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Depression in Persons with Autism: Implications for Research and Clinical Care

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Although several studies have investigated the occurrence of medical and neurological conditions in persons with autism, relatively few reports have focused on the phenomenology and treatment of psychiatric disorders in this population. There is emerging evidence that depression is probably the most common psychiatric disorder that occurs in autistic persons. In this review, we examine the factors that influence the presence of depression in this population, such as the level of intelligence, age, gender, associated medical conditions, and the role of genetic factors and life events. We discuss the various forms of treatment available and highlight the need for early detection.

KEY WORDS: Autism; Asperger syndrome; depression treatment; comorbidity; outcome.

INTRODUCTION

Autism is a neurodevelopmental disorder characterized by reciprocal social deficits, communication impairment, and a range of rigid ritualistic interests (Lord and Rutter, 1994). Although a variety of medical disorders have been described in this condition, relatively little is known about its pattern of psychiatric comorbidity (Ghaziuddin *et al.,* 1992). Although large-scale epidemiological studies have not been done, clinic-based studies on this topic suggest that depression is perhaps the most common psychiatric diagnosis. Mood symptoms in autism have been described since the earliest descriptions of the disorder. For example, several children in Kanner's original series showed symptoms of anxiety and undue fear of objects and events, whereas at least one showed a tendency to lapse into a "momentary fit of depression" (Kanner, 1943). Rutter also noted the occurrence of depression in his series (Rutter, 1970). Earlier studies consisted mainly of case reports and case series (Komoto *et al.,* 1984; Clarke *et al.,* 1989; Ghaziuddin and Tsai, 1991). In a study of 64 children and adolescents with autism referred to a tertiary clinic, Ghaziuddin *et al.* (1992) found that depression was the most common psychiatric disorder, affecting about 2% of the total sample. This figure was probably an underestimate because direct interviews focusing on the presence of depression were not conducted. Studies of higher-functioning persons with autism, including those with Asperger syndrome (often regarded as a milder variant of autism), have yielded higher estimates. For example, in Wing's series of 34 adults with Asperger syndrome, the most common psychiatric diagnosis was depression, occurring in at least 10 subjects (about 30%) (Wing, 1981). Similar rates were reported by another study of Asperger syndrome using different methods of assessment (Ghaziuddin *et al.,* 1998). Based on semi-structured interviews, the authors found that depression was the most common diagnosis in adolescents and adults, occurring in 13 of 35 subjects (37%) with Asperger syndrome (Ghaziuddin *et al.,* 1998). Again, in Tantam's series of 60 subjects with social eccentricity/Asperger syndrome, depression was the

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most common diagnosis (Tantam, 1988). Lainhart and Folstein (1994) reviewed the literature on affective disorders in autism and, on the basis of the 17 published cases, suggested that the condition was underdiagnosed. More recent findings have been consistent with these studies. In a questionnaire study of 59 children with autism and Asperger syndrome, Kim and colleagues (2000) found that compared with a community sample of 1751 children, those with autism and Asperger syndrome showed increased rates of mood and anxiety problems. Although major depression (APA, 1994) is perhaps the most common condition, other types of mood disorders, such as bipolar disorder, have also been reported. For example, Gillberg described a patient with Asperger syndrome with a positive family history of bipolar disorder who later developed an episode of that disorder (1985). Realmuto 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. Although depression itself is a heterogeneous condition "characterized by anything from an exaggeration of the occasional lowering of mood seen in most people from time to time to frank psychosis" (Rutter, 1990, p. 61), the present review focuses mainly on the occurrence of major depression (unipolar depression) in autism. The concept of comorbidity has been the subject of ongoing discussion (see Caron and Rutter 1991), but the main purpose of this report was to examine the correlates and consequences of the co-occurrences of autism and depression, without suggesting a direct link between them. Studies of major depression, especially those published since the last review by Lainhart and Folstein (1994), are examined, and implications for research and clinical care discussed.

