Review Article

How and Why is Autism Spectrum Disorder Misdiagnosed in Adult Patients? - From Diagnostic Problem to Management for Adjustment -

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ABSTRACT

Autism spectrum disorder (ASD) is often overlooked or misdiagnosed in adult patients especially in those with other psychiatric comorbidities. Several reasons possibly account for this fact, for example, difficulty in obtaining accurate developmental history from a patient, insufficient experience among psychiatrists detecting ASD in adult patients, and mild/atypical autistic traits in contrast to prominent symptoms of psychiatric comorbidities. We conducted a search of databases (PubMed, PsycINFO, and ERIC) for relevant articles published from January 2000 to May 2015 and summarized unrecognized or misdiagnosed cases as well as major psychiatric comorbidities among adults with ASD from previous reports. Five disorders, (i.e., schizophrenia, psychotic disorder, bipolar disorder, major depressive disorder, and personality disorder) were specifically highlighted as misdiagnosed psychiatric diseases or comorbidities responsible for unrecognized ASD. This review also proposes plausible pathways for patterns of maladjustment and processes leading to misdiagnosis among adults with ASD, together with necessary approaches to support their goals of a requisite social life. In conclusion, clinicians should be more concerned with correct diagnosis of ASD as well as treatments of psychiatric comorbidities and need perspective of management for better mental health and social adjustment in ASD patients.

MeSH Headings/Keywords: Adult, Autism spectrum disorder, Mental health, Misdiagnosis.

Introduction

Autism spectrum disorder (ASD) in the DSM-5 [1] consists of two diagnostic criteria: criteria A (social and communication deficits) and criteria B (restricted/repetitive behaviors and abnormal sensory sensitivity). In addition, ASD described in the DSM-5 includes three disorders in the DSM-IV-TR [2], that is, autistic disorder, Asperger's disorder, and a part of pervasive developmental disorder-not otherwise specified (PDD-NOS), while the social communication disorder of the DSM-5 covers the remainder of PDD-NOS (DSM-IV-TR). In this review, we quote many articles using the DSM-IV-TR criteria. Accordingly, the practical meaning of the term ASD used in this review mostly corresponds to the set of three disorders of the DSM-IV-TR, that is, autistic disorder, Asperger's disorder, and PDD-NOS.

The most recently reported prevalence of ASD ranged from 1.16% to 1.47% in children [3,4] whereas it was 0.98% in adults [5]. Thus, ASD is more common than the generally recognized prevalence reported before. Moreover, children [6] and adults [7] with ASD have many other psychiatric disorders. One study indicated that young people with ASD are 2 to 4 times more likely to experience comorbid mental disorders than control subjects of the same generation [8]. The mean number of lifetime psychiatric comorbidities were also greater in individuals with ASD than in those without ASD at both young [9] and adult ages, that is, 6.0 ± 3.4 for subjects with ASD versus 3.5 ± 2.7 for those without ASD [10].

It is surprising that 7% to 16% of patients in psychiatric clinics or hospitals are finally diagnosed with ASD according to recent studies [9, 11-14]. An even more surprising fact is that over half of adults with ASD initially visit general practitioners [15]. Therefore, primary care clinicians might have greater opportunity to encounter adult patients with ASD than previously expected. Nevertheless, several studies have pointed out that ASD in adult patients is usually unrecognized and often misdiagnosed by primary care clinicians due to lack of experiences in detecting autistic features [16,17]. Therefore, this review aimed to summarize unrecognized or misdiagnosed cases and major psychiatric comorbidities in adults with ASD based on previous reports, elucidate the background of and process to misdiagnosis, and refer to necessary management for better mental health and social adjustment in adult patients with ASD.

Previous findings of misdiagnosis and comorbidities in adults with ASD: We conducted a search of medical, psychological, and educational databases (i.e., PubMed, PsycINFO, and ERIC) for relevant articles published from January 2000 to May 2015. Search terms included all possible

combinations of the following terms: autism (including Asperger, pervasive developmental disorder-not otherwise specified, pervasive developmental disorder, and autism spectrum disorder), diagnosis (or misdiagnosis), and adult (or adolescent).

