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Bipolar Disorder and Differential Diagnosis in Adolescents:

Arriving at a Correct Diagnosis

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Title: Bipolar Disorder and Differential Diagnosis in Adolescents: How to Arrive at a Correct Diagnosis

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Abstract

Correctly diagnosing mental health disorders in adolescents is essential. It leads to early evidence-based treatments that result in improved outcomes. However, there is controversy about what is the correct diagnosis in adolescent populations that have chronic irritability, anger, impulsiveness, moodiness and other similar symptomatology. Some practitioners see this as a fundamentally ADHD disorder with associated mood symptoms. Others see it as a mood disorder. The case presented here concerns a 16-year-old male with symptoms noted above. He has been treated for the last 18 months without success. This case shows how imperative it is to correctly diagnose adolescents. It is necessary for evidence-based treatment and recovery. Literature review shows that adolescents with chronic irritability develop anxiety and depression in adulthood and not ADHD or bipolar disorder. There are neurobiological differences in bipolar patients and patients with chronic irritability. This points to different underlying disease processes. Looking at the symptomology longitudinally, asking for historical data and using collateral information will all lead to higher likelihood of a correct diagnosis and better treatment options.

Bipolar Disorder and Differential Diagnosis in Adolescents:

Arriving at a Correct Diagnosis

Many mental health disorders start in adolescence. Early interventions can improve the trajectory of the patients' life. However, proper diagnosis is needed to ensure correct treatment. Adolescents do not display typical symptoms of mental health disorders for variety of reasons. For example, in the most recent Diagnostic and Statistical Manual of Mental Disorders (DSM 5) (2013), major depressive disorder can be diagnosed if the child isn't depressed but has irritability (along with other related symptoms). Bipolar mood spectrum disorders can manifest themselves differently as well. Adolescents with hyperactivity, impulsiveness, inattention, and irritability could be diagnosed with any of the bipolar disorders, attention deficit hyperactivity disorders (ADHD), or even the new diagnosis of disruptive mood dysregulation disorder (DMDD). Being able to differentiate and properly diagnose mood disorders is crucial because correct diagnosis leads to proper evidence-based treatment.

National Institute for Mental Health (NIMH) (2017) states that prevalence of ADHD in 13-18 years old's is 8.7%, and prevalence of bipolar disorder in the same population is about 2.9%. DSM5 (2013) states that the prevalence of DMDD is about 2-5% in the adolescent population. Considering that we have millions of adolescents in the county, we need to ensure that we are properly diagnosing them. Improperly diagnosed adolescents will have worse outcomes later due to erroneous treatment.

Being able to differentiate between bipolar disorders, ADHD, and DMDD is essential. Early intervention allows for an opportunity to improve long term outcomes. It is imperative that we correctly diagnose and provide treatment for symptoms in this specific population.

Case Report

This case concerns a 16-year-old male. He lives with his mom and two younger brothers. Previous diagnosis includes ADHD, DMDD, and oppositional defiant disorder (ODD). Medication from previous provider include guanfacine 4mg at night, citalopram 10mg daily, atomoxetine 25mg daily, and Lamictal 100mg at night. His mom states that he has been on methylphenidate in the past, but his irritability and aggression had significantly increased. As a result, the medication was discontinued.

Mom reports that he has always been an irritable and moody child. He can be manipulative, 'sneaky and cranky'. For example, mom states that he does not follow rules, uses internet beyond approved hours, sneaks phone in his room when he shouldn't, argues and picks fights with siblings and. He has a poor frustration tolerance. He talks 'over people' and will introject in conversations that he is not a part of. He is disruptive, impulsive and doesn't wait his turn. Mom states that he rambles, and it is difficult to talk to him because he monopolizes conversation and can be 'crabby and negative'. He does not apply himself in school and gets bad grades even though he is fully capable of performing well academically. Patient states that he just doesn't have interest in certain subjects and will not do any homework in them, which results in poor academic performance. In subjects that he has interest in he does well. There are no behavioral issues in school, as he is not aggressive or violent. He is social and has friends. He has a part time job and socializes there as well. There are no behavioral issues at work.

He does not have any history of being hospitalized in psychiatric settings. He has been treated for the symptoms described above for about 18 months at another outpatient psychiatric clinic. There is no significant medical history and he does not take any medication for medical issues.

Mom has a diagnosis of bipolar 2 disorder. Dad has a history of substance abuse (alcohol) but has been sober for many years now. Parents are divorced. He has minimal contact with dad. Younger brothers do not have any psychiatric diagnosis currently. However, mom did state that one of the children has been more irritable and moodier lately and that she would like for him to be evaluated by a psychiatric provider as well.

