

Depression in Children with Autism/Pervasive Developmental Disorders: A Case-Control Family History Study

Mohammad Ghaziuddin^{1,2} and John Greden¹

Limited information is available about the occurrence of depression in children with autism and other pervasive developmental disorders (PDD). Although depression has been described in autistic children, questions about its validity have often been raised. One approach to address this issue is to investigate family histories of those autistic children diagnosed with clinical depression. Based on data available in nonautistic children, autistic children with depression would be expected to show an increased family history of depression. Since studies of this nature have not been attempted in autistic children, we compared the family history of 13 autistic/PDD children with depression (11 male; 2 female; M full-scale IQ 86.2, SD 24.2; M age 10.4 years, SD 2.2) with 10 autistic/PDD children without a history of current or previous depression (9 male; 1 female; M full-scale IQ 67, SD 12.9; M age 10.5 years, SD 1.6). Diagnosis of depression was based on the DSM-III-R criteria and confirmed independently by two psychiatrists. Ten (77%) of the depressed children had a positive family history of depression compared to 3 (30%) of the nondepressed group, $t(21) = -2.4$; $p = .02$. These findings lend support to the validity of depression as a distinct condition in some children with autism/PDD and suggest that, as in the normal population, autistic children who suffer from depression are more likely to have a family history of depression.

KEY WORDS: Depression; autism; pervasive developmental disorders; family history.

INTRODUCTION

Autism is a neurodevelopmental disorder characterized by a distinct pattern of social deficits, communication impairment, and a restricted range of interests (Lord & Rutter, 1994). It is classified among a group of conditions collectively termed as pervasive developmental disorders (PDD) of which it forms the main prototype (American Psychiatric Association [APA], 1987, 1994). While considerable research has been done exploring the origins of this disorder since its first description by Kanner (1943), little attention has been paid to the occurrence of psychiatric disor-

ders that can occur in persons with autism. This appears to be particularly true of depression. Lainhart and Folstein (1994) suggested that depression may be underdiagnosed in persons with autism. After a comprehensive computer-assisted search, they could identify only 17 published cases that contained enough information to be included in the review. Besides, most of the published work on this topic appears to be confined to adults. For example, Lainhart and Folstein found only two patients younger than 10 years of age in their review.

Despite the paucity of literature on this topic, reports have continued to describe the occurrence of depression in autism, although no causal links have been proposed between the two conditions. In a series of five adults with autism/PDD, Clarke, Littlejohns, Corbett, and Joseph (1989) described a

¹University of Michigan, Ann Arbor, Michigan 48109-0390.

²Address all correspondence to Mohammad Ghaziuddin, Taubman Center Box 0390, University of Michigan Medical Center, 1500 East Medical Center Drive, Ann Arbor, Michigan 48109-0390.

23-year-old man with autism and depression. Gillberg (1985) described a patient with Asperger syndrome, a type of PDD, who developed bipolar disorder with a positive family history of that disorder. Realmoto and August (1991) described three patients with autism and catatonia and proposed that autistic persons with comorbid psychiatric conditions, such as bipolar disorder, may be susceptible to catatonia. Ghaziuddin and Tsai (1991) described the presentation and treatment of depressive illness in a 17-year-old patient with Down syndrome and autism. The same authors later studied an outpatient sample of 68 children and adolescents with autism and found that 6 (9%) patients suffered from an associated psychiatric disorder; 3 of these 6 patients (50%) were clinically depressed (Ghaziuddin, Tsai, & Ghaziuddin, 1992). In a recent inpatient study, Ghaziuddin, Alessi, and Greden (1995) investigated the role of life events in the onset of depression in 11 children with autism/PDD and found that, as in the normal population, depressed children with autism/PDD were more likely to have sustained a higher prevalence of life events compared to those without comorbid depression.

Despite the emerging interest in the occurrence of depression in autism, the critical issue continues to be one of diagnostic validity. Since no standardized instruments currently exist for the diagnosis of depression in this population, it can be argued that what is being labeled as depression may reflect a constellation of vague behavioral symptoms. After all, depression itself is a heterogeneous condition that can be "characterized by anything from an exaggeration of the occasional lowering of mood seen in most people from time to time to frank psychosis, and by impaired social functioning that ranges from none to severe" (Rutter, 1990, p. 61).

One approach to investigate the diagnostic validity of depression in autism is to study the family psychiatric history of autistic patients diagnosed with depression (Lainhart & Folstein, 1994). In the general population, the risk of depression is increased in the parents of depressed children. Presence of a positive family history of depression is often taken as a factor in making a diagnosis of depression in both children and adults. Children with depressed mothers, for example, are more likely to have an earlier onset of depression compared to those with nondepressed mothers (Weissman et al., 1987). Some family studies of autistic probands have suggested an increased risk for depression in first-degree relatives.

