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Autism spectrum disorder among first-visit depressed adult patients: diagnostic clues from backgrounds and past history

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ABSTRACT

Objective: The present study aimed to extract discriminating indicators for diagnosis of autism spectrum disorder (ASD) from personal backgrounds and past history among depressed adult outpatients.
Methods: Subjects were 430 depressed adults, consisting of patients with ASD ($n=70$) and those without ASD ($n=360$). Group comparison and discriminant analysis was conducted with regard to backgrounds (age, gender, education, marriage, living alone, physical diseases and family history of mood disorders) and past history (school non-attendance, bullied experience, psychotic-like experiences, conduct problems, suicide-related behaviors and interpersonal friction).
Results: Six discriminating indicators (interpersonal friction, bullied experience, psychotic-like experiences, age under 32 years, school non-attendance and university educational level) were identified by stepwise discriminant analysis ($P<.001$). Absence of the first 4 indicators almost excluded ASD diagnosis with the highest negative predictive value (98%) and the least negative likelihood ratio (0.11) whereas one or more out of these 4 indicators showed low positive predictive value (32%) despite high sensitivity (93%).
Conclusions: The abovementioned 4 indicators may be useful clues to cover possible ASD subjects among depressed adults although further detailed ASD focused diagnostic procedure is absolutely necessary to specify true ASD subjects. Meanwhile, absence of these 4 indicators is probably helpful to rule out ASD diagnosis.

1. Introduction

Autism spectrum disorders (ASDs), known as pervasive developmental disorders in the *DSM-IV-TR* [1], are characterized by qualitative impairments in communication, reciprocal social interaction and the presence of restricted and repetitive behaviours or interests. ASDs include Autistic disorder, Asperger's disorder and pervasive developmental disorder not otherwise specified (PDD-NOS) according to the *DSM-IV-TR*. Autistic disorder is defined the presence of above symptoms and onset of symptoms prior to 3 years. Asperger's disorder is distinguished from Autistic disorder by the lack of delay or deviance in early language development, and does not have clinically significant delays in cognitive development. PDD-NOS does not meet full criteria for either Autistic disorder or Asperger's disorder, but with pervasive deficit in social interaction.

Recently, the prevalence of ASD in adults was estimated to be 0.98% [2], which is almost similar to that found in children [3]. Thus, ASD has nowadays become a more common disorder than previously recognized.

Strang et al. [4] indicated that children and adolescents suffering from ASD even with normal intelligence were at greater risk for depression than those in general population. In ASD adults with normal intelligence, Hofvander et al. [5] reported that the most common life-time comorbidity was mood disorder (53%) (median age of subjects was 29 years). Also, Lugnegård et al. [6] reported that the most common life-time comorbidity was major depression (70%) (mean age of subjects was 27 years). In contrast, the prevalence of life-time major depressive disorder from 18 to 29 years was 12.0% in the United States [7]. In the International Consortium of Psychiatric Epidemiology Surveys, lifetime prevalence of major depressive episodes was from 3.0% in Japan to 16.9% in the US [8]. For these reasons, general psychiatrists might encounter many depressed adult outpatients with ASD in usual clinical settings. Early diagnosis of ASD can help promoting non-pharmacological treatment strategies (psychoeducation, social skills training and environmental rearrangements) especially in workers suffering from ASD with comorbid depressive state. However, less attention to these supports may sometimes mislead to miserable consequences, e.g., prolonged depressive episodes, frequent relapse, development of further comorbidities like anxiety disorders, failed rehabilitation, job loss and social withdrawal. Therefore, it is important for clinicians to know some clues, always prompting them to interview for possible diagnosis of ASD when seeing depressed adult outpatients.

However, mild psychopathology of ASD tends to be easily missed or often masked by prominent depressive symptomatology. In particular, fatigue and psychomotor retardation associated with depression can

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mask such symptoms as social withdrawal and abnormal speech patterns of ASD [9]. Furthermore, ASD adults suffering from depressive symptoms rather showed higher cognitive ability and less social impairment than those without depressive symptoms [10]. Therefore, it is often difficult for clinicians to find out modest autistic traits in depressed ASD patients with high social functioning. In addition, it is also difficult for adult patients to precisely describe their childhood developmental history whereas clinicians cannot timely obtain such information from their parents who do not necessarily preserve old memory as accurate.

Accordingly, simple and useful discriminating indicators for potential ASD, based on the patient's backgrounds and past history, are highly expected before initiating detailed diagnostic interview for ASD. It is more desirable that these indicators can be easily asked by clinicians. Thus, the objective of this study is to clarify clinical indicators to pick up patients with ASD among the overall depressed adult outpatients in usual clinical settings.

