

# Irritability in children and adolescents: a challenge for DSM-5

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**Abstract** Irritability has recently become a major focus of interest for clinicians and nosologists alike, and its position in the upcoming DSM-5 is currently debated. However, research on irritability has only recently started emerging. Here, I review the recent findings on irritability and its differentially strong relationship to depressive and generalised anxiety disorders compared to disruptive behaviours. Furthermore, I examine the importance of irritability in the recent debate about bipolar disorder in children and adolescents and discuss findings from research into severe mood dysregulation. I next address the relevance of irritability to the two core aims of developmental sensitivity and dimensionality. Finally, I critically discuss the recently proposed putative DSM-5 category of temper dysregulation disorder with dysphoria and make suggestions about future research directions.

**Keywords** Irritability · Bipolar disorder · Depression · Nosology · Severe mood dysregulation

## Introduction

The American Psychiatric Association DSM-5 Task Force emphasises the urgent need for research into irritability by stating: “Severe irritability is a very prevalent mood symptom that has received relatively little research attention; ... this lack of research attention has been a major

contributor to the current controversy as to how children who present with severe irritability as a chief complaint should be diagnosed and treated” [1].

Irritability is one of the main moods that humans experience and have a name for. It refers to easy annoyance and touchiness, is characterised by the emotion of anger, and temper outbursts can be its behavioural manifestations.

Epidemiologic studies suggest that irritability is common in children and adolescents. The estimates range from 3% for severe irritability (operationalised as severe mood dysregulation [2], see below) in the US Great Smoky Mountain Study to 20% in the Isle of Wight study [3]. However, a study using a dedicated instrument to measure irritability with psychometric data on appropriate thresholds is yet to be performed. Some preliminary data indicate that irritability is also common in child and adolescent psychiatric clinics: in an analysis of the Maudsley Hospital item sheets, approximately a third of referred patients under the age of 16 years were found to be suffering from “morbid irritability” (Professor Eric Taylor, personal communication). In a large generic New York clinic, it was found that approximately 47% of consecutively referred children had rage outbursts at home, in school or both places; about 14% were reported to have severe rages by both parent and teacher report (Professor Gaye Carlson, email communication 5th July 2010).

From the point of view of nosology, there are two pressing reasons to do research in irritability.

First, irritability is present in the criteria of a great number of psychiatric disorders and spans the internalising–externalising divide. Defined as a mood, irritability is present in the DSM-IV and ICD-10 criteria of bipolar disorder across the life span. It is also present in the criteria for depression as well as dysthymia in children (it is a Criterion A in the DSM-IV but not in the ICD-10), but not

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in adults. Moreover, irritability or one of its constituent characteristics such as anger or temper outbursts are also present in the criteria of a wide range of anxiety disorders, including separation anxiety disorder and generalised anxiety disorder (GAD). Perhaps most strikingly, while irritability is considered a mood symptom, it is also one of the main constituents of oppositional defiant disorder (ODD; in the form of temper outbursts, anger and touchiness)—a supposedly disruptive disorder. This very wide presence of irritability can be an obvious nuisance by inflating the rates of overlap between disorders (artificial comorbidity) [4]. Conversely, this wide presence may not just be the result of arbitrary choice of symptom criteria by taxonomists. Rather, irritability could be an example of a mood dimension that cuts across psychopathology. This is an ongoing research question with obvious practical implications.

A second and perhaps more dramatic reason that motivates the study of irritability is the debate on *pediatric bipolar disorder*. In the USA, the rates of diagnosis of bipolar disorder in children and adolescents have shown an increase of about 500% over the last decade [5, 6], leading to controversy [7]. One reason for this dramatic increase may have been the result of the assertion that irritability, which is continually present from a very young age (often from within the first year of life [8]), should be considered the typical mood of early mania [9, 10]. Yet, such “chronic” irritability does not seem to conform to what is usually thought of a mood that occurs within a relatively sharply demarcated episode—in the words of the DSM: “a distinct period of abnormally and persistently elevated, expansive, or irritable mood”. Studying the distinction between episodic and non-episodic mood changes—and more generally the time scales and variability of irritable mood—is crucial for diagnosis and treatment. Moreover, as the recent massive expansion in bipolar diagnoses shows, it may also have important public health implications.

### **The relationship of irritability with psychopathology and adverse outcomes**

Of the relatively little research that have so far been done on irritability, most have been on its relationship to other psychopathology. This is justified given that irritability seems to cut across psychopathology—something that has also led to concerns about its specificity. To draw an analogy from internal medicine: is irritability merely like fever, present in all sorts of different conditions ranging from infections to malignancy and therefore merely an indicator that there is “something wrong” rather than a specific symptom?

