevalence of ASD in an SUD population. Two papers explored the role of personality, three papers studied subgroups of individuals serving prison for violent or sexual crimes, and one paper explored the function of drugs in the ASD patient group. There were no studies testing specific treatment interventions.

CONCLUSIONS: In most of the treatment settings studied, there were relatively few patients with co-occurring ASD and SUD, but due to differences in study samples it was difficult to establish a general prevalence rate. The one consistent finding was the lack of focused treatment studies. There is clearly a need for research on interventions that take account of the special needs of this patient group.

KEYWORDS: substance use disorder, autism spectrum disorder, epidemiology, review

CITATION: Arnevik and Helverschou. Autism Spectrum Disorder and Co-occurring Substance Use Disorder – A Systematic Review. *Substance Abuse: Research and Treatment* 2016:10 69–75 doi: 10.4137/SART.S39921.

TYPE: Review

RECEIVED: April 13, 2016. **RESUBMITTED:** June 16, 2016. **ACCEPTED FOR PUBLICATION:** June 22, 2016.

ACADEMIC EDITOR: Gregory Stuart, Editor in Chief

PEER REVIEW: Four peer reviewers contributed to the peer review report. Reviewers' reports totaled 1107 words, excluding any confidential comments to the academic editor.

FUNDING: Authors disclose no external funding sources.

COMPETING INTERESTS: Authors disclose no potential conflicts of interest.

CORRESPONDENCE: esarne@ous-hf.no

Introduction

About half of the patients seeking treatment for substance use disorder (SUD) drop out before finishing the treatment.[1] To reduce drop out and enhance the effect of therapy, there is a need to develop individualized treatments for the different subgroups that do not feel the effect of regular drug treatment programs. One patient group that may be in need of special attention, but has been little studied, is that of individuals with co-occurring autism spectrum disorder (ASD) and SUD. ASD is a group of neurodevelopmental disorders that are characterized by deficits in communication and social interaction as well as by a restricted repertoire of activities and interests.[2,3] Patients with ASD have characteristics such as poor social functioning, repetitive behavior, anxiety, emotional lability, and eccentricities or fixed habits of behavior that can mimic symptoms of other illnesses, including schizophrenia spectrum disorders, bipolar disorder, attention deficit hyperactivity disorder (ADHD), avoidant personality disorder, social anxiety disorder, and mood disorder.[4–6] These symptoms and co-occurring psychiatric diagnoses are also frequently found in patients with SUD.[7]

A recent review[8] found that screening for SUD among individuals with ASD is not part of routine clinical assessments in psychiatry, although SUD screening is increasingly an integral part of clinical guidelines for many other conditions.[8] The frequency of SUD among individuals with neurodevelopmental disorders is currently unknown, and one might suspect that the comorbidity is underdiagnosed. It is also apparent that little is known about successful interventions for individuals with ASD and SUD; in fact, typical interventions for SUD may be particularly unsuitable for people with ASD. Thus, although group treatment is often the main focus of substance abuse interventions in residential or community-based facilities, "12-step" programs, and self-help groups, forced involvement in group sessions may be anxiety and anger provoking for ASD patients and may precipitate drop out or rejection from the group. The failure of individuals with ASD to socialize and participate in group activities may be interpreted as a

lack of motivation or cooperation, while their social aloofness may induce frustration and helplessness both in other patients and in clinicians, which can result in a failure to receive, or respond to, treatment among individuals with ASD and may induce feelings of failure and exclusion that risk worsening the patients' symptoms and their drug abuse.

Given the lack of information regarding both the frequency of substance abuse in individuals with ASD and potential interventions, the aim of this review is to (1) assess the estimated frequency of the co-occurrence of these two conditions, (2) explore the particular characteristics of this group of patients, (3) obtain a better understanding of the function of substance use in this population, and (4) summarize data on the current treatment interventions that are available for this group of patients.

Method

A search was performed to identify all studies of patients with co-occurring ASD and SUD (inclusion criteria) either as a main focus of the study or as a by-product of other studies. The exclusion criteria were: studies that included individuals younger than 12 years, non-English language articles, reports that were not published in peer-reviewed journals, and studies that did not use structured methods for registering substance use.

