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DEPRESSIVE DISORDERS IN ADULTS WITH DOWN SYNDROME

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"[D]epression has been diagnosed in persons with Down syndrome...[and]...reports demonstrate that diagnostic validity is enhanced when behaviors, rather than subjective feelings, are emphasized as criteria and care is taken to rule out all other medical and psychiatric conditions."

Depression is one of the most frequently diagnosed psychiatric disorders for persons with mental retardation,^{3,17} especially those with Down syndrome.^{6,7,13,22} Prevalence rates range from 6 and 13% for both groups and parallels rates of depression for the general population.²⁶ For adults with Down syndrome, case studies describe depressive symptoms often presenting as behavioral changes such as withdrawal, loss of adaptive living skills, and observable changes in mood. In addition to severe behavioral problems, psychotic features are also a common manifestation of depression.^{12,21,23,25} It is, therefore, critically important that care providers recognize symptoms of depression and consider this diagnosis prior to assuming that such individuals may have Alzheimer's disease or a psychotic disorder, for both would lead to inappropriate treatment.

OVERVIEW OF THE DIFFICULTIES IN DIAGNOSING DEPRESSION IN PERSONS WITH DOWN SYNDROME

The diagnosis of depression is complicated for persons with Down syndrome because of impaired verbal ability, conceptual thinking, and overall cognitive functioning. They all limit the individual's participation in the psychiatric interview process. When mental health clinicians meet with a patient to formulate the diagnosis and treatment plan, they rely on standard diagnostic criteria developed by the American Psychiatric Association.^{1,2} Many of these criteria are based

upon the self-report of subjective feelings (such as verbal expressions of sadness or worthlessness). It is, therefore, of limited value in diagnosing persons who have diminished ability for articulating thoughts and feelings.¹⁸ Also, care providers, also unfamiliar with psychiatric symptomatology, may be aware of critical changes, but not report them to mental health or medical providers due to a lack of understanding of the significance of such manifestations.^{16,19}

The expressive and adaptive limitations of this population may also increase the likelihood of misdiagnosis, particularly of a psychotic disorder, because behavioral changes may appear odd or worrisome to providers unfamiliar with persons who have mental retardation.²⁰ Hallucinatory-like self-talk, skill loss or extreme withdrawal, which frequently accompany a depressive disorder in persons with Down syndrome, may be inaccurately diagnosed as a full-blown psychotic disorder. For this population, diagnosis may also be complicated by medical conditions such as hypothyroidism, vitamin B₁₂ deficiency, and Alzheimer's dementia, all of which have symptoms that can mimic depression.^{10,11,14,22}

Depression and Alzheimer's Dementia

To further complicate matters, depression may coexist with Alzheimer's dementia.^{11,14} In this case, prompt treatment of depression will preserve functioning for some time, even though a downhill course may be inevitable. The following symptoms can be seen in both depression and Alzheimer's dementia: loss of adaptive skills; disruption of sleep cycle; appetite changes; apathy; moodiness; irritability; aggressiveness; psychomotor agitation or retardation; and memory loss. Alzheimer's dementia is particularly difficult to rule out because there is no definitive test for this disorder, and medical providers make the diagnosis by exclusion, i.e., they cannot find another cause for the noted problems.^{10,11}

TABLE 1. PERCENTAGE OF DSM-IV SYMPTOMS OF DEPRESSION

DISPLAYED BY SAMPLE (N=40)

DSM-IV Symptoms of Depression	Percentage
Sadness or unhappiness (also described as loss of liveliness, humor, or spontaneity)	100%
Apathy, loss of interest/participation in activities including withdrawal from family and friends	100%
Loss of self-care or independent skills	70%
Noticeable change in eating habits; less\more	55%
Noticeable change in sleeping habits; less\more	73%
Psychomotor agitation	73%
Psychomotor retardation (activity slowdown)	83%
Loss of energy or overly fatigued	93%
Loss of focus, concentration, or task completion	83%
Self-absorbed, inattentive, or unresponsive (to people\things)	88%
Increase in irritated mood or moodiness	78%
Inappropriate fears or avoidances of people\things	60%
Psychotic features (extreme withdrawal, hallucinatory self-talk, etc.)	70%

