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Psychiatric comorbidity in persons with high-functioning autism spectrum disorders: Findings from a tertiary care neuropsychiatric hospital

Abhinav Nahar[a], Harish Thippeswamy[a,*], Mukku Shiva Shanker Reddy[a], M. Thomas Kishore[b], Santosh K. Chaturvedi[a]

[a] Department of Psychiatry, National Institute of Mental Health and Neuro Sciences (NIMHANS), Bengaluru, 560029, India
[b] Department of Clinical Psychology, National Institute of Mental Health and Neuro Sciences (NIMHANS), Bengaluru, 560029, India

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ABSTRACT

Background: The literature on co-morbid psychiatric illnesses in adults with high-functioning autism (HFA) spectrum disorder is sparse.
Purpose: To examine the nature of psychiatric comorbidity and treatment response in adults with HFA spectrum disorder.
Materials and Methods: Case records of subjects (age ≥17 years) who presented over a period of 16 years with primary psychiatric symptoms and further detected to have an HFA spectrum disorder, were analyzed. Autism spectrum disorders (ASD) along with near normal to normal verbal communication and general intelligence were considered as HFA spectrum disorders.
Results: 33 subjects met the study criteria. Nine subjects (27%) were diagnosed to have an underlying Asperger's syndrome and the rest 24 (73%) had pervasive developmental disorders unspecified (PDD NOS). None of the subjects were diagnosed to be suffering from ASD prior to the visit to our hospital. Mean age at the time of psychiatric consultation was 22.7 (s.d = 4.8) years and mean age at the onset of psychiatric comorbidity was 16.48 (s.d = 4.4) years. Nearly half of the sample had more than one type of psychiatric illness. Most common lifetime psychiatric diagnosis was obsessive-compulsive disorder (OCD) (n = 16, 48.4%). Bipolar disorder (BD) was the second most common type of psychiatric manifestation (n = 13, 39.3%) followed by psychotic spectrum disorders (n = 9, 27.2%). Overall response to treatment was minimal.
Conclusions: Individuals with HFA spectrum disorders suffer from multiple psychiatric comorbidities. OCD is the most common type of psychiatric comorbidity followed by BD and psychotic spectrum disorders. Comorbid psychiatric illnesses in individuals with HFA show poor response to treatment.

1. Introduction

Autism spectrum disorders (ASD) are characterized by persistent impairment in reciprocal social communication and interaction, restricted and repetitive patterns of behavior, interests, or activities, which are present from early childhood and are not explained better by intellectual disability or global developmental delay (American Psychiatric association, 2013). Studies from Asia, Europe, and North America have reported prevalence rates for ASD in the range of 1% to 2% for ASD (Hossain et al., 2017). Individuals with ASD with near normal to normal intelligence levels are considered to have high-functioning autism (HFA) spectrum disorders (Goldstein et al., 2008). Such individuals are likely to present to a psychiatrist for their interpersonal problems or comorbid psychiatric illness during adulthood (Joshi et al., 2013; Simonoff et al., 2013). Understanding the clinical outcomes of ASD in adults would help in the planning of services to improve the quality of life (Buck et al., 2014).

Higher rates of comorbid depression and anxiety disorders have been reported in adult subjects with HFA spectrum disorder (Marriage et al., 2009; Rydén and Bejerot, 2008). Prevalence rates of psychosis and obsessive-compulsive disorder (OCD) have been found to be higher among persons with HFA spectrum disorder as compared to the general population (Russell et al., 2005; Hofvander et al., 2009; Joshi et al., 2013). Psychiatric comorbidities in ASD are now being identified as independent diagnoses as compared to the past practice of attributing the psychiatric manifestations solely to underlying autism (Romero

* Corresponding author.
E-mail addresses: abhinavnahar2002@gmail.com (A. Nahar), docharisht@gmail.com (H. Thippeswamy), shivakmc55@gmail.com (M.S. Shanker Reddy), mtkpsy@gmail.com (M.T. Kishore), skchatur@gmail.com (S.K. Chaturvedi).

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et al., 2016). Analysis of comorbid psychiatric manifestations in ASD helps to understand the etiology and improves the process of nosology (Gadow et al., 2012). The comorbid psychiatric symptoms can have atypical manifestations and pose difficulty in recognition of symptoms (Giovinazzo et al., 2013). Further, co-occurring psychiatric conditions among adults with ASD have considerable influence on the clinical outcomes (Buck et al., 2014).