Does irritability have specific associations?

If, indeed, irritability is a mood state characterised by anger and easy annoyance, it is plausible to hypothesise that it will be differentially related to other mood disorders. This prediction seems to hold true, at least under certain conditions.

In response to the bipolar controversy, Leibenluft et al. proposed the ad hoc generated category of severe mood dysregulation (SMD) with the explicit aim of testing the relationship between chronic irritability and mania in children and adolescents. Hence, the main characteristic of SMD is severe irritability that does not conform to the commonly accepted patterns of episodicity, i.e. SMD-irritability lacks clearly demarcated episodes of irritable mood of several days’ duration. The group has previously presented evidence about the necessity to distinguish between chronic and episodic irritability [10]. In addition, SMD requires frequent and impairing anger outbursts, combined with at least three of the “B” criteria of mania (pressured speech, agitation, insomnia and flight of ideas/racing thoughts) and one (distractibility) that is also common to ADHD [9]. A community-based follow-up study suggested that SMD was common, with a lifetime prevalence of 3.3% in those who are 9–19 years of age [2]. Moreover, in the same sample, SMD was a significant predictor of depressive disorders (but not bipolar disorder) at the 7-year follow-up in youths.

Motivated by considerations about the central position that ODD occupies in developmental psychopathology [11], Stringaris and Goodman proposed three distinct dimensions within oppositionality, each differentially predicting other psychopathology: an irritable dimension that predicts primarily depression and generalised anxiety (GAD); a headstrong dimension as the predictor of attention deficit/hyperactivity disorder (ADHD) and nonaggressive CD; and a hurtful dimension predicting aggressive conduct problems and callous/unemotional traits. In these studies, irritability was operationalised on the basis of three symptoms: temper tantrums, being touchy or easily annoyed, and being angry–resentful. The differential associations of the three dimensions have been demonstrated in cross-sectional and longitudinal community-based samples [12, 13]. An important finding from these studies is that irritability is a specific predictor of depression and GAD in two ways: firstly, by showing that it is irritability, rather than other symptoms of oppositionality, which best predicts depression and GAD; secondly, by showing that irritability does just predict all sorts of psychopathology—in fact, headstrong and hurtful behaviours, but not irritability, predict ADHD and conduct problems in multivariate analyses. Also, the prediction to depression and GAD held after controlling for other psychiatric

disorders at baseline. A significant prediction from irritability to depression, dysthymia and GAD, but not phobias, personality (Axis II in the DSM-IV) or bipolar disorders, even after controlling for these disorders at baseline, has also been demonstrated in a 20-year follow-up study of a community-based sample [14]. Importantly, in this sample, the predictions held across informants: parent-reported irritability in youth predicted to self-reported disorders 20 years later. An obvious concern when predicting from irritability to depression is the problem of item overlap. However, it is unlikely that this relationship is accounted for by the presence of irritability in the criteria of depression or GAD: the prediction holds even when using the ICD-10 instead of the DSM-IV depression category (the former does not include irritability as a criterion for children and adolescents). Moreover, the association remains when predicting from childhood irritability to depression and dysthymia in adults—where the criteria do not include irritability.

#### Is non-episodic irritability related to BP?

The assertion that children with non-episodic irritability may be suffering from bipolar disorder [8] was tested in further research. Mick et al. reported that children with very severe forms of irritability were several times more likely to suffer from BP. However, this group's assessment of BP in children is known to include children with what others have described as chronic irritability (i.e. onset in the first year of life with duration over several years) making it difficult to compare it with the commonly accepted construct of bipolar disorder. A major contribution to the question about how irritability relates to bipolar disorder has been through testing the associations of the ad hoc generated construct of SMD [9]. So far, the results show that SMD and BP are distinct in terms of: (a) family history [15], in that SMD youth are significantly less likely than children with classical BP to have parents with BP; (b) longitudinal predictions, showing that SMD predicts major depression, but not BP, in a community sample [2] and that SMD children are very unlikely to show episodes of (hypo-)mania in a 2-year follow-up [16]; (c) processing of emotional stimuli [17]. These findings are in agreement with a clinic study showing that a diagnosis of BP is rarely justified in children who present with chronic persistent irritability [18].

Taken together, the evidence so far suggests that it is very unlikely that chronic irritability, as commonly seen in child psychiatric clinics, may be the predominant mood manifestation of bipolar disorder. This does not seem to hold even for the majority of those with severe non-episodic irritability. However, the conclusion that non-episodic irritability is not specifically related to BP should not

lead to the interpretation that chronic persistent irritability is not relevant to those with BP. Clinically, it will be of particular interest to find out whether, in those with BP or at high risk of BP, baseline irritability levels (i.e. outside an episode) are predictive of outcome. Also, it is worth noting the shared deficits between BP and SMD, such as in emotion labeling [19, 20] and cognitive flexibility [21], although these may be mediated by different brain pathways [17].

