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SYSTEMATIC REVIEWS

# Autism spectrum disorder and personality disorders: Comorbidity and differential diagnosis

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# **Abstract**

#### **BACKGROUND**

Differential diagnosis, comorbidities and overlaps with other psychiatric disorders are common among adults with autism spectrum disorder (ASD), but clinical assessments often omit screening for personality disorders (PD), which are especially common in individuals with high-functioning ASD where there is less need for support.

#### AIN

To summarize the research findings on PD in adults with ASD and without intellectual disability, focusing on comorbidity and differential diagnosis.

#### **METHODS**

PubMed searches were performed using the key words "Asperger's Syndrome", "Autism", "Personality", "Personality disorder" and "comorbidity" in order to identify relevant articles published in English. Grey literature was identified through searching Google Scholar. The literature reviews and reference sections of selected papers were also examined for additional potential studies. The search was restricted to studies published up to April 2020. This review is based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses method.

#### **RESULTS**

The search found 22 studies carried out on ASD adults without intellectual disability that met the inclusion criteria: 16 evaluated personality profiles or PD in ASD (comorbidity), five compared ASD and PD (differential diagnosis) and one performed both tasks. There were significant differences in the methodological



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approaches, including the ASD diagnostic instruments and personality measures. Cluster A and cluster C PD are the most frequent co-occurring PD, but overlapping features should be considered. Data on differential diagnosis were only found with cluster A and cluster B PD.

#### CONCLUSION

ASD in high-functioning adults is associated with a distinct personality profile even if variability exists. Further studies are needed to explore the complex relationship between ASD and PD.

**Key Words:** Autism spectrum disorder; Asperger's Syndrome; Personality disorder; Adulthood; Comorbidity; Differential diagnosis

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**Core Tip:** Differential diagnosis, comorbidities and overlaps with other psychiatric disorders are common among adults with autism spectrum disorder (ASD). Findings of most studies support that ASD in high-functioning adults is associated with a distinct personality profile even if variability exists. Cluster A and cluster C personality disorders (PD) are the most frequent co-occurring PD in ASD, but overlapping features should be considered.

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# INTRODUCTION

Autism spectrum disorder (ASD) is a neurodevelopmental disorder with an early onset and a genetic component. ASD is characterized by deficits in socio-emotional reciprocity, by impaired verbal and non-verbal communication skills, and by an inability to develop and maintain adequate social relationships with peers, and is associated with the presence of repetitive verbal and motor behaviours, restricted patterns of interest, the need for an unchanging (or at least predictable and stable) environment and hypo- or hypersensitivity to sensory inputs. The onset of clinical symptoms occurs during the early years of life[1].

The severity of ASD symptoms, intellectual functioning, age at diagnosis and psychiatric comorbidity have been shown to account for heterogeneity in clinical presentation, functioning and outcome[2-4].

The Diagnostic and Statistical Manual of Mental Disorders, 5th Edition[1] classifies three levels of ASD functioning. Level 1, which requires support, is the best functioning and includes the previous definitions of high-functioning ASD (a term commonly used in clinical practice) and Asperger's syndrome (AS), the closest to neurotypical functioning[1]. ASD level 1 may not have been diagnosed in adulthood and may also have been misdiagnosed as a psychiatric disorder[5,6]. Late-diagnosed individuals show higher levels of co-occurring psychiatric conditions, potentially related to the long-term stress in adaptation to daily life in society[7].

The most common coexisting psychiatric disorders in subjects with ASD include attention deficit hyperactivity disorder (ADHD)[8], obsessive-compulsive disorder[9, 10], psychosis[11-13] and mood and anxiety disorders[14-16]. It is possible that adults with ASD level 1 are vulnerable to such disorders[17], in part because of their greater insight into their deficits[18] and greater sensitivity to discrimination[19].

The high frequency of co-occurring disorders and the development of learnt or camouflaging strategies[20] make it difficult to diagnose ASD in adults, especially in women[21,22]. Misdiagnosis, differential diagnoses, comorbidities and overlapping behaviour with other psychiatric diagnoses, as well as personality disorders (PD), should be considered[23]. While these patients are usually screened for the presence of Axis I disorders, Axis II comorbidities are less often evaluated in this sample of patients[15]. However, in a recent survey Keller *et al*[24] found a PD comorbidity in ASD in 24% of the sample.

PD are enduring and pervasive patterns of inner experience and behaviour that deviate markedly from the expectations of the individual's culture, resulting in distress and impairment[1]. Both PD and ASD are life-long and egosyntonic disorders.

There is a growing interest in exploring the complex relationship between ASD and PD, because a better understanding of this topic may enhance the diagnostic process and also inform targeted interventions.

The purpose of this review is to summarize the research findings on PD in adults with ASD, focusing on comorbidity and differential diagnosis.

#### **MATERIALS AND METHODS**

The present review adhered to the standards set out in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[25]. A systematic review of the literature was performed through PubMed, using combinations of the following search terms: Asperger's Syndrome or/Autism + Personality/Personality disorder or + comorbidity. The search was restricted to studies published up to April 2020. Grey literature was identified through searching Google Scholar. The literature reviews and reference sections of selected papers were also examined for additional potential studies. All records that remained following the removal of duplicates were screened for the inclusion criteria.

Studies were included in this review if they examined PD (as a comorbid or differential diagnosis) in ASD samples. Only studies published in the English language and performed on adults without intellectual disability were selected. In studies for which IQ data were not reported, the participants had to be diagnosed with AS or high-functioning autism (HFA)/ASD level 1. Investigations carried out on non-clinical samples were excluded. Studies evaluating autistic traits in PD patients were also excluded. There were no restrictions made for the geographical region or setting of the study.

#### **RESULTS**

Figure 1 shows a PRISMA flow diagram of the systematic research process. The database search yielded a total of 6936 articles. Three additional records were identified through other techniques (ancestry method, grey literature searches and expert consultation). Following the removal of duplicates, 5808 articles remained for screening.

Upon screening of the records, a further 5735 articles were excluded for a variety of reasons, including a focus on different research topics or a failure to satisfy the inclusion criteria. Thus, the full texts of 74 articles were assessed, 22 of which qualified for inclusion.

In order to perform a better analysis, the studies were grouped into two main classes: Those examining personality or PD in ASD adults using categorical and dimensional models (comorbidity); and those comparing ASD with PD on personality traits or psychological functioning (differential diagnosis). In addition, one study[26] performed both tasks.

