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ORIGINAL ARTICLE

A Systematic Literature Review on the Relationship Between Autism Spectrum Disorder and Substance Use Among Adults and Adolescents

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Abstract

Autism spectrum disorder has often been assumed to be a protective factor against substance use, yet the extent of substance use in this population has been difficult to determine as limited research has been done on these interacting variables. This systematic literature review examined 26 studies published between 2009 and 2019 to uncover the relationship between autism spectrum disorder and substance use. The types of participants included from the primary studies are adults and adolescents. A significant indication that this population is more susceptible to substance use and related disorders was found, yet this may only remain true for adults. Various interacting environmental and genetic/neurological factors combine and may contribute towards this vulnerability such as feelings of isolation, deficits in executive functioning and genetic heritability. High comorbidity rates of depression, anxiety disorders and attention deficit/hyperactivity disorder may further strengthen this vulnerability. Screening for substance use in these patients is not a common practice and the treatment of substance use disorder remains a challenge suggesting that many individuals may remain underdiagnosed. This research paper thus demonstrates the need and importance of more primary research to be done and for greater awareness of this vulnerability within mental health settings.

Keywords Autism spectrum disorder (ASD) · Comorbidity · Neurodevelopmental disorders · Substance use · Substance use disorder (SUD) · Systematic literature review

Autism spectrum disorder (ASD) and substance use both carry social stigma and are poorly understood by society at large. One may not always consider those with ASD as being potential users of drugs; thus, limited primary and secondary research has been conducted on this possibility (Sizoo et al. 2010b). This research paper sets out to perform a systematic literature review that intends to search for, screen and analyse primary research from various academic databases and scholars containing the topics or subtopics of ASD and substance use in adults and adolescents to uncover the relationships among these variables within this group of people.

Autism spectrum disorder (ASD) is a neurodevelopmental disorder that first becomes evident in early childhood and remains throughout adolescence and adulthood. This disorder ranges from high-functioning to low-functioning spectrums and is associated with impaired cognitive functioning, behavioural challenges, social and communication difficulties, repetitive behaviours and fixated interests (Lever and Geurts 2016). ASD affects approximately 1% of the global population (Hofvander et al. 2009). As many as 69% of individuals with ASD present a comorbid diagnosis or psychiatric symptoms with depression and anxiety disorders being common (Lever and Geurts 2016).

Similarly, substance use also presents a high rate of comorbidity. 'Substances' in this paper refer to chemicals that alter the user's awareness, behaviour and mood by altering their brain function. These substances may be legal or illegal to consume (McLellan 2017). Substances in this paper will also refer to self-administered drugs for recreational purposes as well as substances that are prescribed for medical purposes but are used in high doses or in inappropriate situations. Substance use may lead to the abuse of substances or dependence that often leads to harmful side effects, changes in

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behaviour and physical withdrawal symptoms when removed from the substance. The use of substances can therefore lead to a substance use disorder (SUD) (McLellan 2017). Unlike other mental disorders such as schizophrenia, mandatory drug tests are not required for individuals with ASD in most routine clinical assessments and hence substance use in this population is under-recognised (Palmqvist et al. 2014). The potential for those with ASD to be struggling with substance use or dependency seems to be overlooked in modern-day mental health practices as well as in academic literature (Arnevik and Helverschou 2016).

One known systematic review on the topic of ASD and SUD was published in 2016 by Arnevik and Helverschou. Their subtopics were epidemiology, patient characteristics and the function of drug use and treatment, sourcing a total of 18 papers. That systematic review had its strengths, although it used a limited amount of literature, did not discuss the types of substances used, had an extremely limited discussion on the potential neurological and social deficits that contribute to substance use and lastly and focused mainly on the limited treatment interventions available. Some updated literature has been published on this subject matter after January of 2016 when the researchers last performed their database search (Arnevik and Helverschou 2016).

However, this research paper intends to incorporate a variety of, and updated research using various databases, some of which are different from those used by Arnevik and Helverschou (2016). Additionally, this systematic literature review aims not only to discuss the prevalence of substance use but also to focus on any potential social and neurological deficits that may make an individual with ASD more susceptible to substance use. Furthermore, this paper seeks to understand why the relationship between ASD and substance use may occur as well as the types of substances used and possible explanations and implications of this usage to investigate a possible comorbid relationship.

Extensive research has been conducted on the possible link between substance use and addictive behaviours among people with attention deficit hyperactivity disorder (ADHD), another neurodevelopmental disorder, yet considering substance use as a possible struggle faced among individuals with ASD has only started to gain some psychological and psychiatric attention (Sizoo et al. 2010a, b). Ortiz-Medina et al. (2014) suggested that substance use rates in ASD may be equivalent to other psychiatric disorders, yet some claim that SUD is vastly underdiagnosed in those with ASD (Palmqvist et al. 2014). Furthermore, the available information and data on ASD's relationship with substance use remains extremely limited and warrants more investigation (Ortiz-Medina et al. 2014).

Many articles about ASD focus on maternal prenatal risk factors such as substance usage during pregnancy and how this may affect the development of ASD in children. The topic of substance use by either adolescents or adults with this disorder remains under-researched. The aetiology of ASD alone remains an important area of investigation, although seeking to understand individuals with ASD's potential coping mechanisms, risks and how it affects individuals throughout their lifetimes is a significant area of focus as well. The purpose of this systematic literature review is to fill the gap within contemporary literature by providing a comprehensive picture of the extent and nature of the interaction of ASD and substance use. Available literature has tended to focus on one aspect of substance use among people with ASD such as the prevalence of SUD, whilst this paper aims to discuss possible explanations and factors that account for this relationship dynamic from a wider lens.

Lalanne et al. (2017) suggested that it is important to train professionals to identify addiction early in those with ASD and to raise awareness of this potential comorbidity among mental health workers. It is imperative to improve our understanding of substance use in addition to its impact on mental and neurodevelopmental disorders. The limited research and literature provided on this subject matter provides some challenges but also emphasises the importance of performing such a literature review as a lack of understanding or awareness of this vulnerable subgroup may lead to them suffering in silence and a worsening in symptoms.

This review involves performing an extensive search of several applicable databases to discover relevant primary research papers of either a qualitative or quantitative nature from the last 10 years (2009–2019). These studies include the subject of ASD and its relationship with substance use as a main or subtopic. Overall, this research paper seeks out to understand to which extent living with ASD creates an increased risk for substance use through the following objectives:

- To determine the prevalence and types of substances used
- To determine the social and environmental causes of substance use in those with ASD
- To determine the potential genetic and neurological vulnerabilities
- To determine the prevention, screening, treatment and care issues among this population

Method

Relevant articles were sought through a carefully structured process in which seven databases were searched (SpringerLink, Research Gate, Cengage Learning, Journal of Autism and Developmental Disorders, PubMed, Medline and Psych Info) for full-text scholarly literature which had been published between 2009 and 2019. These searches were limited to English using a combination of keywords in each

database. The keywords used are as follows: Autism AND substance use OR substance abuse OR drug use OR addiction OR drug addiction OR drug dependency OR heroin OR cannabis OR alcohol OR LSD OR methamphetamines OR crack cocaine OR cocaine OR hallucinogens OR ecstasy OR tobacco OR inhalants OR ketamine OR crystal meth OR meth OR weed OR marijuana OR benzodiazepines OR recreational drugs. A total of 940 articles were found across the following databases, Journal of Autism and Developmental Disorders (9); SpringerLink (46); Cengage Learning (49); Research Gate (65); PubMed (249); Medline (328); and Psych Info (194). These articles were critiqued using the inclusion and exclusion criteria in Table 1. Only articles discussing adults and adolescents were included. There are various interpretations of the age which adolescence begins; Curtis (2015) defines adolescence as starting from 11 years of age due to the earliest potential initiation of puberty and ending at 18 years of age when an individual enters the early adulthood stage. Articles that fit the inclusion criteria were imported using RefWorks and duplicates were removed. The database search was concluded on the 15th of May 2019. This process has been demonstrated by the PRISMA flow diagram in Fig. 1.

Results

Included Studies

This section describes the origin and nature of the 26 studies that were derived from 671 studies found after duplicates had been removed. A comprehensive summary of all 26 studies is included in Table 2. Twenty out of the 26 studies found were from European countries. Only six out of the 26 studies were performed in other parts of the world such as the USA (4), China (1) and Australia (1). Apart from China, it is evident that the given studies came from developed countries, where people generally have a higher quality of life and more access to healthcare compared to developing countries (Lake and Turner 2017). Only three of the 26 studies consisted of longitudinal studies, making most of the studies cross-sectional. Eleven out of the 26 studies included participants with both ADHD and ASD. This may be because these two disorders share similar developmental pathways and behaviours; thus, it may be hypothesised that they share the same risk for substance use-related problems (Lundstrom et al. 2011).