A total of 2067 articles were identified through the electronic search. Next, the first author (K.T.) read the titles and abstracts of all 2067 articles and then selected case studies that dealt with unrecognized or misdiagnosed cases with ASD (mainly within normal intelligence). In addition, out of the 2067 articles, K.T. selected the articles examining psychiatric comorbidities among adults with ASD according to the following criteria: 50 or more subjects in the study and articles reported in a peer-reviewed English language journal.

Table 1 [18-32] summarizes previous case reports and case series of unrecognized or misdiagnosed individuals with ASD. Most subjects with ASD were misdiagnosed with the following five disorders: schizophrenia, psychotic disorder, bipolar disorder, major depressive disorder, and personality disorder. Among these, schizophrenia, bipolar disorder, and major depressive disorder remained as the final psychiatric comorbidities after reassessing the diagnosis.

Table 2 [8, 10, 33-43] shows major psychiatric comorbidities (≥10%) in adults with ASD. Psychiatric comorbidities, which were commonly seen in previous reports, consisted of mood disorders (including major depressive disorder), anxiety disorders, obsessive-compulsive disorder, attention-deficit/hyperactivity disorder, psychotic disorder, and personality disorder.

ASD and schizophrenia/psychotic disorders: Several studies have pointed out that it is difficult for clinicians to distinguish ASD from schizophrenia since poor social communication skills, unique thinking and bizarre behaviors of ASD resemble negative symptoms and disorganized thoughts/behaviors of schizophrenia [29, 44, 45]. In addition, genetic studies have indicated a close linkage between ASD and schizophrenia [46]. Moreover, several environmental risk factors overlap between autism and schizophrenia, for example, advanced paternal age, maternal diabetes, bleeding during pregnancy, and migrant status [47].

Although previous studies demonstrated a wide range (0% to 28%) of lifetime prevalence of schizophrenia in ASD subjects [8, 35, 36, 38, 41, 43, 48-50], most of them reported a prevalence of under 4% [8,35,36,41,43,48-50]. Neurocognitive impairments such as executive dysfunction [51] and deficits in theory of mind [52] in subjects with ASD are considered a vulnerability for future psychosis according to studies on prodromal psychosis [53-55]. Moreover, one study found that three underlying symptoms (i.e., unusual fears, thought disorder, and bizarre anxiety reactions) are related to psychosis in ASD [56]. As ASD has been mostly regarded as a risk factor for psychotic experiences [57] or non-affective psychotic disorder in several cohort studies [58], clinicians may need to make a differential diagnosis between onset of endogenous psychosis as comorbidity and transient psychotic reaction to a stressful situation in ASD individuals. In other words, it is suggested that clinicians should avoid overdiagnosis of spontaneous psychotic disorders including schizophrenia and rather consider vulnerability to psychotic reaction in ASD individuals.

As one of the above-mentioned reasons for the close relationship between ASD and psychosis, past experiences with bullying may play an important role for future vulnerability to psychosis in ASD individuals [59,60], since they are usually at an elevated risk for becoming bully-victims [61,62] and indeed report extremely high frequency of bullying experiences (75% to 95%) [63, 64] . As additional reason, abuse experiences also seem to be an important risk factor for psychosis [65,66], since individuals with ASD are at an elevated risk for abuse [67,68] and report physical abuse (19%) in their childhood [69] or sexual abuse (40%) in women with higher levels of autistic traits [68]. Posttraumatic stress disorder (PTSD) often results from psychological trauma, such as childhood experiences with bullying and abuse [70-72]. Interestingly, the prevalence of PTSD is also higher (11% to 17%) in individuals with ASD [10, 68, 73] than in the general population (0.3% to 6.1%) [74]. Since PTSD has been regarded as an increased risk factor for psychotic experiences and psychosis [75-77], it could at least partly explain the higher incidence of psychotic comorbidities among ASD individuals.