PHENOMENOLOGY

Presentation of depression in autism depends on a variety of factors. Apart from the more general symptoms of persistent sadness and loss of interest in usual activities, depressed autistic persons may present with certain unique features. Because of their deficits in affective and cognitive systems (Hobson, 1989; Rutter, 1983), persons with autism find it difficult to understand the emotions and feelings of others and of themselves. Kanner proposed that autistic children come "into the world with innate inability to form the usual, biologically provided affective contact with people" (Kanner, 1943). This difficulty in connecting with other people may be related to their deficits in integrating affect with attention, and to their restricted range of emotional expression (Capps *et al.*, 1993). For example, people with autism are known to have difficulties with facial expressions (Macdonald *et al.*, 1989) and with matching their facial expressions with their feelings. At times, the facial expressions might seem inappropriate to the social situation. Sometimes their difficulty in showing appropriate emotional reactions may be compounded by their poverty of nonverbal communication, including the use of gestures (Attwood *et al.*, 1988). However, difficulty in understanding and expressing emotions and feelings does not necessarily confer immunity against a common psychiatric illness such as depression. Although autistic people may at times show inappropriate responses, there is little evidence that they are immune or resistant to experiencing negative affect. Besides, experiencing affective states is not an all-or-none phenomenon. Just as people with autism, contrary to popular belief, can form attachments to their caregivers (Sigman and Mundy, 1989), they can also experience feelings of depression and sadness, although the way in which these are expressed is often different.

FACTORS AFFECTING THE OCCURRENCE OF DEPRESSION

Age

Most of the cases of depression in autism have been described in adolescents or young adults. While this may in part be due to problems of assessment of psychiatric disorders in children, clinical experience suggests that the rate of depression in autism and related disorders rises with age (Ghaziuddin *et al.*, 1998). Thus, some of the behavioral deterioration that occurs in autistic children at the time of adolescence may be related to the emergence of depressive symptoms. The same may apply to older adults with autism, although very little is presently known about the health care needs of older individuals with autism (Howlin, 1997).

Gender

Although Lainhart and Folstein (1994) found an excess of females in the published reports, it is not known if depression is indeed more common in females than in males with autism, because most of these reports are based on clinic samples. However, because females with autism are generally more impaired than males, it is important to investigate if the occurrence of depression is correlated with the severity of depres-

sive symptoms. No gender differences are found before puberty, but women are known to suffer from a higher prevalence of depression than men in the general population. Studies have suggested that changes in androgen and estrogen levels are responsible for the increase of depression seen in girls around puberty (Angold *et al.,* 1999). Similar studies have not been done in persons with autism and related disorders.

Other Psychiatric Disorders

In the general population, depression often occurs with other psychiatric conditions, such as anxiety disorders. Autistic patients with depression also often show evidence of other psychiatric symptoms. Some depressed patients may show an increase in their obsessive-compulsive behaviors, and, quite often, these behaviors tend to become morbid in nature. Ruminations and perseverations may become intense (Ghaziuddin *et al.,* 1995). An increase in stereotypic behaviors, such as rocking and flapping of hands, may also occur, especially in low-functioning persons. Similarly, symptoms of hyperactivity can sometimes be mixed with depression. Preliminary data suggest that a significant number of higher functioning children with autism/Asperger syndrome present with hyperactivity, impulsivity, and distractibility (meeting the criteria for the diagnosis of attention deficit hyperactivity disorder) in their prepubertal years and with depressive symptoms during adolescence (Ghaziuddin *et al.,* 1998).

Other Medical Disorders

Autism occurs with known medical conditions in at least 10% of cases (Rutter *et al.,* 1994). These conditions may increase the vulnerability to depression and modify its symptoms. For example, seizure disorder occurs in about 30% of persons with autism, usually around adolescence or before 5 years (Volkmar *et al.,* and Nelson, 1990). Association of seizure disorder with depression is well established (Hermann *et al.,* 2000). However, it is not known to what extent the risk of depression is increased in autism in the presence of seizures. The same applies to mental retardation. Because mental retardation alone increases the risk to psychiatric disorders (Rutter *et al.,* 1976) and about 70% of patients with autism suffer from mental retardation, the risk of depression in autism is likely to be increased in the presence of mental retardation. However, systematic studies have not been done to investigate this issue, in part because the diagnosis of depression in people with mental retardation, especially in those with severe and profound degrees of retardation, is extremely difficult (Sovner and Hurley, 1983).

