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ADHD and DMDD Comorbidities, Similarities and Distinctions

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Abstract

Since the mid-90s, the number of children treated for bipolar disorder has increased considerably. Although the need to avoid a confusing terminology regarding bipolar disorder was generally accepted, agreement on diagnosis for this population was difficult to conclude. In particular, the controversy concerned children with chronic irritability and high comorbidity with ADHD. The DSM-5 working group on mood disorders proposed a new diagnosis: Dysruptive Mood Dysregulation Disorder (DMDD). If the distinction with bipolar appears now clear, high comorbidity with ADHD is concerning and makes the nosological limits unclear. However, differences are present and these two diseases must be distinguished in order to recognize their particular problems. Investigation of overlaps between ADHD and DMDD should help clarify their etiology, course and outcome.

Keywords: ADHD; DMDD; Pedopsychiatry; Similarities; Comorbidities

Introduction

Since the mid-90s, the number of children and teenagers diagnosed and treated for bipolar disorder has increased considerably. Yet, only a few of them actually had a diagnosis that was considered to be a "typical" bipolar illness. Indeed, the younger the child, the rarer is the bipolar disorder. Although the need to avoid a confusing terminology regarding bipolar disorder was generally accepted, agreement on diagnosis for this population was difficult to conclude particularly due to the net difference between North American and European clinical practices. In particular, the controversy concerned children and adolescents with chronic irritability and high comorbidity with attention deficit hyperactivity disorders (ADHD). In addition to having a clinical picture akin to mood disorders, these children frequently suffered from ADHD. The DSM-5 working group on mood disorders in children and adolescents proposed a new diagnosis: Dysruptive Mood Dysregulation Disorder (DMDD). This is a diagnosis still in evolution whose purpose is to avoid confusion between an emotional dysregulation and bipolar disorder. If the distinction with the latter appears clear, high comorbidity with ADHD is concerning and makes the nosological limits unclear. Thus, this new diagnosis, its meaning and its management are still studied and discussed. In this review, we shall first describe the DMDD and then its comorbidity with ADHD. Subsequently, we will discuss their similarities and their distinctions.

DMDD

Attribution of diagnosis of bipolarity has particularly increased in the last few years, but nevertheless the epidemiological data do not show any increase of prevalence of this pathology [1]. The American Psychiatric Association (APA) quoted an article of the Wall Street Journal where a typical case was described: an 11-year-old boy having received a diagnosis of bipolarity at the age of 4 was never able to be successfully treated for its severe recurrent temper outbursts [2]. Many children were never able to receive an adequate diagnosis because they had a disorder which had not been defined yet. Thus, the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) longs to give a name disruptive mood dysregulation disorder (DMDD), to the suffering of these children and to ensure they receive the care they need.

The first works dedicated to the developmental approach of mood disorders go back to the 1960s by the publication of retrospective and prospective studies with repeated evaluations [3,4]. These studies highlighted the early beginning of some mood disorders and their developmental continuity with certain emotional disorders but also with certain behavior disorders. For the child's mania, the debate turned to the more or less "wide" definition of the notion of mania, which caused a major variation in the estimations of prevalence of bipolar disorder in pediatric population. Indeed, during the last ten years, diagnosis of bipolar disorders in children almost doubled [5].

According to Blader and Carlson [6], the rate of children diagnosed as bipolar between 1996 and 2003 increased from 1.3 to 7.3 per 10,000. This increase corresponds to a period which follows one that was characterized by the under-diagnosis of bipolarity in children and to the necessity of answering the suffering that it had engendered. Today, the DSM-5 specifies and enriches the diagnosis spectrum in pedopsychiatry, knowing that the DSM-IV was mainly realized from observation of adult's clinic. In the context of this increase of bipolarity's diagnosis in children, the DSM-5 workgroup on mood disorders in pedopsychiatry revaluated the limits of bipolarity [7]. With the aim of deepening the distinctions in the disorders, the workgroup on disorders in children got closer to the workgroup on the mood disorders by having three precise purposes: (1) to learn to distinguish episodes of hypomania from episodes of mania, (2) to know if a severe chronic irritability corresponds to a mania state in process of maturation in children, and (3) to define the nosologic status of episodes of hypomania with a duration superior to 4 days. At that time, the question concerning the link between this severe chronic irritability with a bipolar disorder in development remained a major

point to be resolved. For its analysis, the workgroup used scientific data while taking into account the clinical necessity of specifying mood disorders in pedopsychiatry. They discovered that the "classic" phenotype of bipolarity was actually rare in young children. Indeed, many bipolar children showed unusual symptoms of bipolarity and were actually DMDD.