Five studies discuss the use of one or many substances as a subtopic, whereas the rest of the 21 studies have substance use as a main variable and topic of interest. From the years 2009 to 2019, the given papers seem to be equally spread among the 10 years. Five studies contained 1–11 participants, another five studies used 11–100 participants, eight of the studies had a sample of 101–200 participants, three studies used 201–600 participants and five studies had 600+ participants. As stated by Sizoo et al. (2010a) who used a sample of 61 ASD and 49 ADHD participants, 'Given the modest sample sizes it must be emphasised that the results are preliminary, calling for replication' (p. 41). Most of the studies contain 101 to 200 participants or more, although 10 studies still used less than 100 participants. This is because some studies were of a qualitative nature which tended to use a smaller population sample.

All the studies had men as the dominant represented gender. This may be because ASD and autistic traits are more commonly seen in males (Kreiser and White 2015). Most of the studies (17) included participants that were either treatment-seeking, outpatients or in psychiatric care. Other types of populations included in the studies consisted of offenders (1), college students (1) and homeless people (1). The remaining six studies contained individuals from various locations which were uncategorised.

As described in the inclusion criteria, studies containing adolescents above the age of 11 years and adults were searched for. The only study that included children under the age of 11 years was the Swedish national cohort study by Lundstrom et al. (2011), although the study excluded their child participants when measuring mood disorders and SUD.

Table 1 Inclusion and exclusion criteria

Inclusion	Exclusion
Literature published between 2009 and 2019	Literature that focuses on persons under 11 years of age
Written in English	Substance use among caretakers of individuals with ASD to cope
Literature that includes both ASD and substance use as either their main or subtopic	Maternal prenatal substance use and its impact on ASD
Substance use that is either for recreational purposes or the misuse of prescribed substances	Other addictions that are not substance use such as Internet and gambling addiction
Primary research studies and case studies/reports	Secondary research papers, including literature reviews
Studies that are either qualitative, quantitative or mixed method	A focus on the treatment of ASD using substances that are correctly prescribed or administered by a medical professional, such as medical marijuana

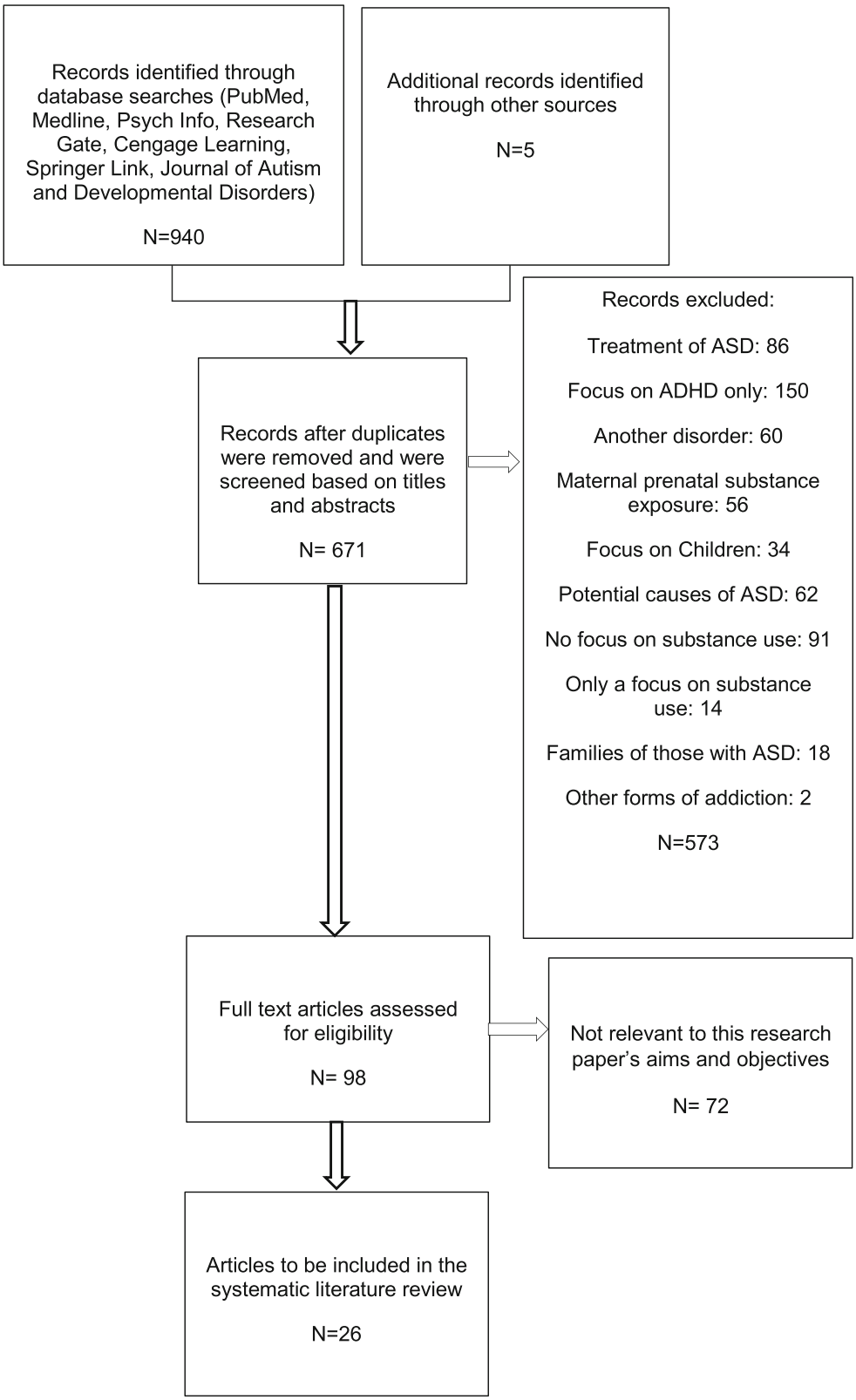

Fig. 1 PRISMA flow diagram. This diagram represents the process of identifying and screening papers for eligibility that were included in this research paper

Only three of the studies had a specific focus on adolescents. Sixteen studies of a quantitative nature mainly focused on the prevalence of substance use, types of substances used or the effectiveness of treating SUD among this sample. Ten qualitative studies made use of interviews and case studies and primarily aimed to understand the underlying reasons as to

Table 2 Characteristics of included studies in ascending order by date

Title	Author(s)	Year	Place of origin	Aim	Methodology	Sample of population	Outcomes/findings
Personality characteristics of adults with autism spectrum disorders or attention deficit hyperactivity disorder with and without substance use disorders	Sizoo, van den Brink, Gorissen-van Eenige & van der Gaag	2009	The Netherla-nds	Examines the temperament of individuals with either ASD or ADHD to see how these profiles differ when substances are used	Participants were tested in 2 sessions Cloninger's temperament and character inventory short version was used to test personality traits Statistical analysis was done using ANOVA	128 adults with either ADHD or ASD with or without SUD from two Dutch-specialised diagnostic centres	14% of participants suffered from current SUD. 8% have had a history with SUD. These patients were mostly male and had a lower IQ score than those unaffected by SUD
Using the Autism-Spectrum Quotient to Discriminate Autism Spectrum Disorder from ADHD in Adult Patients with and Without Comorbid Substance Use Disorder	Sizoo, van den Brink, Gorissen-van Eenige, Koeter, van Wijngaarden-Crem-ers & van der Gaag	2009	The Netherla-nds	To see whether the autism spectrum quotient (AQ) can discriminate between ASD and ADHD with or without comorbid SUD	ANOVAs were used to analyse the mean scores of participants with either ASD or ADHD. Receiver operating characteristic (ROC) computations were applied to assess discriminant powers	129 adult participants recently diagnosed with ASD or ADHD from two specialised Dutch clinics	All but one of the mean AQ (sub)scores were significantly higher for adults with ASD compared to those with ADHD. The SUD status, in general, was not significantly associated with AQ scores. On the social skills subscale patients with ASD and comorbid SUD
Psychiatric and psychosocial problems in adults with normal-intelligence autism spectrum disorders	Hofvander, Delorme, Chaste, Nyden, Wentz, Stahlberg, Herbrecht, Stop in, Anckarsater, Gillberg, Rastam & Leboyer	2009	Sweden and France	Describes the clinical psychiatric presentation and important outcome measures of a large group of normal-intelligence adult patients with ASD	All participants had a structured DSM-5-based clinical interview supplemented with a lifetime DSM-5 symptom checklist	122 participants aged 16 to 60. 5 with autism disorder, 67 Asperger's disorder and 50 with pervasive developmental disorder not otherwise specified (PDD NOS)	Antisocial personality disorder and substance abuse were more common in the PDD NOS group than in the autism disorder group. 16% of the participants reported substance use-related disorders. SUD was not more common in these participants than in the general population
Risk factors for violent offending in autism spectrum disorder: a national study of hospitalized individuals	Langstrom, Grann, Ruchkin, Sjostedt & Fazel	2009	Sweden	Examines potential risk factors that may contribute to violent offences among those with ASD	Data used from Swedish longitudinal registers were compared with those committing violent/sexual offences with those who did not. 31 individuals with ASD were convicted of violent nonsexual crimes and 2 of sexual offences	422 individuals hospitalised with autistic disorder or Asperger's syndrome during 1988-2000 who committed offences. The average age is 26. 317 individuals with autism (69.4% males) and 105 individuals with Asperger's syndrome	16.1% of violent offenders with ASD were comorbid with SUD and 0.5% in a non-violent conviction Psychotic disorder, any substance use and personality disorder significantly correlated with violent crimes
Treatment seeking adults with autism or ADHD and	Sizoo, van den Brink, Koeter, van der	2010		Examines how adults with ASD compared to adults	Interviews to explore current disability and risk factors	123 treatment-seeking adults. 70 with ASD and	Prevalence of comorbid SUD was higher in ADHD than