The characteristics of the studies included in this review are summarized in Table 1. Seven reviews on psychiatric comorbidity/differential diagnosis of adults with ASD that also referred to PD were found[5,27-32], but only two papers were specifically focused on PD[33,34].

#### Personality disorders as comorbid diagnosis

Among studies exploring personality features in ASD, only a few assessed PD as a categorical diagnosis using the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II)[35,36] or the International Personality Disorder Examination (IPDE)[37] (see Table 2). As autistic traits overlap with aspects of several PD, dimensional measures were preferred to assess personality in adults with ASD.

#### Structured Clinical Interview for DSM-IV

A study[14] carried out on 117 patients with ASD found that 62% of the sample met



Ref.	Setting	Aim	Statistical methods	Limitations
Soderstrom <i>et al</i> [50], 2002	NeuropsychiatricClinic in Sweden	To study the personality characteristics of adults with AS	One sample <i>t</i> -test	Small sample size
Anckarsäter <i>et al</i> [47], 2006	Neuropsychiatric Clinic in Sweden	To describe PD in relations to ADHD and ASD symptoms	One sample <i>t</i> - test	Non-specific symptoms may be overselected
Ketelaars <i>et al</i> [43], 2008	Center of Expertise for Autism in Netherlands	To explore difference between patients with mild ASD and patients without ASD in term of AQ scores and psychiatric comorbidity	$X^2$ test	Small sample size
Rydén and Bejerot[40], 2008	Psychiatric setting (tertiary unit) in Sweden	To characterize psychiatric patients with ASD in regard to demographical factors, psychiatric comorbidity and personality traits and compare the ASD group with a psychiatric control group; to compare differences of personality traits between females and males in the ASD group.	Fisher exact test; test; Kruskal-Wallis test	Not ADOS/ADI-R for assessing ASD; A naturalistic study
Hofvander <i>et al</i> [14], 2009	Neuropsychiatric Hospital in France NeuropsychiatricClinic in Sweden	To describe the clinical presentation and psychosocial outcome of a group of normal intelligence adults with ASD	$X^2$ test	Lack of comparison group; Two studies sites; Prevalence of comorbid psychiatric conditions may be overestimated
Sizoo <i>et al</i> [49], 2009	Two diagnostic centers specialized for adult patients with developmental disorders in Netherlands	To test whether adults with ASD or ADHD have distinct personality profiles, to assess how personality profiles in these groups differed by SUD status	One sample <i>t</i> -test	The clinically based diagnostic procedures; The absence of a psychiatric control group; All participants were diagnosed in adulthood
Geurts and Jansen[44], 2011	Tertiary psychiatric unit from diagnosing ASD in Netherlands	To draw the pathway to a diagnosis for adults referred to ASD assessment	Mann-Whitney $U$ tests; Kruskal-Wallis tests; $X^2$ test	Retrospective chart study; Not standardized clinical interviews for assessing axis I and axis II diagnosis
Kanai <i>et al</i> [59], 2011	University Hospital in Japan	To examine the clinical characteristics of adults with AS	Spearman's rank correlation coefficient	Small sample size
Kanai <i>et al</i> [67], 2011	University Hospital in Japan	To examine the clinical characteristics of adults with AS	Mann-Whitney $U$ test	Small sample size
Lugnegård <i>et al</i> [38], 2012	Neuropsychiatric clinics in Sweden	To explore the presence of PD in young adults with AS	$X^2$ test	Small sample size
Schriber <i>et al</i> [55], 2014	Local recruitment by physicians, psychologists, speech and language pathologists, occupational therapists, advocacy groups, regional centers, ASD support groups in United States	To compare self-reports of Big Five personality traits in adults with ASD to those of typically developing adults.	Independent sample <i>t</i> -test	Small sample size
Hesselmark <i>et al</i> [62], 2015	Tertiary psychiatric unit for diagnosing ASD; a community based facility for ASD, a website for ASD	To test validity and reliability of self-report data using the NEO-PI-R in adults with $\ensuremath{ASD}$	Independent sample <i>t</i> -test	Small sample size
Strunz <i>et al</i> [26], 2015	Department of Psychiatry at a University Hospital in Germany	To identify personality traits in adults with ASD and to differentiate them from patients with NPD, BPD and NCC	MANOVA	Selection bias (BPD and NPD were inpatients, while ASD were outpatients)
Helles <i>et al</i> [52], 2016	Neuropsychiatric Centre in Sweden	To examine temperament and character in males who were diagnosed with AS in childhood and followed prospectively over almost two decades	E-test; Kruskal-Wallis H testDunn's post hoc test	Only men with AS

Independent sample t Online administration of self-report questionnaires; Sample was not representative of adult population with ASD	f-test Only men with ASD	Independent sample Small sample size 1-test	ANOVA Self-reports of interpersonal ER; ToM was not assessed	ANOVA Diagnosis was based on self-report of patients	Kruskal-Wallis H test No control for the potential influence of medication on cognitive functioning	uskal- Wallis tests Small sample size	f-test SSPD sample consisted of non-clinical individuals
To assess and compare personality traits of adults with and without elevated ASD Ir traits using; the Five Factor Model of personality	To investigated temperament and character dimensions of men with ASD by individual case matching to a comparison group.	To explore personality and psychopathology in adult with ASD	To examine use of different interpersonal ER strategies in BPD and AS compared to normative control participants	To compare ASC, BPD, and comorbid patients in terms of autistic traits, empathy, A and systemizing	To compare the ToM performance of three forensic patient groups (AS, Schizophrenia and PD patients)	To compare Social Cognition in ASD and SPD using functional magnetic resonance Kruskal-Wallis tests imaging (fMRI).	To compare the ToM performance of a group of HFA and SSPD with a matched HC group
On line recruitment United States	Expertise Centre for Autism in Netherland	University Child and Adolescent specialized clinic in United States	López-Pérez et al Four different mental health institutions in Spain [95], 2017	CARD, online responders to a website	High security psychiatric care in UK	Clinical and support services in Scotland; Nonpsychotic people who had previously participated in the EHRS of schizophrenia	Patients and relatives of schizophrenia patients attending psychiatric service at a hospital in Spain; Public
Schwartzman et al[56], 2016	Vuijk <i>et al</i> [51], 2018	Ozonoff <i>et al</i> [65], 2005	López-Pérez <i>et al</i> [95], 2017	Dudas et al[92], 2017	Murphy[100], 2006	Stanfield <i>et al</i> [87], 2017	Booules-Katri <i>et al</i> [84], 2019