Despite these difficulties, depression has been diagnosed in persons with Down syndrome.^{12,21,23,25} These reports demonstrate that diagnostic validity is enhanced when behaviors, rather than subjective feelings, are emphasized as criteria and care is taken to rule out all other medical and psychiatric conditions. Additionally, these studies suggest that differential diagnosis of depression and Alzheimer's dementia can be accomplished by paying close attention to symptom course. Depression tends to show an up-and-down pattern of decline that with time and treatment will show improvement and an eventual return to pre-morbid levels of functioning. Symptoms of Alzheimer's dementia tend to fluctuate in the early stages, but over time will show a progressive and nonreversible pattern of decline.^{11,14,25}

Co-morbid Psychiatric Disorders

Individuals who are suffering from depression may also concurrently have another psychiatric disorder (called a co-morbid condition). A large and growing body of literature has shown a significant co-morbidity of depressive and anxiety disorders.^{27,28} Symptoms of anxiety are common and associated with depressive symptoms in the literature on persons with mental retardation.^{3,12,17,21,25} Behavioral and obsessive-compulsive disorders are also common disorders found in the literature on people with mental retardation.^{3,6,9,17,24}

A SURVEY OF DEPRESSIVE DISORDERS IN A SAMPLE OF PERSONS WITH DOWN SYNDROME

In this article, we will review our clinic findings for 40 people with Down syndrome who were diagnosed with depressive disorders and present five illustrative case examples. These patients were followed in the Adult Down Syndrome Center, a multidisciplinary clinic that follows 272 adults with Down syndrome.⁸ About one-third of these 272 patients use the clinic for their primary care. Another third uses the clinic for yearly physical assessments and continues to be followed by other primary care physicians. The remaining patients come to the clinic for annual assessments and use its resources for the diagnosis and treatment of specific issues, such as depression. (For additional information about the Center and its referral base see Chicoine et al.⁸)

Study Sample

There were 40 patients in the sample, 23 men and 17 women. The average age was 31 with an age range from 19 to 58. These individuals were followed over a period of 36 months (from January 1992 to January 1995).

TABLE 2. PERCENTAGE OF DSM-IV COMORBID DISORDERS DISPLAYED BY SAMPLE (N=40)

DSM-IV Co-morbid Disorders and Symptoms	Percentage
Medical condition, hypothyroid disorder	22%
Medical condition, vitamin B ₁₂ deficiency disorder	2%
Anxiety disorder (agitation, body tension, hyperactivity, and self-injurious behavior)	35%
Behavior disorder (verbal and physical aggression)	12%
Behavioral symptoms (verbal but not physical aggression)	22%
Obsessive-compulsive symptoms (most often as increase in pre-existing compulsions)	33%

Diagnostic Criteria

Depression

A diagnosis of depression was made by the authors in collaboration with psychiatric and other medical consultants. A thorough medical examination was performed at the time of diagnosis to rule out any medical cause of symptoms.⁸ The criteria used were taken from the Diagnostic and Statistical Manual of Mental Disorders, Third Edition - Revised (DSM-III-R),¹ adjusted for the adaptive and expressive limitations of this population.^{16,19} The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV),² which was available in the later months of the study period, was used as well. The criteria used with this sample emphasized the use of caregiver reports and observable behaviors and were similar to those developed by Sovner¹⁹ for persons with mental retardation.

Co-morbid Psychiatric Disorders

Due to the absence of adequate criteria in the literature, the diagnosis of a co-morbid anxiety disorder was based on an adaption of DSM-III-R criteria by the authors. The criteria used in this sample was similar to a measure by Vitello and colleagues²⁴ for diagnosis of obsessive-compulsive disorder. Vitello et al's measure relied on observed symptoms of this disorder (such as irrational repetitious behaviors) because of the difficulties in self-reporting of anxiety by persons with mental retardation. Similarly, the criteria used to diagnose anxiety disorders in this sample relied on observed indicators of anxiety (such as agitation, restlessness and increased body tension) rather than self-reporting of anxious thoughts and feelings. Diagnosis was nonetheless complicated because symptoms, such as agitation and restlessness, overlap both depressive and anxiety disorders. Because of this, an anxiety disorder was diagnosed only when the severity and persistence of such symptoms were clearly noted by caregivers and other observers.

Adaptive and Cognitive Function

No formal evaluation of cognitive functioning was completed as part of the diagnostic evaluation. To assist in clinical diagnosis, estimates of participants' pre-symptomatic, adaptive living skills were obtained from caregivers.