ASD and mood disorders: Major depressive disorder is the most common psychiatric comorbidity in adults with ASD as shown in Table 2. Even in children with ASD, major depressive disorder is one of the most common psychiatric comorbidities [78,79]. Furthermore, depressive symptoms increase from school age through young adulthood in individuals with ASD due to poor emotional regulation, lower life satisfaction, and greater social difficulties [80]. In adulthood, individuals with ASD experience greater perceived stress than those without ASD [81, 82], and their stress may result from social communication deficits [81], low coping ability [82] and anxiety [83,84]. Furthermore, the awareness of their own social communication deficits can intensify the depressed state in individuals with ASD (especially individuals with higher cognitive ability) [85-87].

Various backgrounds should be taken into consideration when treating depressed adults with ASD, such as past negative experiences bullying [14,88], interpersonal friction [14, 16, 21, 89], and school maladjustment [14, 90]), psychological vulnerability (loneliness [89, 91], lowered self-esteem [87, 91 92], poor emotional regulation [80], and difficulty in identifying distress [93]) and other cognitive/social problems (communication difficulty [94], inflexibility [95], and low life satisfaction [80,91]).

It has also been suggested that there is a close relationship between ASD and bipolar disorder in family studies [96-98] and a genetic study [99]. In addition, a cohort study has showed that ASD is a risk factor for bipolar disorder [58]. In fact, the prevalence of bipolar disorder is higher in individuals with ASD (6% to 21%) [100] than in the general population (2.4%) [101]. Furthermore, some studies reported that the proportion of bipolar disorder together with psychotic symptoms was 7% in adult patients with ASD [35] and 23% in adult patients with ASD in psychiatric intensive care units [102]. Therefore, if clinicians encounter a patient with a history of repetitive depressive episodes together with occasional manic/mixed/

Table 1: Summary of previous case reports and case series of unrecognized or misdiagnosed cases with autism spectrum disorders

Gender (M/F)	Psychiatric diagnosis before reassessment	Psychiatric comorbidity after reassessment	ASD subtypes	Age at first diagnosis (years)	Age at re-assessment (years)	References
M	Schizophrenia	No	Asperger	Between 7- 11	40	Perlman [18]
F	Schizophrenia	No	Asperger	5	42	
M	Depression, mania with psychotic symptom	Bipolar disorder	Asperger	About 23	25	Ng et al. [19]
M	Depression	Depression	Asperger	Unknown	66	Naidu et al. [20]
M	Depression	No	Asperger	About 63	67	James et al. [21]
M	Health anxiety	No	Asperger	Unknown	69	
M	Memory difficulties	Same symptom	Asperger	71	71	
M	Financial problems	Same symptom	Asperger	83	83	
M	Delirium, dementia	Dementia	Asperger	84	84	
M	Inter-ictal psychosis (epilepsy)	No	HFA	Unknown	8	Dossetor [22]
M	Depressed mood, psychosis	Intellectual disability	ASD	Unknown	16	
F	Psychosis, intellectual disability	Intellectual disability	PDD-NOS	Unknown	13	
F	Depressive psychosis	Generalized anxiety disorder	Asperger	14	16	
M	Bipolar disorder	Intellectual disability	PDD-NOS	14	14	Tiffin et al. [23]
F	Personality disorder (with mixed "dissocial" and "borderline" features)	No	Asperger	Unknown	17	
M	Psychosis, mental retardation, OCD, depression	Bipolar disorder	Asperger	Unknown	25	Raja and Azzoni [24]
M	Depression	Bipolar disorder	Asperger	Unknown	30	
F	Psychosis, bipolar disorder, Borderline personality disorder	Bipolar disorder (mixed state)	Asperger	Junior high school	19	
M	Alcohol abuse, psychosis	Alcohol abuse	Asperger	18	22	Radley and Shaherbano [25]
M	Depression, alcohol dependence, adjustment disorder, Cluster B personality disorder	Depression, Alcohol dependence	Asperger	Undergraduate age	44	Spencer et al. [26]
M	OCD, obsessive-compulsive personality disorder, depression,	Depression	HFA	35	78	van Niekerk et al. [27]
M	Depression, personality disorder	Depression, anxiety disorder	HFA	64	72	
M	Depressed mood	No	Asperger	Unknown	83	

