Review

Irritability in child and adolescent psychopathology: An integrative review for ICD-11

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HIGHLIGHTS

- Severe irritability in youth poses a significant challenge for assessment and diagnosis.
- The development of ICD-11 aims to improve the diagnostic classification of youth irritability.
- To this end, we first review the literature on severe mood dysregulation and DMDD.
- Second, we summarize the research on the irritable dimension of ODD symptoms.
- Based on the evidence, we recommend a subtype, ODD with chronic irritability-anger, for ICD-11.

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ABSTRACT

In preparation for the World Health Organization's development of the Eleventh Revision of the *International Classification of Diseases and Related Health Problems* (ICD-11) chapter on Mental and Behavioral Disorders, this article reviews the literature pertaining to severe irritability in child and adolescent psychopathology. First, research on severe mood dysregulation suggests that youth with irritability and temper outbursts, among other features of hyperactivity and arousal, demonstrate cross-sectional correlates and developmental outcomes that distinguish them from youth with bipolar disorder. Second, other evidence points to an irritable dimension of Oppositional Defiant Disorder symptomatology, which is uniquely associated with concurrent and subsequent internalizing problems. In contrast to the *Diagnostic and Statistical Manual of Mental Disorders'* (5th ed.) Disruptive Mood Dysregulation Disorder, our review of the literature supports a different solution: a subtype, *Oppositional Defiant Disorder with chronic irritability/anger* (proposal included in Appendix). This solution is more consistent with the available evidence and is a better fit with global public health considerations such as harm/benefit potential, clinical utility, and cross-cultural applicability. Implications for assessment, treatment, and research are discussed.

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1. Introduction

The World Health Organization (WHO) is revising its *International Classification of Diseases and Related Health Problems*, currently in its Tenth Revision (ICD-10; WHO, 1993), including the chapter on Mental and Behavioral Disorders (WHO, 1993). The forthcoming Eleventh Revision (ICD-11) is anticipated in 2018 (WHO, 2016). Several recent reviews (e.g., Leibenluft, 2011; Rutter, 2011) have underscored the need for changes in the diagnostic classification of child behavioral and emotional disorders in ICD-11. In addition, the recent revision of the American Psychiatric Association's (APA; 2013) *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) has illustrated some of the difficulties, possible solutions, and unresolved questions in the classification of child psychopathology. For ICD-11, the necessity of proposed changes must be weighed against considerations of clinical utility, global public health, and implications for clinicians, families, and children affected (Keeley et al., 2016; Reed, 2010).

An important question facing the present ICD revision is whether to include a new diagnostic entity representing a syndrome of frequent temper outbursts and persistent irritability in children and adolescents (Axelson et al., 2011; Leibenluft, 2011; Lochman et al., 2015; Parens, Johnston, & Carlson, 2010; Stringaris, 2011). Irritability is both a normal human emotion with typical developmental manifestations as well as a diagnostic feature of over a dozen common psychological conditions (e.g., ODD, depression, generalized anxiety) and an associated feature of many more (e.g., ADHD, autism spectrum disorders, sleep problems; APA, 2013; Carlson, 2016; Stringaris & Taylor, 2015; Vidal-Ribas, Brotman, Valdivieso, Leibenluft, & Stringaris, 2016). It is therefore not surprising that irritability poses challenges for assessment and diagnosis, and may also help account for the high rates of comorbidity in child and adolescent mental health (Angold et al., 1999; Caron & Rutter, 1991). A rapidly growing body of evidence shows that children with severe irritability, anger, and temper outbursts are likely to exhibit a pattern of correlates and outcomes that differentiates them from other children who may have the same diagnosis. Such findings are clearly relevant to the classification of emotional and behavioral disorders in ICD-11. And this is more than an esoteric nosological question. The manner in which ICD-11 handles irritability will affect the identification of youth in need of services and the accuracy of the diagnosis they receive, which, in turn, determines the selection of appropriate interventions and the outcome expectancies of parents and clinicians (Lochman et al., 2015).

The aims of this article are to provide a comprehensive and integrative review of the available research on severe irritability/anger in children, and present the empirical basis and public health rationale for how childhood irritability and anger should be considered in ICD-11. Specifically, this paper reviews two distinct but related bodies of research on youth irritability. These are briefly introduced below, with more thorough discussion later in the article (see Table 1 for abbreviations used in this article).

First, Leibenluft and colleagues (Leibenluft, 2011; Leibenluft, Charney, Towbin, Bhangoo, & Pine, 2003) have carried out a program of longitudinal and laboratory-based research investigating severe mood dysregulation (SMD)—a provisional research syndrome characterized by chronic irritability, temper outbursts, and hyperarousal—in order to clarify the diagnostic boundaries of pediatric bipolar disorder (BD). Unlike BD, SMD was found to be associated with later anxiety and depressive episodes, but not manic episodes (Leibenluft, 2011). The subsequent decision to include Disruptive Mood Dysregulation Disorder (DMDD) in DSM-5 was based in large measure on these investigations of SMD (APA, 2013; Leibenluft, 2011), despite several key differences in how these diagnostic constructs have been defined and operationalized. The literature on SMD and DMDD is summarized in part 1 of this review.

Table 1
Abbreviations.

APA	American Psychiatric Association
ADHD	Attention-deficit/hyperactivity disorder
BD	Bipolar disorder
CD	Conduct disorder
CFA	Confirmatory factor analysis
DSM	Diagnostic and Statistical Manual of Mental Disorders
DBD	Disruptive behavior disorder
DMDD	Disruptive Mood Dysregulation Disorder
EFA	Exploratory factor analysis
ICD	International Classification of Diseases
LCA	Latent class analysis
ODD	Oppositional Defiant Disorder
SMD	Severe mood dysregulation
WHO	World Health Organization

Second, several research groups have shown that the 8 symptoms of Oppositional Defiant Disorder (ODD) reflect at least two different dimensions as well as a single diagnostic category. In particular, the "irritable dimension" (e.g., touchy or easily annoyed, angry and resentful) is consistently supported, showing distinct associations with anxiety and depression, both cross-sectionally and across development (e.g., Burke, 2012; Burke, Hipwell, & Loeber, 2010; Ezpeleta, Granero, de la Osa, Penelo, & Domenech, 2012; Stringaris & Goodman, 2009a, 2009b). Part 2 of this review discusses this research.