Multiple procedures were used to develop an adequate and wide search query. In the first search, we used the Medical Subject Headings (MeSH) indexing system terms, Substance abuse disorder (exploded) and Drugs, and combined them with the MeSH terms, Asperger syndrome (exploded) and Autism spectrum disorder (exploded). We further refined the search query using specific and generic terms referring to drugs that are typical of substance abuse (Alcohol* OR Drug* OR Substance* OR Heroin* OR Opioid* OR Cannabis* OR Marijuana* OR Cocaine* OR Crack* OR Amphetamine* OR Methamphetamine* OR Hallucinogen*). The initial search was conducted in March 2014, and an updated search was conducted in January 2016. The search included the following databases: PubMed, PsycINFO, and MEDLINE (Ovid). A total of 1454 studies were identified, among which 308 were identified as duplicates and removed. The titles and abstracts of 1146 studies were screened manually, and 1124 studies were excluded because of the lack of relevance of the title, abstract, or keywords. The remaining 22 studies were read in full. Among them, 11 articles were excluded because they failed to address the topic of comorbidity, did not mention SUD at all, or were mainly oriented toward children with ASD. The remaining 11 articles were included in the study.

In the second search, the same string was used, but the search was restricted to the study setting of interest, namely, Treatment or Rehabilitation (Treat* OR Rehab*). Different procedures (GRADE, AGREE, etc.) were used to develop national and international guidelines for treatment. Some of these methods or procedures include clinical knowledge and patient knowledge in addition to empirical data when making recommendations for clinical practice. We applied the string to national or international guidelines to explore if there was any systematic work for guiding clinicians. The search was carried out in BMJ Best Practice, UpToDate, Norwegian national guidelines, Fagprosedyrer.no, Swedish national guidelines, Danish national guidelines, National Guideline Clearinghouse, National Institute for Health and Care Excellence guidelines, and the Norwegian Knowledge Centre for the Health Services. The search found no studies that fulfilled the criteria.

Finally, we performed a third manual search to check reference lists from a selection of textbooks in the ASD field. The selection was performed by the authors. This search resulted in seven additional articles that addressed the co-occurrence of ASD and SUD.

Results

A total of 18 studies were included in the analysis (see Fig. 1).

The findings are divided into five main sections: (1) studies of substance abuse in clinical populations with ASD, (2) studies of ASD in clinical populations with SUD, (3) studies of the characteristics of individuals with ASD who have SUD, (4) studies of the functions and/or consequences of SUD in individuals with ASD, and (5) studies of intervention strategies.

Studies of substance abuse in populations with ASD (prevalence). We identified 12 articles in which the prevalence of reported drug or alcohol abuse was investigated in clinical samples of individuals with ASD (see Table 1).

Santosh and Mijovic.[9] *Sample*: $N = 98$ treatment-seeking adolescents with pervasive developmental disorders (PDDs). *Aim*: To compare the rates of reported drug or alcohol use with those of a psychiatric control population ($N = 1387$). *Results*: Only three (3.1%) individuals with PDD reported abuse of

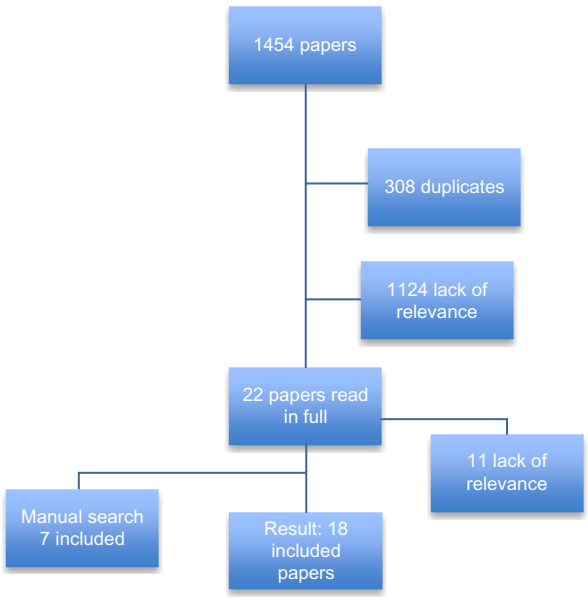

Figure 1. Search flow chart.

drug and/or alcohol. All were male and of normal intelligence. In the psychiatric control population, the drug and/or alcohol abuse frequency was 16.7%.