ADHD: Attention deficit hyperactivity disorder; ADI-R: Autism diagnostic interview - revised; ADOS: Autism diagnostic observation schedule-generic; AQ: Autism quotient; AS: Asperger Syndrome; ASC: Autism spectrum condition; ASD: Autism spectrum disorder; BPD: Borderline personality disorder; Er: emotion regulation; HC: Health control; HFA: High-functioning autism; NCC: Non-clinical controls; NEO-PI-R: NEO personality inventory revised; NPD: Narcissistic personality disorder; PD: Personality disorder; SPD: Schizotypal personality disorder; SSPD: Schizotypal-schizoid personality disorder; SUD: Substance use disorder; ToM: Theory of mind.

the criteria for at least one PD: primarily obsessive-compulsive (32%), avoidant (25%) and schizoid PD (21%). Concerning cluster B PD, rates of comorbidity were low, but antisocial disorder was common in the pervasive developmental disorder subgroup. A high number of patients (35%) had more than two PD. The prevalence of PD did not differ between genders, with the exception of schizoid PD, which was significantly more common among women.

Lugnegård *et al* [38] reported that 48% of a sample of 54 young adults with AS fulfilled the criteria for a cluster A or cluster C PD diagnosis. This evidence was in line with Gillberg and Billstedt's review[27] reporting no cluster B PD comorbidity in this sample of patients. It is surprising that paranoid and dependent PD diagnoses were not found. There was a significant difference in PD prevalence between genders: 65% in males versus 32% in females. Patients with AS and a concomitant PD showed more marked autistic features according to the autism spectrum quotient (AQ)[39].

Similarly, no cluster B PD comorbidity was found by Strunz et al[26]. In research examining personality pathology in ASD compared to specific PD, 45% of ASD patients met the criteria for an Axis II PD diagnosis. In particular, 36% of ASD patients



Table 2 Summary of included studies exploring comorbid personality disorders diagnosis (according to DSM-IV) in autism spectrum disorder patients

Ref.	Participants	Measures	PD assessment instrument	PD Prevalence (at least one PD)
Ketelaars et al[43], 2008	n = 15 (4 AS, 10 PDD-NOS, 1 HFA)	AQ, SCAN-2.1	IPDE	> 50%
Rydén and Bejerot[40], 2008	n = 84 (5 autistic disorder, 51 AS, 28 PDD-NOS); 37% comorbid ADHD	SCID-I, WAIS III, ASSQ, ASDI, ASRS, MADRS,Y- BOCS, GAF, CGI-S, WRAADDS	SCID-II screen; SPP	> 40%
Hofvander <i>et al</i> [14], 2009	<i>n</i> = 117 (5 autistic disorder, 62 AS, 50 PDD-NOS)	WAIS-R or WAIS-IIISCID-I, ASDI	SCID-II	62%
Lugnegård <i>et al</i> [38], 2012	n = 54  (AS)	WAIS-III, DISCOS-11AQ	SCID-II or a structured DSM-IV-based clinical interview	48%
Strunz <i>et al</i> [26], 2015	n = 59 (49 AS, 10 HFA)	ADOS, ADI-R, MINI, SCID-I, DAPP-BQ,NEO-PI-R	SCID-II	45%
Geurts and Jansen[44], 2011	n = 105 (27 autistic disorder, 28 AS, 50 PDD- NOS); 34% of sample with intellectual disability	Former DSM-IV Axis I diagnosis reported	Former DSM-IV Axis II diagnosis reported	15%
Anckarsäter et al[47], 2006	n = 174 subjects with childhood onset neuropsychiatric disorder (47 ASD, 27 ASD+ADHD, 81 ADHD, 19 other diagnosis)	SCID-I, ASDI, Y-BOCS; ASHFAQ, TCI	SCID- II	75%

ADHD: Attention deficit hyperactivity disorder; ADI-R: Autism Diagnostic interview-revised; ADOS: Autism diagnostic observation schedule-generic; AS: Asperger syndrome; ASD: Autism spectrum disorder; ASDI: Asperger syndrome diagnostic interview; ASHFAQ: Asperger syndrome and highfunctioning autism screening questionnaire; ASRS: Adult ADHD self-report scale; ASSQ: Autism spectrum disorder in adults screening questionnaire; ASDI: Asperger syndrome diagnostic interview; AQ: Autism spectrum quotient; CGI-S: Clinical global impression severity of illness; DAPP-BQ: Dimensional assessment of personality pathology; DISCOS-11: Diagnostic interview for social an communication disorder; GAF: Global assessment of functioning; HFA: High-functioning autism; IPDE: International personality disorder examination; MADRS: Montgomery asberg depression rating scale; MINI: Mini international neuropsychiatric interview; NEO-PI-R: Neo personality inventory revised; PDD-NOS: Pervasive developmental disorder not otherwise specified; SCAN-2.1: Schedules for clinical assessment in neuropsychiatry; SCID-I: Structured clinical interview for DSM-IV axis I disorders; SCID-II: Structured clinical interview for DSM-IV personality disorders; SPP: Swedish universities scales of personality; TCI: Temperament and character inventory; Y-BOCS: Yale -brown obsessive compulsive scale; WAIS-R: Wechsler adult intelligence scale-revised; WAIS-III: Wechsler adult intelligence scale-III; WRAADDS: Wender-reimherr adult attention deficit disorder scale.

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met the criteria for schizoid PD, 17% for obsessive-compulsive PD and 2% for avoidant and paranoid PD diagnoses.

These findings are in line with those reported by Rydén and Bejerot[40]. They assessed adults with ASD having no intellectual disability using the structured clinical interview for DSM-IV (SCID-II) screen[41] and the Swedish Universities Scales of Personality[42]. Avoidant and schizotypal personality traits were more common in patients with ASD compared to the control group (patients without ASD). Patients with ASD scored higher on detachment and stress susceptibility and had a median of four PD compared to two in the control group. More than 40% of the ASD group reached the cut-off score for avoidant, borderline and obsessive-compulsive PD, more than a third had depressive, schizotypal, schizoid and narcissistic PD and at least 25% reached the cut-off for paranoid and passive-aggressive PD. Females with ASD scored significantly higher than males on borderline and passive-aggressive traits.