#### Irritability and other important outcomes

In a recent 30-year follow-up study of the Isle of Wight sample, Pickles et al. [3] used a single question addressed to the parents of the participants when they were 14 years: “is your child irritable?” They showed that irritability was a significant predictor of suicidality in adulthood (depression or other psychopathology at outcome was not assessed in relation to irritability in this study). In the Children in the Community study, parent-rated irritability at mean age 13.8 years was a significant predictor of low income and poor educational attainment [14]. Importantly, path analysis showed that this association was only partially mediated through the presence of depression, GAD or dysthymia at outcome [14].

#### What should be the position of irritability in psychiatric nosology?

It is clear that there is much that we do not yet know about irritability and that a precocious attempt to secure a taxonomical position for irritability may lead to its undue reification. However, several of the new findings in this area may provide a reasonable first approximation on how to deal with irritability in future classifications. Here, we discuss two declared aims of the DSM-5 [22] that seem particularly relevant to irritability before addressing the question of an irritability category.

The first is that this classification is meant to be *developmentally sensitive*, rectifying the unrealistically abrupt discontinuities between childhood and adult disorders. Irritability may serve as a case example: it appears early in life, and is part of ODD, one of the most common disruptive behaviour disorders. There is little doubt that irritable children may also be disruptive; however, including irritable mood as part of the diagnostic criteria for disruptive disorders risks confusing behavioural consequences (oppositonality and defiance) with their possible causes (anger or easy annoyance). Importantly, the longitudinal research suggests that irritability is *much less* related to later antisocial problems than to later depression, dysthymia and generalised anxiety. Distinguishing between

moods and their consequences across development will therefore be an important task for DSM-5 with implications for pathophysiological research and treatment.

The second important aspect of the new version of DSM is meant to be its strong emphasis on a *dimensional approach*. There is discussion about incorporating an irritability scale into the DSM-5 as part of a range of scales that will measure things such as impulsivity or sadness and will have a primary-care screening use (personal communication Professor David Shaffer, May 2010). Again, irritability could be a case example on how to tackle the dimensions issue in the DSM-5. Irritability appears to have the properties of a dimension in psychopathology: it cuts across a range of psychiatric disorders and seems to be measurable as a continuum. At the same time, irritability seems to be specifically related to depression, GAD and dysthymia in multivariate analyses. Studying irritability as a dimension that cuts across psychopathology could help remove it from the criterion sets of such a wide range of psychiatric disorders (and, thus, possibly reduce the likelihood of artificial comorbidity). Also, such scales can help clinicians quantify their clinical impression and establish whether any of the treatments they use is helpful in changing irritability. Moreover, the coding of irritability as a dimension could potentially function as a risk index for the occurrence of depression or GAD—in a way analogous

to how, say, hypertension is a risk for stroke. In this context, it is of course important to emphasise that the predictions from irritability to depression are by no means deterministic and that the effect sizes of the association are by no means large.

### The proposed temper dysregulation disorder category in the DSM-5

Of course, many clinical decisions—especially those relating to treatment—are by their nature binary (“should I treat or not?”). The DSM-5 task force has recently proposed the putative category of temper dysregulation disorder with dysphoria (TDDD, DSM-5 proposed criteria listed in Table 1) as a way of dealing diagnostically with children who suffer from severe irritability. TDDD is designed to capture what seems to be a very pertinent clinical phenomenon: children with frequent temper tantrums occurring against the background of a chronically irritable mood. Part of the rationale for TDDD is to provide a diagnostic home for those children with severe non-episodic irritability. In a way, therefore, introduction of TDDD may be seen as an attempt to defend against the over-diagnosis of bipolar disorder in the USA. TDDD has not been systematically studied so far, although findings