We conclude in part 3 with a critical integration of the research and application to the diagnostic classification of irritability. Specifically, we recommend that ICD-11 should recognize a pattern of severe irritability and anger in youth, which was not identified by previous editions of the ICD or DSM. However, the research seems insufficient to justify, and to some extent manifestly argues against, including a freestanding diagnosis such as DMDD in ICD-11. Upon thorough examination of the available evidence, and in consideration of global public health implications, we recommend that ICD-11 include a subtype, *ODD with chronic irritability/anger* (see Appendix).

Several recent publications have offered useful reviews of different portions of the literature addressed in the present article. The literature regarding SMD and DMDD has been summarized elsewhere (e.g., Baweja, Mayes, Hameed, & Waxmonsky, 2016; Leibenluft, 2011; Mikita & Stringaris, 2013; Roy, Lopes, & Klein, 2014; Parens & Johnston, 2010; Stringaris, 2011), including some critical reviews (e.g., Axelson et al., 2011; Lochman et al., 2015). Although no articles have specifically reviewed the research on ODD symptom dimensions, a few have addressed the relations between ODD and internalizing problems (e.g., Boylan, Vaillancourt, Boyle, & Szatmari, 2007; Burke & Loeber, 2010; Fraire & Ollendick, 2012; Greene & Doyle, 1999). Others have offered more general, transdiagnostic treatments of irritability and anger (e.g., Fernandez & Johnson, 2016; Krieger, Leibenluft, Stringaris & Polanczyk, 2013; Leibenluft & Stoddard, 2013; Meyers, DeSerisy, & Roy, 2016; Stringaris & Taylor, 2015), including a recent meta-analysis and conceptual review (Vidal-Ribas et al., 2016). Finally, a few articles have offered more clinically oriented reviews (e.g., Sukhodolsky, Smith, et al., 2016; Towbin, Axelson, Leibenluft, & Birmaher, 2013; Tourian et al., 2015).

This review is a novel contribution in that it critically integrates these two bodies of research. In an earlier, brief commentary (Lochman et al., 2015), we presented a succinct summary of selected literature. Here, we provide a comprehensive and up-to-date review of this rapidly expanding evidence base, with specific recommendations for the diagnostic classification of irritability/anger in ICD-11. To identify relevant articles, literature searches were conducted in PsycINFO, PubMed, and Google Scholar. Search terms were tailored to identify peer-reviewed empirical articles related to irritability in child and adolescent psychopathology in the two areas noted above. Specifically, we searched for (a) studies directly investigating SMD, DMDD, or closely related proxies such as chronic irritability; and (b) studies that used diagnostic features of ODD as a means to investigating dimensional or categorical subcomponents of ODD symptomatology.[1] Searches were last conducted in August 2016.

2. Syndromes and disorders of mood dysregulation in children

The recent interest in severe childhood irritability was in part sparked by concerns about the diagnosis of BD in children. Data collected between 1990 and 2006 indicate that rates of pediatric BD increased

as much as 5-fold in inpatient populations (Blader & Carlson, 2007; Case, Olfson, Marcus, & Siegel, 2007) and as much as 40-fold in outpatient clinics (Moreno et al., 2007). Notably, this rate of change was substantially greater than that of BD in adults and that of other disorders in children. While these findings may indicate an alarming trend in the diagnosis of pediatric BD, the prevalence of pediatric BD remains relatively low (approximately 1–3%; Van Meter, Moreira, & Youngstrom, 2011).

An observed increase in any diagnostic estimate could reflect a true change in prevalence or a change in diagnostic practices. Changing clinical practices could, in turn, represent an improvement (more accurate case identification), a problem (overdiagnosis and misdiagnosis), or some combination of both (Stringaris & Youngstrom, 2014). In the case of the U.S. pediatric BD diagnoses, the upsurge has been largely attributed to changes in diagnostic conventions. On the one hand, there was growing professional consensus that the classic symptoms of mania do sometimes present in children, warranting a BD diagnosis according to current diagnostic systems and guidelines. On the other hand, some portion of clinicians and researchers went one step further, adopting the belief that childhood mania could be detected, perhaps in a prodromal or modified form of BD, based on the presence of irritable mood rather than the cardinal manic symptoms characteristic of adults with BD (Leibenluft, 2011; Parens & Johnston, 2010). Subsequent research has shown that the purportedly increasing rates of pediatric BD could be accounted for by variability in research and clinical diagnostic methods used in the U.S. rather than true changes in prevalence over time or differences between countries (James et al., 2014; Stringaris & Youngstrom, 2014; Van Meter et al., 2011). Whether these changing diagnostic practices of some U.S. clinicians were for better or for worse remains a matter of debate. Nonetheless, when it comes to the reliability, validity, and utility of a diagnosis, variability across clinicians represents a significant problem for clinical practice and an open question for research.

In an effort to help clarify the boundaries of BD in youth, Leibenluft et al. (2003) established a broad phenotype[2] of pediatric BD, "severe mood and behavioral dysregulation," later known as "severe mood dysregulation" (SMD). Initially, SMD was a provisional research syndrome defined by three primary features: (a) non-episodic, abnormal mood (i.e., anger or sadness); (b) symptoms of hyperarousal (e.g., insomnia, agitation, distractibility); and (c) heightened reactivity, manifest through verbal or behavioral outbursts (Leibenluft et al., 2003). By comparing children with SMD to those with BD, research could hopefully determine whether these were two distinct syndromes or different manifestations of the same underlying disorder (Leibenluft, 2011). Subsequent findings have been interpreted as evidence supporting the validity of SMD and, by extension, DMDD (DSM-5 Child and Adolescent Disorders Work Group, 2010; Leibenluft, 2011), despite the noteworthy distinctions between the two constructs and considerable variability in how they have been operationalized (discussed later in the article).

2.1. The evidence for SMD

2.1.1. Longitudinal and cross-sectional behavioral findings

Perhaps the most compelling evidence for SMD comes from large longitudinal studies. Using an existing longitudinal epidemiological dataset, Brotman et al. (2006) found that a post hoc SMD diagnosis in childhood emerged as a unique, robust predictor of depressive disorders in early adulthood. Similar analyses could not be conducted for BD in that sample, but subsequent studies have tested such hypotheses. For

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[1] Case studies, commentaries, and review articles were not included. Intervention studies were included only if they examined SMD, DMDD, or ODD-irritability as a moderator or similarly relevant analyses. Studies of dimensions of disruptive behavior were excluded if they included a broader range of symptoms beyond the core features of ODD (e.g., ADHD, conduct problems, depressive symptoms, emotion lability/dysregulation). Articles broadly related to irritability or temper outbursts, but not SMD, DMDD, or ODD, were also excluded.