In a pilot study on adults with mild ASD, Ketelaars et al[43] found partial or complete PD, assessed by the IPDE[37], in more than half of the sample. Schizoid and avoidance were the most frequent PD. There were no significant differences in the pattern of Axis II comorbidity between the ASD and the non-ASD patients.

Instead, in a retrospective chart study[44] on adults screened for ASD, only 15% of ASD patients had a lifetime PD diagnosis. This lower comorbidity is probably due to the fact that one third of the patient group had an intellectual disability. People with autism and an intellectual disability were less likely to receive a diagnosis of PD[45,

In a study on Temperament Character Inventory (TCI) profiles in ASD and ADHD [47], the presence of PD was assessed with the SCID-II in a subgroup of patients with childhood onset of a neuropsychiatric disorder: 75% of the sample met the criteria for at least one PD. Specific PD prevalences are presented in Table 3.

Table 3 Specific personality disorders (Structured clinical interview for DSM-IV axis II diagnosis) prevalence in autism spectrum disorder samples

PD	Lugnegård et al[38], 2012	Hofvander et al[14], 2009	Anckarsäter et al[47], 2006	Strunz et al[26], 2015
Paranoid	0%	19%	25.5 % ASD; 25.9% ASD + ADHD	2%
Schizoid	26%	13%	31.9% ASD; 22.2% ASD + ADHD	36%
Schizotypal	2%	21%	23.4% ASD; 11.1% ASD + ADHD	0%
Antisocial	0%	3%	0% ASD; 18.5% ASD + ADHD	0%
Histrionic	0%	0%	0%	0%
Borderline	0%	9%	10.6% ASD; 14.8% ASD + ADHD	0%
Narcissistic	0%	3%	6.4% ASD; 3.7% ASD + ADHD	0%
Avoidant	13%	25%	34% ASD; 11.1% ASD + ADHD	2%
Obsessive-compulsive	19%	32%	42.6% ASD; 29.6% ASD + ADHD	17%
Dependent	0%	5%	8.5% ASD; 22.2% ASD + ADHD	0%

PD: Personality disorders; ASD: Autism spectrum disorder; ADHD: Attention deficit hyperactivity disorder.

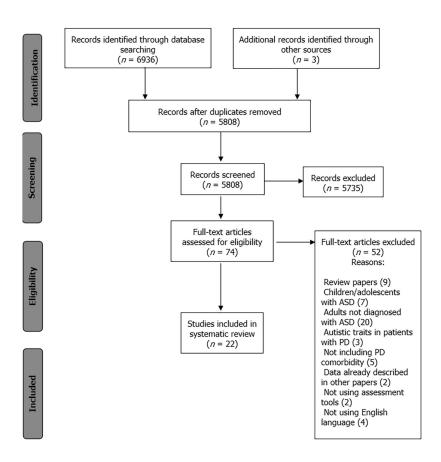


Figure 1 Preferred reporting items for systematic reviews and meta-analyses flow diagram of the systematic research process.

#### Temperament and character inventory

Studies using the temperament and character inventory (TCI) to evaluate personality in patients with ASD are presented in Table 4[48]. Four TCI studies on adults with ASD[47,49-51] found low scores on the character dimensions of self-directedness and cooperativeness. Moreover, ASD was associated with high harm avoidance, low reward dependence, low novelty seeking and high self-transcendence. The high level of rare answer scores also reflects the oddity and social insensitivity inherent in the self-descriptions of subjects with ASD[50,52]. Cluster A and cluster C PD were more common in patients with ASD assessed with the TCI and confirmed with the SCID-II

Table 4 Summary of studies using temperament character inventory to evaluate personality in adults with autism spectrum disorder

Ref.	Participants	Comparison group	Measures	Personality measures	Results
Anckarsäter et al[47], 2006	<ul><li>n = 113 (6 autistic disorder, 46</li><li>AS, 66 Atypical Autism);</li><li>47ASD+ADHD 66 ASD</li></ul>	Age and sex matched group	SCID-I; ASDI; Y- BOCS; ASHFAQ; TCI	TCI; SCID-II	Lower NS, RD, SD, C; Higher HA; Cluster A and Cluster C PD were common
Soderstrom et al[50], 2002	n = 31 AS	Age and sex matched group	WAIS-III	TCI	Higher HA ST; Lower NS, RD, SD, C
Sizoo <i>et al</i> [49], 2009	n = 75 (53 without SUD, 8 with past SUD, 14 with current SUD)	n = 657 NC	ADI-R; ADOS; DSM-IV criteria checklists; WAIS-III	VTCI	Higher HA, ST; Lower RD, SD, C; Lower NS and RD for ASD without SUD; Higher P for subgroups with current or past SUD
Vuijk et al[51], 2018	n = 66 (15 ASD, 25 AS, 26 PDD-NOS)	Matched comparison group (age, education, marital status)		TCI	Higher HA, lower NS, RD, SD, C
Helles <i>et al</i> [52], 2016	n = 40 AS	Within comparison group (no longer ASD/ASD pure/ASD plus)	GAFWAIS-IIIASDI; BDI; ASRS	TCI	Higher RD in no longer ASD; Higher HA, lower NS in ASD pure; Higher HA, lower C, SD in ASD plus

C: Cooperativeness; HA: Harm avoidance; NC: Neurotypical controls; NS: Novelty Seeking; P: Persistence; RD: Reward dependence; SD: Self-directedness; ST: Self-transcendence; SUD: Substance use disorder; SUD: No history of SUD; VTCI: Short version of temperament character inventory.

In the sample of AS patients included in another TCI study[50], the obsessional type of PD was the most frequent, followed by the passive-dependent, explosive and passive-aggressive types.

The TCI profiles differed somewhat when ASD was combined with a comorbid disorder such as ADHD[47] or substance abuse[49]. When ASD was comorbid with ADHD this was associated with higher levels of novelty seeking, whereas when ASD was comorbid with substance abuse this was associated with a higher degree of persistence and a lower degree of self-directedness compared to ASD patients without the comorbidity.