For example, DeLong and Dwyer (1988) reported increased rates of bipolar disorder among relatives of autistic probands. Piven et al. (1990) also found elevated rates of mood disorders in relatives of autistic probands compared to controls. However, it is not known if this increased risk in relatives is correlated with a history of depression in the autistic probands. This issue is important because increased rates of depression in the first-degree relatives of autistic probands with depression would lend support to the diagnostic validity of depression in this population (Lainhart & Folstein, 1994). Since studies of this nature have, to our knowledge, not been attempted in children with autism, the aim of the present study is to compare the family history of depressed autistic/PDD children with a control group of nondepressed children with autism/PDD. Based on evidence from general population, we hypothesize that depressed autistic/PDD children show a higher prevalence of depression in their first-degree relatives than nondepressed children with autism/PDD.

METHOD

The study was conducted at the University of Michigan Child Psychiatry inpatient unit over a period of 4 years. This short-term 10-bed unit is staffed by two board-certified child psychiatrists; two child psychiatry fellows; and a multidisciplinary team consisting of paramedical personnel such as speech therapists, teachers, and social workers. To be eligible, patients had to be at least 7 years old and have a full-scale IQ of 50 or above. This IQ score cutoff was chosen because assessment of depression in children with severe or profound mental retardation is extremely difficult. Also, at the time of the evaluation, patients had to be living with at least one biological parent who was able to give a detailed family history. Biological parents (one or both) were directly interviewed about the family psychiatric history in the first-degree relatives. Family history was collected blind to the group membership (depressed vs. nondepressed) and was based on the Family History Research Diagnostic Criteria (FH-RDC; Andreasen et al., 1977). No attempt was made to differentiate between the onset of depression in parents before and after the birth of the child since it was assumed that the impact of stress of bringing up a child with chronic disabilities will be equally applicable to both the groups.

Diagnosis of pervasive developmental disorders was based on the DSM-III-R criteria (APA, 1987). Patients underwent a standard diagnostic protocol consisting of parent interviews, psychiatric observation of the child, psychological testing, educational assessment, and speech and language evaluation. The Autism Behavior Checklist (ABC; Krug, Arick, & Almond, 1980), completed by one or both parents and/or caregivers, was also used to provide additional information. Patients who met less than the required 8 of the criteria on the symptom checklist of autistic disorder were given a diagnosis of pervasive developmental disorders not otherwise specified (PDDNOS).

Diagnosis of depression was based on the DSM-III-R criteria and included the categories of major depression, dysthymia, and depression not otherwise specified. These were further divided into two groups: definite depression and probable depression. As explained in detail elsewhere (Ghaziuddin et al., 1995), assessment was based on a checklist derived from the DSM-III-R. Only those with definite depression were included. Also, to increase the homogeneity of the two groups (depressed vs. nondepressed), patients had to be depressed at the time of the evaluation; those with a past history suggestive of depression were excluded. Moreover, although irritability alone may qualify for the diagnosis of dysthymia in children, clear evidence of depressed mood was necessary for inclusion in the study. This is because many autistic children may, at times, show symptoms of irritability and temper tantrums that may not indicate underlying depression. Therefore, for a diagnosis of depression, a history of depressed mood, either with a clear onset or a history of a qualitative change in mood suggestive of depression, was necessary. The Reiss scale (1990), a comprehensive measure for assessment of psychopathology in children with mental retardation and psychiatric disorders, was also used to support the clinical diagnosis, where applicable. This is an observer-rated scale that takes into account the last 3 months of behavior and is completed with the help of direct-care-givers. Except in one subject, the scale was completed in all those who were mentally retarded. A "best estimate" diagnosis was arrived at within a week of admission on the basis of all available information. Subsequently, another child psychiatrist evaluated the data and confirmed the diagnosis. Patients were excluded if agreement between the two psychiatrists was not reached. Because of the difficulty inherent in performing structured psychiatric interviews in this population, no such inter-

views were attempted (Young, O'Brian, Gutterman, & Cohen, 1987).