[2] The broad phenotype, not captured by DSM-IV criteria, was operationalized in order to be contrasted with other, narrower phenotypes (also articulated by Leibenluft et al., 2003) which were diagnosable through DSM-IV. These included *intermediate phenotypes* (defined by mania/hypomania not otherwise specified, or mania/hypomania comprised of irritable but not elated mood), and a *narrow phenotype* (defined by the hallmark criteria of mania/hypomania including both the minimum 7- or 4-day duration and the elevated/expansive mood or grandiosity).

example, Leibenluft, Cohen, Gorrindo, Brook, and Pine (2006) found that although *episodic irritability* (characteristic of BD) in early adolescence was predictive of anxiety and mania in adolescence/adulthood, *chronic irritability* (characteristic of SMD) was predictive of later ODD, ADHD, and Major Depressive Disorder. Additionally, Stringaris, Cohen, Pine, and Leibenluft (2009) examined a similar construct of irritability, consisting of having tantrums and being angry, measured in early adolescence. Over a 20-year follow-up period, even after controlling for baseline psychopathology, parent-reported irritability predicted self-reported outcomes of Major Depressive Disorder, Generalized Anxiety Disorder, and Dysthymia, but not BD or personality disorders (Stringaris et al., 2009).

To our knowledge, only two longitudinal studies have examined actual SMD diagnoses prospectively. First, Stringaris et al. (2010) assessed a sample of 177 youth with either SMD or BD at baseline and 4 subsequent points at 6-month intervals. Compared to children with SMD, those with BD were approximately 50 times more likely to exhibit a manic, hypomanic, or mixed episode at some point over the next two years (Stringaris et al., 2010). Second, Deveney et al. (2015) reported the results of a 4-year prospective study of a sample of 200 youth with SMD. At 2- and 4-year follow-ups, respectively, only 49% and 40% of the returning samples continued to meet criteria for SMD, and another 42% and 37% continued to show clinically significant irritability symptoms. Here, several caveats should be noted. First, both studies had relatively low follow-up response rates due to attrition and rolling enrollment (i.e., participants' duration in study varied). Second, both studies reported a wide range of comorbidities in the SMD sample at baseline, including ADHD (>80%), ODD (>75%), anxiety disorders (30–56%), depressive disorders (23–33%), and CD (about 5%), and Deveney et al. (2015) reported that participants had an average of 4 to 5 lifetime diagnoses. Finally, all of the above studies may have been poorly designed for the assessment of bipolar disorder at longitudinal follow-up. A recent meta-analysis (Youngstrom, Genzlinger, Egerton, & Van Meter, 2015) demonstrated that caregivers' reports are best for differentiating between youth with BD vs. those without, with a large effect size that was over twice that of youth report. Thus, studies utilizing only self-report at follow-up (e.g., Brotman et al., 2006; Deveney et al., 2015; Stringaris et al., 2009, 2010) are more susceptible to false negatives in the identification of BD.

In addition to these longitudinal findings, several cross-sectional studies also suggested distinctions between SMD and BD. Children with BD were more likely to have parents with BD than were children with SMD (Brotman et al., 2007). A number of other studies (e.g., Birmaher et al., 2009; Brotman et al., 2006; Stringaris et al., 2010) collectively demonstrate that SMD is more common among males than females, whereas BD shows a roughly equal gender distribution in youth (DSM-5 Childhood and Adolescent Disorders Work Group, 2010). And in the development of Stringaris, Zavos, et al.,'s (2012) parent- and self-report rating scale, the Affective Reactivity Index, youth with SMD had higher irritability scores than youth with BD, who in turn had higher scores than healthy comparison youth. Using the same measure, Stoddard et al. (2014) found that youth with SMD and comorbid anxiety disorders showed higher overall irritability than youth with anxiety alone, but not more than youth with SMD alone; and all anxiety and SMD groups showed higher levels of irritability than healthy controls. With respect to characterizing SMD, these studies demonstrate what is already known: youth with SMD are more irritable than other youth. But is it also the case that irritable youth are more likely to have SMD? Interestingly, in one outpatient clinical sample of 51 children referred specifically for severe, frequent, and impairing temper outbursts, only 22% met criteria for SMD whereas ODD (88%), ADHD (75%), anxiety disorders (49%), and depressive disorders (33%) were far more common (Roy et al., 2013). Lastly, Giacobo, Jané, Bonillo, Ballespí, and Díaz-Regañon (2012) found that SMD, unlike anxiety, was not associated with somatic symptoms in a sample of preschoolers.

2.1.2. Laboratory findings

Research over the past decade has shed light on the pathophysiology of severe irritability using various neuropsychological, neuroimaging, and physiological methodologies to compare youth with SMD to healthy controls, youth with BD, and those with other disorders. This research focused largely on the core processes thought to underlie irritability and anger: deficits in cognitive flexibility and impaired processing of emotional stimuli (Leibenluft, 2011; Leibenluft & Stoddard, 2013; Stringaris & Taylor, 2015). It has been hypothesized that these deficits collectively contribute to increased likelihood of encountering frustrating circumstances, a reduced threshold for frustration, and amplification of irritability and anger (Leibenluft, 2011).

Neuropsychological and behavioral research paradigms have been used to investigate cognitive flexibility among these groups. Dickstein et al. (2007, 2010) demonstrated that youth with BD exhibit clear deficits in reversal learning, but there were only a few small effects and marginal trends that differentiated youth with SMD from healthy controls. Indeed, with regard to behavioral measures of neuropsychological function, most studies have not found results that significantly differentiate youth with SMD from healthy controls. While Adleman et al. (2011) found that youth with SMD had fewer total correct trials on a response reversal task than BD and healthy youth, Deveney, Connolly, et al. (2012) found no behavioral differences between BD, SMD, and controls on a motor inhibition task (however, see contrasting results below regarding imaging differences). Independent from these studies, Uran and Kılıç (2015a) conducted a host of neuropsychological tests (Wisconsin Card Sort, Stroop, trail-making, controlled oral word associations, and category naming) and found that ADHD youth, but not SMD youth, could be significantly differentiated from healthy controls on these tasks. Studies among youth with high-functioning autism have found that irritable mood is associated with dampened physiological reactivity (Mikita et al., 2015), but not with card-sort or trail-making performance after controlling for IQ (Simonoff et al., 2012). A slightly different story emerges, however, when response reversal tasks are combined with functional magnetic resonance imaging. Youth with BD and SMD appear to share common deficits in caudate activity in response to errors, suggesting common dopamine-related learning deficits. However, only youth with SMD showed such abnormalities in the inferior frontal gyrus, suggesting unique deficits in behavioral inhibition (Adleman et al., 2011). Yet, during failed attempts at motor inhibition, SMD youth do not appear to show any differences from controls, whereas BD youth showed deficits in the right anterior cingulate cortex and right nucleus accumbens. In sum, whether looking at brain activity or not, youth with SMD appear to generally resemble healthy controls during response reversal/inhibition paradigms. Although there are some differences in some studies, SMD youth are not nearly as distinct from healthy controls as are ADHD or BD youth.

