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Bipolar Disorder and Down Syndrome: Six Cases

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This article describes six cases of bipolar disorder in persons with Down syndrome, and only eight cases have previously been reported. A family history was obtainable in only four persons, but three of the four had a positive history of bipolar disorder. Five of the six individuals are males. Potential relevance of these findings are discussed.

Only eight persons with bipolar disorder and Down syndrome (DS) have been reported in the scientific literature. This fact suggests that bipolar disorder is rare in DS. It is impossible, however, to determine prevalence based on reported cases. In a population survey of 11,277 persons in California with DS, no one was diagnosed with bipolar disorder. The population survey confirmed the clinical impression that the coexistence of bipolar disorder and DS is fairly rare. Thus, it is clinically significant when a person with DS also has probable bipolar disorder. The following reports are from four university centers and describe bipolar disorder in six persons with DS.

**Case Reports**

Mr. A. was in his 20's with moderate mental retardation and DS. (see Table 1) His maternal great-aunt and two maternal aunts have bipolar disorder. He presented with a seven-year history of cyclic behavior. His manic phase would last three to six weeks. During this time he would have increased energy, irritability, increased arguing, increased vocalizations, decreased concentration, increased masturbation, decreased sleep with laughing while in bed. During these "up" phases he believed coworkers talked about him. His behavior also precluded workshop attendance, and he would do silly things such as put milk in the microwave instead of the refrigerator. Just prior to his "up" phases, he had one or two days when he functioned at his best and may well have been hypomanic. Although his parents referred to his "non-up" phase as his low phase, he slept longer, had a good appetite, never cried or made self-deprecating statements, and functioned reasonably well. He could attend the workshop and ride the bus. He was placed on valproic acid and lithium. Both were titrated to a therapeutic range (lithium 0.7 mmol/L and valproic acid 485 micromol/L). He was diagnosed with rapid cycling bipolar disorder and had a partial response (decrease in the duration of the "up" cycles).

Mr. B., in his mid-30's, had DS and profound mental retardation. He was initially seen because of cyclic hitting, kicking, throwing himself on the floor and disruptive sleep. On review of symptoms, staff noted that he had crying spells, temper outbursts, a previous diagnosis of depression and also dental problems. Although he was diagnosed with depression, he did not respond to two trials of antidepressants. After several months, his diagnosis and treatment were reevaluated. Twelve days prior to the re-evaluation, he responded to a staff prompt by kicking, screaming, and biting. Two days later, staff reported that he was "wound up all night." He masturbated for much of the night to the point of causing tissue injury to his penis. He jumped on the bed until the mattress and box spring were knocked to the floor. He had both laughing and crying spells. He sang different tunes. By 2:30 a.m., another client complained because Mr. B. was so disruptive. Mr. B. ignored redirection and continued to masturbate and sing for the remainder of the night. The next day he teased other clients and tried to provoke them into fights. He repeatedly made a fist in front of a peer. He also had two crying spells. The following week he had another episode and was up half the night. The following night he made funny noises.
and laughed for about three hours. He was started on valproic acid, 500mg a.m. and 750mg h.s. His depakote level was generally in the 70's. He remained stable for approximately a year, but then displayed a milder version of his manic symptoms. Depakote was increased; he again responded and was euthymic for another year.

Mr. C. had DS and mild mental retardation. He was in his thirties. He had a history of acting on his wishes as though the wishes were real. In his manic phases, he contacted car dealerships about buying a car even though he had no driver's license. He also phoned a printer to make his wedding invitations even though he was not dating. During his depressed periods, he had eating binges with significant weight gain, crying spells and anhedonia (no motivation to exercise). His mood swings could be severe and rapid. Within minutes, he could shift from smiling about wanting to buy a sports franchise to crying about his family. His family history was positive for bipolar disorder. Mr. C.'s past medical history was positive for seizure disorder and heart disease. His symptoms were controlled with lithium and carbamazepine. Although he would still experience rapid mood swings, the duration and intensity were diminished with psychopharmacology.