Survey Results

Of the 40 individuals diagnosed with depressive disorders, 16 were diagnosed with major depression alone, 14 with major depression and co-morbid disorders, and 10 were diagnosed with mood disorder due to a general medical condition. Nine of the latter ten had hypothyroidism, and one other had a vitamin B₁₂ deficiency. These individuals were treated both for the medical condition and their depression (which was treated with antidepressant therapy and supportive counseling). Table 1 presents the symptoms displayed by our patients. Table 2 displays the co-morbid problem findings and Table 3 presents five illustrative case histories.

Depressive Symptom Presentation

For the 16 individuals diagnosed with major depression, symptoms included fatigue or exhaustion, the appearance of sadness (described also as a loss of liveliness, humor and spontaneity), loss of concentration or task completion, irritability and moodiness, increase in aggressive verbal behaviors, agitation, sleeping disturbance, weight loss or gain, self-absorption, inattentiveness to people and surroundings, withdrawal, and a lack of interest or participation in all or most activities. Psychomotor retardation often presented as a general slowdown in all areas as well as extreme slowdown in self-care activities such as dressing and eating.

Fearfulness was also reported, most often as a fear of public places and strangers. Some increases in pre-existing compulsive or ritualistic behaviors were also noted. For several individuals, extreme sleep problems were also evident including severe insomnia, reversals of day and night sleeping patterns, and nocturnal activities such as roaming the house.

TABLE 3. FIVE CASES OF DEPRESSION IN ASSOCIATION WITH DOWN SYNDROME

CASE DESCRIPTION	COMMENT
<p>Case 1. Major depression, single episode, mild to moderate degree of severity</p> <p>Mr. A., a 43-year-old man living in a group home, became sullen, withdrawn and unresponsive to fellow residents, staff and family members. He complained of exhaustion and showed no interest in social and recreational activities. He had difficulty concentrating and following through on tasks at work, resulting in a noticeable drop in production. He had a decreased appetite and lost weight. Over the course of the year he became more withdrawn and self-absorbed. He was negligent about his own hygiene. His activity level slowed down, and he needed more and more prompting to do even basic tasks. Staff in the group home noted the loss of a long term caregiver and several recent deaths in his family as possible precipitants to this depressive episode.</p> <p>A course of individual treatment and consultation with caregivers, coupled with the use of an antidepressant medication (paroxetine 20 mg daily), resulted in a gradual lifting of the depression and a return to normal functioning.</p>	<p>This individual presented with very typical symptoms: weight loss, self-absorption, exhaustion, social withdrawal, and loss of concentration. As the untreated disorder progressed, the withdrawal and self-absorption became more pronounced, and work performance, as well as daily living skills, declined.</p>
<p>Case 2. Major depression, more severe symptoms and psychotic features</p> <p>In her third year in a food service job, Ms. B., a 24-year-old woman, became extremely withdrawn, listless and self-absorbed. She would sit and stare as if in a trance for hours. She exhibited what appeared to be hallucinations involving animated and at times angry or indecipherable conversations with imaginary other(s). She was moody, irritated and at times aggressive with her parents. Her movements and activity level slowed drastically. She was fearful of being out in public. She stopped going to her job, lost interest or motivation for self-care skills and for attending social and recreational activities (despite a previously active social life).</p> <p>When seen first at the Adult Down Syndrome Center, Ms. B. was on an antidepressant - nortriptyline (Pamelor®) 80 mg daily and haloperidol (Haldol®) 1 mg daily, which were prescribed by a previous psychiatrist. Both medications were gradually discontinued because of extrapyramidal side effects (dry mouth, loss of appetite, and urinary retention) and a sedation, which appeared to increase the severity of her withdrawal and psychomotor retardation. A different antidepressant was prescribed when she was seen at the clinic (paroxetine (Paxil®) 20 mg daily) and it was better tolerated. This medication along with individual and family counseling resulted in a gradual lifting of depressive symptoms. Ms. B. was also encouraged to return to a work setting to facilitate the rehabilitative process and to relieve stress on her family caregivers.</p>	<p>This individual displayed symptoms which were severe and included psychotic ones. In addition to hallucinations, she developed fears and a marked slowness that appeared quite odd and bizarre. She did, however, respond to antidepressant therapy alone.</p>
<p>Case 3. Mood disorder due to general medical condition, hypothyroidism, more severe symptoms and psychotic features</p> <p>Ms. C., a 26-year-old woman, became increasingly withdrawn and self-absorbed. Despite a previous good employment record she lost her job in a fast food restaurant because of a lack of attentiveness to duties and because her self-talk was increasingly noticeable to others. Her family noticed a similar absorption with her own thoughts and self-conversations. Despite an active social life and good-natured personality she became increasingly withdrawn, apathetic, listless and flat in her affect. Her activities and movements were slowed dramatically. Her sleeping was erratic and she gained weight. She became less attentive to her own hygiene and she grew fearful of going to public places.</p> <p>When she attended the Adult Down Syndrome Center, a hypothyroidism was diagnosed. Treatment of this disorder with thyroid hormone therapy (Synthroid®) 0.1 mg daily was partially effective. She completely responded to treatment with fluoxetine (Prozac®) 20 mg daily and supportive counseling for Ms. C. and her family.</p>	<p>Although the etiology of depressive symptoms may have been due to a medical condition (hypothyroidism), the symptoms were very similar to those displayed by persons with depression, who were not found to have a medical condition. In this case, the symptoms were very severe and included psychotic ones. Treatment of the hypothyroidism as well as the addition of an antidepressant and supportive counseling, resulted in the alleviation of symptoms.</p>