M	Depression, ODD, ADHD	No	ASD	Unknown	10	
M	Depression, anxiety disorder, ODD	Anxiety disorder, ADHD	ASD	Unknown	11	
M	Depression, bipolar disorder, Anxiety disorder, ODD, ADHD	Depression	ASD	Unknown	12	Mazefsky et al. [28]
M	Bipolar disorder, ODD, ADHD	Depression	ASD	Unknown	12	
M	Depression, OCD, ODD, ADHD	Depression	ASD	Unknown	17	
F	ODD, ADHD	ADHD	ASD	Unknown	12	
F	Depression, anxiety disorder	Depression	ASD	Unknown	13	
F	Depression, bipolar disorder, Anxiety disorder, OCD, ODD, ADHD	Depression, anxiety disorder	ASD	Unknown	16	
M	Schizophrenia	Schizophrenia	Autism	11	16	
M	Schizophrenia	Schizophrenia	Autism	14	17	
M	Schizophrenia	Schizophrenia	Atypical autism	15	16	Waris et al. [29]
M	Schizophrenia	Schizophrenia	Atypical autism	16	17	
M	Schizophrenia	Schizophrenia	Asperger	16	16	
F	Schizophrenia	Schizophrenia	Asperger	9	13	
F	Schizophrenia	Schizophrenia	Atypical autism	12	14	
F	Schizophrenia	Schizophrenia	Asperger	14	15	
F	Schizophrenia	Intellectual disability	Autism	14	38	Crivelli and Rocca [30]
M	A mixed episode with psychotic symptoms	Psychotic disorder	ASD	23	23	Simoncini et al. [31]
M	Bipolar disorder, schizophrenia	No	HFA	Middle school age	16	
M	Schizophrenia	Intellectual disability	PDD-NOS	Puberty	17	Van Schalkwyk et al. [32]
M	Schizophrenia	No	PDD-NOS	14	16	
M	Bipolar disorder, psychosis	Bipolar disorder	Autism	14	21	
F	Schizoaffective disorder	No	ASD	After graduating from special school	19	

ASD: autism spectrum disorder, Autism: autistic disorder, Asperger: Asperger's disorder, PDD-NOS: pervasive developmental disorder-not otherwise specified. HFA: high functioning autism, Depression: major depressive disorder, ODD: oppositional defiant disorder, OCD: obsessive-compulsive disorder, ADHD: attention-deficit/hyperactivity disorder.

psychotic periods, they should suspect an underlying ASD diagnosis (especially a patient with an early onset age of mood episodes [103]).

ASD and personality disorders: Major subtypes of personality disorders, such as cluster A personality disorders (i.e., schizoid and schizotypal personality disorders) and cluster C personality disorders (i.e., avoidant and obsessive-compulsive personality disorders) according to the DSM-IV-TR (Table 2) are reported psychiatric comorbidities with ASD. Actually, many studies have indicated that there is a phenomenological overlap between ASD and the above-mentioned personality disorders [36, 104-106]. Nevertheless, borderline personality disorder (BPD) as a cluster B personality disorder seems to be an important psychiatric comorbidity that can mask autistic features and easily lead to misdiagnosis of ASD patients, as shown in Table 1. In fact, the proportion of comorbid BPD ranged from 9% to 14% in ASD patients [10,36,42,107]

ASD is characterized by neurocognitive deficits, such as

Table 2: Major psychiatric comorbidities in adults with autism spectrum disorders.