Mr. D. was in his early 40's and had DS. He was first seen one year ago; there was no previous psychiatric history. He had an insidious onset of mood swings and was first prescribed a hypnotic for sleep seven years prior to initial assessment. When first seen, he had been depressed during the past year in May, high in July and again manic in August, and seemed to be rapid cycling. During depressed phases he woke up tearful, had initial insomnia and talked at night about killing himself. He believed no one liked him anymore. He had early morning waking. He was withdrawn socially, slow moving, talked less, and said he was sick. His depressed phases lasted up to two weeks at a time; his manic phases lasted three to four days. These symptoms included an elevated mood, slightly pressured speech, marked flight of ideas, paranoid ideas of reference and complaints about being unable to sleep. He also had grandiose beliefs about being Elton John's brother and Lucille Ball's son. No significant increased energy or agitation was noted. The home staff were most concerned about the depressed phases because of the suicidal talk and some attempts (e.g., towel around his neck). He had a brother with schizophrenia, as well as a mother and sister with bipolar disorder who were on lithium and doing well.

During the following January, Mr. D.'s mood became depressed. Lithium treatment was started with some improvement in mood. Three months later, he had muscle weakness and tremor. Even though the level was only 0.9, lithium was reduced. His strength returned, his concentration was better, and he was more motivated when seen two months later. Seven months after starting lithium, his mood was down again. His level was only 0.14 and lithium was increased. In summary, Mr. D. had rapid cycling bipolar disorder, and a strong family history of manic depression. The prominent features were grandiosity when high, suicidal talk when depressed. His non-depressive symptoms seemed attenuated and less severe compared to the average manic patient and were probably hypomanic according to the clinician who knew him well.

Ms. E., in her 20's, was a woman with hypothyroidism and physical stigmata of DS. She developed a sleep disorder as a teenager. Her level of mental retardation was uncertain as English was not her native language, and she was not motivated to do testing. In her native country, she did high school work (could read and write), but

<table>
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<tr>
<th>SUBJECT</th>
<th>AGE</th>
<th>MR LEVEL</th>
<th>FAMILY HISTORY</th>
<th>SYMPTOMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mr. A.</td>
<td>20's</td>
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<td>+ bipolar</td>
<td>abdeklmwb'c'</td>
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<tr>
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<td>+ bipolar</td>
<td>acikopqv</td>
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<tr>
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<td>unspecified</td>
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<tr>
<td>Mr. F.</td>
<td>30's</td>
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Symptoms Key: a=euphoria; b=irritability; c=grandiosity; d=decreased need for sleep; e=more talkative/vocalizations; f=pressured speech; g=flight of ideas; h=distractibility; i=increase in goal=directed activity; j=psychomotor agitation; k=excessive pleasurable activity w/potential painful consequences; l=increased energy; m=cyclic behavior; n=depression; o=crying spells; p=anhedonia; q=weight loss/gain; r=insomnia/hypersomnia; s=psychomotor retardation; t=fatigue; u=recurrent thoughts of death/suicidal ideation/plan; v=labile mood; w=delusions; x=leasling; y=physical aggression; z=withdrawn; a=SIB; b=rapid cycling; c=silly behavior; d=hallucinations.
current tests suggested an IQ of less than 20. She would go as long as 75 hours without sleeping; typically, she slept only three to four nights a week. When she did sleep, she would sleep for as many as twelve hours. When initially seen, she did not have hypersexuality or increased verbalization. Correction of her hypothyroidism did not resolve her psychiatric symptoms. Family history was negative for any psychiatric illnesses. Initially, she was thought to be depressed and was given nortriptyline and amitriptyline, but without response. Thiothixene resulted in less aggression and improvement in sleep but family decreased the dose because she looked too sedated. Clomipramine (25mg at h.s.) resulted in an increase in irritable behavior and was discontinued. She was diagnosed with bipolar based on a recent past history of restlessness, sleeplessness, high energy levels at night, hallucinations, food refusal, and self-injurious behavior. When she was treated with lithium 300 mg BID, her sleep improved, her activity level was normal and she was much calmer.