He does not attend any form of psychotherapy and does not feel that this would help. He agrees with mom and stated that he does get angry, crabby and irritable. He attributes this to siblings that annoy him. He states that it is easy for him to be sad and depressed. At other times he feels that he has more energy and wants to be more social. He understands that following rules is important but feels that if he isn't hurting anyone that it is ok to break them. He agrees that he should work harder in school but states that he just doesn't have any motivation to attend some classes. He would like to learn better ways of coping with his irritability.

Being able to truly differentiate diagnosis and correctly diagnose this patient will result in improved mood, more positive family dynamics and better academic performance. Many of the symptoms outlined above overlap with the bipolar spectrum disorders, ADHD or DMDD. Understanding all the nuances that come with a proper diagnosis is difficult but essential. Interventions proscribed, including medication, will be based on a correct diagnosis. Treating target behaviors is essential. Surest way to fail in treatment is to treat something that the patient doesn't have. Appropriate diagnosis will lead to the use of evidenced based treatments which will increase chances of success. This case study is a good example of the difficulty in diagnosing adolescents with irritability (among other symptoms outlined), and the following literature review will provide some insight into new ways we can look at the problem. Furthermore, the literature review will provide possible treatment options as well.

Literature review

The issue of what exactly constitutes a bipolar disorder, DMDD, ODD, or ADHD in children and adolescents is an ongoing, unanswered question in psychiatry. Carlson & Klein (2014) state that the main issue began at the transition point when in Diagnostic and Statistical Manual of Mental Disorders 3 (1980) the irritable and hyperactive children were separated into two distinct categories. Before this separation, the children who were irritable and hyperactive (exhibited mood and behavioral problems) were diagnosed with 'hyperkinetic reaction of childhood'. In the DSM3 these children were diagnosed with hyperkinetic reaction of childhood. However, the mood symptoms were not a part of the main diagnostic criteria but were labeled as 'associated symptoms'. The mood and the irritability were re-categorized under the various mood disorders. In the DSM 5 (2013), youth with similar symptoms could be diagnosed with ADHD as associated symptoms in ADHD include low frustration tolerance, irritability and mood lability.

In the current DSM, the definition of bipolar illness has undergone changes as well. In the DSM3 bipolar disorder required a 'distinct period' which wasn't the case in previous editions. There was no mention of what the 'distinct period' meant, and no discussion if the symptoms should represent a change from previous functioning (Carlson & Klein, 2014). This created a problem where chronically irritable teens with other similar mood symptoms could be diagnosed with bipolar illness. The issue is whether bipolar illness (manic episode) should represent a distinct episode or if chronically irritable mood should be included as a prodromal part of a manic episode. In the current DSM5, the manic episode is labeled as 'distinct period lasting at least a week with constant elevated, expansive or irritable mood'. The problem there is that there is no end point. The question is at what point would a manic episode stop in an

untreated patient? In the DSM5 there is no endpoint and thus a constantly elevated, irritable youth could, theoretically, be considered manic which would earn them the diagnosis of a bipolar disorder. The question is, does an adolescent with constantly irritable mood (and the usual accompanying symptoms of disagreeableness, argumentativeness, etc.) have mania and thus bipolar disorder or do they need to exhibit episodic change from previous functioning to be diagnosed with the bipolar disorder?

There is an understanding that depressive symptoms can occur without person meeting criteria for a major depressive disorder. Looking at a bipolar disorder in such a way can be helpful. Carlson (2012) writes that there is evidence that hypomanic symptoms occur much more frequently than manic episodes and cut across many conditions. Without a clear manic episode, it can be difficult to differentiate between bipolar and other illnesses in youth with symptoms of irritability, rapid speech, etc.

Perhaps the most important diagnosis that a clinician must consider in children and adolescents with emotional and behavioral issues in addition to bipolar disorder is ADHD. ADHD, due to its hyperactivity and impulsive nature, can often manifest itself in a child as irritable and disruptive (Goldstein, Birmaher & Youngstrom, 2020). In addition, associated symptoms in the DSM 5 (2013) include low frustration tolerance, irritability and mood lability which complicates the picture further. These youths can develop behavioral problems due to conflicts with parents, teachers and other authority figures. Pataki & Carlson (2013) state that the issue is that if we look at symptoms that some youth have such as hyperactivity, impulsiveness, emotional lability, pleasure seeking, distractibility, and irritability, the question becomes are these behaviors due to untreated ADHD or to an emerging manic episode. Carlson & Klein (2014) advise that we should not look at the symptoms as a snapshot in time but consider their

historical development. We can make a good differentiation between ADHD and bipolar symptoms if we look at the symptoms longitudinally. ADHD is a neurodevelopmental disorder that begins in early childhood and bipolar disorder needs certain periodicity and fluctuations.