Table 2 (continued)

Title	Author(s)	Year	Place of origin	Aim	Methodology	Sample of population	Outcomes/findings
co-morbid Substance Use Disorder: Prevalence, risk factors and functional disability	Gaag, van Eenige & van Wijngaarden-Cremers		The Netherlands	with ADHD on prevalence and risk factors for comorbid SUD and disability levels associated with SUD	affecting those with ASD or ADHD	53 with ADHD into current, former and no history of SUD	in ASD. Patients with lifetime SUD started regular smoking early in life, had more challenging upbringings and had more parental SUD. ASD and ADHD share similar risk factors for SUD. Patients with past SUD may have a higher level of functioning before the onset of SUD in comparison to those without SUD
Do candidate genes discriminate patients with an autism spectrum disorder from those with attention-deficit/hyperactivity disorder and is there an effect of lifetime substance use disorders?	Sizoo, van den Brink, Franke, Vasquez, van Wijngaarden-Cremers & van der Gaag	2010	The Netherlands	Assess whether the genetic overlap of ASD and ADHD is influenced by comorbid substance use-related disorders	Polymorphisms were genotyped in five known candidate genes for (one of) the disorders. Genotyping was by Taqman-based analysis or by simple sequence length analysis	A total of 110 adult patients. 61 with ASD and 49 with ADHD	ASD could be distinguished from ADHD with nominal statistical significance. The results were independent of lifetime SUD status. Serotonergic genes could prove to play an important role in differentiating between ASD and ADHD
Autistic-like traits and their association with mental health problems in two nationwide twin cohorts of children and adults	Lundstrom, Chang, Kerekes, Gumpert, Rastam, Gillberg, Lichtenstein & Anckarsater	2011	Sweden	Examines whether the variability in ALTs (autistic-like traits) is a meaningful risk factor for ADHD, anxiety, conduct problems, depression and substance abuse, and to assess common genetic and environmental susceptibilities	Participants filled out an online survey assessing DSM- 5 based symptoms. The twins were divided into groups based on their degree of ALTs and the risk for mental health problems was calculated for each group. Genetic and environmental susceptibilities common to ALTs and the other problem types were examined	Two nationwide twin cohorts from Sweden (consisting of 11 222 children and 18 349 adults)	2.5% of the sample stated that they experienced some type of problem with drugs or alcohol in their lives. It was estimated that there is a 7.5% association with ASD and the risk of developing substance abuse and an 8.2% risk for those the rate high in autistic-like traits. It is proposed that this is due to a genetic correlation
Psychiatric Comorbidity and Functioning in a Clinically Referred Population of Adults with Autism Spectrum Disorders: A Comparative Study	Joshi, Wozniak, Petty, Martelon, Fried, Bolfek, Kotte, Stevens, Furtak, Bourgeois, Caruso, Caron & Biederman	2013	The United States of America	To examine the comorbidity and functioning in clinically referred adults with ASD	Participants received an assessment, a diagnostic interview and a psychiatric interview. A caretaker completed a diagnostic interview. The diagnosis of ASD was established by	63 adults with ASD	Adults with ASD have high levels of psychiatric comorbidity and dysfunction comparable to a clinically referred population of adults without ASD. up to

Table 2 (continued)

Title	Author(s)	Year	Place of origin	Aim	Methodology	Sample of population	Outcomes/findings
					a psychiatrist. Information from various sources was used		one-third of the ASD population in this study had SUD, consistent with the rates observed in the non-ASD psychiatrically referred population
Attitude and risk of substance use in adolescents diagnosed with Asperger syndrome	Ramos, Boada, Moreno, Llorente, Romo & Parellada	2013	Spain	To assess the risk of drug use in adolescents with Asperger's syndrome and compare it with that risk in control subjects. A secondary objective was to analyse the personality factors that may be associated with substance use in the same two groups	Three self-administered questionnaires, one for drug risk assessment (FRIDA) and the other two for personality trait assessment (MACI and SSS-V)	26 adolescent participants diagnosed with Asperger's syndrome and 28 healthy controls	Both identified personality factors and other variables associated with the Asperger's syndrome contribute to the low risk of drug abuse observed in this population
Attention-Deficit/Hyperactivity Disorder, Autistic Traits, and Substance Use Among Missouri Adolescents	Mulligan, Reiersen & Todorov	2014	The United States	Examined rates of substance use among adolescents with elevated ASD symptoms, with or without comorbid ADHD	Samples were assessed for ADHD, autistic traits and substance use with the use of parent-report questionnaires	2937 adolescents between 13 and 17 years old	Adolescents with high levels of autistic traits are at elevated risk for alcohol and tobacco use if they have comorbid ADHD; also, they may be at high risk for another drug use, even if they do not have comorbid ADHD
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	Kronenberg, Slager-Visscher, Goossens, van den Brink & van Achterberg	2014	The Netherla-nds	To improve treatment, it is necessary to identify the everyday life consequences of SUD and co-occurring ADHD or ASD in adult patients	Participants were interviewed. The interview transcripts were coded and analysed according to the seven steps for descriptive phenomenology by Colaizzi	11 participants with SUD and ADHD and 12 with SUD and ASD. Age 18 to 65. Outpatients from the treatment centre	Substance use is reported to solve some ADHD or ASD related difficulties in the short run but have negative consequences in the long run and can contribute to already impaired cognitive functioning. Substances can be used to deal with social anxiety, increase focus and reduce feelings of insecurity and overstimulation
Addiction and Autism: A Remarkable Comorbidity?	Van Wijngaarden-Crem-ers, van den Brink & van der Gaag	2014	The Netherla-nds	Explores the comorbidity between ASD and addiction and their underlying explanation	A year cohort of 200 consecutive admissions in an adult addiction psychiatry unit was	8 male patients diagnosed with ASD out of 118 patients	50% of patients abused alcohol, 50% abused soft drugs and 62.5% abused hard drugs. This study

Table 2 (continued)