Number of subjects (male/female)	Mean age (years)	ASD subtypes (%)	Ratio of subjects with IQ 70 or higher	Major psychiatric comorbidities (types and proportions)		References
270	31	ASD	88%	Psychotic disorders	21%	Nylander et al. [33]
(187/83)				Mood disorders	17%	
				Anxiety disorders	17%	
				Personality disorders	15%	
129	36	ASD	24%	Anxiety disorder (lifetime)	53%	Buck et al. [34]
(97/32)				OCD (lifetime)	36%	
				Major depressive disorder (lifetime)	13%	
				Psychotic disorder (lifetime)	10%	
129	31	Autism (10%)	Unknown	ADHD	38%	Stahlberg et al. [35]
(79/50)		Asperger (38%)				
		Atypical autism (52%)				
122	29 (median)	Autism (4%)	100%	Mood disorder (lifetime)	53%	Hofvander et al. [36]
(82/40)		Asperger (55%)		Anxiety disorder (lifetime)	50%	
		PDD-NOS (41%)		ADHD (lifetime)	43%	
				OCD (lifetime)	24%	
				Chronic tic disorders (lifetime)	20%	
				Substance related disorders (lifetime)	16%	
				Psychotic disorders (lifetime)	12%	

117	Unknown	Autism (4%)	100%	Obsessive personality disorder (lifetime)	32%	
(77/44)		Asperger (53%)		Avoidant personality disorder (lifetime)	25%	
		PDD-NOS (43%)		Schizoid personality disorder (lifetime)	21%	Hofvander et al. [36]
				Paranoid personality disorder (lifetime)	19%	
				Schizotypal personality disorder (lifetime)	13%	
105	31	Autism (26%)	66%	Personality disorder (lifetime)	15%	
(80/25)	(median)	Asperger (27%)		Mood disorder (lifetime)	13%	Geurts et al. [37]
		PDD-NOS (47%)		Anxiety disorder (lifetime)	10%	
89	37	Atypical autism	60%	Schizophrenia spectrum disorders (lifetime)	35%	
(58/31)				Mood disorders (lifetime)	11%	
				Organic disorders (lifetime)	10%	Mouridsen et al.[38]
				Alcohol or drug use disorder (lifetime)	10%	
84	20	Autism	21%	Mood disorders (12-month prevalence)	17%	
(69/15)				Anxiety disorders (12-month prevalence)	12%	
				Disruptive behavior disorders (12-month prevalence)	12%	Moseley et al. [8]

70 (55/15)	34	ASD	100%	Substance use disorders (lifetime)	30%	Sizoo et al. [39]
63 (41/22)	29	Autism (65%) Asperger (25%) PDD-NOS (10%)	97%	Major depressive disorder (lifetime)	77%	Joshi et al. [10]
				ADHD (lifetime)	68%	
				Social phobia (lifetime)	56%	
				Oppositional defiant disorder (lifetime)	53%	
				Agoraphobia (lifetime)	35%	
				Generalized anxiety disorder (lifetime)	35%	
				Substance use disorders (lifetime)	33%	
				Specific phobia (lifetime)	32%	
				(psychiatric comorbidities under 30% were excluded)		
62 (45/17)	24	Autism	0% (all subjects with intellectual disability)	Major depressive disorder	37%	Bakken et al. [40]
				Anxiety disorder	34%	
				Psychosis	25%	
				OCD	13%	
54 (26/28)	27	Asperger	100%	Major depressive disorder (lifetime)	70%	Lugnegård et al. [41]
				Any anxiety disorder (lifetime)	56%	
				ADHD (lifetime)	30%	
				Recurrent hallucinations (lifetime)	13%	

53*	30	ASD	100%	Major depressive disorder	49%	Rydén et al. [42]
(Unknown)				OCD	23%	
				Social phobia	17%	
				Borderline personality disorder	14%	
				Anorexia Nervosa	13%	
50	36	Asperger	100%	Major depressive disorder (lifetime)	48%	
(34/16)				Phobias (lifetime)	26%	
				Dysthymia (lifetime)	24%	Roy et al. [43]
				OCD (lifetime)	14%	
				Panic disorder (lifetime)	14%	