The largest body of evidence regarding the neural mechanisms of SMD relate to processing emotional stimuli. In comparison to healthy controls and other diagnostic groups (ADHD/CD, MDD/ANX), youth with BD and those with SMD both display similar deficits in their ability to accurately label emotions via facial expressions in both children and adults (Guyer et al., 2007; Kim et al., 2013; Rich et al., 2008). Similarly, Deveney, Brotman, et al., (2012) found that SMD youth made more errors than healthy controls, and were not different from BD youth, in labeling emotion via prosody in both children and adults. Some evidence suggests that these emotion-labeling deficits are associated with poor social reciprocity skills among youth with BD, but with dysfunctional family relationships among youth with SMD (Rich et al., 2008), as well as with youth with SMD paying less attention to eyes compared to healthy children (Kim et al., 2013). In a visual probe paradigm, youth with SMD show evidence of increased threat bias relative to healthy controls and independent from the presence or absence of depressive and anxiety disorders (Hommer et al., 2014). At the same time, however, youth with SMD show no attentional bias toward positive or negative images, unlike youth with BD and healthy controls (Rich et al., 2010).

These ostensibly conflicting findings might be reconciled by neuro-imaging data. Youth with SMD showed low activation in the left amygdala when completing subjective fear ratings of neutral faces, whereas non-irritable youth showed high activation, compared to BD youth and healthy controls. Interestingly, however, SMD and BD youth reported higher subjective ratings of their own fear relative to healthy controls (Brotman et al., 2010). In a similar task, youth with SMD and BD both exhibited higher levels of activation in the right amygdala, relative to healthy controls, when processing emotional and neutral faces; however, in parietal regions responsible for monitoring and integrating information, SMD youth uniquely showed deactivation in response to fearful expressions, whereas BD youth uniquely showed deactivation in response to angry expressions (Thomas et al., 2013). In another study, Thomas et al. (2012) presented youth with faces that morphed from neutral to varying levels of anger or happiness. In response, healthy controls exhibited increasing activity in the left amygdala and in the left posterior cingulate, while those with BD and SMD showed no change in amygdala activity and decreasing activity in the left posterior cingulate, suggesting disengagement from increasing anger. Conversely, as faces morphed from neutral to happy, healthy volunteers showed no change, BD showed decreasing, and SMD showed increasing activity in the right inferior parietal lobule, left middle occipital gyrus and fusiform gyrus, right middle occipital gyrus and cuneus, and left middle/superior frontal gyrus (Thomas et al., 2012). Thus, SMD irritability may be associated with aberrant activity in the amygdala, parietal, occipital, and frontal regions in response to a variety of neutral and emotional facial expressions.

Indeed, there is some evidence that SMD youth show increased activity in certain occipital gyrus clusters and ventromedial prefrontal cortex (regions associated with visual stream and emotion processing) during non-aware vs. aware processing of emotional stimuli, whereas healthy controls show increased activity during the aware conditions (Thomas et al., 2014; Tseng et al., 2016). These studies also found, with some consistency, that SMD youth show elevated activity while processing angry faces, and decreased activity while processing happy faces, in areas associated with emotional face processing and social cognition. This might support the notion of threat bias in SMD youth. However, results were inconsistent, and neither of these studies found the hypothesized group differences in amygdala activity.

Another line of work has examined irritable children presented with irritating circumstances. One common paradigm of this type is the Posner task, which utilizes a simulated game with positive, negative, and rigged negative feedback. Compared to healthy controls, SMD youth show unique decreased N1 amplitude across all conditions, suggesting deficits in initial attention regardless of emotional context, whereas youth with BD show unique decreased P3 amplitude only during frustrating circumstances (Rich et al., 2007). However, post hoc analyses revealed that the decreased N1 amplitude was accounted for by ODD symptoms rather than SMD status (Rich et al., 2007). In a subsequent magnetencephalography study, Rich et al. (2011) found that SMD youth responded to negative feedback with increased activity, and to positive feedback with reduced activity, in the left anterior cingulate cortex and right medial frontal gyrus relative to healthy controls. In contrast, youth with BD uniquely showed greater superior frontal gyrus activation and decreased insula activation in response to negative feedback. Subjectively, SMD and BD youth both reported feeling less happy during the rigged condition compared to controls, although SMD youth reported greater agitation following negative feedback (Rich et al., 2011). Further, when frustrated, SMD youth showed deactivation in the left amygdala, left and right striatum, parietal cortex, and posterior cingulate—regions associated with spatial attention, reward processing, and emotional salience (Deveney et al., 2013). Lastly, using a different frustration paradigm with younger children, Perlman et al. (2015) found that clinically irritable youth showed greater anterior cingulate and middle frontal gyrus activation during reward, but less activation during frustration, relative to healthy children. Conversely, irritable youth showed less activation of the posterior cingulate during winning and more activation during losing. Taken together, these results suggest dysfunction in regions related to reward processing, error monitoring, and emotion regulation.

A few studies have examined neural structure, function, and chemistry in SMD youth during resting states apart from any neuropsychological tasks. Dickstein et al. (2008) found that youth with SMD had lower temporal myo-inositol, a secondary messenger that plays a role in BD and other psychiatric disorders. However, this finding did not survive correction for 16 overall comparisons. In a longitudinal MRI study, Adleman et al. (2012) found that BD and SMD were associated with reduced gray matter in the insula and dorsolateral prefrontal cortex, regions that mediate cognitive and motor control. However, BD youth—not SMD or controls—showed increased volume in the globus pallidus cross-sectionally, and an increase in the volume in parietal regions longitudinally. Perhaps at odds with the amygdala aberrations found by others, Stoddard et al. (2015) found that youth with BD exhibited hyperconnectivity in the amygdala compared to healthy controls and SMD youth, who did not differ. Finally, research on reward processing in youth with SMD has yielded few results. Rau et al. (2008) found no between-group differences between BD, SMD and healthy youth in processing reward and punishment, a paradigm which has previously been found to be a neuropsychological marker of psychopathy and callous-unemotional traits. Likewise, Rich et al. (2005) found no differences between BD, SMD, and healthy youth in their physiological startle response, regardless of its timing or association with reward.