Leibenluft [8] first described the diagnostic criteria of Severe Mood Dysregulation (SMD) in order to study the relations between bipolarity and severe chronic irritability [8]. The DSM-5 workgroup then proposed another terminology, the Temper Dysregulation Disorder Dysphoria (TDDD). In the end, it was the expression Disruptive Mood Dysregulation Disorder (DMDD) that was retained for the release of the DSM-5 in May 2013. The clinical picture given in the below section is very similar to the one described by Leibenluft except for hyperarousal.

Diagnostic Criteria of Disruptive Mood Dysregulation Disorder (DSM-5; 2013)

- Severe recurrent temper outbursts manifested verbally and/or behaviorally that is grossly out of proportion in intensity or duration to the situation or provocation.
- The temper outbursts are inconsistent with developmental level.
- The temper outbursts occur, on average, three or more times a week.
- The mood between temper outbursts is persistently irritable or angry most of the day, nearly every day, and is observable by others.
- Criteria A-D have to be present for 12 or more months. Throughout that time, the individual has not had a period lasting 3 or more consecutive months without all of the symptoms in Criteria A-D.
- Criteria A and D are present in at least two or three settings and are severe in at least one of these.
- The diagnosis should not be made for the first time before age 6 or after age 18 years.
- By history or observation, the age of onset of criteria A-E is before 10 years.
- There has never been a distinct period lasting more than 1 day during which the full symptom criteria, except duration, for a manic or hypomanic episode have been met.
- The behaviors do not occur exclusively during an episode of major depressive disorder and are not better explained by another mental disorder.

The symptoms are not attributable to the physiological effect of a substance or to another medical or neurological disorder.

Data concerning DMDD correspond to a pathological concept that is still in evolution. The values presented below are based on current knowledge still in movement for this new diagnosis. Prevalence found for DMDD is 3.3% in subjects from 9 to 19 years-old, among which 1.8% have a severe form [9] (American general population). This prevalence is higher than the depressive syndrome (2%) [10,11] or bipolarity (1.5%) [12,13] in children. According to Dickstein [14], average age is 11.04 and we find 78.1% of boys. There is thus a male ascendancy for DMDD [15], while both sexes are represented in an equivalent way in young bipolar people [1,16].

Many children were diagnosed with bipolar disorder but also ADHD while actually being DMMD, pathology which itself causes severe psychiatric consequences. The creation of a different clinical entity seemed necessary and will contribute significantly to the understanding of developmental trajectories of mood disorders.

Comorbidities

If we examine the association of DMDD with Axis I diagnoses, a clinical trial by Dickstein [14] showed that 93.8% of young people with DMDD presented criteria of ADHD, 84.4% the criteria Oppositional Defiant Disorder (ODD) and 46.9% the criteria of anxiety disorders. We also find comorbidities in the American study entitled "The Great Smoky Mountains Study" [10] (Table 1), however with lower rates. In Leibenluft's study [8], 84.9% of young people with DMDD presented an oppositional defiant disorder (ODD) and 86.9% an associated ADHD. We also find 58.2% of children with associated anxiety disorders and 16.4% having presented a depressive episode.

Similarly, according to a study by Kessler [17], comorbidities with DMDD amounted to more than 25% for ADHD and ODD. In these cases of comorbidity, impairment for children with DMDD runs deeper. Furthermore, these children often have symptoms similar to a depressive syndrome or to anxiety disorders which cause an even more difficult classification. Indeed, this child DMDD presents more often depressive disorders than average. In front of prevalence and severity of symptomatology, it is important that we can make a precise diagnosis for the young carriers of these disorders. We find a significant difference for comorbidity in young persons between ADHD and DMDD on one hand, and ADHD and bipolar disorder on the other. Being frequently associated with bipolar disorder (60.6%), ADHD is found even more often with DMDD (86.7%). Besides, the comorbidity rate of ADHD/ODD will differ depending on whether the child is bipolar or DMDD. Only 26.7% of bipolar children present the toxic combination (ADHD/ODD/bipolar) against 80.8% in the case of those diagnosed DMDD (ADHD/ODD/DMDD). This latter very high rate of comorbidity may lead one to reconsider the limits of the diagnotic entity of DMDD [17].