ASD: autism spectrum disorder, Autism: autistic disorder, Asperger: Asperger's disorder, PDD-NOS: pervasive developmental disorder-not otherwise specified, OCD: obsessive-compulsive disorder, ADHD: attention-deficit/hyperactivity disorder, IQ: intelligence quotient.
*Psychiatric diagnosis prior to assessment in 53 patients with ASD.

emotional dysregulation [108,109], executive dysfunction [51, 110], and deficits in cognition of facial emotion [111], whereas BPD also comprises emotional dysregulation, executive dysfunction (i.e., impairments in attention, flexibility, learning, and planning), and deficits in cognition of facial emotion [112-113]. Additionally, another study showed that patients with ASD and patients with personality disorders (almost all subjects were patients with cluster B or cluster C personality disorder) did not differ in their ability to read and regulate emotions [114]. Moreover, as a common risk factor, both subjects with ASD [67-69] and BPD [115,116] have greater incidences of childhood abuse than healthy controls. For these reasons, both patients with ASD and BPD are susceptible to stressful situations and easily reveal an unstable psychology and impulsive behaviors, for example, intense anger, interpersonal hypersensitivity, self-injuring behaviors, and identity diffusion [117].

Nevertheless, it is important for psychiatrists to distinguish comorbid BPD with ASD ("BPD on ASD") from BPD without ASD ("pure BPD") when planning treatment strategies. Although it is necessary for an ASD diagnosis to confirm a history of developmental disability in early childhood, the following three points may be useful to extract potential autism spectrum ("BPD on ASD") from heterogeneous symptoms superficially diagnosed as BPD [118] especially in females with frequent suicide attempts (≥5 suicide attempts), a lower score in the global assessment of functioning, and absence of comorbid substance abuse [107].

Difficulty in diagnosing mild type of ASD: An epidemiological study showed that the proportion of the total subjects with Asperger's disorder and PDD-NOS in ASD was approximately 67% (Asperger's disorder 9%; PDD-NOS 58%) [119]. As for PDD-NOS, it is not only a milder form of ASD but also has atypical features, that is, social communication deficits without repetitive and stereotyped behaviors [120], most of which meet the diagnostic criteria of social communication disorder in the DSM-5. Furthermore, 88% of individuals with PDD-NOS is within normal intelligence [121]. As stated above, more than half of ASD individuals have an IQ (intelligence quotient) of over 70 [4, 121], and most of their ASD symptom are mild or atypical. On the other hand, most of the previous research on adults with ASD contained a high proportion of subjects with Asperger' s disorder and PDD-NOS, as shown in Table 2. Thus, what we need is to sensitively distinguish mild and atypical autistic traits from potential ASD in individuals with normal intelligence in common clinical settings.

Many individuals with subtle autistic symptomatology, who are cognitively high functioning, are often unrecognized in early childhood [122,123]. Such individuals may repetitively experience interpersonal problems and failed social adaptation without knowledge of their autistic traits until delayed diagnosis of ASD at an adult age [14, 16]. Therefore, the severity of ASD symptom does not necessarily correlate with subjective psychological stress or risk of psychiatric comorbidity since individuals with mild or atypical autistic traits may have been covertly suffering from mental health problems associated with interpersonal friction or maladaptation to society. Even if an adult patient does not have a medical history with an ASD diagnosis in childhood, repetitive discouraging experiences

may be suggestive of potential autistic traits hidden in his or her personal life and history.

In particular, the female gender is more associated with difficulty in detecting mild/atypical autistic traits because females generally show fewer ASD symptoms with age than males due to acquired compensatory social skills [124] and less restricted interests [124,125]. Moreover, there may be a gender bias in ASD diagnosis since girls are less likely to meet diagnostic criteria for ASD than boys even at equivalent levels of autistic traits if they show fewer behavioral problems and normal intellectual level [126]. Meanwhile, abnormal sensory response (e. g., taste, smell and touch response) may be a considerable characteristic of females with ASD and provide a hint for potential ASD diagnosis [124, 127].