POSSIBLE CAUSAL MECHANISMS

Depression is caused by a variety of factors, both genetic and environmental. Relatively little is known about the causes that underlie the occurrence of depression in persons with autism. However, based on preliminary reports, a few generalizations can be made.

Genetic Factors

Family genetic factors play an important role in the etiology of depression in the general population, in both children and adults (Sullivan, Neale, & Kendler, 2000). Autistic children who suffer from depression are more likely to have a family history of depression (Ghaziuddin & Greden, 1998). Although depression does not appear to be part of the broader phenotype of autism (Bolton *et al.,* 1998), it is possible that autism with comorbid depression may form a distinct subgroup. De Long and Dwyer (1988) proposed an etiological relationship between Asperger syndrome and bipolar disorder. In a family history study of a sample of autistic subjects grouped on the basis of language function, they found that the rate of bipolar disorder in the first-degree relatives with high-functioning autism, especially Asperger syndrome, was higher than that of the general population. DeLong (1999) put forth the hypothesis that there are two distinct forms of autism. One form is characterized by bilateral damage to the brain in early life (e.g., tuberous sclerosis), and the other, more common idiopathic form, is related to familial mood disorders, and is a severe early-life form of major mood disorder itself (DeLong, 1999). Although no direct link can be proposed between autism and depression at this stage, the two disorders seem to cluster in some families, suggesting that in a subgroup of patients, common genetic factors may be responsible. Studies have also found an excess of depression in first degree relatives of autistic persons compared with controls with Down syndrome; this excess of depression in families does not seem to be related to the stress of raising a child with autism (Piven and Palmer, 1999). Furthermore, it has been shown that parents of autistic children who show altered serotonin levels themselves score high on depression and anxiety symptoms (Cook *et al.,* 1994), which suggests an interplay of common neurochemical factors between depression and autism, at least in some cases.

Life Events

Life events play an important role in the onset of depression (Kendler *et al.,* 1999). Negative events such as death, parental divorce, and so on have been linked with clinical depression in both children and adults. Studies in autistic persons have yielded similar findings, suggesting that autistic children who develop clinical depression experience more negative life events compared with controls. Thus, in a study of 11 subjects with autism and depression, Ghaziuddin and colleagues (1995) found that the depressed group had experienced an excess of negative life events, such as bereavement, parental marital discord, and others in the 12 months before the onset of depression. Similar studies have not been done in adults with autism. Another issue that needs to be investigated is the interaction between the level of functioning and the response to life events. It is not clear, for example, if high-functioning subjects respond more severely to negative life events than those who have varying degrees of mental retardation. It is likely that autistic persons who respond with depressive symptoms to negative events do so because they are genetically predisposed to depression, although systematic studies of this nature have not been done. Thus, it remains to be seen to what extent the response to life events and the onset of depression in this group is mediated by genetic factors. Although adverse events are known to trigger depressive episodes, there is growing evidence that both depression and adversity (as measured by life events) are familial and genetically influenced (Plomin and Bergman, 1991).

COMPLICATIONS

The prognosis of autism is determined mainly by the level of intelligence and of communication (Rutter, 1973). However, clinical evidence suggests that the presence of psychiatric disorders, especially depression, may also affect the long-term outcome of autism. The effects of depression can be wide ranging, both on the patient and on the family. Depressive symptoms can result in increasing social withdrawal and oppositional and aggressive behavior and can interfere with the person's placement in the community. In some cases, catatonia may develop as a complication. In this condition, the patient becomes extremely slow in his movements, and shows regression of self-care skills. In a recent study, Wing and Shah (2000) found a high prevalence of catatonia in referrals autistic persons to a tertiary diagnostic center. Of a total of 506 children and adults referred to the center, 30 presented with features of catatonia. While the psychiatric diagnosis of these patients was not given, there were several features in the history, such as an onset after exposure to stressful events, which suggested that a substantial number could have been clinically depressed. In extreme cases, suicidal behavior can also result. For example, in one series of 149 patients with schizoid personality disorder, defined in a manner closely resembling Asperger syndrome, Wolf (1995) found that six (4%) committed suicide. In this context, it is worth noting that no systematic study has focused on the correlates of suicidal behavior in persons with autism.