High comorbidities are also found in a study by Leibenluft [18]. DMDD in general pediatric population is associated with the following disorders: 26.9% with ADHD, 25.9% with conduct disorders, 24.5% with ODD, 14.7% with anxiety disorders and 13.4% with depressive disorders [18]. In pedopsychiatric population, comorbid disorders with DMDD were particularly frequent: 93.8% of ADHD, 84.4% of ODD and 46.9% of anxiety disorders. Also, according to Brotman and al [19], diagnoses of Axis I most associated with DMDD are ADHD (26.9%), ODD (24.5%), anxiety disorders (14.7%) and depressive disorders (13.7%) [9].

Finally, in Carlson's study [20] based on a series of 151 consecutive admissions in a department of pedopsychiatry of children from 4 to 12 years-old, 54.6% of these were admitted for behavioral disorders with aggressiveness and agitation crisis. A little more than a third of these children had a new crisis during their hospitalization. The diagnoses associated to these emotional states were mainly ADHD. The delay between the first agitation crisis and the admission was of 6 days on average. The fact of having at least one agitation crisis during the hospitalization appeared as being strongly connected to the comorbidity of ADHD with another typical behavior conducts disorder, ODD, or the existence of a learning's disorder. In this prepubescent population, neither the mania nor the other disorders

were significantly associated with the probability of agitation crisis because of the young age of the population. Other factors were found in the context of agitation crisis: low intellectual efficiency, exposure to violence and negative effects. This study evokes that these agitation crisis correspond to rage outbursts of DMDD, alone or comorbid of an ADHD.

We see that in all these studies, comorbidity of DMDD with ADHD is extremely high and the question of overlapping between these pathologies is imperative.

Diagnoses	% DMDD	% Non-DMDD	OR	IC	p-value
Other diagnoses	38.9	24.5	1.91	0.79-4.57	0.15
Mood disorders	9.8	6.1	1.73	0.42-7.21	0.45
Behaviorals disorders	33.1	19.6	1.78	0.69-4.59	0.24
Anxiety disorders	4	4.5	0.78	0.09-6.59	0.82
Depressive disorders	7.8	2.2	7.21	1.34-38.85	0.02
Addictions	7.8	8.8	0.73	0.15-3.44	0.69
ADHD	21.9	0.7	0.99	0.06-16.94	0.99
Antisocial disorders	3.8	1	0.92	0.08-9.97	0.95
ODD	2.1	0.6	3.94	0.2-79.09	0.37
OR: Odds-ratio IC: confidence interval					

Table 1: Comparison of the prevalence of Axis I diagnoses in young people with DMDD and without DMDD in the GSMS study.

Similarities

In Mulrany's study [21], 20% of children with ADHD met the criteria for DMDD and it was found that males were at a greater risk of developing ADHD with DMDD which is consistent with previous data. Those results also demonstrated that DMDD exacerbates social difficulties in children with ADHD and has a stronger impact on family functioning. Apart from the exacerbation of certain dysfunctions, there were an overlap in the context of the symptoms of ADHD and DMDD. Cardinal symptoms of DMDD, such as severe recurrent temper outbursts manifested verbally and/or behaviorally possibly associated with aggressivity, frequently co-occurs with ADHD with or without ODD or CD. More specifically, DMDD comprises hyperreactivity to negative stimuli and a reactive aggressiveness with tantrums, both of which could be found and attributed to ADHD. Likewise, there are close similarities between ADHD and DMDD concerning patterns of poor adaptative functioning and increased psychopathology [22].