In sum, neurocognitive and imaging studies provide some support for distinctions among SMD, BD, and healthy controls. Youth with SMD may have difficulty with cognitive flexibility and modulating their attention to emotional stimuli in their environment. They exhibit signs of threat bias and atypical neural activity in the amygdala, parietal, occipital, and frontal regions. In some respects these aberrations set them apart from healthy controls relative to youth with BD; in other respects, however, the opposite pattern is observed. Given the limited research and mixed findings in these areas, it seems premature to draw firm conclusions regarding the underlying neural mechanisms of SMD.

2.2. The evidence for DMDD

Based largely on SMD literature reviewed above, the DSM-5 Child and Adolescent Disorders Work Group (2010) argued for the inclusion of DMDD in DSM-5. Given the differences between the operationalization of SMD in the literature and the definition of DMDD, virtually no evidence regarding DMDD existed at the time of its inclusion in the DSM-5. Since 2010, a handful of research groups have examined the prevalence, comorbidities, and correlates of DMDD using existing datasets. The publication of these secondary analyses and the collection of new data have increased in recent years, much of which has been compiled in special issues and sections (e.g., Carlson, 2016; Stringaris, Rowe and Maughan, 2012).

Across community- and population-based studies, there is a clear trend toward DMDD prevalence rates being higher in younger samples and when criteria are not strictly applied. For example, in three community samples, ages 2–17 collectively, the DMDD criteria for temper outbursts were met by approximately half of the children and adolescents and by 81% of the preschoolers (Copeland, Angold, Costello, & Egger, 2013). However, when the mood, duration, frequency, and persistence criteria were also applied, DMDD prevalence rates were reduced to 1–3%. Similarly, in a large community sample of adolescents, Althoff et al. (2016) found that 5% met the loosest criteria for DMDD, but this estimate fell below 2% after applying the DSM-5 frequency and hierarchy rules. Of those with DMDD, 93% had at least one other diagnosis, most commonly ODD/CD (68%), and these youth were more likely to be receiving mental health services of all types, exhibit higher disability in daily activities, suicidality, and learning disability—but these characteristics did not differentiate DMDD youth from those with a BD diagnosis.

Overall, these findings suggest that DMDD is not clearly distinct from other disorders in population-based, cross-sectional analyses. When followed longitudinally in to adulthood, however, SMD youth appear to have higher rates of psychiatric disorders (particularly anxiety and depression) as well as poorer health, economic, and academic outcomes, relative to both healthy and psychiatric comparison samples (Copeland, Shanahan, Egger, Angold, & Costello, 2014).

With respect to younger children, Dougherty et al. found an age 6 rate of DMDD of 8%, which fell to 1% by age 9 (Carlson, Danzig, Dougherty, Bufferd, & Klein, 2016; Dougherty et al., 2014, 2016). Predictors at age 3 of age 6 DMDD included ADHD, ODD, high CBCL dysregulation profile, poorer peer functioning, and temperament, with parenting behaviors and parental lifetime substance abuse also playing a role (Dougherty et al., 2014). Further, DMDD at age 6 in turn predicted DMDD, depressive disorder, and ADHD at age 9, as well as higher levels of depressive, ADHD, and DBD symptoms, and poorer social, educational, and overall functioning (Dougherty et al., 2016). Importantly, losing temper, irritability, and tantrums are relatively common in both clinical and community samples of young children, but with significant qualitative and quantitative differences (Carlson et al., 2016).

Mayes and colleagues recently published several studies examining the longitudinal stability and diagnostic specificity of DMDD among population and clinical samples. In an 8-year longitudinal study, Mayes et al. (2015) found that about 9% of youth in a community sample showed elevated symptoms of DMDD (irritable-angry mood and temper outbursts) at baseline (6–12 years of age); however, only 29% of these youth continued to show symptoms 8 years later, and over half (55%) of those who did show symptoms at follow-up were new cases. In a separate analysis of the same sample (Mayes, Waxmonsky, Calhoun, & Bixler, 2016), 92% of children with elevated DMDD symptoms also met criteria for ODD, and 98% were identified as having ODD or other clinically significant problems. Moreover, two-thirds of those with ODD also had elevated DMDD symptoms, while only 3% of those without ODD showed elevated DMDD symptoms. Finally, Mayes, Calhoun, et al. (2016) found that ODD accounted for the majority of the variance in DMDD, while covariates (age, gender, IQ, race, parent occupation) explained only 2–3%, a pattern which was strikingly consistent across population and psychiatric samples broken down by diagnosis (ADHD, autism, ODD).

Studies of DMDD in clinical populations have yielded broadly similar results to those among community based samples. Margulies, Weintraub, Basile, Grover, and Carlson (2012) applied the DMDD criteria to an inpatient sample of children ages 5–12. Two-thirds of participants had a history of chronic irritability and explosiveness; however, less than half of those met criteria for DMDD by parent report (31%), and even fewer according to behavioral observation by hospital staff (16%). Similarly, Axelson et al. (2012) found that 26% of their child outpatient sample met full criteria for DMDD at intake, with 40% meeting criteria at some point over the course of two years. The DMDD diagnosis showed low longitudinal stability, high diagnostic overlap, and could not be differentiated from other disorders—especially DBDs—based on course or parental histories (Axelson et al., 2012). Similarly, a chart review study (Tufan et al., 2016) found that 11% of codable files met criteria for DMDD, most of these patients were male (78%) with family histories of psychopathology (78%) and a median of 2 other psychiatric diagnoses (most commonly ADHD, ODD, and BD spectrum disorders). And although DSM-5 does not permit the diagnosis prior to age 6, Martin et al. (2016) found that in an early childhood psychiatric day program (ages 4–6), 42% of children met criteria for DMDD, of which 83% had ODD and 67% had ADHD. This group also exhibited higher levels of emotional reactivity and aggression, and lower receptive language skills.

Freeman, Youngstrom, Youngstrom, and Findling (2016) recently examined DMDD in a large community mental health center sample of children and adolescents. Results showed that 31% met criteria for DMDD even though only 27% of the sample met criteria for SMD.

Those with DMDD had more total diagnoses at baseline ($M = 3.0$, $SD = 1.3$); 96% had a comorbid diagnosis of ODD, and 81% had comorbid ADHD. Interestingly, although youth with DMDD showed more severe difficulties compared to non-DMDD youth, analyses revealed no significant differences between youth with ODD vs. youth with DMDD (i.e., ignoring DSM-5 hierarchical rules). Moreover, the interactions between ODD and DMDD diagnostic status were nonsignificant, suggesting that the additional diagnosis of DMDD did not identify greater severity or different problems than what was already identified by the diagnosis of ODD (Freeman et al., 2016).