Depression in the child with autism can affect the family in several ways. Children with autism who suffer from comorbid depression are more likely to have parents with a history of depression than those who do not suffer from depression. Apart from this reason, depression in the child can result in a variety of behavioral problems, in particular aggression, that can have a negative impact on the family and on social relationships. (Kim *et al.,* 2000). Increased rates of depression and other behavioral problems in siblings can also occur (Gold, 1993).

ASSESSMENT OF DEPRESSION

Features in High-Functioning Autistic Persons

Because the diagnosis of depression depends primarily on verbal and communication skills, verbal autistic persons are better able to communicate their depressive symptoms than those who are lower functioning. However, even in the higher-functioning group, expression of feelings such as sadness is difficult. Of particular diagnostic value is a recent change in the character and flavor of autistic preoccupations. Obsessions and rituals in autism are often viewed as anxiety-reducing behaviors that provide the autistic child with an element of control (Jolliffe *et al.,* 1992). However, in some cases, an increase in these behaviors may index the onset of depression. For example, a high-functioning autistic youngster with a special interest in science and space may become fixated on the "dark hole of space" and overtaken with fear that he might fall into the "space-hole" and disappear (Ghaziuddin *et al.,* 1998). In addition, there may be increasing social withdrawal, beyond what is considered "normal" for the autistic individual. Other patients may show an apparent increase in obsessive-compulsive behaviors, such as repeatedly washing hands. Features such as crying spells, a persistently depressed mood, sleep disturbance, and prob-

lems with appetite, can also be present. Sometimes, a total loss of interest in the usual autistic preoccupations may herald the onset of depression. Some authors have suggested that higher-functioning persons with autism may be more vulnerable to depression than those who suffer from comorbid mental retardation. Support for this view comes from the reports that autistic individuals with normal intelligence consider themselves less competent and tend to have a lower self-worth (Capps *et al.,* 1995). Also, the more able the autistic person, the higher the reported social adjustment and the ability to understand others, and the more negatively they tend to view themselves (Sigman *et al.,* 1997). This suggests that higher-functioning people, because of their vulnerability to lower self-worth, may be more predisposed to depression. However, there is no systematic epidemiological evidence to support this view. The same possibility applies to persons with Asperger syndrome (see Ghaziuddin *et al.,* 1998). It has been speculated that persons with Asperger syndrome are more prone to depressive episodes than those with traditional autism. For example, Rourke *et al.,* (1989) suggested that children and adolescents with nonverbal learning disability are prone to depressive episodes. Because there is some neuropsychological overlap between nonverbal learning disability and Asperger syndrome, the prevalence of depression may be increased in this group, although no studies have specifically investigated this issue.

Features in Low-Functioning Autistic Persons

Assessments of depression in lower functioning persons depends more on the presence of the so-called vegetative signs of depression than on the presence of depressed mood. These signs include a change in the level of functioning, regression of skills, such as incontinence, severe appetite, sleep and weight disturbance, and, in some cases, presence of aggression. While every aggressive outburst does not suggest the presence of underlying depression, every autistic person who has a recent history of aggressive outbursts, in the setting of irritability, and sleep and appetite disturbance, should be screened for depression. This is especially true in those who are lower functioning. Presence of a family history of depression in first-degree relatives is of obvious diagnostic significance in both high- and low-functioning autism. In some cases, unusual features, such as catatonia and other "psychotic behaviors," may suggest the presence of depression. Despite the difficulties involved in the assessment of depression in low-functioning autistic persons, rating scales and instruments designed for persons with mental retardation, such as the Reiss scales (1990), may be useful.

TREATMENT ISSUES

Few studies have focused on the treatment of depression in persons with autism. However, findings from intervention studies suggest that a variety of psychosocial techniques and psychopharmacological agents can be adapted for this purpose. Although psychodynamic psychotherapy is of limited value in the treatment of persons with autism (Riddle, 1987), some high-functioning individuals with good verbal skills may benefit from it, if the approach used is highly structured and directive (Wing, 1983). Most studies advocate the use of a structured form of psychotherapy, along with appropriate behavioral and educational interventions. In more able and older persons with autism, cognitive-behavioral strategies may help to cope with anger and depression, although these are seldom successful in isolation (Howlin, 1998).