The literature on comorbid psychiatric illnesses in adults with HFA spectrum disorders is sparse despite the likely detrimental impact of psychiatric comorbidities on educational, social, community participation and employment outcomes (Giovinazzo et al., 2013; Lever and Geurts, 2016). The current study was undertaken to examine the nature of comorbid psychiatric symptoms and their response to treatment in adults with HFA spectrum disorder at a tertiary care neuropsychiatric hospital.

2. Materials and methods

This study is a retrospective chart review of persons diagnosed with HFA spectrum disorders who were evaluated at the National Institute of Mental Health and Neuro Sciences (NIMHANS), Bangalore, India, from the year 2000 to 2016. The study was approved by the Institute ethics committee. NIMHANS is a well-known psychiatric research Institute in India with a postgraduate residency training program and provides both inpatient and outpatient care. Subjects are initially screened for psychiatric symptoms and are further evaluated in detail, as clinically indicated. The detailed evaluation of the subjects is done by a postgraduate resident doctor using a semi-structured clinical proforma. The case histories are then discussed with a consultant followed by a clinical interview for final diagnosis as per 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) (World Health Organization, 1992). Case records of subjects (age ≥17 years) with ASD and behavioral symptoms without any clinical history suggestive of intellectual impairment were scrutinized. Subjects were first evaluated clinically for impairment in intelligence and were referred for a formal intelligence testing if an impairment was found. Individuals with HFA, without any clinical evidence for impairment of intelligence or with an intelligence quotient (IQ) more than 70 on formal testing were included in the study. Socio-demographic details, birth, and developmental history, vocational history, education level, clinical diagnosis, family history, psychiatric comorbidity, medication details, psychological assessments and improvement of symptoms based on clinical observation were noted.

3. Results

During the mentioned review period, 33 subjects were identified to have HFA spectrum disorder out of total 169,596 subjects who consulted adult psychiatry services. Twenty-five (75.6%) subjects availed inpatient services. Twenty-six (78%) subjects were males and 7 (22%) were females. None of the subjects were diagnosed to have a HFA spectrum disorder prior to their visit to our hospital. The mean age of the subjects at the time of consultation to NIMHANS was 22.76 (SD = 4.8; range = 17–37) years. One subject had not received formal education. The mean number of years of a formal education for rest 32 subjects was 11.72 (SD = 2.9) years. Among these, 10 (30.3%) subjects were either pursuing or had completed a graduation. Only 2 subjects who had completed graduation were employed and none of the subjects were married (Table 1).

Nine subjects (27%) were diagnosed to have Asperger's syndrome and the rest 24 (73%) subjects were diagnosed as having pervasive developmental disorders unspecified (PDD NOS). There was no language delay in any of the 33 subjects. Special skills in music, calendar calculation, mathematics, and painting were present in 7 of the 9 subjects with Asperger's syndrome. IQ assessment using standardized intelligence scales was done for 11 subjects who were suspected to have intellectual impairments on initial clinical evaluation and all 11 subjects were found to have an IQ of 70 and above (Mean = 83; SD = 13). The family history of mental illness was present among 7 (21.2%) subjects. Seizure disorder was present in 4 (12.1%) subjects (generalized seizures and focal seizures in two subjects each).

Table 1
Socio-demographic profile and clinical details of adults with high functioning autism (N = 33).

Variable	n (%)
Male	26 (78.7%)
Mean age at which ASD was Diagnosed (Years)	22.76 ± 4.88
Mean no. of years of education	11.72 ± 2.9
Married	0 (0)
Still pursuing education	4 (12.1%)
Employed	2 (6.0%)
Significant antenatal events	3 (9.0%)
Birth asphyxia	7 (21.2%)
Seizure disorder	4 (12.1%)
Generalized seizures	2 (6.05%)
Focal seizures	2 (6.05%)
Subjects who underwent IQ testing	11(36.7%)

3.1. Birth and developmental history

Mothers of 3 (8.8%) subjects had significant antenatal events with 2 mothers having a history of pre-eclampsia and one mother having typhoid fever at six months gestation. Twenty-one subjects (63%) were the firstborn in the birth order. All subjects were born out of singleton pregnancies. Five subjects (15%) were born through a caesarian section and 28 through vaginal delivery (85%). Among 28 subjects who were born through vaginal delivery, there was a history of prolonged labor in 8 subjects (28.6%) and 6 of these subjects had forceps-assisted delivery. Only one subject had a pre-term delivery (3%). Birth asphyxia was reported in 7 (21%) subjects.