The sample overlapped with that from our earlier study that investigated the role of life events and depression in children with autism/PDD (Ghaziuddin et al., 1995). Eighteen autistic/PDD children with depression were eligible to participate in the study. However, 2 depressed patients were excluded because family history was not available (patients were adopted); 1 patient was excluded because depression was categorized as doubtful; 1 was excluded because the full-scale IQ was lower than 50; and another was excluded because agreement was not reached between the investigators regarding the presence of depression. The final sample, therefore, consisted of 13 patients with autism/PDD with comorbid depression (11 male; M full-scale IQ: 86.2, SD 24.2; M age: 10.4 years, SD 2.2; 2 autistic disorder, 11 PDDNOS). Six patients met the criteria for major depression, while the remaining 5 were categorized as suffering from depressive disorder not otherwise specified. Controls were chosen from a pool of nondepressed autistic/PDD patients admitted consecutively to the same unit during the same index period, and matched on age, sex, and as close to the IQ as possible (9 male; M full-scale IQ: 66.9, SD 12.9; M : 10.5 years, SD 1.6; 4 autistic disorder; 7 PDDNOS). Four patients in the depressed group and 6 in the nondepressed group were mentally retarded (full-scale IQ < 70).

Fisher's Exact Test (two-tailed) was used to determine the significance of the results.

RESULTS

Ten of the 13 (77 %) patients with depression gave a family history of depression in either parent, compared to 3 of the 10 (30%) in the controls, $t(21) = -2.4, p = .02$. The two groups did not differ so far as the mean age and the sex distribution were concerned. However, there were significant differences between the two groups in their IQ distribution; depressed patients had a higher full-scale IQ than the nondepressed group (M : 86 vs. 67; unpaired $t = 2.3, p = .03$). These results are shown in Table I.

DISCUSSION

Most of the depressed children presented with a positive family history of depression: 77% of de-

Table I. Differences Between Depressed and Nondepressed Patients

	Depressed	Nondepressed	<i>p</i>
Male: Female	11:2	9:1	ns
Age (years, <i>M</i> ± <i>SD</i>)	10.4 ± 2.2	10.5 ± 1.6	ns
Full-scale IQ (<i>M</i> ± <i>SD</i>)	86 ± 24	67 ± 13	.03
Family history of depression [(n(%))]	10 (77)	3 (30)	.02

pressed autistic/PDD children had a family history of depression compared to 30% of patients without depression. These results, which suggest that children with autism/PDD who suffer from depression are more likely to have parents with a history of depression compared to nondepressed children with autism/PDD, are consistent with those noted in children without autism/PDD. In the absence of standardized measures for the assessment of depression in autism, the findings provide support to the diagnostic validity of depression in this group of patients (Lainhart & Folstein, 1994).

Aggregation of depressive disorders seen in some families with autistic children could result from several mechanisms. First, depression in parents of disabled children could be the result of the stress involved in bringing up such children. Such a mechanism is not likely to operate in the present study because the control group also consisted of patients with similar disabilities. Second, it could be due to the effect of environmental stressors and life events. However, while there is some evidence that children with autism/PDD who get depressed present with an increased prevalence of life events prior to the onset of their depression (Ghaziuddin et al., 1995), it is not known how this relates to the presence of family history of depression in this group of patients. Finally, it may reflect underlying genetic mechanisms common to both disorders, at least in some individuals with autism (Smalley, 1991).

One reason why few reports have investigated the presence of depression in children with autism is the complicating variable of mental retardation. In this study, we attempted to control for this variable by excluding children with severe mental retardation (i.e., those with a full-scale IQ lower than 50). Therefore, the finding of excess family history of depression in the depressed group cannot be attributed to mental retardation. However, it is important to note that the depressed group did have a significantly higher full-scale IQ compared to the nondepressed group. The significance of this is unclear. It may be

that depressed children with autism have a higher IQ or that those with a higher IQ are more likely to report depression; at the same time, it may also mean that depression is more likely to be suspected and diagnosed in the presence of relatively higher level of intelligence.

Although this was not an epidemiological study, the fact that 13 patients were diagnosed with definite depression over the index period emphasizes the importance of screening for mood disorders in this population. That patients with a full scale IQ under 50 and those with "doubtful" depression were excluded suggests that the actual rate of depression, at least in children referred for inpatient services, is likely to be higher than that obtained in this study. For example, Richard, a 10-year-old, was admitted following a suicidal gesture. He had wrapped a tape round his neck and attempted to put a pair of scissors to his neck. He had also attempted to jump out of the bedroom window because of increasing difficulties at school resulting from his social awkwardness and idiosyncracies. He was described as intelligent but odd with a verbal IQ of 117, a performance IQ of 84 and a full-scale IQ of 101. Among other problems, he had told a class-mate that he wanted to rape her. He had never been diagnosed as autistic/PDD in the past. On admission, a diagnosis of PDDNOS was made. However, his father decided to discharge him against medical advice before his mood disorder could be fully evaluated. Thus, despite preliminary evidence that he might have been depressed, he was excluded from the sample because the diagnosis was not established. At the same time, it is important to note that the findings are based on an inpatient sample where children with severe psychopathology are admitted. Therefore, it is unclear to what extent the results can be generalized to outpatients and to community samples. Another point that needs to be emphasized is that the sample consisted of prepubertal children. To what extent, therefore, the results apply to adolescents and adults with autism and depression is not known.