Title	Author(s)	Year	Place of origin	Aim	Methodology	Sample of population	Outcomes/findings
					studied as well as 2 case studies		suggests ASD and addiction may share developmental dysregulations
ADHD Symptoms, Autistic Traits, and Substance Use and Misuse in Adult Australian Twins	De Alwis, Agrawal, Reiersen, Constantino, Henders, Martin & Lynskey	2014	Australia	How ADHD symptoms, autistic traits and their combined effects are associated with nicotine, alcohol and cannabis use and use disorders in the general population	Cross-sectional interviews and self-reports were used to measure ADHD, autistic traits, substance use and SUD. Logistic regression analyses were used for comparing the associations between measures	3,080 adult Australian twins between the age of 27 and 40 years old. (mean age 31.9 years)	Greater autistic traits scores were associated with elevated levels of regular smoking, cannabis use and nicotine, alcohol and cannabis use disorders. for alcohol use, those with high autistic traits scores were less likely to report drinking to intoxication but were at elevated risk for developing alcohol dependence
Screening for substance use disorders in neurodevelopmental disorders: a clinical routine?	Palmqvist, Gedman & Bölte	2014	Sweden	Investigates whether drug and alcohol screening are a clinical routine in the assessment of two prominent neurodevelopmental disorders, namely ADHD and ASD	Structured telephone interviews mapping SUD screening procedures were conducted with department representatives in charge	34 general adolescent and 29 adult psychiatric outpatient departments	Findings reveal that screening for SUD in ADHD/ASD is not a part of routine clinical assessments, although gradually an integral part of many clinical guidelines. SUD might be underdiagnosed in neurodevelopmental disorders
Smoking, alcohol consumption, and drug use among adolescents with psychiatric disorders compared with a population-based sample	Mangerud, Bjerkeset, Holmen, Lydersen & Indredavik	2014	Norway	Tests the types of substance use and their frequency in adolescences with psychiatric disorders	Recorded the frequencies of smoking, alcohol use and illicit drug use in the participants and compared them with 8173 adolescents from the general population in Norway	566 adolescent psychiatric patients aged 13 to 18. 39 of those having ASD	Only 7.7% of those with ASD claimed to be alcohol users and none claimed to have tried illicit drugs or are current smokers. This study suggests that those with ASD may not put themselves in settings where substances are present
The Evidence for the Contribution of the Autism Susceptibility Candidate 2 (AUTS2) Gene in Heroin Dependence Susceptibility	Wei Dang, Qian Zhang, Yong-Sheng Zhu & Xiao-Yun Lu	2014	China	To see if the single-nucleotide polymorphisms (SNP) rs6943555 in autism susceptibility candidate 2	This study identified different genotypes in participants to identify if having the AUTS2 gene, commonly associated with	426 patients with heroin dependence and 416 healthy controls	Results confirmed that in the SNP rs6943555 of AUTS2 may play an important role in the

Table 2 (continued)

Title	Author(s)	Year	Place of origin	Aim	Methodology	Sample of population	Outcomes/findings
				(AUTS2) has any association with the likelihood of heroin use	autism links to substance use		aetiology of heroin and alcohol dependence
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)	Kronenberg, Goossens, van Etten, van Achterberg & van den Brink	2015	The Netherla-nds	To identify the care needs of adult SUD patients with and without co-occurring ADHD or ASD	An exploratory study using the European Addiction Severity Index, the Camberwell Assessment of Needs, and the Manchester Short Assessment of Quality of Life to assess and compare care needs and perceived quality of life	72 patients from an outpatient's dual diagnosis department and 51 from an addiction clinic all with ASD/ADHD and SUD. Ages range from 18 to 65	SUD patients have fewer care needs than SUD patients with co-occurring ADHD or ASD. The SUD and SUD and ADHD groups report needs in similar domains. The SUD and ASD group showed a greater number of and more extensive care needs. Differences in the care needs of adult SUD patients with/without ASD should be considered
Coping styles in substance use disorder (SUD) patients with and without co-occurring attention-deficit/hyperactivity disorder (ADHD) or autism spectrum disorder (ASD)	Kronenberg, Goossens, van Busschbach, van Achterberg &. van den Brink	2015	The Netherla-nds	To improve treatment for these patient groups, it is important to identify and compare the various coping styles between SUD patients with and without ADHD or ASD and with subjects from a general population sample	Cross-sectional study using the Utrecht Coping List (UCL) and 15-minute interviews	122 participants. 50 participants with SUD, 41 participants with SUD and ADHD, 31 participants with SUD and ASD	Compared with the reference group, all three SUD groups showed a significantly higher mean on the palliative reaction, avoidance and passive reaction subscales of the UCL. The scores for all UCL subscales of the groups were remarkably similar. The SUD and ASD group scored higher on passive reaction and lower on reassuring thoughts than the SUD and the SUD and ADHD groups and lower on expression of emotions
ASD Traits and Co-occurring Psychopathology: The Moderating Role of Gender	Kreiser & White	2015	The United States	This study aims to compare male and females with ASD or ASD traits to find different severities of comorbid disorders in each	Phase 1: online survey Phase 2: group interviews	84 Undergraduate students at a public university	33% of males with high level and 39% low-level autism had SUD. Females of 14% high and 17% of low-level autism More comorbid in autistic males
		2015	France				

Table 2 (continued)

Title	Author(s)	Year	Place of origin	Aim	Methodology	Sample of population	Outcomes/findings
Substance-use disorder in high-functioning autism: clinical and neurocognitive insights from two case reports	Lalanne, Weiner, Trojak, Berna & Bertschy			Analyses how neurocognitive traits associated with high-functioning autism may be potential triggers for SUD	Interviewed two adults with high-functioning autism	Two cases of high-functioning autistic adults who use alcohol and psychostimulants	Better identification of autism and its cognitive impairments, which may be vulnerability traits for developing SUD, could help improve the diagnosis and treatment of SUD among this population
Burden and Expressed Emotion of Caregivers in Cases of Adult Substance Use Disorder with and Without Attention-Deficit/Hyperactivity Disorder or Autism Spectrum Disorder	Kronenberg, Goossens, van Busschbach, van Achterberg & van den Brink	2016	The Netherlands	To identify and compare caregiver burden and expressed emotion in SUD patients with and without comorbid ADHD or ASD. To examine differences in correlations between caregiver burden and expressed emotion across patient groups	A cross-sectional study with measures of perceived burden, subjective stress and perceptions of expressed emotion in informal caregivers for patients with an SUD, SUD and ADHD or SUD and ASD	122 participants with ASD or ADHD or SUD and their caregivers	Informal caregivers for patients with only SUD show higher levels of burden and caregivers for patients with SUD and ASD. This difference was largely explained by the higher number of contact hours between patient and caregiver in the SUD only group
Cigarette smoking, alcohol and cannabis use in patients with pervasive developmental disorders	Schapir, Lahav, Zalsman, Krivoy, Sever, Weizman & Shoval	2016	North America	This study aims to examine the rates of smoking, alcohol and cannabis use among patients with a pervasive developmental disorder (PDD), to determine whether they are protected from developing substance-related behaviours	Data were collected from the participant's electronic medical records which included data on substance use	85 participants (71 men and 14 women) diagnosed with either autism, Asperger's syndrome or PDD- NOS. The minimum age is 14 and the average age is 23	PDD is associated with 5-8-fold lower adjusted risk of smoking, alcohol and cannabis use compared to other non-psychotic psychiatric patients
Brief Report: Autism Spectrum Disorder and Substance Use Disorder: A Review and Case Study	Rengit, McKowen, O'Brien, Howe & McDougle	2016	The United States	This review and case study seeks to illustrate risk factors which predispose individuals with ASD to developing an SUD and discuss the obstacles of treatments for SUD	Review and case study	A 28-year-old male with ASD and alcohol use disorder	Those with ASD without an intellectual disability are more at risk for substance misuse than those with both ASD and intellectual disability. This study highlights the need for special addiction intervention for this group
Increased Risk for Substance Use-Related Problems in Autism Spectrum Disorders:	Butwicka, Langstrom, Larsson, Lundstrom, Serlachius,	2017	Sweden	This study aimed to find an association between ASD, ADHD and substance use to see if substance misuse	Swedish longitudinal databases were used to investigate any association between ASD/ADHD and	26,986 individuals diagnosed with ASD during 1973–2009, and	Substance use-related problems were highest among individuals with ASD and ADHD. The

Table 2 (continued)

Title	Author(s)	Year	Place of origin	Aim	Methodology	Sample of population	Outcomes/findings
A Population-Based Cohort Study	Almqvist, Frisen & Lichtenstein			is a risk factor for those with ASD/ADHD and their unaffected family members	substance use-related problems. They also examined the pattern of substance use-related problems among unaffected relatives of individuals with ASD	their 96,557 non-ASD relatives	risks of substance use-related problems were increased among full siblings of ASD probands, half-siblings and parents. ASD is a risk factor for substance use-related problems. The higher risks among relatives of probands with ASD suggest common familial (genetic and/or shared environmental) liability
The prevalence of Autistic Traits in a homeless population	Churchard, Ryder, Greenhill & Mandy	2019	United Kingdo-m	This study aims to find the prevalence of autistic traits and comorbid disorders among the homeless population	Homeless individuals were selected and screened for ASD as well as other comorbidities	106 homeless individuals between 36 and 57 years old	ASD may be a risk factor for homelessness. 12 out of 22 homeless individuals with elevated Autistic traits reported using alcohol and drugs
Treating Patients with Co-occurring Autism Spectrum Disorder and Substance Use Disorder: A Clinical Explorative Study	Helverschou, Brunvold, & Arnevik	2019	Norway	This study addresses ways of improving services for individuals with ASD and SUD by enhancing the competence of professionals in ordinary SUD outpatient clinics	Participants were given cognitive behavioural therapy (CBT) modified for ASD over a minimum of 10 sessions. The therapies lasted between 8 and 15 months. Standardised assessments were conducted pre-and post-treatment	4 male patients with ASD and intelligence quotient (IQ) ⩾ 70	2 participants had ended their drug and alcohol abuse, 1 had reduced his abuse and 1 still had a heavy abuse of alcohol. Physical well-being was the most prevalent reported positive aspect of drug or alcohol use, whereas the experience of being left out from social interaction was the most frequent negative aspects of intoxication

why the population in question may or may not use substances.