In some cases, there can be a comorbidity of ADHD and bipolar disorder. If there is comorbidity, the outcome is worse compared to if they only had one disorder because mania isn't treated as effectively in patients with both (Pataki & Carlson, 2013). ADHD is an independent risk factor for development of a bipolar disorder and increases its risk for suicide (in patients with both diagnosis) compared to patients with just a bipolar disorder (Lan et. al., 2015). However, the rates of true comorbidity aren't high. Some studies report comorbidity in adolescents at 40% and other studies at 18.6% (Pataki & Carlson, 2013). However, longitudinal studies show that in adulthood the rates of bipolar disorder in people with ADHD are comparable to general population which is about 1-5% (Pataki & Carlson, 2013). It is probably the case that in adolescents, some clinicians count the same symptom for both disorders thus inflating the number of diagnosis and increasing the comorbidity rates.

Carlson (2012) outlines some of the symptoms that can make the differential diagnosis difficult for clinicians. They include:

- Silly, disinhibited behavior of a child with ADHD vs emerging elevated mood in mania
- Impulsivity in ADHD vs pleasure seeking without caring for the consequences in mania
- Resistance to sleep vs no need for sleep
- Emergence of ADHD symptoms due to increase in demand in middle school vs emerging mania
- Odd or distracted language in autisms or ADHD vs flight of ideas in mania

- “Hallucinations” in anxiety disorders vs psychosis in mania

Symptoms of grandiosity and elation can be a cardinal sign of bipolar disorder and is certainly not a symptom in ADHD and can be used as a differentiation even though it is rare in adolescents (Carlson & Meyer, 2006). In addition, we should get collateral information from multiple sources as using only one source will increase the prevalence of this disorder (Carlson & Meyer, 2006). If symptom development is abrupt this indicates a bipolar disorder. However, if it is gradual, differentiating between bipolar disorder, irritable depression, ODD and other similar diagnosis is very difficult. Lastly, symptoms of mania such as severe emotional dysregulation, anger, and agitation can occur due to early trauma resulting in PTSD (Carlson & Meyer, 2006). The subsequent mood issues and behavioral problems shouldn't be looked as emergence of mania but dysregulation due to PTSD.

When diagnosing children with behavioral and mood symptoms, it helps to look at the issue longitudinally. One way we can clarify the issue is to see if chronically irritable children and adolescents progress to having classically defined bipolar disorder in adulthood with distinct mood episodes or develop other mental health problems. Stringaris et al. (2009) reported that of 631 individuals followed from age 13.8 (SD=2.6), to age 33.2 years (SD=2.9), chronic irritability in adolescence was a predictor of major depressive disorder at age 33 (odds ratio 1.33), generalized anxiety disorder (odds ratio=1.72), and dysthymia (odds ratio=1.81). This study supports the idea that chronic irritability is more likely to result in development of anxiety and depression in adulthood instead of bipolar disorder. Leibenluft (2011) presents an article where children with severe mood dysregulation disorder had 2.7% of parents with bipolar disorder while bipolar children had parents with a bipolar disorder at a rate of 33.3%. This shows that children with chronic problems of irritability have more genetical loading for depressive and

anxiety disorders while children with bipolar parents are more likely to be bipolar themselves. We need to take a longitudinal view which can clarify the length of the episode, what is provoking the irritable reaction and whether it is episodic or chronic.

Leibnluft (2011) also cites research that point to pathophysiological differences and similarities between bipolar adolescents as compared to adolescents with severe mood dysregulation (where main symptoms are chronic irritability and moodiness). Both groups have negative evaluation of face emotion identification compared to healthy controls. This suggests that there is some sharing of pathological processes between the two conditions. Poor emotional face identification is correlated with poor social reciprocity skills in bipolar youth but with dysfunctional family relationships in youth with SMD (Evans et al., 2017). However, the mechanisms appear different. Youths with severe emotional dysregulation had lower amygdala activity than bipolar or healthy comparison group (Leibnluft, 2011).

Poor frustration tolerance can be measured with neuroimaging while the participant completes a frustrating task. Leibnluft (2011) shows that children and adolescents with bipolar disorder had deficient top-down processing (decreased parietal P3 waves) during completion of frustrating task, while adolescents with mood dysregulation had deficits in bottom up processing (decreased parietal, temporal and central N1 and P1 waves). Evans et al. (2017) state that in response reversal task which examines adaptation to changing environmental stimuli (poor responders are more frustrated), mood dysregulated youth are similar to controls while bipolar youth performed worse. Youths with SMD had increased threat bias relative to healthy controls as well as elevated processing during angry faces and lowered processing with happy faces (Evans et al., 2017). This points to increased threat vigilance and dysregulated performance of amygdala, parietal, and frontal regions of the cortex. Interestingly, bipolar youth showed less

activity in response to angry faces which could show disengagement from increasing anger (Evans et al., 2017).