Research among different diagnostic populations also provides useful information about DMDD. In one large study, 79% of youth with ODD, 45% of youth with autism, 39% of youth with ADHD-C, 12% of youth with ADHD-I, and 3% of typically developing children met criteria for DMDD. Of those with DMDD, 91% met criteria for ODD, and most of the remainder had autism (Mayes, Waxmonsky, Calhoun, Kokotovich et al., 2016). Similarly, Mulraney et al. (2016) examined a community sample of children (ages 6–8) with ADHD and found that 22% of the full sample had DMDD. Nearly all (95%) of those with DMDD had at least one other diagnosis (ODD, 90%; anxiety disorder, 41%; conduct disorder, 26%), although depressive disorder diagnoses were similarly rare (<3%) in both the DMDD and the non-DMDD groups. Further, compared to children with ADHD but no DMDD, children with ADHD and DMDD showed higher levels of bullying and lower levels of self-control, but few overall individual or family differences (Mulraney et al., 2016). Other studies suggest key differences across informants. In an outpatient sample, parents and teachers exhibited low agreement in rating DMDD symptoms, with mothers and fathers consistently reporting greater symptom levels (Mayes, Waxmonsky, Waschbusch, et al., 2016). Similarly, Uran and Kılıç (2015b) found that DMDD youth could largely be differentiated from ADHD youth and healthy controls by parent report (i.e., higher scores on virtually all Conners subscales, poorer overall family functioning) but not by teacher report.

If DMDD was established to facilitate more accurate differentiation from BD, recent studies raise questions about the extent to which this goal been achieved. In terms of their clinical histories, demographics, symptom trajectories, and clinical presentation, youth with DMDD and BD-NOS have been found to be more similar than different (Fristad et al., 2016). Among the few exceptions were that youth with DMDD were slightly younger, more often male, and more often had a DBD, whereas those with BD-NOS showed more symptoms of mania and family histories of BD. Of those with DMDD, 84% had ADHD and 98% had a DBD. Similarly, Mitchell et al. (2016) estimate that DMDD occurred in approximately 25% of their clinical sample of adolescents with BD-I, BD-II, or BD-NOS. Further, DMDD was associated with home conflict, assault history, and functional impairment; but most of these correlations did not survive corrections for multiple comparisons (Mitchell et al., 2016). Notably, of these youth with BD and DMDD, 100% had ODD and 63% had ADHD. Lastly, in another study (Sparks et al., 2014), family history of BD was found to increase children's risk for DMDD by over 5 times, and the chronic irritability phenotype was also associated with BD, depression, ADHD, and DBDs.

Consistently across studies, the vast majority of those with DMDD usually also received a diagnosis of ODD. In fact, our review identified only one study in which ODD did not occur among at least half of those with DMDD. Investigating an outpatient clinical sample in India, Tiwari, Agarwal, Arya, Gupta, and Mahour (2016) found that only 19% of those diagnosed with DMDD were also diagnosed with ODD. However, this study was limited by a very small sample size ($n = 21$ with DMDD) and the absence of any sort of comparison group.

To our knowledge, the DSM-5 Field Trials are the only studies of DMDD with original data and actual DSM-5 diagnoses. Interrater reliability for DMDD was "unacceptable" at 2 of 3 sites, yielding a "questionable" pooled kappa of 0.25 (Regier et al., 2013)—the lowest of any child diagnoses included in DSM-5. Only recently have researchers begun to examine the etiological mechanisms underlying DMDD rather than

SMD (e.g., Kessel et al., 2016; Stoddard et al., 2016; Wiggins et al., 2016), and it is too soon to tell which findings will be supported and replicated.

2.3. Conclusions regarding SMD and DMDD

SMD and DMDD identify populations of youth with clinically significant behavioral and emotional problems. These youth exhibit some notable neural, neuropsychological, and behavioral characteristics, as well as longitudinal associations with depression, anxiety, and continued symptoms and impairment over time. Diagnostically, these youth are generally already *identified* (i.e., they would receive at least one diagnosis of some kind, most often ODD or ADHD) but not adequately *described* by existing diagnostic systems (i.e., these diagnoses do not communicate clinically important information about their irritable mood and temper outbursts, and may make differential diagnosis and treatment more difficult).

At the same time, the SMD/DMDD literature has several significant limitations. Most of the neurocognitive and imaging studies of SMD have been limited by small samples characterized by limited/unknown diversity[3] and comprised mostly of adolescents. The majority of the laboratory-based evidence has emanated from a single U.S. research group, while most of the behavioral and longitudinal evidence comes from secondary analyses of existing data. Thus, independent replication and new data collection are greatly needed. Further, the measurement of SMD, chronic irritability, and DMDD has been inconsistent across studies, often based on post hoc approximations. Researchers have operationalized SMD and DMDD by piecing together items from diagnostic interviews and rating scales, providing little evidence of validity and reliability. This is complicated by changes to the construct itself in its evolution from SMD to DMDD. For example, youth must demonstrate several symptoms of hyperarousal and an IQ of 80 or greater to meet criteria for SMD; neither is true for DMDD. Thus, evidence for SMD may not generalize to DMDD. Equally disconcerting is the absence of any null hypothesis. That is, if the findings reviewed above are interpreted as evidence for SMD as a distinct entity (Leibenluft, 2011), what, then, is the counterfactual scenario? What results would have indicated that SMD is not a unique diagnostic entity? One could argue that establishing SMD as a provisional research syndrome may have paved the way for either its validation (Leibenluft, 2011) or its reification (Hyman, 2010).

The available research on DMDD suggests that comorbidities will be common and diagnostic assessment will be difficult. Prevalence is not likely to be high, and may vary widely across populations, assessment techniques, and clinicians, given its low interrater reliability. Generally, rates are likely to be higher in various clinical populations, younger children, and when criteria are not applied with clinical judgment based on data from multiple sources. Longitudinally, DMDD appears to show low stability, but is also associated with various continued subthreshold difficulties.

Evidence concerning the existence of a problem should not be interpreted as evidence for a particular solution. The research on SMD and DMDD does potentially suggest a "blind spot" in ICD-10 and DSM-IV; but it does not follow that ICD-11 should therefore include a new, freestanding diagnosis based on irritability, anger, and temper outbursts. What kind of diagnostic entity would best capture this phenomenon remains unclear. To help resolve this question, we will now turn to separate but related body of research on child irritability/anger.