2. Methods

2.1. Subjects

We conducted a case-control study in a retrospective manner to extract discriminating indicators for diagnosis of ASD. Subjects were depressed adult outpatients without apparent intellectual problems, i.e., receiving mainstream education, who newly visited our clinic from January 2009 to December 2012. Their age ranged from 18 to 87 years. Their final diagnosis was confirmed in January 2014. Among 483 depressed patients who were collected from the medical records, 53 patients (9% of total) did not have precise description of their backgrounds and personal history, and thereafter were excluded from the study as missing data. Ultimately, we extracted 430 depressed outpatients, whose mean age (±Standard Deviation) was 40.4 (±14.7) years and proportion of females was 60%. These depressed patients included the patients with adjustment disorder (n=89), major depressive disorder (n=215) and bipolar disorder (n=126).

2.2. Diagnostic procedure of ASD subjects

Axis-I psychiatric morbidity was assessed using the Structured Clinical Interview for *DSM-IV* Axis I Disorders (SCID-I) [11]. Although psychotic symptoms such as hallucinations and delusions were noted separately during the SCID-I interview, there were no patients fulfilling the sufficient criteria for the diagnosis of schizophrenia and other psychotic disorder. *DSM-IV-TR* criteria was used for diagnosis of ASD. Developmental history in ASD subjects was confirmed from their parents by the psychiatrists who were qualified as Certified Supervising Psychiatrist of the Japanese Board of Psychiatry, and were in charge of outpatient clinic for both child-adolescent and adult psychiatry. Parents were requested to bring suitable records (maternal and children health handbook, school reports in primary and middle school) as references. The criteria for the allocation to the ASD group were the Autism-Spectrum Quotient Score of at least 26, explained in the next section, and a confirmation of diagnosis in an expert interview. Among 430 depressed subjects, 70 subjects were diagnosed as ASD (ASD group).

2.3. Assessment the autistic traits of ASD subjects

We assessed the autistic traits of ASD subjects by the Japanese version of Autism-Spectrum Quotient (AQ-J) [12]. The original version of AQ is a 50-item self-administered questionnaire for adults with normal intelligence to assess the presence of autistic traits, which consists of five domains such as social skill, attention switching, attention to detail, communication and imagination [13]. The AQ score ranges from 0 to 50, and the higher AQ score indicates higher autistic tendency. Although AQ is not a diagnostic tool, it is a useful screening tool [14]. For AQ-J, its most optimal cut-off score for distinguishing ASD from non-ASD subjects was 26 or more, with modest sensitivity (0.76)/specificity (0.71), low positive predictive value (0.24) and high negative predictive value (0.96) [12].

2.4. Backgrounds and past history for analyses

As the candidates for discriminating indicators of ASD, the following factors were selected from various studies. These were patients' backgrounds (age, gender, education level, marital history, living alone, physical diseases [15,16] and family history of mood disorders [17]), age of onset for psychiatric comorbidity, and past history affecting social function and adjustment (school non-attendance [18–20], bullied experience [21–23], psychotic-like experiences [6,24,25], conduct problems [26,27], suicide-related behaviors [24,28] and interpersonal friction at work/school [29]). These variables can be easily asked by clinicians without information from parents of the patients. Presence or absence of these variables were confirmed by simply answering either "yes" or "no" by patients. For bullied experience, we asked such questions like "Have you ever been bullied during your school days? For example, being frequently targeted or routinely harassed in any way?". For interpersonal friction at work/school, we asked questions like "Have you ever experienced interpersonal problems at work/school? For example, having a quarrel or an interpersonal conflict with colleague or your boss?".

2.5. Statistical analyses

Abovementioned variables were compared between depressed subjects with ASD and those without ASD. Comparisons (Table 1) were made by using the Mann–Whitney U test (for continuous variables), the chi-squared test (for categorical variables) or Fischer's exact test (when one of the expected values in a 2×2 table is less than 5). The step-wise discriminant analysis with Maha-lanobis' distance measure (Table 2) was performed to reveal possible contributing factors for ASD diagnosis among the overall depressed subjects. The best cut-off point for ASD diagnosis when using significant discriminators (Table 3) were examined by calculating the area under the curve (AUC) of the receiver operating characteristic curve. An AUC >0.7 is generally considered an acceptable test performance [30]. The optimal cut-off point was calculated as the best balance in a trade-off between sensitivity and specificity, using maximal values derived from the Youden Index, i. e., sensitivity+specificity−1 [31].

SPSS 19.0 for Windows (SPSS Japan, Tokyo, Japan) and XLSTAT version 2014. 1 (Addinsoft, Tokyo, Japan) were used for the statistical analyses. A two-tailed P value less than .05 was regarded as statistically significant.

2.6. Ethics

We had informed the patients of anonymous inclusion of our ASD subjects in this retrospective study and the data analyses as coded and grouped on the Web site of our department, together with information that the study was approved by the Ethics Committee of the University of the Ryukyus. These also included the sentence that the participants could withdraw from this study without any penalty or loss of benefits for their treatments, although no patients refused to participate in this study.

3. Results

3.1. Diagnostic profiles of ASD subjects

Seventy (16%) out of 430 total depressed adults were diagnosed as ASD. Among these 70 subjects with ASD, the majority was 45 subjects diagnosed as PDD-NOS (64%) while 6 subjects were diagnosed as autistic disorder (9%) and 19 subjects as Asperger's disorder (27%).