Hofvander et al.[10] *Sample*: *N* = 122 normal-intelligence adults with ASD. *Aim*: To describe clinical psychiatric presentation and core outcome measures. *Results*: Four (6%) of the adults with ASD had co-occurring SUD.

Sizoo et al.[11,12] *Sample*: *N* = 123 treatment-seeking patients with ASD and ADHD. *Aim*: To compare the prevalence of SUD in patients with ASD and ADHD. *Results*: SUD rates were significantly lower in patients with ASD (30%) than they were in patients with ADHD (58%). There were no group differences in risk factors or disability scores.

Abdallah et al.[13] *Sample*: *N* = 414 cases with ASD taken from a national register of individuals born in Denmark between 1982 and 2004. *Aim*: To report rates of psychiatric comorbidity. *Results*: Only three (0.7%) individuals were diagnosed as having co-occurring alcohol-related disorders according to the ICD-8.

Lugnegård et al.[14] *Sample*: *N* = 54 young adults with Asperger syndrome (AS). *Aim*: To examine systematically psychiatric comorbidity in individuals with developmental disorders who were referred to clinical services. *Results*: Among the six (11%) individuals who were identified as having co-occurring lifetime substance dependence disorders, all but one were male.

Lundström et al.[15] *Sample*: Two nationwide twin cohorts from Sweden (age/IQ range). *Aim*: To identify substance and alcohol abuse among individuals with autistic-like traits (ALT) using a single dichotomous item. *Results*: In the sample with ALT, 159 (2.5%) individuals were identified as having experienced problems with alcohol or drugs at some time in their life.

Mandell et al.[16] *Sample*: *N* = 14 psychiatrically hospitalized adults with ASD. *Aim*: To compare the rates of SUD in this population with the rates detected in a group of patients without ASD. *Results*: Five (36%) adults in the ASD population had substance use/abuse, which was not significantly different from that observed in the non-ASD clinical population.

Joshi et al.[5] *Sample*: *N* = 63 adults with ASD who were referred to special services for complex cases of ASD. *Aim*: To compare patterns of psychiatric comorbidity and functioning with those of a clinical sample without ASD. *Results*: Seven (11%) adults in the ASD sample had current SUD (33% lifetime prevalence); between 3% and 6% of the individuals had a current drug abuse or drug addiction (13%–29% lifetime). Although the rates were lower than those observed in the non-ASD sample, the difference was not statistically significant.

Søndenaa et al.[17] *Sample*: *N* = 33 offenders with ASD who were charged with sexual or violent crime (a subsample of the next study). *Aim*: To compare and contrast the characteristics of sexual and violent offenders and identify the presence of autistic traits in the presentation of the offending behavior. *Results*: Twelve individuals (36%) reported substance abuse, mainly linked to alcohol consumption. However, only three individuals (10%, all in the violent offender group) were formally diagnosed with SUD by forensic psychiatric experts.

Helverschou et al.[18] *Sample*: *N* = 48 offenders with ASD who were examined during a 10-year period. *Aim*: To describe the characteristics of offenders with ASD who were examined by forensic psychiatric experts and compare the findings with available data on non-ASD offenders. *Results*: A total of 18 individuals (38%) reported any substance or alcohol use. Substance dependency was identified in 7 (15%) individuals, and intoxication related to the charges was described in 10 (21%) individuals.

Studies of ASD in clinical populations with SUD. Among the studies reviewed here, only one reported the prevalence of ASD in clinical SUD populations.

Ståhlberg et al.[19] *Sample*: *N* = 100 adolescents in institutional care (age, 12–19 years; mean age, 16 years; IQ). *Aim*: To assess the prevalence of psychiatric disorders among adolescents. *Results*: A total of 14% of individuals with SUD had ASD; 2% of those with SUD had AS.

Studies of the characteristics of individuals with ASD and SUD. We identified two articles that explored the role of personality traits in combination with ASD and SUD. We also found three reports that studied subgroups of individuals with ASD who were in prison for violent or sexual crimes.