The schematic diagram (Figure 1) demonstrates patterns of maladjustment and the process to misdiagnosis in adults with ASD, which can be adapted to other small closed groups like school situations. This schematic diagram might be helpful for readers to understand the major reasons for repetitive discouraging experiences and misdiagnosis with other mental disorders among adult patients with ASD.

Executive functioning and mental health in individuals with ASD: ASD is associated with deficits in executive functioning [51], which covers quick mental shifts, adaptation to diverse situations, initiation and preservation of goal-directed activity, inhibition of inappropriate behaviors and emotional control [128]. Although deficits in executive functioning are not a specific feature of ASD individuals, they have more problems associated with executive dysfunction than healthy controls [108, 129,130]. Furthermore, problems of executive dysfunction are not necessarily related to the severity of ASD symptoms [131-133]. Even though individuals, who at a young age were diagnosed with an ASD, are no longer met diagnostic criteria for ASD with age, these individuals still have more difficulty in several components of executive functioning (e.g., set-shifting and working memory) than healthy controls [130].

Executive functioning is associated with daily living skills in individuals with ASD [110, 134,135]. On the other hand, daily living skills are not strongly dependent on the severity of ASD symptom [136,137]. In fact, many high-functioning individuals with less severe ASD symptoms have deficits in daily living skills [136-138]. It should also be noted that daily living skills are positively correlated with increased independence and optimal outcomes in adulthood [137, 139]. Unfortunately, it was shown that adults with ASD who lived independently and were competitively employed comprised only 12% in ASD subjects whose mean performance IQ was 80 [140], and 24% in ASD subjects whose mean full IQ was 89 [139]. These findings imply that we should assess total mental health and quality of life not only with respect to severity of ASD symptoms or existence of psychiatric comorbidity but also include patients' executive functioning and daily living skills.

The World Health Organization proposes that mental health is a state of well-being in which an individual realizes his or her own ability, can cope with the normal stresses of life, can work productively and is able to make a contribution to his or her community [141]. In other words, it is necessary for individuals with ASD to acquire daily living skills and ability to work for a better quality of life. Figure 2 shows a schematic diagram of the goals of mental health and social life and the necessary approaches to support individuals on the autism spectrum, which is based on previous reports [142-146]. Although executive functioning in individuals with ASD matures at a slower rate than it does in those without ASD [129, 132], clinicians may need to focus not only on alleviation of ASD symptoms and other comorbidities in their treatment but also on improving patients' daily living skills and work capability as interventions for better mental health and social life.

Assessments of adjustment and functioning beyond symptomatology: Although several tools are useful to assess daily living skills and executive functioning in individuals with ASD [147-149], it is still necessary for clinicians to pay attention to a mismatch between patients' intellectual ability (intelligence and academic achievement) and their actual performance or adaptation to their position at work if they are employed [43, 150]. Such a gap can indicate the existence of underlying deficits in executive functioning and/or interpersonal/social skills in adults on the autism spectrum and can sometimes cause deterioration in their mental health. Therefore, beyond symptomatology of ASD and psychiatric comorbidity, clinicians should also focus on patients' cognition and past/current adjustments (e.g., work history, reasons for job changes, work style/performance/productivity, patterns of interpersonal relationship and interpretation of other's thought/feeling).

Even if patients cannot verbally express their inner thoughts and feelings, a careful observation of their behaviors and interaction with others is helpful for therapists to determine adjustment