3.2. Comorbid psychiatric manifestations

Remaining 31 (94%) subjects had atleast one type of prominent psychiatric manifestation (Table 2). The mean age at the onset of psychiatric comorbidity was 16.48 (SD = 4.4) years. Fifteen (45.4%)

Table 2
Psychiatric comorbidities in adults with high functioning autism (N = 33).

Comorbid psychiatric illness	n (%)
Subjects with psychiatric comorbidity	31 (93.9%)
Subjects with more than one psychiatric diagnosis	15 (45.4%)
Obsessive-compulsive disorder (OCD)/OC symptoms	11/5
Lifetime diagnosis	16 subjects
Current	15 subjects
Bipolar affective disorder (BD)	13 subjects
Lifetime diagnosis	10 subjects
Current	
Psychotic spectrum disorder	9 subjects
Lifetime diagnosis	9 subjects
Current	
Depression	1 subject
Lifetime diagnosis	0
Current	
Substance use disorder	1 subject
Lifetime diagnosis	1 subject
Current	
Behavioral addiction	3 subjects
Lifetime	3 subjects
Current	
ADHD	4 subjects
Lifetime diagnosis	2 subjects
Current	

subjects had more than one type of psychiatric manifestation. OCD was the most common lifetime psychiatric diagnosis and was present among 16 subjects (48.4%), followed by bipolar affective disorder (BD) in 13 subjects (39.3%), psychotic spectrum disorders in 9 subjects (27.2%) and depressive disorder in 1 subject (3%). Insight was recorded as partial to poor in all subjects who presented with OCD. Substance use in the form of cannabis harmful use was present in 1 subject (3%) and behavioral addictions in the form of computer gaming and internet addiction were present in 3 subjects (9%). Lifetime diagnosis of attention-deficit hyperactivity disorder (ADHD) was present in subjects (12%). Only 2 subjects (6%) did not have any psychiatric comorbidity and they presented with complaints of poor social interaction and stereotyped patterns of behavior and interests.

Among 33 subjects, 23 (69.6%) received antipsychotics, 13 (39.3%) received antidepressants, 17 (51.5%) received mood stabilizers, and two (6.0%) received benzodiazepines. Four subjects (12%) developed extrapyramidal symptoms, one subject (3%) developed tardive dyskinesia while on anti-psychotics and another subject (3%) developed hyperammonemia while on valproate. In addition to pharmacotherapy, 8 subjects (24.2%) received individual therapy in the form of anger management techniques, problem-solving skills; 4 subjects (12.1%) received social skill training, 3 subjects (9%) received vocational training, and subjects (12.1%) received behavioral therapy.

3.3. Response to treatment

The overall improvement was found to be minimal in 11 out of 15 subjects (73.3%) with OCD. The minimal improvement pattern was observed in 6 out of 7 subjects with psychosis (85.5%) and 9 out of 11 subjects with BD (81.8%).

4. Discussion

This study was undertaken to examine the nature of psychiatric comorbidity in adults with HFA spectrum disorders. We observed high rates of psychiatric comorbidity in the form of OCD, BD, psychotic spectrum disorders as compared to the earlier studies where depression and anxiety disorders were reported to be common (Joshi et al., 2013; Hofvander et al., 2009; Mazzone et al., 2012). This observation could be due to a referral bias and also for the reason that milder symptoms of anxiety and depression may have escaped attention from individuals and their family members.