In conclusion, this preliminary study of depression in children with autism and depression found increased family history of depression. These findings are consistent with those seen in the normal population and provide support to the validity of depression in some children with autism/PDD. From a clinical standpoint, the findings underscore the importance of screening for depression in children with autism, especially when there is a family history of that disorder. Studies are needed to investigate the presentation of mood disorders in autistic children and explore the mechanism of coaggregation of autism and depression seen in some families.

ACKNOWLEDGMENT

The authors acknowledge that support of Norman Alessi, MD, and staff of the inpatient unit.

REFERENCES

- American Psychiatric Association. (1987). *Diagnostic and statistical manual of mental disorders* (3rd ed., rev.). Washington, DC: Author.
- American Psychiatric Association (1994). *Diagnostic and statistical manual for mental disorders* (4th ed.). Washington, DC: Author.
- Andreasen, N. C., Endicott, J., Spitzer, R. L. and Winokur, G. (1977). The family history method using diagnostic criteria. Reliability and validity. *Archives of General Psychiatry*, 34(10), 1229-1235.
- Clarke, D. J., Littlejohns, C. S., Corbett, J. A., & Joseph, S. (1989). Pervasive developmental disorders and psychoses in adult life. *British Journal of Psychiatry*, 155, 692-699.
- DeLong, G.R., and Dwyer, J. T. (1988). Correlation of family history with specific subgroups: Asperger syndrome and bipolar affective disorder. *Journal of Autism and Developmental Disorders*, 18, 593-600.
- Ghaziuddin, M., & Tsai, L. (1991). Depression in autistic disorder. *British Journal of Psychiatry*, 159, 721-723.
- Ghaziuddin, M., Tsai, L., & Ghaziuddin, N. (1992). Comorbidity of autistic disorder in children and adolescents. *European Child and Adolescent Psychiatry*, 1(4), 209-213.
- Ghaziuddin, M., Alessi, N., and Greden, J. (1995). Life events and depression in children with Pervasive Developmental Disorders. *Journal of Autism and Developmental Disorders*, 25, 495-502.
- Gillberg, C. (1985). Asperger's syndrome and recurrent psychosis—A case study. *Journal of Autism and Developmental Disorders*, 15, 389-397.
- Kanner, L. (1943). Autistic disturbances of affective contact. *Nervous Child*, 2, 217-230.
- Krug, D. A., Arick, J., & Almond, P. (1980). Behavior checklist for identifying severely handicapped individuals with high levels of autistic behavior. *Journal of Child Psychology and Psychiatry*, 21, 221-229.
- Lainhart, J. E. & Folstein, S. E. (1994). Affective Disorders in people with autism: A review of published cases. *Journal of Autism and Developmental Disorders*, 24, 587-601.
- Lord, C., & Rutter, M. (1994). Autism and other pervasive developmental disorders. In M. Rutter, E. Taylor, & L. Hersov (Eds.), *Child and Adolescent Psychiatry, Modern Approaches* (3rd ed.). Oxford, U.K.: Blackwell.
- Piven, J., Gayle, J., Chase, G. A., Fink, B., Landa, R., Wzorek, M. A., & Folstein, S. (1990). A family history study of neuropsychiatric disorders in the adult siblings of autistic individuals. *Journal of the American Academy of Child and Adolescent Psychiatry*, 29, 177-183.
- Realmoto, G. M., & August, G. J. (1991). Catatonia in Autistic Disorder: A sign of comorbidity or variable expression. *Journal of Autism and Developmental Disorders*, 21, 517-528.
- Reiss, S. (1990). *Reiss Scales for Children's Dual Diagnosis (mental retardation and psychopathology)*. Worthington, OH: International Diagnostic Systems, Inc.
- Rutter, M. (1990). Commentary: Some focus and process considerations regarding effects of parental depression on children. *Developmental Psychology*, 26, 60-67.
- Smalley, S. (1991). Genetic influences in autism. *Psychiatric Clinics of North America*, 14, 125-139.
- Weissman, M. M., Gammon, G. D., John, K., Merikangas, K. R., Warner, V., Prusoff, B. A., & Sholomskas, D. (1987). Children of depressed parents. Increased psychopathology and early onset of major depression. *Archives of General Psychiatry*, 44, 847-853.
- Young, J. G., O'Brian, J. D., Gutterman, E. M., & Cohen, P. (1987). Research on the clinical interview. *Journal of the American Academy of Child and Adolescent Psychiatry*, 26, 613-620.