3. The irritable dimension of Oppositional Defiant Disorder

ODD is characterized by symptoms that have been largely consistent for three decades (APA, 1987, 1994, 2000, 2013; WHO, 1993, 2016), and which include both emotional and behavioral features. These 8 symptoms include often losing temper, arguing, defying, annoying others, blaming others, being touchy or easily annoyed, angry and resentful, and spiteful or vindictive. The majority of children with ODD only exhibit about 4 or 5 symptoms (Waschbusch & Sparkes, 2003), allowing for heterogeneity in the development and presentation of ODD-related behaviors (Greene & Doyle, 1999). Rates of comorbidity are extremely high, with 92% of those with lifetime ODD also meeting criteria for another lifetime mental disorder diagnosis (Nock, Kazdin, Hirpi, & Kessler, 2007). ODD is especially notable because it demonstrates both homotypic (e.g., ODD with ADHD or CD) and heterotypic (e.g., ODD with anxiety or depression) comorbidity and developmental continuity with other disorders (Boylan et al., 2007; Burke & Loeber, 2010; Burke, Loeber, Lahey, & Ralthouz, 2005; Copeland, Shanahan, Costello, & Angold, 2009; Kim-Cohen et al., 2003).

Researchers have recently identified at least 2 major dimensions of ODD that help account for the overlap of ODD with both behavioral and emotional disorders. With slight variations[4], all studies identify one dimension of irritability, characterized by anger, touchiness, and temper outbursts, and another dimension defined by defiant and argumentative behavior. The irritable dimension of ODD is associated with distinct correlates and outcomes, suggesting that current models of ODD do not adequately capture clinically meaningful variance within the disorder. In general, the evidence concerning ODD dimensions can be organized according to a confirmatory vs. exploratory framework, with more recent studies seeking to reconcile competing models and test new applications.

3.1. Conceptual/confirmatory models

Reflecting on the heterogeneity and multifinality of ODD, Stringaris and Goodman (2009b) defined three a priori dimensions of ODD—irritable (touchy, angry, temper), defiant (defies, argues, blames, annoys), and hurtful (spiteful, vindictive)—based on theory and the limited available evidence. In large community-based studies, Stringaris and Goodman found cross-sectional (Stringaris & Goodman, 2009b) and 3-year longitudinal (Stringaris & Goodman, 2009a) evidence that the irritable dimension of ODD was uniquely associated with depression and anxiety, the defiant dimension with ADHD and CD, and the hurtful dimension with aggressive conduct problems. Kolko and Pardini (2010), in a sample of children with CD or ODD, found that the hurtful dimension predicted a range of continued conduct problems (violence, theft, vandalism) and overall externalizing problems, whereas the irritable dimension predicted later internalizing symptoms, social problems, greater functional impairment, and treatment-resistant ODD and ADHD.

Other studies have adopted these same 3 symptoms (touchy, angry, temper) to investigate the irritable dimension of ODD, with little or no attention to the other symptoms. Mick, Spencer, Wozniak, and Biederman (2005) found that ODD-type irritability symptoms occurred in large majorities of their sample of children with ADHD, both with and without comorbid mood disorders. In contrast, more severe forms of irritability (non-ODD-type) were more specifically linked to mood disorders and greater levels of impairment (Mick et al., 2005). In two other studies, Drabick and Gadow compared youth (a) with ODD symptoms including irritability, (b) with only the non-irritable symptoms of ODD, and (c) without any ODD symptoms.[5] By both parent and teacher

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[3] Few of the studies reviewed reported information regarding the ethnic, family, or socioeconomic background of their sample, but those that did suggest limited diversity. For example, Kim et al. (2013) and Guyer et al. (2007) both report that over 90% of their SMD participants were White.

[4] For clarity, we use the terms "irritable," "defiant," and "hurtful" to refer to the three ODD symptom dimensions (even if the studies used different terms) and specify which symptoms were included in which dimensions.

[5] The irritable and defiant groups in these two studies are not directly comparable given that the latter were comprised of only those who did not meet criteria for the former, and therefore had lower symptom severity overall.

report, the irritable group showed higher levels of depressive and anxiety symptoms relative to the other groups (Drabick & Gadow, 2012). The severity of co-occurring symptoms and impairment differed depending on whether parent or teacher report was used (Gadow & Drabick, 2012).

In contrast to the above, other studies have directly tested ODD dimensionality using CFA, with some differing from the Stringaris/DSM-5 model. Aebi et al. (2010), using a large sample of youth with ADHD, found that a 3-dimensional model, consisting of irritable (touchy, angry, temper), defiant (argues, blames, defies) and hurtful (annoys, spiteful) dimensions fit the data best. Further, the irritability dimension was predicted by emotional problems and lability, unlike the hurtful and defiant dimensions. In another study (Whelan, Stringaris, Maughan, & Barker, 2013), irritability showed continuity and independence from the other ODD dimensions up through age 13, distinctly predicting depression at age 16. Defiant behavior (argues, takes no notice of rules, refuses to do as told) at age 10 predicted subsequent irritability, and at age 13 uniquely predicted subsequent conduct problems and callous attitude, but not depression. However, the hurtful dimension (spiteful, tried to get others back) failed to predict to any outcomes (Whelan et al., 2013).

Finally, Leadbeater and Homel (2015) found that a 2-factor model demonstrated measurement invariance across gender and over time from age 12 to 25. Whereas defiant behavior (defiant, argues, blames others) declined over time, irritability (easily annoyed, angry, cranky) remained stable. Concurrently, irritability was more strongly linked to internalizing problems than conduct problems, while defiance was linked to both conduct problems and internalizing problems throughout adolescence. Longitudinally, however, the patterns were not so clear. For example, cross-lagged path models suggested bidirectional longitudinal associations (e.g., internalizing problems predicting irritability and vice versa), with inconsistencies across development (different cross-lagged paths at different ages), and somewhat less specificity than hypothesized (e.g., conduct problems predicting irritability in adolescence, defiant behavior predicting internalizing problems in adulthood).

3.2. Empirical/exploratory models

In contrast to the hypothesis-driven approaches described above, other researchers have utilized more data-driven methods to examine the heterogeneity of ODD. Burke et al. (2005) hypothesized that affective components of ODD could account for its unique homotypic and heterotypic continuity with other disorders. Applying EFA to data from a large community sample of girls (Burke et al., 2010), results supported a 3-factor model of irritability (touchy, angry, spiteful), defiant behavior (temper, argues, defies), and hurtful behavior (annoys, blames). The irritability dimension predicted later depression, whereas, for some girls, all 3 dimensions predicted later CD. In following this sample to mid-adolescence (age 16), Hipwell et al. (2011) found that the irritable dimension explained links from CD to depression. In a clinical sample of boys followed from childhood, defiant behavior, but not irritability, predicted borderline personality symptoms in adulthood (Burke & Stepp, 2012). This lack of an association between irritability and personality disorders was consistent with previous findings (Stringaris et al., 2009).