There was also some evidence indicating an association between temperament and character dimensions and long-term ASD diagnostic stability and psychiatric comorbidity. In a longitudinal cohort study by Helles et al[52], the TCI was used to assess 40 males who were diagnosed with AS in childhood and followed prospectively over almost two decades. Three distinct temperament and character profiles emerged. Those no longer meeting the criteria for ASD had high reward dependence. It is also interesting to note that in another study[50] 35.5% of the sample had reward dependence scores above the general population mean, suggesting that a subgroup of individuals with AS desire closer social interaction than they are able to establish. The participants with a stable ASD diagnosis and no current psychiatric comorbidity ('ASD pure group') were characterized by lower novelty seeking and higher harm avoidance compared with normative data; however, compared to the other groups harm avoidance was lower than for the 'ASD plus group' (those with a stable ASD diagnosis and psychiatric comorbidity), which showed elevated harm avoidance and low selfdirectedness and cooperativeness. In the ASD plus group, comorbidity disorders were depression, anxiety disorder and/or ADHD.

Vuijk et al[51] performed a re-analysis of scores on the TCI administered to a sample of 66 ASD men by individual case matching. Compared to the general population, patients with ASD scored significantly higher on the scale for harm avoidance, and lower on novelty seeking, reward dependence, self-directedness, and cooperativeness. These findings confirmed the results emerging from their previous research published in Dutch[53].

#### Big five personality traits

In Table 5 a summary of studies measuring the Big Five personality traits[54] in ASD patients is presented.

Schriber et al[55] investigated personality differences between ASD adults and neurotypical control adults using self-reports of the Big Five personality traits. Individuals with ASD were more neurotic, and less extraverted, agreeable, conscientious and open to experience, than neurotypical controls. The same

BFI: Big five inventory; L-SAS: Liebowitz social anxiety scale; HADS: Hospital anxiety and depression scale; IPIP-NEO-120: International personality item pool representation of the NEO-PI-R; NEO-PI-R: Neo personality inventory revised.

personality differences were confirmed when controlling for age, gender and self- and parent reports. The findings indicated that the personality profile distinguished between ASD and neurotypical controls but did not significantly distinguish severity symptoms between individuals with ASD.

In another study, Schwartzman *et al*[56] compared adults with and without ASD using the International Personality Item Pool Representation of the NEO-PI-R (IPIP-NEO-120) as a trait measure. The IPIP-NEO-120, following the full-length version of the NEO[57,58], consists of 24 items per factor and 4 items per facet for a total of 120 items. The Big Five facets accounted for 70% of the variance in autism trait scores measured with the Ritvo Autism Asperger's Diagnostic Scale Revised (RAADS-R)[59]. Neuroticism correlated positively with autism symptom severity, whereas extraversion, openness to experience, agreeableness and conscientiousness correlated negatively with autism symptom severity.

The clinical characteristics of AS adults, including depression, anxiety and personality (NEO Five-Factor Inventory, NEO-FFI)[57], were examined by Kanai *et al* [59]. The AQ[39], Hospital Anxiety and Depression Scale (HADS)[60], Liebowitz Social Anxiety Scale (L-SAS)[61] and neuroticism scores were significantly higher in adults with AS than in controls, whereas the extraversion, agreeableness and conscientiousness scores were significantly lower. The total score of the AQ correlated with the anxiety subscale score of the HADS and the extraversion, openness and conscien-

tiousness subscale scores of the NEO-FFI in adults with AS, but not in the controls.

Strunz et al[26] assessed personality traits using the NEO-PI-R[62] and personality pathology using the Dimensional Assessment of Personality Pathology (DAPP-BQ)[63, 64] in four samples of adults: ASD, narcissistic PD, borderline PD and non-clinical controls. Personality traits and personality pathology specific to ASD could be identified: ASD individuals, when compared to non-clinical controls, showed significantly higher scores on the NEO-PI-R neuroticism and DAPP-BQ emotional dysregulation dimensions and lower agreeableness scores; ASD individuals had significantly lower scores on the NEO-PI-R extraversion and openness to experience scales and significantly higher scores on the DAPP-BQ inhibitedness and compulsivity scales, relative to all other groups.

Moreover, individuals with ASD scored significantly higher than all other groups on the NEO-PI-R straightforwardness (frankness in expression) subscale. The results of the comparison with PD will be described later as differential diagnosis features.

#### Minnesota multiphasic personality inventory

Table 6 shows a summary of studies using other assessment measures to evaluate personality in ASD.

Only one study[65] explored personality in HFA by administering the minnesota multiphasic personality inventory (MMPI-2)[66]. The ASD sample had higher scores on the L (Lie) validity scale, Clinical Scale Depression (D) and Social Introversion (Si), Content Scale Social Discomfort (SOD), Supplementary Scale Repression (R) and Personality Psychopathology Five (PSY-5) Introversion (INTR) scales than a matched sample of college students.

In ASD, sample comorbidity conditions were major depression, anxiety disorder and ADHD. The MMPI-2 profile reflected social isolation, interpersonal difficulties, depressed mood and coping deficits. This study also found medium-sized group differences from the control sample and elevations in 30%-40% of the ASD group on Scale 8 (Schizophrenia). These results could be related to psychotic symptoms but also to social alienation and general maladjustment. A high rate of elevation (30%) on the L scale reflects a desire to present a favourable impression and is quite unusual in this sample of patients.

# Eysenck personality questionnaire

Kanai et al[67] examined 112 adults with AS using the eysenck personality questionnaire (EPQ)[68] and the Schizotypal Personality Questionnaire (SPQ)[69]. Patients scored higher than controls on the SPQ, higher on the neuroticism and psychoticism scores of the EPQ and lower on the extraversion and lie scores of the EPQ. The SPQ subscale scores (unusual perceptual experiences, odd behaviour and suspiciousness) were correlated with the total scores of the AQ in AS.

#### Personality disorders as differential diagnosis

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In the literature investigating the relationship between PD and ASD, differential diagnosis is less explored than comorbidity. Studies comparing individuals with ASD or PD on different assessment measures are shown in Table 7, and each PD cluster is described in terms of differential diagnosis with ASD.

# Cluster A personality disorders

Autism and schizophrenia spectrum disorders are classified separately in the DSM-5, but empirical findings suggest that these two disorders share overlapping features [70-72]. In clinical practice the most common difficulties are in the differential diagnosis of adults with ASD from those suffering from schizoid or schizotypal PD[29,73]. It is suggested that attention should be paid to the developmental history of the person, the prodrome and onset of the condition, its course and the absence of positive symptoms 74].