Mr. F. was in his 30's with moderate mental retardation, DS and hypothyroidism. He was initially seen to determine if he still needed thioridazine. He had a past history of allegedly paranoid ideation about individuals trying to kill him. He had a past diagnosis of bipolar disorder and was placed on lithium ten years prior to the initial consultation. Eight years ago, however, the diagnosis had been changed from bipolar to a psychotic disorder, and lithium was discontinued. When initially seen, no psychiatric disorder was obvious and thioridazine 75mg was gradually tapered over six months.

Two months after thioridazine was discontinued, Mr. F. developed sleep problems and talked about seeing a wrestler at the airport who knew him. When he was seen four months after stopping thioridazine, he said that Hulk Hogan knew him. He had pressured speech, his work production fell and he argued more frequently. On exam, his mood was bright. It was unclear whether he understood the question about knowing Hulk Hogan; he did not have psychomotor agitation. Consequently, no medication was prescribed. His thyroid function was checked to ensure that he was not hyperthyroid, and his sleep/wake activity was charted.

Over the next two months, he continued to show a reduced need for sleep. Mr. F. usually went to bed after 11 p.m. or 11:30 p.m. and awoke between 4 a.m. to 5 a.m. He believed that people on the TV talked about him. He also talked about a party that he attended with Hulk Hogan. His caregiver, however, noted that neither the beliefs about people talking about him on TV nor partying with Hulk Hogan greatly affected Mr. F.’s daily life. He told his speech therapist that he played with scissors because he was afraid staff would kill him. At the next appointment, he did not voice any paranoid beliefs. He said he knew Hulk Hogan, but did not fixate on it, nor did the belief affect his behavior or actions during the exam. Furthermore, there was no evidence that he was responding to internal stimuli. He did have some unusual actions such as pouring out cans of sugar and flour so he could put in his coffee. Although a bipolar or psychotic disorder was considered, it was decided to first try buspirone for possible anxiety-like features. (In retrospect, Mr. F.’s anxiety symptoms were unimpressive, but buspsirone was a "milder" psychotropic than an antipsychotic or a mood stabilizer.)

A three month trial of buspirone was unsuccessful. He was now going to bed at 8 p.m. or 9 p.m. and awakening between 12:30 a.m. and 2:30 a.m. Furthermore, when he awoke, he disturbed the sleep of the other residents. His mood was irritable. Staff reported his energy was increased. During the exam, no clear delusional ideation could be elicited. Following pre-lithium baseline labs, lithium 300 BID was started.

Three months after starting medication, he was averaging 6.5 hours of sleep. He had not talked about Hulk Hogan or people on TV knowing him as he had previously. On exam, he wore a wresting mania hat, but did not say that Hulk Hogan knew him. There was no pressured speech nor psychomotor agitation. His mood was euthymic. Six months after starting lithium, he consistently slept 6.5 hours, started a new job and made more money than he had previously. No delusions were noted. His mood was euthymic, and he had no psychomotor agitation. Nine months after starting lithium, there was no mention about TV personalities or wrestlers knowing him. Staff felt that there was a partial response, but they were concerned that he was "stealing" items such as scissors. There was no indication that he felt he needed the scissors to defend himself. His mood was subdued (compared to previous appointments). Mr. F. was referred for behavioral interventions for the "stealing" and was lost to follow-up.