Definitions of ASD and Substance Use

The selected studies observed different aspects of substance use. Some make use of the terms 'substance use-related problems' (Butwicka et al. 2017), 'substance-related behaviours' (Schapir et al. 2016) or 'addiction' (Van Wijngaarden-Cremers et al. 2014). This variance provides a challenge when it comes to comparing the results. Most studies concerned SUD, which indicates that this is a disorder that has been diagnosed in the individual although many individuals may have a pathological relationship with substances but may not have been formally diagnosed with an SUD (Palmqvist et al. 2014).

Studies also differed with their classification of ASD. Some studies used different terms linked to ASD such as 'autistic traits' or 'autistic-like traits' which may indicate some symptoms of ASD but not a formal diagnosis. Some studies differentiate high-level and low-level autism which may act as a beneficial distinction to help identify who is at risk. One study by Ramos et al. (2013) exclusively included Asperger's syndrome which is on the high-functioning spectrum with standard cognitive functioning but severe deficits in social skills (Casartelli and Chiamulera 2016).

Some studies included pervasive developmental disorder (PDD) or Pervasive Developmental Disorders Not Otherwise Specified (PDD NOS) which is a disorder like Autism but that does not reach the full criteria (Cascio and Kilmon 1997). The current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) has revised the criteria for autism by using the term ASD in replacement of PDD suggesting that autism presents itself in different levels of functioning rather than different subtypes (Maenner et al. 2014). The DSM-5, which was released in 2013, no longer contains various subtypes of autism such as Asperger's syndrome or PPD NOS as seen in some of the studies in this systematic literature review. Maenner et al. (2014) further suggested that ASD prevalence estimates may be lower under the DSM-5 criteria than under earlier versions of the DSM. This poses a challenge when comparing older studies to more recent studies. Furthermore, studies that fail to differentiate high-functioning from low-functioning ASD can be problematic as studies that distinguish this assist in identifying a precise population that may be vulnerable to substance use instead of generalising the entire spectrum.

Conflicting Literature Regarding the Comorbidity of ASD and Substance Use

The extent of substance use in those with ASD has been difficult to determine as limited research has been done on these interacting variables (Lundstrom et al. 2011). Most studies found have suggested a higher vulnerability or a link between ASD and the likelihood of the development of an SUD. Out of the 26 studies, five studies seem to disagree, namely, Hofvander et al. (2009), Ramos et al. (2013), Schapir et al. (2016), Mangerud et al. (2014) and lastly Churchard et al. (2019). Hofvander et al. (2009) found that the ASD population was no more at risk for substance use-related disorders compared to other psychiatric populations.

The remaining four studies (Churchard et al. 2019; Mangerud et al. 2014; Ramos et al. 2013; Schapir et al. 2016) found a lower risk of substance use within the ASD population. Churchard et al. (2019) studied autistic traits among the homeless population. They hypothesised that homeless individuals with autistic traits had a lowered risk of substance use compared to their non-ASD homeless counterparts. Out of 22 homeless individuals with autistic traits, 12 (55%) of them reported using substances. This number was lower than the homeless population without autistic traits; out of 72 participants, 56 (78%) reported using substances (Churchard et al. 2019). This study is challenging to compare to other studies, given its unique population sample of homeless individuals.

Schapir et al. (2016) found a lower risk of substance use-related problems among people with ASD which will be discussed in the next section. Ramos et al. (2013) studied 26 participants with Asperger's syndrome and concluded that there was a low risk for drug use. Mangerud et al. (2014) suggested that those with ASD are less likely to use substances because they are less likely to be found spending time in situations where substances are used. Both Ramos et al. (2013) and Mangerud et al. (2014) exclusively studied an adolescent population, whereas Schapir et al. (2016) studied a young ASD sample as well, with the youngest participants being 14 years old and the mean age being 23 years old. These variances in results may be due to the age of onset of substance use within this population, especially as this population demonstrates various developmental delays (Casartelli and Chiamulera 2016). Adolescents with ASD may also be more sheltered compared to their non-ASD counterparts, thus making it more difficult to obtain substances at an early age through their peers.

Prevalence and Types of Substances Used

A total of 11 papers specified the different types of substances used among the ASD population within their studies, rather than simply measuring SUD only. Those that were mentioned having users were alcohol (11), alcohol and cannabis (1), alcohol and cocaine (1), alcohol and unspecified medication (1), alcohol and unspecified drugs (1), cannabis (9), cigarette/tobacco use (4), heroin (2), cocaine (3), methadone (2), amphetamines (3),

hallucinogens (1), benzodiazepines (1), others or unspecified (4), polydrug (3), hard drugs (1) and soft drugs (1). Substances that fall within 'hard' and 'soft' drugs are often subjective and lack proper scientific classification. Janik et al. (2017) found that in literature, soft drugs often referred to cannabis, alcohol and tobacco. Hard drugs, on the other hand, may refer to opioids, amphetamines and cocaine. The results of the 11 studies will be discussed following the ascending order of publication.

One of the earliest studies on the link between ASD and SUD was done by Sizoo et al. (2009b). They used 75 ASD participants, 18% of whom had a current SUD and 11% presented a former SUD. In total, 75% of former and 36% of participants with current SUD had an alcohol-related SUD. Methadone, polydrug and methamphetamine both had a 7% SUD rate. A total of 29% of participants had a current cannabis-related SUD and 14% had both alcohol and drug-related SUD. No participants reported a disorder related to sedatives or cocaine.

The next study by Sizoo et al. (2009a, b) initially compared the results from both ASD and ADHD samples. The ASD sample consisted of 76 participants. A total of 28% of the ASD sample reported having a lifetime of SUD, whereas the ADHD group reported 60% lifetime SUD. The alcohol subtype of SUD was reported in 47% of the ASD participants, drastically more than the ADHD group (25%). Cannabis abuse was seen in 29% of the ASD group. This systematic literature review does not include gambling addiction; however, drugs and gambling disorder was a combined category and was reported at 24%. These figures may not be representative of the whole ASD or ADHD population given its small sample size.

A 2010 study was done by Sizoo et al. Out of the 61 ASD participants, 30% reported having a lifetime SUD. A total of 53% were reported to have the alcohol dependence subtype of SUD, 26% had the cannabis dependence subtype and 21% fell within the 'other' category of SUD. These categories were somewhat broad, although this was one of the earlier publications on this topic. This study also measured SUD in a sample with ADHD. Lifetime SUD was seen to be higher within the ADHD group (57%), but the alcohol dependence type SUD was significantly higher in the ASD group (Sizoo et al. 2010a, b).

Another similar study by Sizoo et al. also was done in 2010 with a sample of 70 ASD participants. A total of 70% of individuals reported having no history of SUD. The abuse of alcohol was seen in 14% of the sample. Methadone was reported at 2%. Amphetamines were reported in 2% of the sample, cannabis was at 7%, alcohol with drug use was at 3% and polydrug was at 2%. There were no users of sedatives, hypnotics, anxiolytics and cocaine (Sizoo et al. 2010a, b). These percentages are a lot lower than seen in the previous 2010 study.

A study by Joshi et al. (2013) measured the types of substances used among the ASD treatment population, and 33% of the participants reportedly had an SUD. Joshi et al. (2013) stated that this is consistent with the rates observed in other psychiatrically referred populations with other disorders. Among the participants, 29% had met the criteria for lifetime alcohol abuse and 6% for current alcohol abuse. Furthermore, 13% met the criteria for a lifetime and 3% met the criteria for current alcohol dependence. A total of 11% reported cigarette smoking in their lifetime yet no one still smoked at the time. Five percent met the criteria for lifetime drug dependence and 2% had it at the time of participation. Two of the nine participants who met the criteria for drug abuse reported to actively be using at the time of assessment. Most of the participants were described as using more than one drug (6 out of 9 participants). Cannabis was used by all participants with a history of substance use. The use of hallucinogens was reported at 55.5% (5 out of 9), benzodiazepines at 50% (4 out of 9) and cocaine use at 33.3% (3 out of 9), which was also notably common (Joshi et al. 2013).