Sizoo et al.[11] *Sample*: *N* = 75 patients with ASD. *Aim*: To compare the temperament and character profiles of ASD individuals with those of a group of patients with ADHD (*N* = 53) and to explore the impact of SUD. *Results*: Differences between the ASD/ADHD groups were found regarding harm avoidance, pessimism, and social inhibition; the ASD group also had low scores for reward dependence, which indicated reduced social attachment. These differences were affected by SUD status. Thus, IQ scores were significantly lower in the SUD group compared with the non-SUD group. These results also suggest that adults with ASD who turn to alcohol and drug use are more socially engaged than those without a history of SUD.

Ramos et al.[20] *Sample*: *N* = 22 young patients with AS (mean age, 15 years; IQ). *Aim*: To compare personality factors that may be associated with substance use between the AS group and non-AS controls (*N* = 28). *Results*: The AS group had a generally lower risk for drug use than did the controls. They also scored lower than did controls on all sensation-seeking traits, but scored higher on introversion and inhibited and doleful traits. Individuals with AS were less likely to engage in risky activities, such as going to places where drugs are used, and their friends tended to be nonusers and to have negative attitudes toward drugs. The authors speculated that adherence to social rules and reduced social contact lead adolescents with AS to be less influenced by peers when it comes to experimenting with substances.

Søndenaa et al.[17] *Sample*: *N* = 33 individuals with ASD; 21 charged with violent crime and 12 charged with sexual crime.

Aim: To explore the differences between the two groups. *Results*: Twelve individuals (36%) reported having abuse problems, mostly of alcohol, but only three individuals (10%) were diagnosed with SUD by the forensic psychiatric experts.

Studies of the functions and/or consequences of SUD in individuals with ASD. We identified three articles that described the function of the drug misuse.

Kronenberg et al.[21] *Sample*: $N = 12$ adult patients with co-occurring ASD and SUD. *Aim*: To identify the everyday life consequences of this co-occurrence using qualitative methods. *Results*: Various reasons for using alcohol and illegal drugs were identified: to forget problems, to clear their minds, to act more socially, to attain peace of mind, to get through the day, or to get over frustration. Substance use was reported as having solved some ASD-related problems in the short term, and also as having negative consequences in the long term (ie, as contributing to already impaired cognitive functioning). The study noted that substance use disorganizes the individuals' lives and that the absence of structure contributes to substance use; this becomes a vicious circle that needs to be broken for effective treatment and care.

Kronenberg et al.[22] *Sample*: $N = 31$ patients with co-occurring ASD and SUD. *Aim*: To identify and compare different coping styles in patients with ASD and SUD and in those with other psychiatric illnesses. *Results*: Patients with SUD and co-occurring ASD were different from the other groups in their coping styles; they scored higher on passive reaction and lower on reassuring thoughts.

Lalanne et al.[23] *Sample*: $N = 2$. The study was a case report describing two adults with high-functioning autism who were diagnosed late and consumed high quantities of alcohol and psychostimulants. It was reported that the two patients drank alcohol to reduce their anxiety associated with different events and to improve their social skills. Their clinical picture was masked by their SUD, which resulted in a delayed diagnosis of their developmental illness. The authors conclude that its prevalence might be underestimated and that the cognitive inflexibility and change-related anxiety found in these patients might be a vulnerability trait for developing SUD and should be addressed specifically during treatment.

Studies of intervention strategies. *Kronenberg et al.*[22,24,25] *Sample*: $N = 31$ patients with co-occurring SUD and ASD recruited from mental health services and addiction treatment services. *Aim*: To compare the ASD group with patients with co-occurring SUD and ADHD and other psychiatric illnesses. *Results*: The three articles from this study provided useful information on treatment needs, although they did not test specified interventions. The authors note that the nursing needs of patients with SUD and co-occurring ASD are more extensive and more severe than those of individuals with SUD and ADHD or individuals with SUD and other psychiatric diagnoses with respect to: alcohol problems, psychiatric health, unemployment, finance, family/social relations, daytime activity, looking after the home, and sexual life. They also report that the process of recovery is similar in all groups, although an instructional and directive attitude seems to be preferred by most patients with co-occurring SUD and ASD.