Disruptive behavior may serve a combination of functions, such as the need to seek attention, to escape from stressful situations, to obtain stimulation, and to avoid unwanted events (Durand and Carr, 1991). While disruptive behavior may be a symptom of depression, other causes should be carefully examined. Thus, when behavioral and mood symptoms occur, patients should be carefully screened for environmental stresses, including physical illnesses (Ghaziuddin, 1988). People with autism are not able to "mind-read," that is, to understand other people's ideas, feelings, and emotions, which may contribute to their social problems (see Baron-Cohen, 1995). Since social problems may compound the occurrence of depression, recent approaches incorporating interventions based on the "theory of mind" deficits should be tried.

In addition to behavioral and psychological interventions, medications are being increasingly used for the control of mood and behavioral symptoms in autism. However, despite the current popularity of psychopharmacologic agents, little systematic research has focused on their use in persons with autism. Ideally, medications should be used as part of a comprehensive treatment package, using other types of treatments as well. In their survey of psychotropic drug use in 109 subjects with higher-functioning autism and other pervasive developmental disorders, Martin and colleagues (1999) found that the most commonly used medications were antidepressants. About a third of the subjects (31.1%) were receiving antidepressants during

the index period of the study. Selective serotonin reuptake inhibitors (SSRIs) are being increasingly used in autism, because of their role in the control of depression and aggression. However, a recent review of these agents in autism concluded that of the 40 studies, only 6% were controlled trials (King, 2000). Some reports have speculated on the use of SSRIs for a variety of symptoms of autism, such as language impairment (DeLong *et al.*, 1998), whereas others have proposed that they work best in the presence of depression (Ghaziuddin *et al.*, 1991). Reports have also described the use of non-SSRI antidepressants in persons with autism, even when the symptoms of depression are not marked (e.g., Hollander *et al.*, 2000; Steingard *et al.*, 1997). Neuroleptics alone or in combination are seldom effective (Lainhart and Folstein, 1994), although they may have a role in some patients who show psychotic features with depression. Interestingly, there have been a few reports of the use of electroconvulsive therapy in persons with "developmental disabilities," many of whom suffer from autism. While the core symptoms of autism do not respond to electroconvulsive therapy (Bertagnoli & Borchardt, 1990), this form of treatment should be reserved for life-threatening and refractory forms of depression. A recent report, for example, described the successful treatment of catatonic stupor and depression in a 14-year-old boy with autism (Zaw *et al.*, 1999).

CONCLUSION

Depression is a common psychiatric illness, with an annual prevalence of about 10% and a lifetime prevalence of about 17% (Angst, 1999). It can occur with a variety of neuropsychiatric conditions, including autism. Although its exact prevalence in the community is not known, clinic-based studies suggest that depression is probably the most common psychiatric disorder seen in persons with autism. Depressed people with autism present with a wide range of symptoms ranging from irritability and sadness to aggressive outbursts and suicidal behavior. These symptoms can cause problems both to the patient and his family, at times leading to institutional care. While depression can be reliably diagnosed in high functioning persons using the same criteria as for the general population, the diagnosis can be extremely difficult in those with severe cognitive and communication impairment. It is important, therefore, to maintain a high index of suspicion, especially when there is history of a recent change in the level of functioning, particularly around puberty. A variety of factors may contribute to the emergence of depression. While in some cases depression in autism could occur by chance, in others it could result from a combination of genetic or environmental factors or both. Indeed, depression seems to cluster in some families with autism, although there is no evidence at this stage that it forms part of the broader phenotype of autism. Presence of other medical disorders, such as seizure disorder, may also contribute to the association. Future studies should compare the prevalence of depression in autism with that complicating other developmental disorders, particularly in community samples. Impact of depression on the long-term outcome of autistic persons should be examined and systematic studies undertaken to investigate the presentation of symptoms, especially in those who suffer from marked communication deficits. In addition, efforts should be made to examine the efficacy of treatment, including the use of medications and psychotherapy. While treatment of depression does not cure autistic symptoms, it often results in a substantial degree of improvement in the quality of life of the affected person and lessens the burden of care of the family.

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