Kronenberg et al. (2014) measured the abuse of substances that occurred for more than 3 years. A total of 25% of participants reported abusing alcohol and 8% abused cannabis, although 42% used both alcohol and cannabis together. A total of 27% abused both alcohol and cocaine. Finally, 8% abused alcohol and medication. It is notable that in this study, alcohol and cannabis used together was the most common combination of substance use, followed by alcohol and cocaine.

Van Wijngaarden-Cremers et al. (2014) performed a pilot study on eight ASD males. Four out of eight (50%) had an alcohol-related SUD, a further 50% were reported to have a soft drug-related SUD and 62.5% were reported to have a hard drug-related SUD. Five out of the eight participants had more than one SUD. These figures appear drastically high and may be because of the small sample size.

De Alwis et al. (2014) studied the frequency of alcohol, cannabis and tobacco smoking in 3080 Australian twins with ADHD symptoms and autistic traits. The more autistic traits the individual had, the higher the rates of tobacco smoking and nicotine dependence were noted. Those with autistic traits were 11 times more likely to report using cannabis than the general population. Additionally, cannabis dependence was associated with both higher ADHD and autistic traits with individuals displaying three or more symptoms. Higher autistic trait symptoms decreased the chances of individuals drinking monthly or drinking to the point of intoxication. However, individuals with six or more autistic traits were more positively correlated with alcohol dependence, conditional to monthly use.

A 2015 study analysed a group of participants with both ASD and SUD to find out their primary drug of use. Three percent reported no primary drug used and 71% of participants abused alcohol. No participants claimed to use heroin, 7% of

those used cocaine, 3% used amphetamines and 13% reported cannabis abuse. Only 3% used more than one type of substance. It is evident within this study that alcohol was the most favoured substance of choice among this sample (Kronenberg et al. 2015b).

In the following study from 2016, smoking, alcohol or other substance use was defined as lifetime use if it occurred for a period of at least 6 months (Schapir et al. 2016). This study used the term PDD and compared the use of substances among PDD to non-PDD controls. PDD consists of the whole spectrum of autistic disorders. Out of 85 PDD participants, only 3.5% reported alcohol use, 20% reported smoking cigarettes and 2.4% used cannabis. All these percentages were significantly lower compared to the 85 non-PDD groups where 10% used alcohol, 52.9% smoked cigarettes and 10.6% used cannabis. This study's findings suggest that the PDD group face a lesser risk of developing an SUD. This contrasts with the rest of the studies discussed here.

The 2017 study by Butwicka et al. had a large population sample of 26,986 patients with ASD and 1,349,300 non-ASD controls. The ASD sample had higher rates of SUD and drug, tobacco use and alcohol-related disorders. The rates of SUD for the ASD group were at 3.6% which was notably higher than the rate amount non-ASD individuals which were 0.8%. This study showed that alcohol and drug-related disorders had the same prevalence of 2.1% whereas tobacco use was only at 0.1%. All substance use rates were higher for the ASD group than the non-ASD group. ASD was associated with an increased risk for a variety of substance use-related problems. The data from family members in this study suggested that this was due to a shared link between ASD and substance use problems between relatives (Butwicka et al. 2017). This has been the most recent primary study found, which discusses the different types of substances used and does not simply just report on the prevalence of substance use in general. In summary, this study suggested a higher prevalence of SUD and related problems among the ASD participants, especially without intellectual disability disorder compared to the non-ASD controls.

Social and Environmental Factors Associated with Substance Use in ASD

The possible social and environmental reasons why those with ASD may use alcohol or other substances are discussed in this section based on the included studies. Sizoo et al. (2010a, b) found risk factors for those with ASD to develop SUD to be, early onset of smoking, having parents who have an SUD and adverse family history of child mistreatment. The exact role of the social environment outside of the home remains unclear. Based on their case study of a 28-year-old male with ASD and alcohol dependence disorder, Rengit et al. (2016) suggested that the ASD population may be more likely to use substances outside social settings. Sizoo et al. (2010a, b), however, found that people with ASD with a current or past substance dependency may express more social interest compared to those with ASD without a history of an SUD. De Alwis et al. (2014) acknowledge that those with autistic traits stereotypically have lessened exposure to social settings, where the pressure of alcohol consumption often takes place.

In contrast, De Alwis et al. (2014) further stated that the lack of social support, stressful social events and related comorbidities may encourage the development of alcohol dependence. Sizoo et al. (2009a, b) hypothesised that using substances, particularly alcohol, alters people with ASD's perception, reducing their awareness of their poor social skills which may create the illusion of improved social interactions without truly improving performance. To further suggest this, Sizoo et al. (2009a, b), in another paper, found that those with ASD with current or previous SUDs may have substance-induced problems with reality testing.

Those with ASD may be more vulnerable to stress due to restricted access to appropriate coping mechanisms (Hofvander et al. 2009). Social and communication impairments associated with ASD may contribute to substance use as a coping mechanism (Rengit et al. 2016). The qualitative study by Lalanne et al. (2015) found that their two participants, both with high-functioning ASD, drank alcohol to decrease their anxiety linked to unexpected life events, sensory abnormalities and their lack of confidence when socialising. Both individuals studied presented deficits in attention span and executive functioning and thus, apart from alcohol, tried improving their performance with stimulants such as caffeine, nicotine and tea (Lalanne et al. 2015).

The study by Kronenberg et al. (2014) aimed to understand the everyday life consequences of individuals with ASD who also have an SUD. The study found that those with ASD and an SUD struggled to make sense of and express emotions accurately. Chaotic thoughts and emotions often lead to a vicious cycle of negative thinking and substance use. Chaotic thoughts and emotions may also lead to an overload of stimulus making them feel hopeless and dejected, thus overall contributed to a decreased life satisfaction, and can lead to social isolation and feelings of loneliness. The use of substances was consequently aimed to muffle these chaotic thoughts and feelings as well as to assist them to relax and eradicate feelings of boredom.

Participants further expressed that they used substances to be able to interact with others, as the previous study suggested (Lalanne et al. 2015). Substance use reportedly helped with decreasing overstimulation or oversensitivity and helped participants to focus and react more appropriately in social settings. The participants expressed how structure in their lives was important for them to be motivated and productive, although substance use leads to the dissolving of structure within their lives in the long term. Furthermore, this lack of

structure created a perpetuating cycle, as chaotic thoughts increased, leading to more negative feelings, and using of substances as a coping mechanism (Kronenberg et al. 2014). Correspondingly, a study by Sizoo et al. (2010a, b) found that the ability to perform domestic chores and taking part in society was the most negatively impacted by substance use.

Little research has been done on gender differences and their impact on comorbid SUDs and ASD. One study, however, by Kreiser and White (2015) aimed to do so. It was found that males with ASD were more likely to have an SUD compared to their female counterparts. A total of 33% of high-functioning males and 37% of low-functioning males had met the criteria for an SUD. Only 14% of high and 17% of low-functioning females met the criteria. Kreiser and White (2015) hypothesised that females with ASD are more likely to display internal disorders as comorbidities such as anxiety and depression, as opposed to more external disorders (SUD). Females with ASD are also known to present less restrictive and repetitive behaviours compared to males with ASD (Kreiser and White 2015). This is relevant because according to van Wijngaarden-Cremers et al. (2014), substance addiction and ASD share behavioural similarities such as the high levels of detailed perception and rigid or compulsive habits. These restrictive and repetitive behaviours which males with ASD are more likely to possess may be a risk factor for SUDs.

Långström et al. (2009) looked at violent offenders with ASD compared to non-violent offenders with ASD. It was found that 16.1% of violent offenders with ASD had an SUD, yet only 0.5% of non-violent offenders with ASD had an SUD. The misuse of substances significantly correlated with violent offenders but not non-violent offenders. This may be because substance use reduces the ability for those with ASD to anticipate the consequences of their behaviour and makes it challenging to act appropriately and acceptably in social situations (Helverschou et al. 2019).