Discussion

The impact of ASD on the lives of individuals is strongly influenced by co-occurring medical, developmental, or psychiatric conditions. SUD is one important, but little studied, co-occurring condition. This review of the existing literature indicates that this co-occurrence has a larger variation in clinical populations than that recognized previously. However, the number of studies that explored the relationship between ASD and SUD is limited, with very few having addressed the characteristics of individuals with the dual diagnosis, or the possible functions of substance abuse in individuals with ASD. In particular, we did not identify any studies of specific treatment interventions.

Only 18 studies were identified that examined the association between ASD and substance abuse in a systematic manner. Eleven articles explored the frequency of SUD in patients with ASD but reported that the rates ranged widely, from 0.7% to 36%, and most studies involved highly selected samples, such as offenders or patients in mental hospitals. Sample sizes were variable, and the age, intellectual level, and sex distribution of participants varied between samples. Few studies reported formal diagnostic criteria for SUD, and definitions of SUD ranged from "having experienced trouble with alcohol or drugs" to "current substance addiction". Such inconsistencies limit the comparisons between studies and render it difficult to establish an overall rate for the co-occurrence of ASD and SUD based on the existing research. No systematic prevalence studies of non-biased samples have been published, and the lack of studies of ASD in SUD populations is striking. Thus, formal prevalence studies that include representative ASD and SUD samples are required to report the rates of SUD in patients with ASD more accurately.

Despite these caveats, it appears that the rates of SUD were generally lower in ASD samples compared with other clinical cohorts, although the difference was not statistically significant in all studies. It has been suggested that the relatively low frequency of SUD detected in individuals with ASD may be caused by their limited social contacts, which reduces the influence of peers, and/or to their literal interpretation of social "rules", which makes them less likely to experiment with drugs and other illegal substances.[20] The one group in which substance abuse was most likely to occur was that of criminal offenders with ASD, as some of these individuals reported to be using several illegal drugs and to have performed criminal acts while intoxicated.

Although not all articles report IQ scores, one might speculate on whether some of the subpopulations of ASD and SUD consist of individuals who have mainly higher cognitive functioning. If that is the case, then SUD may be more prevalent in patients with high-functioning ASD. IQ is one

Table 1. Prevalence of SUD in populations with AS or ASD.

REFERENCE	POPULATION	N	GENDER (MALE:FEMALE)	IQ	PREVALENCE
Santosh et al., 2006	PDD	97	4.4:1	60.8% IQ ≥ 70	3.1%
Hofvander et al., 2009	AS	122	2:1	All IQ ≥ 70	6.0%
Sizoo et al., 2009, 2010	ASD	123	3.8:1	103.9	30.0%
Abdallah et al., 2011	ASD	414	4.2:1	78.7% IQ ≥ 70	0.7%
Lugnegård et al., 2011	AS	54	0.9:1	Mean 102	11.0%
Lundstrøm et al., 2011	ALT	159	–	–	2.5%
Mandell et al., 2012	*ASD*	14	2.5:1	35.1% IQ ≥ 70	36.0%
Joshi et al., 2013	*ASD*	63	1.9:1	97% IQ ≥ 70	11.0%
Søndenaa et al., 2014	ASD	33	5.6:1	75% IQ ≥ 70	10.0%
Helverschou et al, 2015	ASD	48	5.9:1	67% IQ ≥ 70	15.0%
Ståhlberg et al., 2010 AS ASD	SUD*	100	11.5:1	Mean 85.3	2.0% 14.0%

Abbreviations: AS, Asperger Syndrome; ASD, Autism Spectrum Disorder; ALT, Autistic-like traits; PDD, Pervasive Developmental Disorder. SUD*, A population in institutional care having Substance Use Disorder. Percentage with AS and ASD in this population is presented.

of the factors that may predict outcome in ASD generally.[26] Thus, one might predict that the effect of treatment would be more promising in this group. Furthermore, the finding that adults with ASD and SUD are more socially engaged than are individuals with ASD without SUD[11] might also suggest that the former subgroup represents individuals who might have the possibility of a better outcome of treatment. Both of these hypotheses should be addressed in further studies.