TABLE 3. FIVE CASES OF DEPRESSION IN ASSOCIATION WITH DOWN SYNDROME (Cont.)

CASE DESCRIPTION	COMMENT
<p>Case 4. Major depression and anxiety disorder</p> <p>Ms. D., a 24-year-old woman and her ill elderly mother moved to another city to be closer to an older sister. In the year after, she became extremely withdrawn with extended periods of engaging in animated fantasies with "imaginary others." She slowed down dramatically in all activities including work and self-care. She became uncharacteristically moody and irritated and had lost her liveliness and sense of humor. She was agitated, restless, and could not seem to relax. She began to chew on her fingers, causing unsightly cuts and sores. She showed an increase in exhaustion and a pattern of sleeping days and staying awake at night. During this period she was hospitalized with a bleeding ulcer which her doctor attributed to stress.</p> <p>Her family was reluctant to permit the use of antidepressant medication. Believing that her symptoms were due in part to the loss of her former support network and an over-sensitivity to her elderly mother's illness, a nearby group home was located for Ms. D. With much time and counseling she made new friends and developed new interests in her new setting. This resulted in a gradual cessation of depressive and anxiety symptoms.</p>	<p>The presentation of this individual was very odd and bizarre. Her self-talk with "imaginary friends" may have developed to ease her loneliness. The loss of self-care activities was dramatic. Self-injury, such as chewing on her fingers, also added to an unusual presentation. The family's reluctance to use an antidepressant may have prolonged symptoms. Nonetheless, this case example shows that situational changes should not be overlooked when considering treatment options. Also, a spontaneous remission may have occurred.</p>
<p>Case 5. Major depression, anxiety and behavior disorder</p> <p>In his last year of school, and due to unknown causes, Mr. E. began to have the same symptoms that he had displayed 10 years earlier following abuse from a fellow student. For this second bout of symptoms, he became progressively tense, irritable, and withdrawn. He refused to go to school in the mornings and would explode with an outburst of yelling and throwing things when attempts were made to force him to go. He began to masturbate openly, and to display a number of self-stimulating behaviors such as rocking and hand-flapping. He became more ritualistic about the exact order and placement of a large and growing number of items in his household. In time his aggressive behaviors became more frequent and more assaultive of his parents. His compulsive requirements for the placement of objects became more rigid, his withdrawal from his parents and friends more extreme, his masturbatory behavior more open and more frequent, and his anxiety, agitation, and self-stimulatory behavior more pronounced.</p> <p>As a result of the severity of symptoms, Mr. E. was hospitalized briefly in a psychiatric hospital and treated with psychotropic medications (propranolol (Inderal®) 20 mg daily, Lithium 1200 mg daily; and lorazepam (Ativan®) 2 mg daily). In addition, he had a carefully designed behavior management program. This treatment continued after he was discharged.</p> <p>Over time, his depressive and anxious symptoms have gradually dissipated and his behavior problem has become more manageable. He recently transferred to a residential facility where he continues to live successfully with only brief periods when there is a recurrence of depressive, anxious or behavioral symptoms.</p>	<p>Depressive symptoms were quite extreme and presented with severe anxiety and behavioral disorders which were not manageable in an outpatient clinic. The severity of symptoms may have resulted from the cognitive and expressive language limitations of this individual which may have prevented him from conceptualizing and expressing his depression in more typical ways.</p>

Five of the patients with major depression had a single episode of mild severity. (See Case Example 1 in Table 3) Their symptoms lasted an average of 12 months. Moderate impairments in social relationships and mild impairments in work/school functioning or daily living skills were noted by caregivers.