Genetic and Neurological Vulnerabilities

Genetic and neurological vulnerabilities may increase the risk for those with ASD to misuse substances, although little primary research has been done on this topic. Casartelli and Chiamulera (2016) suggested that irregularities in motor cognition may affect social functioning in individuals with ASD and help explain the pathways of drug-seeking behaviours through creating repetitive and compulsive behaviours. The main neurocognitive deficits associated with ASD that were identified by one study were social and cognitive impairments, a lack of processing bias, weak central coherence and executive functioning impairments (Kronenberg et al. 2014). Executive function is responsible for decision-making, planning, assessing risks and the breaking of habits (Craig et al. 2016). According to Kronenberg et al. (2014), this lack of executive functioning may influence their inability to understand the consequences of substance use. It is, therefore, possible that substance use with ASD leads to further accumulation of executive functioning deficits. Furthermore, according to Lalanne et al. (2015), the abovementioned deficits may be risk factors for developing alcohol dependency as they relate to anxiety and social problem-solving skills.

Rengit et al. (2016) suggested that people with ASD have an elevated threshold for frontal cortical dopamine depletion meaning that they are less receptive to cognitive rewards compared to the non-ASD population. This is hypothesised to make them more inclined to seek out substances. Those who have ASD also often suffer from oversensitivity from external stimuli. To cope with this, they may develop highly rigid and repetitive comfort-seeking behaviours. This may potentially involve substance use for some (Sizoo et al. 2009a, b).

ASD and ADHD are suggested to share similarities in behavioural, cognitive and genetic traits (Craig et al. 2016). ASD and ADHD seem to be comorbid developmental disorders (Kronenberg et al. 2015a). Around 50 to 70% of the contributing genetic factors of ADHD and ASD show an overlap (Craig et al. 2016). Studies have suggested similar aetiologies of ASD and ADHD, signifying an increase of rare copy number variants at locus 16p13.11 in those with ADHD, an area where microdeletions and microduplications have been reported in association with ASD (Lundstrom et al. 2011). The relationship between ADHD and substance use has been thoroughly investigated. The co-occurrence of adult ADHD and alcohol abuse ranges from 35 to 71% and the co-occurrence of adult ADHD with substance abuse ranges from 15 to 25%. If ADHD creates a high risk of substance use and related disorders, ASD may have an increased risk as well. Furthermore, Mulligan et al. (2014) suggested that adolescents with high levels of autistic traits are at an elevated risk for alcohol and tobacco use if they have comorbid ADHD. Considering the similarities among ASD and ADHD, the influences that encourage SUDs in those with ADHD may have the same effect in those with ASD.

Dang et al. 2014) studied the autism susceptibility trait candidate 2 (AUTS2) on a genetic level. This gene, when disrupted, is strongly associated with ASD, epilepsy, dyslexia and ADHD. It has also been found that it acts as a vulnerability gene for heroin and alcohol dependence. It is further suggested that anomalies with the AUTS2 gene may also increase the susceptibility to cannabis or nicotine dependence. ASD and SUD can both be perceived as developmental disorders in which a genetic predisposition and vulnerability play a role (Van Wijngaarden-Cremers et al. 2014). Regardless of this information, more primary studies need to be done to investigate the potential neurological relationship between ASD and SUD.

Prevention, Screening, Treatment and Care Issues

This section sets out to discuss possible preventative solutions and challenges, issues with caring for those with ASD and an SUD, issues with screening and possible treatments and their challenges, based on four studies that were included in the review (Helverschou et al. 2019; Kronenberg et al. 2016; Rengit et al. 2016; Palmqvist et al. 2014). Based on one case study, the prevention of substance misuse among members of the ASD population may be a challenging task (Rengit et al. 2016). ASD serves as a risk factor for many other comorbid disorders such as anxiety disorders and depression (Kreiser and White 2015). These disorders may further perpetuate a cycle of substance use due to feelings of isolation and loneliness (Kronenberg et al. 2014).

As stated earlier, substance use is often assumed to be a peer activity but with ASD, it may occur more frequently in isolation (Rengit et al. 2016). Thus, the availability of substances in the home and a family history of substance abuse should be considered (Sizoo et al. 2009a, b). For a person with ASD, certain protective factors such as family support, management of comorbid disorders and possible social skills training may minimise the risk of substance abuse (Rengit et al. 2016). Getting someone with ASD and SUD to seek treatment serves as another challenge as it involves intensive social interaction (Helverschou et al. 2019). It can therefore be suggested that group therapy is not likely to be as effective among this population. With other forms of therapy, it is important to work with the behavioural and cognitive abnormalities of ASD when treating substance use problems or dependency (Rengit et al. 2016).

A second study compared the levels of burden and expressed emotions among those caring for individuals with just SUD or of those with both ASD and SUD (Kronenberg et al. 2016). It was found that ASD alongside SUD created a significantly higher feeling of distress as reported by their caregivers. However, it was found that ASD did not contribute to an increased feeling of burden. This means the caretakers of those with both ASD and SUD reported fewer feelings of a burden than caretakers of individuals who just had SUD. This may be because SUD alone contains more social stigma and is seen as a weakness, whereas ASD is seen as an uncontrollable disorder. Those with ASD may also have been cared for long before they were diagnosed with an SUD; thus, caregivers have become more accustomed to the given levels of distress (Kronenberg et al. 2016).

Palmqvist et al. (2014) found that screening for SUD among both adult and adolescent psychiatric patients with ASD was not a common practice in Sweden despite it being part of their neurodevelopmental disorder guidelines. This suggests that SUD may be significantly underdiagnosed among those with ASD or even ADHD. Being under the influence of substances such as hypnotics or cannabis may imitate autistic-like behaviours, such as poor self-regulation and lack of inhibitory control, making it difficult to create a differential diagnosis (Palmqvist et al. 2014). This needs to be considered more seriously in current clinical assessment practices.

A fourth study suggested that current treatment methods of SUD may not always be suitable for those with ASD. Helverschou et al. (2019) performed a clinical explorative study on effective treatment methods with those with comorbid ASD and SUD. Within their study, four male patients with both ASD and SUD were given cognitive behavioural therapy (CBT) for a minimum of 10 sessions to treat SUD. This therapy had been modified to accommodate the challenges that ASD may present such as communication difficulties. This resulted in two participants ending their substance use, one participant reduced their substance use, and another remained heavily dependent on alcohol. Although this type of psychotherapy had a fair success rate, ASD provided additional challenges. It was reported that the participants' communication styles made them challenging to work with. Participants also needed more sessions than recommended and it was thus more time-consuming. Therapists noted that participants had difficulty in understanding the nature and purpose of the therapy sessions and struggled to understand the professional nature of the therapeutic process (Helverschou et al. 2019).

This study suggests that knowledge and experience with ASD are necessary for the therapist to successfully treat drug and alcohol use within this disorder. Additionally, family and community support are important to facilitate early intervention and help with factors such as housing and employment. Loneliness was noted to be significantly prevalent within the participants making social support networks even more essential for treating SUD. Overall, CBT remains a promising form of treatment for those with ASD and SUD, especially when it is modified to accommodate ASD (Helverschou et al. 2019).

Discussion

The aims and objectives of this systematic literature review were to explore the relationship between substance use and ASD concerning potential comorbidity, prevalence, types of substances used, social or environmental causes of substance use, genetic and neurological vulnerabilities and lastly, potential prevention, treatment and care. The overall objective was to ascertain to what extent living with ASD creates an increased risk for substance use. Out of the 26 studies found, five studies found that the ASD population were at either a decreased risk or had no less of a risk than the average psychiatric population for developing a SUD, whilst Hofvander et al. (2009) found that the ASD population had the same risk for substance use-related disorders as other psychiatric populations. Churchard et al. (2019), Ramos et al.

(2013), Schapir et al. (2016) and Mangerud et al. (2014) found a decreased risk in the ASD population for substance use. A common theme among the studies done by Ramos et al. (2013), Schapir et al. (2016) and Mangerud et al. (2014) which found a decreased risk of SUD in the ASD population was that their samples consisted of adolescents or young adults. A suggestion for further research would be to compare younger and older ASD populations concerning SUD to identify a potential age of onset.

The rest of the 21 studies picked up on a distinct pattern suggesting that individuals with ASD may use more or be more at risk for abusing substances, further suggesting a likely comorbid relationship between ASD and SUD. Although, the participants in the study by Schapir et al. (2016) had the highest rate of cigarette smoking compared to all given studies in this paper that measured cigarette smoking, with 20% of the ASD/PDD population within these studies even though this was a lot less compared to the non-ASD/PDD control group (52.9%). This is much higher than what was reported in the study by Butwicka et al. (2017) where only 0.1% smoked tobacco and Joshi et al.'s (2015) study that reported 11% of lifetime tobacco usage.