Recognizing the function of substance use is crucial in designing individual treatments. This has been rarely studied in patients with co-occurring ASD and SUD. Substance abuse may represent a particular vulnerability factor, as the intoxication may further decrease the ability of individuals with ASD to anticipate the consequences of their behavior and make it even more difficult to behave according to formal and informal laws.[27] This might have important clinical implications and should be studied further. The effect of anxiety in individuals with ASD and SUD might be an important topic of study. There is a high prevalence of anxiety reported in ASD generally, and possible links between anxiety and substance abuse as self-medication have been hypothesized by several authors.[6,27,28] Cannabis and other legal and illegal substances have been reported as risk factors associated with reduced quality of life, mental health disorders (including suicide attempts), and premature death because of overdoses, accidents, violence, and suicide.[29–31] In ASD populations, there is also a heightened risk of suicidal behavior. An article published in *The Lancet* in 2014[32] reported that, among 374 adults (256 men and 118 women) diagnosed with AS, 66% self-reported suicidal ideation, 35 reported plans or attempts at suicide, and 116 (31%) reported depression. With a heightened risk in both populations, it would be reasonable to suggest that there is a heightened risk in patients with co-occurring disorders.

The main limitations of this review were that it included few studies that used different methods; thus, its generalizability is low. Because of the low number of studies included here, we were not able to use methods that were developed to perform meta-studies.

Clinical Implications

No studies of specific treatment strategies were found, although the studies reported by Kronenberg et al.[22,24,25] provided valuable information for a better understanding of the needs of patients with co-occurring ASD and SUD. SUD treatment requires medical, psychological, and social interventions, as well as support for housing, schooling, transportation, and legal services. Failing to address such needs simultaneously could sabotage treatment success. Behavioral therapies, delivered by trained clinicians, help patients remain drug free by strengthening their motivation to change. This can be achieved by providing incentives for abstinence, building skills to resist and refuse substances and deal with triggers or craving, replacing drug use with constructive and rewarding activities, improving problem-solving skills, and facilitating better interpersonal relationships. Studies including persons with ASD and comorbid psychiatric disorders indicate that cognitive behavioral treatment approaches adapted to the individuals' level of functioning are most frequently recommended for this group.[33,34] The support of family members and friends is important for the recovery of patients. The findings from the Netherlands[25] point to the potential value of an instructional and directive approach when delivering treatment to

SUD + ASD patients. Despite these studies, there is a lack of intervention studies in this population. One reason for this lack might be that the population in question is a small population with complex co-occurring disorders. Both disorders require long-term treatment and involve multiple parts and levels of both specialized treatment facilities and support in the primary health services. That sort of study requires a large and expensive research project that might be difficult to finance. Moreover, further studies should aim to extend the range of evidence-based interventions that target specifically patients with co-occurring ASD and SUD. To date, no specific guidelines for clinicians working with these patients have been published; thus, these individuals have to rely on clinical expertise and common guidelines for the two disorders. Group treatment is, in many settings, a fundamental and important component of intervention for SUD patients. However, the difficulties experienced in social situations and social relations experienced by patients with ASD seem to indicate the value of a more individual approach. Clinicians should be aware of the prevalence of ASD and the possibility for specialized interventions for this group.

Summary

Although individuals with co-occurring ASD and SUD are a small subgroup in most clinical settings, diagnostic assessment of these conditions is often limited and little research has addressed the likely causes of substance abuse; moreover, even less is known about potentially effective interventions for this group of patients. To improve the treatment offered to these patients, we advise more specific studies of individuals with co-occurring ASD and SUD. First, there is a need for large, well-designed epidemiological studies. Second, studies targeting the function of substance use in patients with ASD are needed. Last, there is a need to develop well-designed intervention studies. Screening for SUD in ASD is increasingly becoming a part of clinical guidelines, although it is not yet an integral part of the routine clinical assessments in psychiatry. Thus, SUD might be underdiagnosed among neurodevelopmental disorders.[35] When diagnosing co-occurring SUD and ASD, it is important to recognize that self-report instruments may provide useful information; however, caution must be exercised in their interpretation.[36] While waiting for additional research on this subgroup of patients, clinicians should be aware of the prevalence of SUD in ASD populations and of ASD in SUD populations. Finally, when working with these patients, it is important to provide special help with socialization, to adopt a more instructional attitude and to carefully consider treatment modes and approaches.

Acknowledgment

Thank you to Professor Emiritus Patricia Howlin at Institute of Psychiatry, London, UK, for contributing in a final discussion on the manuscript and help with language.