Social cognition (SC) deficits are points of overlap between ASD and schizophrenia spectrum disorders. SC includes cognitive mechanisms involved in the processing and interpretation of the social world[75-79]. Most studies on this topic directly examined patients with autism and schizophrenia[80-83] rather than schizoid or schizotypal patients. Only two studies meeting the inclusion criteria were found.

Booules-Katri et al[84] investigated differences in Theory of Mind (ToM), a main component of SC, which refers to the ability to understand the emotional and mental states of other people[75,78,79,85,86]. They used three advanced ToM tests in 35 patients with HFA, 30 patients with schizotypal-schizoid PD (SSPD) and 36 healthy controls: individuals with HFA showed worse performance and no dissociation

Table 6 Summary of studies using different assessment measures to evaluate personality in adults with autism spectrum disorder

Ref.	Participants	Comparison group	Measures	Personality measures	Results
Ozonoff <i>et al</i> [65], 2005	n = 20 HFA	24 NC (age, intelligence and gender matched college students)	WAIS-R	MMPI-2	Higher Depression, Social Introversion, Social Discomfort, Repression and PSY-5 scale Introversion
Kanai <i>et al</i> [59], 2011	n = 55 AS	57 NC	WAIS-R	SPQEPQ	SPQ: AS>NC; SPQ subscale scores (unusual perceptual experiences, odd behaviour, and suspiciousness) were correlated with total scores of the AQ in the AS group; Higher 'Neuroticism' and 'Psychoticism'; Lower 'Extraversion' and 'Lie'

EPQ: Eysenck personality questionnaire; MMPI-2: Minnesota multiphasic personality inventory; SPQ: Schizotypal personality questionnaire.

between affective and cognitive ToM components when compared with the SSPD patients; and the SSPD individuals scored significantly lower on cognitive than affective ToM tasks.

Stanfield et al[87] compared SC in ASD and schizotypal PD (SPD) using functional magnetic resonance imaging (fMRI). In the Ekman 60-Faces Test and the social judgement task there were no significant differences between the ASD, the SPD and the comorbid groups on any measure. All groups had similar patterns of impairment in the SC tests and few differences in clinical symptoms, but clear differences were seen between the ASD and SPD groups using fMRI during the social judgement task. Hyperactivation in SPD compared to ASD was found in the amygdala and the cerebellum. The fMRI findings for the comorbid group showed differences compared to the ASD group and similarities with the SPD group. The findings supported the hypo- and hyper-mentalizing theory of ASD and schizophrenia, highlighting the difficulty and importance of considering SPD as a differential diagnosis for ASD.

# Cluster B personality disorders

In recent years there has been a growing interest in investigating deficits in SC, given the symptomatic overlap between autistic spectrum conditions and borderline PD (BPD)[88-91].

An investigation[92] into the difference and overlap between ASD and BPD was performed by evaluating autistic traits and empathizing and systemizing abilities in four samples: ASD, BPD, comorbid ASD+BPD and controls.

Similar to BPD, ASD patients scored higher than controls on the AQ[39] and the Systemizing Quotient-Revised (SQ-R)[93] but had lower empathizing abilities measured with the Empathy Quotient (EQ)[94]. The major limitations of this study were that diagnosis was based on the patients' self-reports, and that there was a preponderance of females in the BPD and control samples. The results support the view that some females with BPD have undiagnosed ASD.

In another study[95], 30 BPD, 30 AS and 60 matched control participants were compared on interpersonal emotion regulation strategies. Both patients with AS and those with BPD engaged less than the controls in interpersonal affect improvement. No differences were found for affect worsening. Individuals with AS did not differ in affect improvement and worsening, tending to generally engage less in interpersonal emotion regulation. Instead, individuals with AS reported using less adaptive (attention deployment, cognitive change) and more maladaptive (expressive suppression) interpersonal emotion regulation strategies compared to individuals with

Differential diagnosis between ASD and narcissistic PD (NPD) may also be difficult. NPD was found to be one of the most prevalent PD in a help-seeking population of adults with suspicion of autism without intellectual disability in whom autism could be excluded[96]. Attwood[97] suggested that individuals with ASD, especially those with superior intellectual abilities, may overcompensate for feelings of inadequacy in social situations by becoming arrogant and egocentric.

Strunz et al[26] compared BPD, NPD and ASD on personality traits (NEO-PI-R) and personality pathology (DAPP-BQ), reporting different profiles. Adults with ASD had significantly higher scores on the NEO-PI-R conscientiousness dimension and significantly lower scores on the DAPP-BQ dissocial behaviour dimension than BPD and NPD patients. On the corresponding DAPP-BQ compulsivity scale, adults with ASD had significantly higher scores than all other groups.