De Alwis et al. (2014) concluded that more autistic traits were associated with an increased vulnerability to SUD including smoking cigarettes and nicotine dependence. Alcohol use and related disorders seemed to be the most common and the highest reported substance of choice according to the given studies, followed by cannabis. Social impairment is one of the main characteristics of ASD. This may explain one reason why the individuals with ASD were less likely to use illegal drugs and more likely to use alcohol, which is legal, and cannabis, which is legal in some places, because the use of illegal drugs requires complex social and communication skills for the attainment of the drugs (Kronenberg et al. 2015a).

Loneliness and isolation were identified as common dilemmas the ASD population faced that contributed towards substance use, both as a coping mechanism and 'self-medication' to increase social abilities (Kronenberg et al. 2014). It can be hypothesised that the lack of social support and societal purpose, such as being unemployed, may make someone with ASD more vulnerable to turn to substances. A chaotic cycle of events has been noticed when ASD participants used substances as a coping mechanism to deal with deficits in communication skills, low self-esteem or environmental overstimulation (Lalanne et al. 2015). This leads to a lack of structure within their lives which further perpetuates substance use. Early identification is thus key to preventing SUD (Rengit et al. 2016). The high comorbidity rate of ASD with disorders such as anxiety, depression and ADHD needs to be highly considered (Kronenberg et al. 2015a). The given qualitative studies were especially beneficial for this systematic literature review in describing and understanding the social and environmental challenges faced by ASD participants and how they led to substance use. Social and environmental risk factors are likely to be merged with neurological/genetic vulnerabilities such as cognitive impairments to create a higher risk overall (Kronenberg et al. 2014).

Limitations of Given Studies

One of the biggest limitations of these studies has been that they were mostly performed in first-world countries, with European countries having most of the studies done. This presents a limiting perspective as countries with a lower quality of life, low socio-economic status and unique life stressors may present different risk factors for vulnerable psychiatric populations to use substances (Lake and Turner 2017). There furthermore remain an extremely limited number of studies that specifically focus on the ASD population and their relationship with substance use making the information not well known or easy to find. There also remains limited primary studies on the genetic and neurological vulnerabilities or links between ASD and substance use such as common deficits. On the other hand, there is a more common focus in the literature on how maternal substance use may lead to child ASD due to neurological deficits or abnormalities in utero. Both environmental and genetic/neurological risk factors should be investigated as it is likely that both are at play to increase comorbidity between ASD and SUD (Sizoo et al. 2010a, b).

Another challenge or limitation is the changes made between the DSM-5 and previous versions of this diagnostic manual. PDD or PDD NOS and various other subtypes of Autism are no longer seen as clinically relevant which poses a challenge when looking at existing studies that are based on these terms or subtypes. For example, the Ramos et al. (2013) study deals with the subtype of Asperger's syndrome whereas that may now be 'high functioning' on the spectrum (Maenner et al. 2014). Individuals who fit the criteria for ASD 10 years ago may not meet the current DSM-5 criteria today, making it imperative that new research is done based on the most updated definitions and to keep the differences in mind when dealing with research-based upon earlier versions of the DSM. Most studies did not make mention of electronic cigarettes and it is often unclear if these have been included in studies that discuss nicotine.

Limitations of this Systematic Literature Review

This systematic literature review set out to utilise primary studies, written in English, published from 2009 to 2019 and accessible through seven different databases. It is possible that valuable studies either written in another language, accessible from a different database or published before 2009 have been excluded. Furthermore, the information conveyed in this

research paper is limited to the extent of information that was able to be provided through available primary studies.

Suggestions for Further Research and Implications for Policy

The role of familial influences on an individual with ASD's vulnerability to misuse substances needs to be more thoroughly explored, not only concerning the social environment but also in terms of genetic susceptibility. This is because SUD and ASD are both exceedingly hereditary disorders (Van Wijngaarden-Cremers et al. 2014). Butwicka et al. (2017) found a higher than usual susceptibility rate of potential SUD among parents and siblings of participants with ASD suggesting a genetic link between ASD and SUD. Dang et al. (2014) found complimentary results stating that the AUTS2 gene commonly associated with ASD may also act as a vulnerability gene to heroin and alcohol dependence. Regarding familial environment factors, early onset of smoking, having parents who have an SUD and adverse family history, or child mistreatment increases the chances for those with ASD to develop an SUD. Therefore, looking at substance availability within the home and family substance use is vital (Sizoo et al. 2010a, b).

As stated earlier, Ramos et al. (2013), Schapir et al. (2016) and Mangerud et al. (2014) found a decreased risk in the ASD population for substance use and the common theme within the three studies was that their samples consisted of adolescents or young adults. A suggestion for further research would be to compare younger and older ASD populations with SUD to identify a potential age of onset. This could be done by comparing younger and older people within the ASD population to recognise the difference of substance use habits and possible age of onset for SUD. Looking into substance use among high- versus low-functioning ASD may also be helpful to understand comorbidity better. Another important aspect to keep in mind is the comorbidity of ADHD, as Mulligan et al. (2014) stated that with comorbid ADHD, adolescents with ASD may be vulnerable to substances.

Although this systematic literature review did not look at the use of drugs as a treatment but rather how they are used recreationally, there remains a lot to uncover regarding the treatment of ASD and related symptoms with substances. A double-blind, randomised pilot study by Danforth et al. (2018) set out to test whether methylenedioxymethamphetamine (MDMA), also known as ecstasy, would be a safe and effective aid alongside psychotherapy for reducing social anxiety in the ASD population. MDMA is a stimulant and hallucinogen that is often viewed as a dangerous recreational substance, although following treatment, a notable reduction in social anxiety among the adult participants with ASD was concluded (Danforth et al. 2018). This could further suggest why some individuals with ASD seek out recreational drugs to attempt to self-medicate and eradicate symptoms of social anxiety. From the chosen studies in this paper, one study identified nine active ASD substance users and five participants used hallucinogens (55.5%) (Joshi et al. 2013).

As of March of 2019, clinical trials have opened in North America aiming to observe changes in symptoms associated with ASD within participants when doses of cannabidiol (CBD) are administered. This is based on the premise that CBD may be able to reduce irritability and anxiety. This clinical trial, however, will focus on participants between the ages of 7 and 17 years [National Library of Medicine (U.S.) 2019]. Given the information from the chosen studies, cannabis, second to alcohol, was a popular choice of substance for the ASD population. Research like this remains scarce and new, and the performance of more clinical trials should enrich our understanding of the potential positive and negative impacts of substances on the psychiatric population.

Continuing to perform research on this subject matter remains imperative, and as discussed in the subsection of prevention, treatment and care, identifying those who are struggling with substance use remains a challenge. As mentioned previously, executive functioning impairments have been considered a core deficit in ASD (Craig et al. 2016). At times, substance use-related symptoms may be mistaken for impaired executive functioning in those with ASD and consequently go undetected (Palmqvist et al. 2014). It is therefore urged that routine testing in psychiatric settings be done for substance use in ASD patients which is thoroughly done with other disorders such as schizophrenia (Palmqvist et al. 2014). With policy implications, such research may encourage more routine testing for substance use in those with ASD may be enforced. As discussed, ordinary therapy for SUD may not be suitable for ASD (Helverschou et al. 2019). The 2019 study by Helverschou et al. is the only study that was found to clinically test the effectiveness of SUD treatment therapy on the ASD population. More in-depth and extensive research may pave the way for specialised therapy methods to best treat those with comorbid ASD and SUD.

Conclusion

In conclusion, the possibility of those with ASD having an increased vulnerability of developing a SUD or struggling with substance use-related behaviours remains a very recent topic of interest. Additionally, it remains a topic of limited research which may produce a detrimental effect on our understanding of ASD; thus, more in-depth research is recommended. The ASD population is likely to struggle with both environmental and genetic/neurological vulnerabilities that make them more likely to turn to substance use as a coping mechanism such as feelings of social isolation and deficits in executive functioning. Most of the literature compiled for this

systematic literature review concludes that there is indeed increased comorbidity, vulnerability or risk factor for those within the ASD population to develop some type of SUD, but this finding was not true for adolescents and younger people. This may be due to the age of onset of substance use within this population, especially as this population demonstrates various developmental delays. This possible age difference has not been commonly recognised by other papers within this topic and may be regarded as new information about ASD and substance use.

Declarations

Conflict of Interest The authors declare that there is no conflict of interest.

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