Author Contributions

Did the search and wrote the main part of the manuscript: EAA. Both the authors designed the study, listed search criteria, and approved the manuscript. All authors reviewed and approved of the final manuscript.

REFERENCES

1. Brorson HH, Ajo Arnevik E, Rand-Hendriksen K, Duckert F. Drop-out from addiction treatment: a systematic review of risk factors. *Clin Psychol Rev*. 2013;33(8):1010–24.
2. WHO. The ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research. Geneva: WHO; 1993.
3. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. Fifth ed. Arlington, VA: American Psychiatric Association; 2013.
4. Ryan RM. Treatment-resistant chronic mental illness: is it Asperger's syndrome? *Hosp Community Psychiatry*. 1992;43(8):807–11.
5. Joshi G, Wozniak J, Petty C, et al. Psychiatric comorbidity and functioning in a clinically referred population of adults with autism spectrum disorders: a comparative study. *J Autism Dev Disord*. 2013;43(6):1314–25.
6. Helverschou SB, Bakken TL, Martinsen H. Psychiatric disorders in people with autism spectrum disorders: phenomenology and recognition. *International Handbook of Autism and Pervasive Developmental Disorders*. New York, NY: Springer Science + Business Media; 2011:53–74.
7. Jane-Llopis EVA, Matytsina I. Mental health and alcohol, drugs and tobacco: a review of the comorbidity between mental disorders and the use of alcohol, tobacco and illicit drugs. *Drug Alcohol Rev*. 2006;25(6):515–36.
8. Palmquist E, Claeson AS, Neely G, Stenberg B, Nordin S. Overlap in prevalence between various types of environmental intolerance. *Int J Hyg Environ Health*. 2014;217(4–5):427–34.
9. Santosh PJ, Mijovic A. Does pervasive developmental disorder protect children and adolescents against drug and alcohol use? *Eur Child Adolesc Psychiatry*. 2006;15(4):183–8.
10. Hofvander B, Delorme R, Chaste P, et al. Psychiatric and psychosocial problems in adults with normal-intelligence autism spectrum disorders. *BMC Psychiatry*. 2009;9:35.
11. Sizoo B, van den Brink W, Gorissen van Eenige M, van der Gaag RJ. Personality characteristics of adults with autism spectrum disorders or attention deficit hyperactivity disorder with and without substance use disorders. *J Nerv Ment Dis*. 2009;197(6):450–4.
12. Sizoo B, van den Brink W, Koeter M, Gorissen van Eenige M, van Wijngaarden-Cremers P, van der Gaag RJ. Treatment seeking adults with autism or ADHD and co-morbid substance use disorder: prevalence, risk factors and functional disability. *Drug Alcohol Depend*. 2010;107(1):44–50.
13. Abdallah MW, Greaves-Lord K, Grove J, Norgaard-Pedersen B, Hougaard DM, Mortensen EL. Psychiatric comorbidities in autism spectrum disorders: findings from a Danish Historic Birth Cohort. *Eur Child Adolesc Psychiatry*. 2011;20(11–2):599–601.
14. Lugnegård T, Hallerback MU, Gillberg C. Psychiatric comorbidity in young adults with a clinical diagnosis of Asperger syndrome. *Res Dev Disabil*. 2011;32(5):1910–7.
15. Lundström S, Chang Z, Kerekes N, et al. Autistic-like traits and their association with mental health problems in two nationwide twin cohorts of children and adults. *Psychol Med*. 2011;41(11):2423–33.
16. Mandell DS, Lawer LJ, Branch K, et al. Prevalence and correlates of autism in a state psychiatric hospital. *Autism*. 2012;16(6):557–67.
17. Søndenaa E, Helverschou SB, Steindal K, Rasmussen K, Nilson B, Nottestad JA. Violence and sexual offending behavior in people with autism spectrum disorder who have undergone a psychiatric forensic examination. *Psychol Rep*. 2014;115(1):32–43.
18. Helverschou SB, Rasmussen K, Steindal K, Søndanaa E, Nilsson B, Nøttestad JA. Offending profiles of individuals with ASD; a study of all individuals with ASD examined by the expert forensic psychiatric service in Norway between 2000 and 2010. *Autism*. 2015;19(7):850–8.
19. Ståhlberg O, Anckarsater H, Nilsson T. Mental health problems in youths committed to juvenile institutions: prevalences and treatment needs. *Eur Child Adolesc Psychiatry*. 2010;19(12):893–903.
20. Ramos M, Boada L, Moreno C, Llorente C, Romo J, Parellada M. Attitude and risk of substance use in adolescents diagnosed with Asperger syndrome. *Drug Alcohol Depend*. 2013;133(2):535–40.
21. Kronenberg LM, Slager-Visscher K, Goossens PJ, van den Brink W, van Achterberg T. Everyday life consequences of substance use in adult patients with a substance use disorder (SUD) and co-occurring attention deficit/hyperactivity disorder (ADHD) or autism spectrum disorder (ASD): a patient's perspective. *BMC Psychiatry*. 2014;14:264.