Table 7 St	udies comparing autism s	pectrum disorder patients with	Table 7 Studies comparing autism spectrum disorder patients with personality disorders patients on different assessment measures	essment measures
Ref.	Participants	Comparison group	Measures	Results
Strunz <i>et al</i> [26], 2015	59 ASD (83% AS, 17% HFA)	62 NPD, 80 BPD, 106 NC	NEO-PI-R; DAPP BQ; SCID-I/MINI; SCID-II	On the NEO-PI-R: Conscientiousness: NCC = ASD > BPD and NPD; Neuroticism: NCC < ASD = NPD < BPD; Extraversion: ASD < BPD, NPD, NCC; Openness for experience: ASD < NCC, BPD, NPD; Agreeableness: ASD = BPD and NPD > NCC; on the DAPP-BQ; Inhibitedness: ASD = BPD > NCC and NPD; Dissocial Behaviour: NCC = ASD < BPD and NPD; Emotional dysregulation: NCC < ASD = NPD < BPD; Compulsivity: ASD > BPD, NPD, NCC
López-Pérez 30 AS et al[95], 2017	2 30 AS	30 BPD60 matched NC	SCID-ISCID-IIEmotion regulation of others and self (two scales: extrinsic affect improvement, extrinsic affect worsening)Interpersonal emotion management	Affect improvement: BPD = AS < NNC; Affect worsening: BPD = AS = NNC; Affect improvement > affect worsening in BPD e NCC; Affect improvement = affect worsening in ASD; Adaptive interpersonal strategies (attention deployment, cognitive change) ASD < BPD and NNC; Maladaptive interpersonal strategies (expressive suppression) ASD > BPD and control.
Dudas et al [92], 2017	624 ASD	23 BPD; 16 ASD+ BPD; 2081 NC	AQ, EQ; SQR; SCID-II	AQ: NC < BPD = ASC < ASC+BPD; EQ:NC = BPD > ASC = ASC+BPD; SQR NC < BPD = ASC = ASC+BPD
Murphy [100]2006	39 AS; Male forensic patients detained in high security psychiatric care	39 PD (antisocial and/or borderline)39 SC with positive symptoms detained in high security psychiatric care	WAIS-R; ToM measures	$IQ\ PD = AS > SC$ ; AS and SC performed worse on two ToM measures (the Revised Eyes Task and the second order mental representation stories)
Stanfield <i>et</i> al[87], 2017	28 ASD	21 SPD; 10 CM; 33 NC	ADOS-G; SCID-II; PANSS; WAISsocial judgment taskEkmann 60 facies task; fRMI task of social judgement	SPD = CM = ASD < controls on social judgment task and Ekman 60-Faces Test; on positive symptoms: ASD < SPD = CM; on negative symptoms ASD = SPD > CM; fRMI: hyperactivation in SPD and CM group compared to ASD was found in the amygdala and the cerebellum
Booules- Katri <i>et al</i> [84], 2019	35 HFA	SSPD ( $n = 30$ ) and a NC ( $n = 36$ )	O-LIFF questionnaire; SCID-I; SCID-II; ADI-R; ADOS; WAIS-III; ToM test	HFA showed greater impairment and no dissociation between affective and cognitive ToM components; SSPD scored significantly lower on cognitive than affective ToM test

BPD: Borderline personality disorder; CM: Comorbid group (SPD+ASD); EQ: Empathy quotient; NPD: Narcissistic personality disorder; O-LIFE questionnaire: Short version of the Oxford-Liverpool Inventory of Feelings and Experiences questionnaire; PANSS: Positive and negative syndrome scale; NC: Non clinical control group; SQR: Systemizing quotient revised; SSPD: Schizotypal-schizoid personality disorder; ToM: Theory of mind.

In BPD, higher levels of neuroticism, extraversion and openness for experience but less conscientiousness and the same level of agreeableness were found on the NEO-PI-R scores. The study also found, using the DAPP-BQ, more emotional dysregulation and dissocial behaviour and less inhibition and compulsivity in BPD patients compared with ASD patients. On the three inhibitedness subscales, no differences were reported. Even if the underlying causes social avoidance differed between BPD and ASD (social skill deficit in ASD versus fear of rejection in BPD), ASD individuals scored lower on the NEO-PI-R openness to experience dimension but significantly higher on the ideas (intellectual curiosity) subscale than BPD patients.

In relation to the difference between autism and narcissism, ASD patients' scores on the NEO-PI-R modesty and compliance subscales were comparable to non-clinical control subjects. Moreover, patients with ASD and non-clinical controls had similar scores on the DAPP-BQ narcissism subscale.

With regard to differential diagnosis with antisocial PD, different empathic dysfunctions in psychopathy and autism have been found[98,99]. Only one study[100] compared the ToM performances of forensic AS, schizophrenia and PD patients. In the PD group there were individuals with dissocial PD and/or BPD, diagnosed by expert clinicians. Patients were male and detained in high security psychiatric care. The results suggested that the AS and SC groups performed worse than the PD patients on the revised eyes task[101] and the second-order mental representation stories. The AS and PD groups did not differ on the Wechsler Adult Intelligence Scale full-scale IQ but both scored more highly than the SC group.

#### Cluster C personality disorders

It is well known that the phenomenology of obsessive-compulsive PD shows similarities to that of ASD[102], so misdiagnosis of ASD as anankastic PD is possible. It is suggested to consider first whether an individual has an underlying autism spectrum condition before diagnosing obsessive-compulsive PD[103]. In ASD, repetitive patterns of behaviour, in particular the pursuit of circumscribed interests, are often associated with pleasure and mastery rather than egodystonicity. Gadelkarim et al[104] suggested that in obsessive-compulsive patients the presence of obsessive-compulsive PD should alert one to the possible recognition of ASD.

No studies comparing ASD patients with cluster C PD patients met the inclusion criteria.

# DISCUSSION

Examining personality in adults with ASD has only become the focus of research in recent years. The current review provides a literature summary of how personality and PD have been studied in high-functioning adults with ASD, focusing on two clinical issues.

The first issue for clinicians evaluating personality in ASD adult patients is to determine whether personality traits are part of the same autistic phenomenology or rather represent different categorical factors (comorbidity). The findings of studies focused on PD comorbidity suggested that approximately 50% of individuals with ASD fulfilled the diagnostic criteria for at least one PD.

The prevalence of PD comorbidity seemed to vary, increasing in samples of patients with other Axis I disorders, especially ADHD, and decreasing in mixed samples with intellectual disabilities. The most common comorbid PD belong to cluster A or cluster C (schizoid, schizotypal, obsessive-compulsive and avoidance PD). High rates of patients with more than one PD were found using the SCID-II. This suggests the utility of completing an assessment with other instruments to answer the question: 'True comorbidity or overlapping features?'[5]. Phenotypic similarities between highfunctioning ASD and both schizoid/schizotypal and obsessive-compulsive PD have been noted, but the available data are sparse, so this could be a diagnostic challenge for clinicians[105,106]. An additional PD to an ASD diagnosis could be considered 'true comorbidity' if it gives relevant information for understanding patient functioning and for developing more specific treatments.

In most of the studies reviewed, the personality of adults with ASD was assessed in order to identify a specific profile differing from that of neurotypical controls. Big Five personality traits and the TCI dimensions are the most commonly used taxonomy for measuring personality in adults with ASD. The findings of these studies support the hypothesis that ASD in adults is associated with a distinct personality profile that is not equivalent to an ASD diagnosis or to a specific PD.

Regarding the Big Five traits, these patients have been shown in all the studies reviewed to be higher in neuroticism and lower in extraversion and agreeableness, and also in most of the studies to be lower in openness to experience and conscientiousness. At the same time, ASD characteristics are statistically independent of the Big Five personality traits in clinical samples.