For the other 11 patients diagnosed to have major depression, symptoms were more severe and often accompanied by psychotic features. (See Case Example 2 in Table 3) For these 11, caregivers reported that symptoms lasted between 24 and 36 months, with an average of 28

Self-talk was found to be common behavior for many of the 272 adults with Down syndrome seen at the Center. However, for the individuals diagnosed with depressive

months. They all had debilitating impairments in at least two functional spheres of social relations, work/school, or activities of daily living.

A common pattern of impairment included isolation from social relationships, job loss or extended absence from work, and a significant reduction in self-care and daily living skills.

For these 11 individuals, psychotic features which were commonly observed included extreme withdrawal or trance-like stupor, delusions, and hallucinatory-like conversations with self and imaginary others (self-talk).

disorders in the sample, incidents of such behaviors were far more numerous, extreme, and more public. Observers also noted these conversations to be more animated, angry in

content and seemingly oblivious to the presence of others or to social convention.

For the nine patients with a co-morbid anxiety disorder, symptoms of the anxiety included agitation, increased body tension, restlessness, hyperactivity, and mild to moderate self-injurious behavior (including hand or finger biting, scratching, hitting self, and hair pulling). Symptom severity was of moderate severity for two and severe for the other seven. (See Case Example 4 in Table 3)

For five others for whom anxiety and behavior disturbances were co-morbid problems, symptoms of anxiety again included agitation, increased body tension, restlessness, hyperactivity, and mild to moderate self-injurious behavior. Additionally all had a marked increase in compulsive symptoms and a concomitant increase in a pre-existing ritualized behavior. Self-stimulating behaviors such as rocking and masturbation were also evident. Behavioral symptoms included physically and verbally aggressive behaviors for all, which were severe at times. Compared to the other 35 individuals who were diagnosed with a depressive disorder, these five were described by caregivers as more intellectually and functionally impaired. (See Case Example 5 in Table 3)

The ten persons diagnosed with a depressive disorder due to a general medical condition, which has been reported to cause depression,^{10,14} had depressive symptoms almost identical to those individuals with major depression. (See Case Example 3 in Table 3)

DISCUSSION AND CONCLUSIONS

The rate of depressive disorders in this sample (14.7%) was slightly higher than the upper end of the range reported in the literature for persons with mental retardation (6 - 13%).^{6,7,13,22} The higher rate may have been due to the inclusion of persons with co-morbid psychiatric disorders and depression secondary to medical conditions, who may have been excluded in other studies. Although anxiety symptoms were present for many of the patients in our sample, the degree and severity of such symptoms merited a separate diagnosis of an anxiety disorder in nine cases. For five others, the severity of anxiety and behavior symptoms merited a separate diagnosis along with depression.

As in other reports, depressive symptoms were most often reported as behavioral changes. It is significant that 32 of the 40 persons with Down syndrome and major depression had more severe, chronic and debilitating symptoms that were often accompanied by psychotic features, and is consistent with other reports.^{12,23,25} Despite the presence of psychotic symptoms (such as hallucinatory self-talk and extreme withdrawal), the diagnosis of a depressive disorder rather than psychotic disorder, was warranted by DSM-III-R¹ and DSM-IV² criteria because depressive symptoms were predominant, preceded and continued well after the cessation of psychotic symptoms. Moreover, Sovner & Hurley²⁰ have cautioned against an overly hasty diagnosis of a psychotic disorder when other disorders cannot be ruled out in this population (such as depression). These authors recommended the use of the term "psychotoform" for psychotic-like symptoms in order to help promote the use of such medications as antidepressants, which have a better risk-benefit ratio than anti-psychotic medications.

Despite the severe and chronic course of many who were diagnosed with depressive disorders in the sample, an eventual pattern of improvement was shown, which does not suggest Alzheimer's dementia. Still, in the absence of a definitive test, Alzheimer's dementia cannot be totally ruled out. These 40 individuals will continue to be followed longitudinally at the Center to assess any significant re-emergence of symptoms or losses in functioning.

The results of these clinical findings suggests that a careful evaluation of behavioral changes, symptom course and medical conditions should help clinicians to better differentiate between depression, medical disorders, Alzheimer's dementia and psychotic disorders in this population. These conditions often have similar symptom presentations and yet have different treatments and prognosis.

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