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 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/
How and why is autism spectrum disorder misdiagnosed in adult patients?  - From diagnostic problem to management for adjustment -

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

| M | Depression, ODD, ADHD | No | ASD | Unknown | 10 | Mazefsky et al. [28] |
| M | Depression, anxiety disorder, ODD | Anxiety disorder, ADHD | ASD | Unknown | 11 |
| M | Depression, bipolar disorder, Anxiety disorder, ODD, ADHD | Depression | ASD | Unknown | 12 |
| 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, ODD, ADHD | Depression, anxiety disorder | ASD | Unknown | 13 |
| F | Schizophrenia | Schizophrenia | Autism | 11 | 16 | Waris et al. [29] |
| M | Schizophrenia | Schizophrenia | Autism | 14 | 17 |
| M | Schizophrenia | Schizophrenia | Atypical autism | 15 | 16 |
| 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, Bipolar disorder, schizophrenia | 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 | 16 | Van Schalkwyk et al. [32] |
| M | Schizophrenia | Intellectual disability | PDD-NOS | 14 |
| M | Bipolar disorder, psychosis, Schizoaffective disorder | No | Bipolar disorder | Autism | 14 | 21 |
| F | Schizoaffective disorder | No | ASD | After graduating from special school | 19 |

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

<table>
<thead>
<tr>
<th>Number of subjects (male/female)</th>
<th>Mean age (years)</th>
<th>ASD subtypes (%)</th>
<th>Ratio of subjects with IQ 70 or higher</th>
<th>Major psychiatric comorbidities (types and proportions)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>270 (187/83)</td>
<td>31</td>
<td>ASD</td>
<td>88%</td>
<td>Psychotic disorders</td>
<td>Nylander et al. [33]</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Mood disorders</td>
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<td>Anxiety disorders</td>
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<td></td>
<td></td>
<td>Personality disorders</td>
<td></td>
</tr>
<tr>
<td>129 (97/32)</td>
<td>36</td>
<td>ASD</td>
<td>24%</td>
<td>Anxiety disorder (lifetime)</td>
<td>Buck et al. [34]</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>OCD (lifetime)</td>
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<td>Major depressive disorder (lifetime)</td>
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<td></td>
<td>Psychotic disorder (lifetime)</td>
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<td>129 (79/50)</td>
<td>31</td>
<td>Autism (10%)</td>
<td></td>
<td>ADHD</td>
<td>Stahlberg et al. [35]</td>
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<td></td>
<td>Asperger (38%)</td>
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<tr>
<td></td>
<td></td>
<td>Atypical autism</td>
<td>(52%)</td>
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<tr>
<td>122 (82/40)</td>
<td>29 (median)</td>
<td>Autism (4%)</td>
<td>100%</td>
<td>Mood disorder (lifetime)</td>
<td>Hofvander et al. [36]</td>
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<tr>
<td></td>
<td></td>
<td>Asperger (55%)</td>
<td></td>
<td>Anxiety disorder (lifetime)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>PDD-NOS (41%)</td>
<td></td>
<td>ADHD (lifetime)</td>
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<td></td>
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<td>OCD (lifetime)</td>
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<td>Chronic tic disorders (lifetime)</td>
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<td>Substance related disorders (lifetime)</td>
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<td></td>
<td></td>
<td>Psychotic disorders (lifetime)</td>
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<tr>
<td>Study</td>
<td>Sample Size</td>
<td>Diagnosis</td>
<td>Prevalence (Lifetime)</td>
<td>Personality Disorder</td>
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<tr>
<td>Hofvander et al. [36]</td>
<td>(77/44)</td>
<td>Asperger (53%)</td>
<td>25%</td>
<td>Avoidant personality disorder (lifetime)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>PDD-NOS (43%)</td>
<td>21%</td>
<td>Schizoid personality disorder (lifetime)</td>
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</tr>
<tr>
<td>Geurts et al. [37]</td>
<td>(80/25) (median)</td>
<td>Asperger (27%)</td>
<td>13%</td>
<td>Mood disorder (lifetime)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>PDD-NOS (47%)</td>
<td>10%</td>
<td>Anxiety disorder (lifetime)</td>
<td></td>
</tr>
<tr>
<td>Mouridsen et al. [38]</td>
<td>(58/31)</td>
<td></td>
<td></td>
<td>Schizophrenia spectrum disorders (lifetime)</td>
<td></td>
</tr>
<tr>
<td>Moseley et al. [8]</td>
<td>(69/15)</td>
<td>Autism (21%)</td>
<td>17%</td>
<td>Mood disorders (12-month prevalence)</td>
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<td></td>
<td>Alcohol or drug use disorder (lifetime)</td>
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<td>Anxiety disorders (12-month prevalence)</td>
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<td>Disruptive behavior disorders (12-month prevalence)</td>
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<tr>
<td>Study</td>
<td>Sample Size</td>
<td>Diagnosis</td>
<td>Comorbidity</td>
<td>Finding</td>
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</tr>
<tr>
<td>Sizoo et al. [39]</td>
<td>(55/15)</td>
<td>ASD 100%</td>
<td>Substance use disorders (lifetime) 30%</td>
<td>How and why is autism spectrum disorder misdiagnosed in adult patients? - From diagnostic problem to management for adjustment -</td>
<td></td>
</tr>
<tr>
<td>Joshi et al. [10]</td>
<td>(41/22)</td>
<td>Autism (65%) 97%</td>
<td>Major depressive disorder (lifetime) 77%</td>
<td>Substance use disorders (lifetime) 30%</td>
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</tr>
<tr>
<td>Bakken et al. [40]</td>
<td>(45/17)</td>
<td>Autism (65%) 97%</td>
<td>Major depressive disorder (lifetime) 37%</td>
<td>Anxiety disorder 34%</td>
<td></td>
</tr>
<tr>
<td>Lugnegård et al. [41]</td>
<td>(26/28)</td>
<td>Asperger (25%) 100%</td>
<td>Major depressive disorder (lifetime) 70%</td>
<td>Any anxiety disorder (lifetime) 56%</td>
<td></td>
</tr>
</tbody>
</table>

(All subjects with intellectual disability)
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/ataypical 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]. This 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

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**Figure 1:** Postulated pathways for patterns of maladjustment and the process to misdiagnosis in adults with autism spectrum disorder.
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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Submitted Oct 14, 2015
Accepted Nov 18, 2015