In summary, there are some differences in how healthy controls, youth with SMD and youth with bipolar disorder process emotional information. As stated, SMD youth are more threat vigilant. Bipolar youth show less activity with anger in amygdala. There are some similarities between bipolar and SMD youth as both have problems with processing of emotional content. Due to limited research and creating of DMDD (which is new version of SMD) there is limited data available about both structural and functional differences in brains of youth who have these disorders. More research is needed to understand the underlying mechanisms.

Due to uncertainty about diagnosing bipolar disorder in adolescents, there are relatively few screening tools available that clinicians can use to make the diagnostic process easier. More work is needed in this area. One promising tool is “The Conners’ Abbreviated Parent Questionnaire”. This 10-item tool can pick out 73% of youths with the bipolar disorder which is a similar sensitivity to screening tools for adults with bipolar disorder (Tillman & Geller, 2005). A positive result will require further assessment by the provider for the presence of bipolar disorder.

One key factor that can make the diagnosis process more difficult is the question of who is providing the information about the patient. If information about manic episodes is gathered from parents, studies show that the information can be unreliable. For example, Pataki & Carlson (2013) show that parents who report symptoms of severe mania, once examined by a clinician, really display anxiety and depression. Parents who reported children with bipolar symptoms where found by teachers to not display any behaviors whatsoever (Pataki & Carlson, 2013). Pataki & Carlson (2013) also show that children whose parents reported bipolar and ADHD

symptoms, only had ADHD symptoms according to teacher reports. This shows that who is providing information can make all the difference in diagnosis. At a minimum, when interviewing adolescents, we need to get information from the caregiver and the teacher as manic episodes should be apparent in school due to extensive period of time that the student spends there (Carlson, 2012). Another methodological issue is double counting of the symptoms. If we count hyperactivity, impulsiveness, pleasure seeking into ADHD, bipolar, and other similar disorders, our patient will have many comorbidities. We need to understand the fundamental reason that is causing the behaviors and look at the symptoms longitudinally. Carlson & Klein (2014) show that the use of collateral information leads to decrease in the rates for both mania and ADHD. Lastly, geographic area can influence diagnosis. For example, when given the same patient case, British clinicians are more likely to diagnose ADHD and ODD while US clinicians diagnosed bipolar comorbid with ADHD (Dubicka, Carlson, Vail & Harrington, 2008). This is due to a conceptual difference in the outlook on mental health disorders between the providers in the two countries.

Implications

Clinicians need to recognize the difference between bipolar, ODD, DMDD, and ADHD in order to select appropriate treatments. Giving stimulants to a bipolar patient can exacerbate the symptoms. Giving antipsychotics to an adolescent with truly ADHD disorder who has associated symptoms of irritability and poor frustration tolerance will not help. Correct diagnosis leads to accurate evidence-based treatment.

Changing of what it means to be bipolar or have ADHD through different DSM reiterations has contributed to the problem. The fact that DSM is an evolving product, it is certain that the DSM 6 will have even further changes. As DSM diagnosis are created by

committees that cluster similar symptoms into disorders, there will always be clinicians that disagree with the conclusions which will result in different diagnosis for same patients.

We should look at the symptoms cluster longitudinally. Clinicians need to ask for historical data to find the root cause of the symptoms. This will clarify the diagnosis. If an adolescent has exhibited new onset of irritability, oppositional behaviors, poor frustration tolerance, etc., we should lean more toward behavioral or mood diagnosis. ADHD can be excluded as it is thought to start before the age of 12 whose symptoms are not acute but chronic. If the same patient does not display episodic nature of these symptoms then diagnosis of depression, adjustment, or anxiety is more likely. Considering historical data can lead to a more accurate diagnosis.

Obtaining collateral information from multiple sources is crucial in adolescent populations. At a minimum, interviewing the primary caregiver in addition to the child is necessary. In addition, receiving reports from teachers or anyone who is in contact with the child regularly will increase the chances of making the correct diagnosis.

The use of screening tools, such as “The Conners’ Abbreviated Parent Questionnaire”, can cue to provider in to assess for the bipolar disorder. It is only a 10-item questionnaire which makes it efficient as it can be done in a timely manner. It will certainly lead to less omissions and more accurate diagnosis.

More research is needed to truly understand the cause of these behaviors in adolescents and children. As DMDD, bipolar disorders, ODD and ADHD can have similar presentations, we need more basic research done to truly understand the cause of the symptoms. It is possible that some of these disorders are in fact just a spectrum of one disorder with different phenotypes.

Understanding the impact of neurotransmitters on the pathophysiology on the brain disorders will hopefully lead to more effective treatment of behaviors.

Due to hormonal changes in adolescents, family dynamics, peer pressure, and brain development, making appropriate diagnosis can be challenging. There are some techniques that are outlined in this paper that can make the diagnosis easier. Looking at the symptoms longitudinally, utilizing more sources of information, and supporting further research in brain science is essential for more precise diagnosis and better treatments.

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