Many children with ADHD have difficulties to regulate their emotion. In their literature review, Shaw, Stringaris, Nigg and Leibenluft [23] found emotion dysregulation is prevalent in ADHD throughout the lifespan and is a major contributor to impairment. Emotion dysregulation may arise from deficits in orienting toward; recognizing, and/or allocating attention to emotional stimuli and the ADHD treatment often ameliorate regulation of emotion. The authors considered 3 models to explain the links between ADHD and emotion dysregulation: they are correlated but distinct dimension; emotion dysregulation is a core diagnostic feature of ADHD or the combination constitutes a nosological entity distinct from both emotion dysregulation alone and ADHD.

From a therapeutic perspective, ADHD and DMDD also have close similarities. According to Pappadopulos et al. [24], psychostimulants were the most frequently used pharmacological agents in their review of the pharmacological treatment of aggression like severe temper outbursts, in children and adolescents [23]. Likewise, according to the review of Tourian et al. [25], methylphenidate is efficient in decreasing aggression and irritability in youth with DMDD. More generally, in this review, it seems that the methylphenidate and the risperidone, but not the lithium, are effective to decrease the symptoms of the DMDD for patients under the age of 18. In the study of Waxmonsky [26], similarities on the therapeutic aspects are also found between a group of children with ADHD and another group of children with ADHD and DMDD indeed, this study found that the DMDD children got closer to hyperactive children from the point of view of the therapeutic answer to the treatment, whether pharmacological (methylphenidate) or psychotherapeutic (cognitive and behavioral remediation, e.g. summer camp with behavioral sessions).

Distinctions

To illustrate these differences, we shall begin with a study of Carlson showing the interest to consider the DMMD as a standalone entity. G. Carlson studied the concept of tantrum, a frequent cause of hospitalization which may be strongly associated to a diagnosis of mania [20]. Among 130 children aged five to 12 years and hospitalized in child psychiatry, 55% had severe tantrums averaging one hour. These children belong to a complex diagnostic group because they may be associated with many diagnoses such as learning disorders, ADHD, ODD and conduct disorder. Furthermore, compared to the pedopsychiatric population, these children are younger, they often received treatment before (mainly atypical neuroleptics) and the duration of hospitalization is longer. Anger outbursts were repeated for 50% of them without any clear improvement and those children pose serious diagnostic and therapeutic problems. However, the other half simply improved through hospitalization and no longer presented a tantrum during it. Finally, while more than a third of these children were diagnosed bipolar I early in the treatment, only five of them had finally received the diagnosis after a reliable expertise. The diagnosis of bipolar disorder in children seems to have been given by excess and confusion between ADHD and DMMD may persist if the symptoms are not clear or if there is comorbidity.

Thus, in spite of visible similarities, DMDD and ADHD must be differentiated. Contrary to DMDD, the persistent dysphoria and chronic irritability are not found in ADHD. Finally, mood stabilizers are a part of therapeutic perspectives for the treatment of DMDD, contrary to ADHD. According to Biederman [27], a strong family psychopathology is found in the case of ADHD children, contrary to the DMDD children. To differentiate the two diseases, the definition of DMMD in the DSM-5, very similar to the initial one by Leibenluft, no longer includes hyperactivity and puts greater emphasis on severe and recurrent temper outbursts in response to common stress situations [8,28]. The working group of the DSM-5 decided to rename the syndrome "DMDD" for a more descriptive name which includes a notion of severity of temper outbursts. Hyperactivity was eliminated as a diagnostic test in order to differentiate it from ADHD, and therefore,

the presence of hyperactivity means that ADHD is associated with DMDD.

Acute emotional crises of DMDD children have a structure that is similar to "developmental" anger, but their duration is longer [29]. An adult recalling a rule and provocations by other children are the main factors of these temper tantrums. The tantrum appears suddenly and disappears gradually. While anger quickly escalates and then disappears, distress is rather constant throughout the crisis. Emotional distress is expressed by crying, withdrawal of interactions and a need for reassurance. Temper outbursts are repeated and have an impact on social, school and family life. We find in DMDD children the difficulty to regulate negative emotions in response to social cues and the predominance of negative mood. This negative mood may include sadness and anger, but chronic dysphoria and chronic irritability are the central dimensions and are not found in ADHD [15].