**Table 1** Proposed criteria for the putative DSM-5 category of temper dysregulation disorder with dysphoria

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- A. The disorder is characterised by severe recurrent *temper outbursts* in response to common stressors
1. The temper outbursts are manifest verbally and/or behaviourally, such as in the form of verbal rages or physical aggression toward people or property
  2. The reaction is grossly out of proportion in intensity or duration to the situation or provocation
  3. The responses are inconsistent with developmental level
- B. Frequency: the temper outbursts occur, on average, three or more times per week
- C. Mood between temper outbursts
1. Nearly every day, the mood between temper outbursts is persistently negative (irritable, angry and/or sad)
  2. The negative mood is observable by others (e.g. parents, teachers, peers)
- D. Duration: Criteria A–C have been present for at least 12 months. Throughout that time, the person has never been without the symptoms of Criteria A–C for more than 3 months at a time
- E. The temper outbursts and/or negative mood are present in at least two settings (at home, at school or with peers) and must be severe in at least in one setting
- F. Chronological age is at least 6 years (or equivalent developmental level)
- G. The onset is before age 10 years
- H. In the past year, there has never been a distinct period lasting more than 1 day during which abnormally elevated or expansive mood was present most of the day for most days, and the abnormally elevated or expansive mood was accompanied by the onset, or worsening, of three of the “B” criteria of mania (i.e. grandiosity or inflated self-esteem, decreased need for sleep, pressured speech, flight of ideas, distractibility, increase in goal-directed activity or excessive involvement in activities with a high potential for painful consequences). Abnormally elevated mood should be differentiated from developmentally appropriate mood elevation, such as it occurs in the context of a highly positive event or its anticipation
- I. The behaviours do not occur exclusively during the course of a psychotic or mood disorder (e.g. major depressive disorder, dysthymic disorder, bipolar disorder) and are not better accounted for by another mental disorder (e.g. pervasive developmental disorder, post-traumatic stress disorder, separation anxiety disorder) (note: this diagnosis can co-exist with oppositional defiant disorder, ADHD, conduct disorder and substance use disorders). The symptoms are not due to the direct physiological effects of a drug of abuse, or to a general medical or neurological condition
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from research in SMD can be reasonably extrapolated to it. For example, it is possible that TDDD will show substantial overlap with ODD. But this could be an advantage, as it would give clinicians the opportunity to code the salient mood components, without having to use a label that necessarily implies disruptive behaviours. Of course, the TDDD label is not entirely without problems. The word “temper” in its name can mislead people into believing that temperament is referred to and that psychiatrists have given diagnostic labels to temperamental variation. Also, there is a clear need for further research into the putative category. In particular, how much of the impairment is caused by severe irritability rather than co-existing conditions (e.g. ADHD), and is there evidence that the category is homogeneous enough for it to be clinically useful? At least in the case of ODD, it is clear that parenting interventions may be very effective (possibly also in reducing irritability).

### Unanswered questions about irritability and future directions for research and classification

The first step in examining the position of irritability within the nexus of psychopathology is well underway. The next important step is to establish causal influences on irritability and the mechanisms by which it exerts its effects. These next steps should inform nosology and will be necessary in the quest for pathophysiologically informed treatments.

*Measurement* and, more generally, further *phenotypic refinement* is the first big future issue for research into irritability. Instruments specifically designed to measure irritability are yet to be developed, although valuable information can and has been extracted using existing scales (such as the CAPA [2], the DAWBA [12, 13] and the DISC [14]). Instruments that are designed to capture the exact temporal dynamics of irritability and the extent to which it is modifiable by environmental cues may help with its phenotypic refinement. In this context, it will also be important to test the relationship between irritability and the related concepts of mood [23] and emotional [24] lability.

*Development* is another important consideration, closely related to measurement issues. For example, is the frequency or duration of early life tantrums predictive of later irritability trajectories? Are there developmentally sensitive periods for the increase of irritability, e.g. puberty? Also, how much is irritability related to neuroticism or temperamental emotionality? Preliminary findings from the Isle of Wight [3] suggest that the relationship between adolescent irritability and adult suicidality is not mediated by adult neuroticism. Conversely, recent longitudinal data

suggest that temperamental emotionality is an important predictor of ODD and of its relationships to internalising disorders.

The *genetics* of irritability are still unexplored as is its relationship to the environment. These should be tested in twin studies. It seems plausible to assume that children’s irritability modifies their own environment as it is to expect that children’s irritability will be affected by the environment they live in. Testing this assumption in longitudinal twin studies offering repeatedly assessed environmental variables can have important practical implications.

Studying *mediation* and *moderation* mechanisms are important in understanding how irritability relates to depression. How much of genetic or environmental risk factors does irritable mood share with sadness or other symptoms of depression? Moreover, is any overlap different to that between antisocial problems and depression?

*Family and situational* factors may also help in distinguishing between types of irritability. Is irritability that occurs only with particular persons the same as irritability that occurs pervasively or irritability that seems to happen out of the blue? Furthermore, family and situational factors may still be very important even if the genetic contribution to irritability were found to be very high. It may well be that the effects of irritability can change dramatically through environmental modification (e.g. following parenting interventions). As has been argued before [25], even disorders that are completely genetically determined, such as phenylketonuria, may be treated successfully by simple environmental modification.

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