22. Kronenberg LM, Goossens PJ, van Etten DM, van Achterberg T, van den Brink W. Need for care and life satisfaction in adult substance use disorder patients with and without attention deficit hyperactivity disorder (ADHD) or autism spectrum disorder (ASD). *Perspect Psychiatr Care*. 2015;51(1):4–15.
23. Lalanne L, Weiner L, Trojak B, Berna F, Bertschy G. Substance-use disorder in high-functioning autism: clinical and neurocognitive insights from two case reports. *BMC Psychiatry*. 2015;15:149.
24. Kronenberg LM, Goossens PJ, van Busschbach J, van Achterberg T, van den Brink W. Coping styles in substance use disorder (SUD) patients with and without co-occurring attention deficit/hyperactivity disorder (ADHD) or autism spectrum disorder (ASD). *BMC Psychiatry*. 2015;15:159.
25. Kronenberg LM, Verkerk-Tamminga R, Goossens PJ, van den Brink W, van Achterberg T. Personal recovery in individuals diagnosed with substance use disorder (SUD) and co-occurring attention deficit/hyperactivity disorder (ADHD) or autism spectrum disorder (ASD). *Arch Psychiatr Nurs*. 2015;29(4):242–8.
26. Howlin P, Moss P. Adults with autism spectrum disorders. *Can J Psychiatry*. 2012;57(5):275–83.
27. Stoddart KP, Burke L, King R. *Asperger Syndrome in Adulthood: A Comprehensive Guide for Clinicians*. New York, NY: WW Norton & Co; 2012.
28. Lai MC, Lombardo MV, Baron-Cohen S. Autism. *Lancet*. 2014;383(9920):896–910.
29. Serafini G, Pompili M, Innamorati M, Rihmer Z, Sher L, Girardi P. Can cannabis increase the suicide risk in psychosis? A critical review. *Curr Pharm Des*. 2012;18(32):5165–87.
30. Brooner RK, King VL, Kidorf M, Schmidt CW Jr, Bigelow GE. Psychiatric and substance use comorbidity among treatment-seeking opioid abusers. *Arch Gen Psychiatry*. 1997;54(1):71–80.
31. Wilcox HC, Conner KR, Caine ED. Association of alcohol and drug use disorders and completed suicide: an empirical review of cohort studies. *Drug Alcohol Depend*. 2004;76(Suppl):S11–9.
32. Cassidy S, Bradley P, Robinson J, Allison C, McHugh M, Baron-Cohen S. Suicidal ideation and suicide plans or attempts in adults with Asperger's syndrome attending a specialist diagnostic clinic: a clinical cohort study. *Lancet Psychiatry*. 2014;1(2):142–7.
33. White TJ. A window into the neurobiology of childhood and adolescent psychopathology. *J Am Acad Child Adolesc Psychiatry*. 2013;52(1):9–11.
34. Wood JJ, Ehrenreich-May J, Alessandri M, et al. Cognitive behavioral therapy for early adolescents with autism spectrum disorders and clinical anxiety: a randomized, controlled trial. *Behav Ther*. 2015;46(1):7–19.
35. Palmqvist M, Edman G, Bolte S. Screening for substance use disorders in neurodevelopmental disorders: a clinical routine? *Eur Child Adolesc Psychiatry*. 2014;23(5):365–8.
36. Mazefsky C, Kao J, Oswald D. Preliminary evidence suggesting caution in the use of psychiatric self-report measures with adolescents with high-functioning autism spectrum disorders. *Res Autism Spectr Disord*. 2011;5(1):164–74.