Finally, in Uran's study [30], it appears that children with DMMD have a higher comorbidity rate than those with ADHD. Results showed that DMDD children's average scores were higher than ADHD children in Conners and in "Communication", "Affective Responsiveness", "Affective Involvement" and "General Functioning" subscales of Family Assessment Device (FAD). In conclusion, children with DMDD were distinguished from children with ADHD by their higher comorbidity rate, greater family dysfunctioning and impaired behavioral patterns.

Pathophysiologycally, the study of amygdala activation during emotion processing of neutral faces in children with DMDD versus ADHD suggested the role of unique neural correlates in face emotion processing [19]. It showed a double dissociation in amygdala activity in youths with DMMD and ADHD when completing fear (emotional) versus non emotional ratings of neural faces. Patients with DMDD manifested hypoactivation while patients ADHD manifested hyperactivation.

The DSM-5 consequently added the DMDD diagnostic to characterize a mood disorder in children and adolescents which differs from that ADHD, a neurodevelopmental disorder [31]. This child symptomatology would be more related to the environmental context and learning disorders. Some people have almost permanently a negative mood. These individuals tend to express negative emotions in the face of everyday life events. The models of personality describe this as a negative emotional style temperament trait, a reactivity style with some stability during development and linked to biological characteristics. We refer to emotional lability, neuroticism or hazard avoidance to describe this mode of emotional reactivity. In pedopsychiatry, the "difficult temperament" is a set of temperamental traits where high emotionality is central and a risk factor for the development of anxiety, depression disorders and externalizing problems. These features, bringing together persistent negative mood and a high reactivity to events of everyday life, recall the semiology of ADHD.

Discussion

For opponents of the DSM-5, the DMDD may diagnose "trivial infantile anger" as a pathology. However, for this diagnosis, we do not refer to "simple" anger but to frequent and violent anger outbursts associated with severe and persistent irritability. Indeed, the criteria are not common (chronic dysphoria with a minimum of three severe anger outbursts per week over a period of at least one year).

Comorbidity between ADHD and DMDD are frequently found. Most studies have found an high comorbidity of at least 20% to 80% while Dickstein goes as high as more than 90% [8,14]. In addition, common features are hyperreactivity to negative stimuli and reactive aggression and similarities on the therapeutical aspect with the effectiveness of methylphenidate to some extent. This data can lead us to question ourselves about the nosological limits and the possibility of a sub-type. Similarities aside, the diagnosis of DMDD aims to avoid mistakenly assigning a diagnosis of ADHD. Indeed, we have seen that the differences between ADHD and DMDD are present. Chronic impact on mood with dysphoria or chronic irritability are among the central criteria of this differentiation. Similarly, the issue of awareness of the existence of DMDD is key for the therapeutic management, with mood stabilizers being a possible treatment differentiating it from ADHD [32].

In summary, it would be necessary for those children to develop effective treatments and have the means to act preventively. This requires the prior identification of the particularities of this pathology without being limited to nosographic categories previously developed. Indeed, knowing that psychiatric nosographies evolve based on new knowledge and cultural influences, the description of DMDD gives to number of children a recognition of their suffering. This diagnosis also changes the image they have, allowing them to evolve in a more peaceful environment. Furthermore, this diagnostic debate reminds how it is necessary in the field of child and adolescent psychopathology to keep a developmental perspective.

Conclusion

The DSM-5 added a new diagnostic disorder, the DMDD, a diagnosis related to mood disorders. For opponents of the DSM-5, the DMDD risks to diagnose "trivial infantile anger" as pathological. But for this diagnosis, we just do not speak 'simple' anger but to frequent and violent tantrums associated with severe and persistent irritability. Indeed, the criteria are not ordinary (chronic dysphoria plus a minimum of three severe tantrums per week over a period of at least one year).

DMDD is frequently comorbid with ADHD and its clinical picture may cause it to be mistaken for ADHD. However, differences are present and these two diseases must be distinguished in order to recognize the particular problems of these children. Possible explanations proposed for such a high association between ADHD and DMDD are that both disorders show similar risk factors (genetic and psychosocial vulnerability) or DMDD may be a subtype of ADHD. Besides in this review, we have not discussed the high comorbidity with ODD, a disease also to be distinguished from DMDD. It is often associated with DMDD which makes its nosological distinction harder.

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