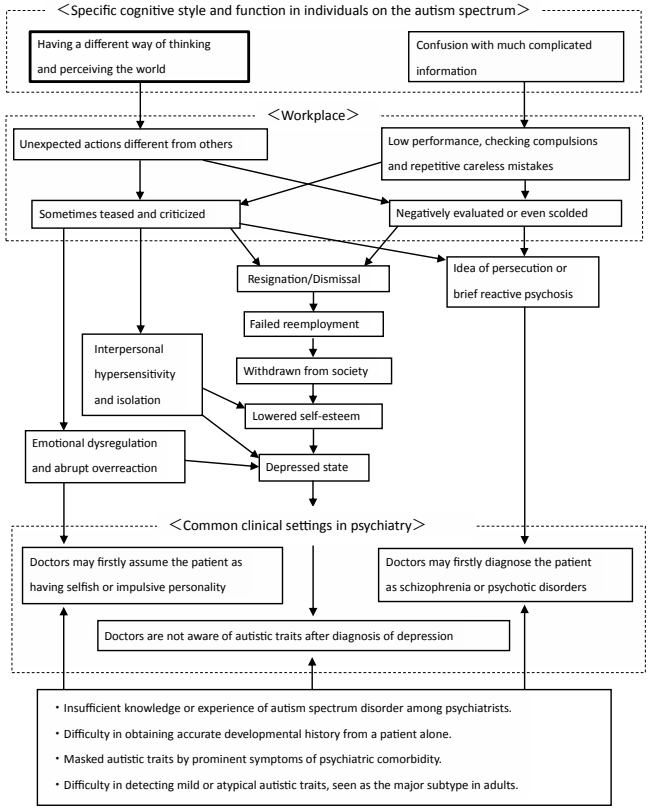

Figure 1: Postulated pathways for patterns of maladjustment and the process to misdiagnosis in adults with autism spectrum disorder.

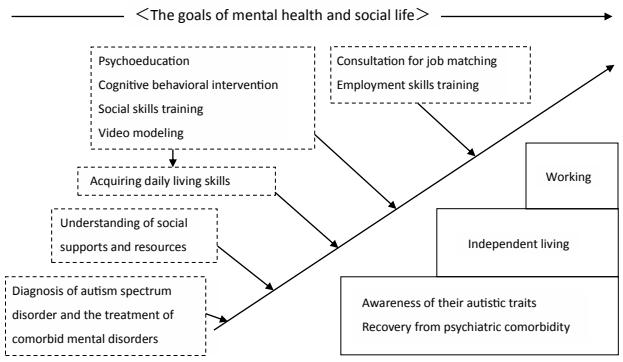

Figure 2: Necessary approaches and supports for the requisite mental health and social life in individuals on the autism spectrum.

problems and executive dysfunction, especially when patients are in a hospitalized situation. Autistic traits can often make their psychiatric comorbidity resistant to standard treatments. In other words, psychiatric comorbidity tends to be prolonged or easily relapses when autistic traits are not dealt with. Therefore, it should be noted that potential autism spectrum is sometimes hidden behind treatment-resistant mental disorders (prolonged illness and frequent relapse) in adult patients with repetitive adjustment problems that do not correspond with their intelligence and ability.

Diagnosing ASD can often improve patients' perspective or lead to positive emotions such as elation and relief [151]. However, being labeled with ASD without intervening management can leave patients disappointed and prejudiced. In order to make their unique features valuable for their work and contribution to society, clinicians should be aware of the specific nature of autistic features (their strengths and difficulties) while referring to information from several guidelines (e.g., NICE clinical guideline 142, AASPIRE Healthcare Toolkit) [152, 153].

Conclusions

Although 7% to 16% of adult patients in the psychiatric clinics or hospitals are finally diagnosed with ASD according to recent studies, ASD is still overlooked or misdiagnosed as other mental disorders (i.e., schizophrenia, mood disorders, and personality disorders) in primary care settings. Several reasons possibly account for this fact, for example, difficulty in obtaining accurate developmental history, insufficient experiences of detecting ASD among clinicians, and mild/atypical autistic traits in contrast to prominent psychiatric comorbidities. Other than diagnostic problems, clinicians should pay more attention to the association between their functioning, adjustment, and mental health beyond symptomatology. For better mental health and social adjustment in patients with ASD, correct diagnosis of ASD, treatments of psychiatric comorbidity, and improvements in functioning and adjustment are comprehensively necessary.

Conflicts of interest

All authors declare that they have no competing interest for this review article.

Authors' contributions

KT designed and collected the studies, interpreted the data, and drafted the manuscript. Tsuyoshi Kondo and Teizo Kuba interpreted the data, and modified the manuscript.

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