Adults with ASD have repeatedly been shown to have a distinct temperament and character compared to neurotypical controls. Concerning the TCI dimensions, lower scores on the character dimensions of self-directedness and cooperativeness indicated a possible personality psychopathology[107,108]. Moreover, ASD was associated with high harm avoidance, low reward dependence, low novelty seeking and high selftranscendence. High harm avoidance reflects pessimism and shyness, and also statedependent anxiety. Low reward dependence indicates impairments in social sensitivity, attachment capacity and adaptability. In individuals with an immature character structure, high self-transcendence may lead to disregard for the basic realities of human interaction and social responsibilities.

As regards other personality measures, such as the EPQ and MMPI-2, the emerging profile reflected social isolation, interpersonal difficulties and psychotic-like

In summary, the overall profile of personality traits and dimensions in ASD puts individuals at risk for other psychiatric disorders and lower functioning, even if variability exists.

Individuals with autism that are not diagnosed in childhood may have a high level of stress in trying to find a lifestyle to survive in a world that is difficult to understand; thus, building their personality with this level of chronic stress could be a trigger for creating a PD. Nevertheless, the neuropsychiatric dysfunctions associated with ASD permit considerable variation in personality. It has been suggested that personality mediates the relationship between autistic symptoms and well-being[109,110]. Exploring personality could provide a more comprehensive picture of adults with ASD, characterizing them through their individual strengths and weaknesses. It could advance the understanding of heterogeneity within patients and help in the development of more specific interventions. Treatment of PD comorbidity in adults with ASD is still in its infancy, but specific programmes have started to be developed 111 .

The second critical issue is differentiating ASD patients from PD patients in clinical samples when searching for an ASD diagnosis. High-functioning ASD patients are frequently misdiagnosed with PD, and few studies were found on differential diagnosis between ASD and PD.

SC deficits could be useful for distinguishing ASD from PD, especially borderline and antisocial PD[112]. Gender could cause specific patterns of PD comorbidity and increase the risk of misdiagnosis, especially in women[14,113]; it has been suggested that some women with BPD have undiagnosed ASD.

Concerning the difference between autism and narcissism, individuals with ASD may appear egocentric because of a limited awareness of when it is appropriate to compliment oneself and when it is not. Nevertheless, ASD patients were found to be comparable to non-clinical controls on scales measuring narcissism in the only available investigation on this topic[26].

Differences in ToM abilities between ASD and cluster A PD have also been found, but functional neuroimaging may be better than SC testing for discriminating between autism and schizophrenia spectrum disorders[87].

Findings on differential diagnosis should be replicated and investigations should be extended to compare ASD patients with cluster C PD patients too.

Differential diagnosis should be based on clinical examination and a very careful history investigation of the first years of development, the first social relationships with other children and adolescents, changes of lifestyle during development and clinical symptoms of ASD in the first years of life.

Interviews such as the Autism Diagnostic Interview-Revised (ADI-R)[114] could help the clinician to collect the first symptoms of ASD. Personality assessment could help in confirming the diagnosis, but has to be used carefully by an expert clinician who knows the ASD cognitive style in order to avoid misunderstandings.

The findings of all the studies included in this review were based on self-reporting questionnaires or structured interviews that collected information only from the patients. This raises concerns about how a person with autism can read and understand the complex questions in a self-report test: individuals with autism could have difficulties in understanding the real meaning because of their literal way of reading a text. Nevertheless, studies have supported the validity of self-report in adults with ASD without intellectual disability[55,62].

# CONCLUSION

This review provides a summary of the main findings in the literature regarding PD in adults with high-functioning ASD without intellectual disability. The aim of the review is to improve knowledge of the complex relationship between ASD and PD. Among the limitations of this review is the exclusion of studies looking for autistic traits in patients with PD or in non-clinical populations, which may be informative for giving a better understanding of overlapping features, as the question of commonality as opposed to comorbidity is not yet resolved. Furthermore, our research was conducted extensively on PubMed only. Future works should be conducted by



optimizing retrieval strategies and also including studies concerning adolescents. Another area little examined is the role of age in modulating the relationship between PD and ASD[115,116]. Longitudinal research on personality and ASD may clarify whether the relationship between personality and ASD increases in adulthood, as has been suggested[55].

# **ARTICLE HIGHLIGHTS**

#### Research background

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by persistent deficits in social communication and social interaction, as well as restricted, repetitive and stereotyped patterns of behaviour. Individuals with high-functioning ASD are more likely to be diagnosed in adulthood, probably due to the development of learnt or camouflaging strategies that make it much harder to identify the underlying difficulties. Late-diagnosed individuals report higher levels of co-occurring psychiatric disorders or misdiagnosis, because some features of ASD can overlap with symptoms of other psychiatric conditions as well as personality disorders (PD). In recent years there has been a growing interest in exploring the complex relationship between ASD and PD, especially for features that overlap with cluster A and cluster C

#### Research motivation

Consideration of the relationship between PD and ASD, with a focus on differential diagnosis and comorbidity, can lead to a better understanding of this complex topic and can improve the diagnostic process as well as supporting the creation of targeted interventions.

# Research objectives

To summarize the research findings on ASD and PD in adulthood, focusing on comorbidity and differential diagnosis.

#### Research methods

The guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) were followed in the present review. A comprehensive literature search was performed through PubMed, including only studies published in the English language and performed on adults without intellectual disability. The research included studies published up to April 2020.

# Research results

The current review provides a literature summary of how personality and PD have been studied in high-functioning adults with ASD. The findings show that approximately 50% of individuals with ASD fulfilled the diagnostic criteria for at least one PD. The most common comorbid PD belong to cluster A or cluster C (schizoid, schizotypal, obsessive-compulsive and avoidance PD). High-functioning ASD patients are frequently misdiagnosed with PD, but only a few studies have been conducted on differential diagnosis. Furthermore, there were significant differences in methodological approaches, including ASD diagnostic instruments and personality measures.

#### Research conclusions

ASD in high-functioning adults is associated with a distinct personality profile even if variability exists. Cluster A and cluster C PD are the most frequent co-occurring PD, but overlapping features should be considered. Exploring personality could provide greater understanding of adults with ASD by identifying strengths and weaknesses, and could give relevant information for the development of specific and individual treatments.

#### Research perspectives

Further studies are needed to explore the relationship between ASD and PD, especially on differential diagnosis. It would be useful to explore the relationship between PD and ASD from a longitudinal perspective, take in account individual's life and development history.

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