OCD was the most common psychiatric diagnosis in our sample and was observed in nearly 50% of the subjects, a rate much higher when to compared to findings from earlier studies (Joshi et al., 2013; Rydén and Bejerot, 2008; Hofvander et al., 2009). A significant overlap of the underlying neural mechanisms of the repetitive behaviors might be the reason for the frequent comorbidity of OCD and ASD (Joshi et al., 2013). Autism-related obsessive-compulsive (OC) phenomena comprise of excessive involvement into one or more circumscribed special interests, repetitive mannerisms, insistence on sameness. These phenomena can be difficult to delineate from typical OC symptoms. Autism-related OC phenomena are usually considered to be ego-syntonic, do not normally cause functional impairment and are accompanied by euphoria rather than anxiety or guilt. However, they can be comorbid with ego-dystonic OCD symptoms causing further difficulty in the delineation of symptoms. Additionally, there can be a progression from autism-related OC phenomena to typical OC symptoms (Fischer-Terworth and Probst, 2009). Our finding of poor insight in persons with comorbid OCD is in line with the earlier findings (Kaur et al., 2016). Poor insight in OCD is associated with an inadequate response to treatment (Kishore et al., 2004a;Kishore et al., 2004b Catapano et al., 2001; Erzegovesi et al., 2001). Nearly, one-third of the study subjects had a lifetime diagnosis of BD. In an earlier study, up to a quarter of subjects with ASD had a lifetime diagnosis of BD (Joshi et al., 2013). However, the rates for comorbid bipolar spectrum disorders have varied widely (3–75%), possibly due to a referral bias (Hofvander et al., 2009; Munesue et al., 2008; Ghaziuddin et al., 1998). In our study, subjects with comorbid BD were treated with either atypical antipsychotics alone or in combination with a mood stabilizer. The overall response to treatment was poor to modest. We also found a higher level of comorbid psychotic spectrum disorders as compared to the previous studies and the overall response to antipsychotics was poor (Joshi et al., 2013; Hofvander et al., 2009; Roy et al., 2015).

Our study finding poor response of all comorbid psychiatric conditions to treatment is striking. Lack of uniformity in documentation prevented us from analyzing the reasons for poor response to treatment. The possible reasons for poor response to treatment could be the higher severity of the comorbid conditions in view of presentation to a tertiary care center, poor insight, and poor compliance. The higher rates of psychiatric comorbidities in our study as compared to earlier studies could be due to the disparity in hospital setting and methodological differences. Subjects in our study consulted general adult psychiatric services unlike in other studies wherein subjects were evaluated for psychiatric comorbidity at a specialty clinic (Joshi et al., 2013; Marriage et al., 2009; Rydén and Bejerot, 2008; Hofvander et al., 2009). The influence of settings on under-diagnosis and over-diagnosis of comorbid psychiatric disorders is quite well-known in other developmental disorders, particularly the intellectual disability (Kishore et al., 2004a,b).

Functioning of the subjects in our study was observed to be impaired across various domains, particularly the occupational functioning. None of the subjects in our sample were married or were in a relationship. Most subjects were staying with their parents and were dependent on them. It is very likely that comorbid psychiatric illnesses may have contributed to the overall socio-occupational dysfunction. A lower level of occupational and social functioning in adults with autism spectrum disorder has been previously reported (Joshi et al., 2013; Rydén and Bejerot, 2008). In this regard, it would be interesting to compare the socio-occupational functioning in HFA spectrum disorders with and without comorbid psychiatric disorders in order to examine the role of comorbidities.

Prenatal factors such as exposure to environmental chemicals and drugs, maternal infections during pregnancy, pre-eclampsia, diabetes mellitus, and autoimmune conditions have been found to be associated with increased risk of ASD. In addition, perinatal factors like birth asphyxia, intrauterine growth retardation, and delivery by cesarean section, are associated with increased risk for ASD (Ornoy et al., 2016; Curran et al., 2015). In our study, adverse antenatal events were present in only a small proportion of subjects but a substantial number had history of birth asphyxia (21.2%).

The limitations of our study include a retrospective approach that limits the verification of the details documented in the charts, referral bias of severe cases reporting to tertiary care settings, small sample size, and lack of a comparison group. Reliance on clinical assessments and minimal use of structured interview schedules and psychological instruments add to the limitations. We were also not able to establish the reasons for the lack of diagnosis of ASD prior to the contact with our services. The awareness about ASD is reported to be low in the community and parents may not seek psychiatric consultations unless there are significant behavioral disturbances (Daley, 2004; Kishore and Basu, 2011);

The present study highlights the presence of psychiatric comorbidity in the form of OCD, BD, and psychotic spectrum disorders among adults with HFA spectrum disorders. The response to treatment was generally poor and there was a significant socio-occupational dysfunction in such individuals. Further research is needed in the area of psychiatric comorbidity and its management among individuals with HFA spectrum disorders.

Declaration of interest

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