**Discussion**

The foregoing contribute six cases to the literature. A potential limitation of this paper is the lack of karyotypes in the said cases. On the other hand, all of the individuals showed typical physical characteristics of DS. They were seen by clinicians in a DS clinic setting or by those experienced in working with persons with developmental disabilities. Karyotyping raises the issue of what benefit it is to an adult who has been diagnosed as having DS all of his/her life and in whom the diagnosis is not clinically questioned. The cases showed a variety of symptomatology that was generally affected by the level of mental retardation. At the higher levels of functioning, psychosis was obvious. Mr. D. believed that Lucille Ball was his mother. At a more moderate level of functioning, Mr. F. believed that Hulk Hogan knew him, although it was uncertain as to whether he really understood the question ("Does Hulk
In his case as well as with Mr. B. and Ms. E., the diagnosis relied on vegetative signs of mania (reduced need for sleep, increased energy and in Mr. B.’s case, excessive masturbation).

Family history was obtained in only four of the six cases, but three out of four had at least one blood relative with bipolar disorder. A family history of manic depression in a person with DS suggests that the individual should be closely monitored for evidence of mania or hypomania.

It is also interesting that all previously reported cases, plus five of the six of this article’s subjects, were male. Along with Ms. E., there is possibly another individual (and another female) described by Kastner's group. The individual is an eight-year-old girl with DS. In the former article she is described as having profound mental retardation, a history of severe self-injury, hyperactivity, irritability, distractibility and impulsive behavior. Problems were noted as early as age three. The child, however, did not have a sleep disorder nor mood lability. Cycling behavior was not mentioned in the earlier article, but was in the later one. She did have a seizure disorder and responded to a depakote level of 111 micrograms/ml. In the later article, the authors note that the child did not meet DSM-III-R criteria for bipolar disorder. Kastner et al linked the affective symptoms and non-paroxysmal electroencephalogram abnormalities in children with severe or profound mental retardation. They wondered if this constituted a new organic psychiatric syndrome. To include this case as one of bipolar disorder and DS is arguable given the lack of mood lability or sleep disorder. When an earlier version of this paper was presented at the AAMR 121st Annual Conference on 5/29/97, however, Kastner raised the possibility that his group’s case report may well be appropriate for inclusion cyclic aspect of behavior.

Four of the six cases (Mr. A., Mr. D., Ms. E. and Mr. F.) showed predominantly hypomanic features (although one could argue that evidence of psychotic beliefs precludes a diagnosis of hypomania). Are manic symptoms attenuated in persons with DS? Nevertheless, both Mr. B.’s behavior and Mr. C.’s grandiosity would be considered as typical manic symptoms in the general population.

An interesting finding is that two of the six cases (Mr. B. and Ms. E.) showed physical aggression. Also interesting was the relative lack of self-injury. Only Mr. B. showed self-injurious behavior (SIB) which was during his excessive masturbation. It is possible that self-injury was not prominent in the other cases and hence was overlooked. Lowry notes that aggression and SIB are more common in mood disorders. Future case reports of bipolar disorder and DS should make a special effort to determine if aggression and/or SIB are present.

Whether there are now fourteen or fifteen individuals in the English-speaking world with DS and bipolar disorder means that this is significantly less than predicted. Craddock and Owen predicted over 1,450 cases of DS and bipolar disorder in the United States and Great Britain. Even with the Kastner et al case, the published cases are still far less than the expected cases.

The strong predominance of males is interesting. In the general population, bipolar disorder is equally common in men and women. Previous studies linking bipolar disorder and the X chromosome have been equivocal and in the opposite direction! The hypothesis of X-linked transmission of manic-depressive illness is based on the observation of a sex ratio of two females with bipolar disorder for every male. At this point, it is unknown why there are reports of thirteen males and only one (or two) female(s) with DS and bipolar disorder.

It has been over ten years since the first DS and bipolar cases were published. It is conceivable that the real issue is an under recognition of bipolar disorder. This is somewhat unlikely as the authors have been actively searching for individuals with bipolar disorder and DS. If ultimately the answer is under recognition, then the solution may be rating scales for bipolar disorder standardized in developmentally disabled populations and especially in persons with DS. Personal communication suggests that there may be several individuals with DS with several more that have not yet been published. Given that one percent of the predicted cases are in the literature, it is quite important that additional cases be described in detail and appear in print.

References


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