Rowe, Costello, Angold, Copeland, and Maughan (2010) also used EFA, in a large longitudinal epidemiological dataset, and found a 2-factor model of irritability (touchy, angry, temper) and defiance (all other ODD symptoms). The irritable and defiant dimensions differentially predicted anxiety and substance use disorders, respectively (though results were nonsignificant for depression, CD, and ODD). Finally, Stringaris, Zavos, Leibenluft, Maughan, and Eley (2012) employed both EFA and CFA in a large sample of youth and found support for a 2-factor model of irritability (hot temper, mood lability, stubborn, sullen, irritable) and defiant/hurtful behavior (mean, destroys, teases,

disobeys school, disobeys home), with one item (argues) cross-loading on both. Results offered phenotypic and genetic evidence that defiant/hurtful behaviors are more strongly linked to delinquency, while irritability is more strongly linked to depression, both cross-sectionally and longitudinally.

A different, person-oriented approach, LCA, has been used by several researchers to differentiate subgroups of youth with ODD based on their symptom profiles. In a clinical sample of boys, Burke (2012) found 3 groups—low symptoms (16%), behavioral symptoms only (48%), and behavioral plus irritable symptoms (36%)—distinguished by the presence or absence of irritable symptoms. Compared to the behavioral-only group, the irritability group showed higher levels of anxiety, depression, and neuroticism in later adolescence and young adulthood (Burke, 2012). In a community sample of Dutch children, Kuny et al. (2013) used LCA and found 4 groups: a defiant class (11–12%), with higher externalizing problems; an irritable class (9–11%) with higher internalizing problems; an all-symptoms class (5–8%), with elevated internalizing and externalizing problems; and a no-symptoms class (69–75%). Similarly, Aebi et al. (2016) found 4 latent classes of adolescent male offenders: irritable (21%), defiant (25%), irritable and defiant (32%), and low symptoms (22%). Irritability in this study was associated with suicidality, anxiety disorders, mood disorders, and likelihood of violent re-offense. Finally, Althoff, Kuny-Slock, Verhulst, Hudziak, and Ende (2014) employed LCA on large Dutch and US community samples, and in both cases identified 4 similar classes based on the CBCL oppositional subscale: no symptoms (35–50%), defiant (7–18%), irritable (22–16%), and all symptoms (36–17%). Youth in the irritable class were more likely to develop mood disorders in adulthood, whereas those in other elevated symptom classes had an increased likelihood of violence in adulthood.

3.3. Finding the irritable dimension of ODD

Although the literature on the multidimensionality of ODD symptoms consistently identifies an irritable dimension, there has been variability in terms of the total number of dimensions and the specific symptoms that comprise them. Table 2 displays how the symptoms of ODD have been identified with different dimensions across a total of 32 empirical studies (34 models) using the 8 core symptoms of ODD. As this table shows, there are definite patterns underlying the variability. Several studies have sought to disentangle these patterns by comparing alternative models of ODD dimensions to one another.

Ezpeleta et al. (2012) assessed the fit of varying models of ODD dimensionality in a community sample of preschoolers, finding the most support for both Stringaris and Goodman's (2009a, 2009b) model and Burke et al.'s (2010) model. In both models, the irritable dimensions were associated with anxiety disorders, internalizing scales, negative affect, anger, and emotional inflexibility, while defiant dimensions were more associated with ADHD, disruptive disorders, externalizing scales, callous-unemotional traits, and CD symptoms. In subsequent analyses, Ezpeleta and Penelo (2015) found that the dimensions of ODD demonstrate metric invariance across boys and girls, but with different results from teacher and parent reports. Additionally, growth mixture models in both clinical and community samples found that trajectories of either high-persistent or increasing irritability from ages 3 to 6 were associated with more DBDs, internalizing and externalizing problems, and functional impairment at age 6 (Ezpeleta, Granero, Osa, Trepat, & Domènech, 2015). Lavigne, Gouze, Bryant, and Hopkins (2014) and Lavigne, Bryant, Hopkins and Gouze (2015) also compared models among a preschool age community sample and found that the 2-factor model comprised of irritability and oppositional behavior fit the data best and showed invariance across gender and age. However, results also suggested that the heterotypic predictions from irritability to subsequent anxiety and depressive symptoms are not as robust as perhaps believed, with little consistency or specificity in cross-lagged models controlling for baseline.

Table 2
Arrangement of ODD symptoms into dimensions in the empirical literature.

ODD symptom	Dimension of ODD symptomatology, n (%)			N studies/models with symptom
	Irritable	Defiant	Hurtful	
Touchy/easily annoyed	34 (100.0)	0	0	34
Angry & resentful	34 (100.0)	0	0	34
Loses temper	25 (73.5)	9 (31.0)	0	34
Spiteful/vindictive	9 (26.5)	8 (27.6)	11 (61.1)	28
Annoys	0	21 (72.4)	7 (38.9)	28
Blames	0	22 (75.9)	6 (33.3)	28
Argues	0	29 (100.0)	0	29
Defies/refuses to comply	0	29 (100.0)	0	29
N studies/models with dimension	34	29	18	
Symptoms per dimension across studies/models				
M	3.00	3.90	1.41	
SD	0.00	0.77	0.51	
Range	3–3	3–5	1–2	

Note: Cell values indicate the frequency with which each symptom has been identified with each dimension in the empirical literature reviewed in this article. Percentages are calculated as the proportion of the number of studies with that dimension that classify the symptom therein. Frequency counts are aggregated across all studies investigating dimensions, clusters, classes, or groups derived from measures corresponding to DSM symptoms of ODD (e.g., DAWBA, DISC); studies using other measures of oppositionality (e.g., CBCL) are not represented here. Studies utilized a variety of analytic and methodological designs. Where multiple models were assessed, results from only the 1-2 preferred or best-fitting model(s) are included, resulting in a total of 34 models from 32 studies.

In a large community sample of Brazilian school-age children (Krieger, Polanczyk, et al., 2013), the touchy-angry-temper model of irritability showed better fit than the touchy-angry-spiteful model and other 1- and 2-factor models. Moreover, irritability was associated with depression and anxiety in the child and a history of depression and suicidality in the mother, whereas the defiant dimension was specifically associated with child and maternal ADHD, and the hurtful dimension with child CD. Likewise, Aebi, Plattner, Metzke, Bessler, and Steinhausen (2013) applied CFA in a large Swiss community sample using items from the parent- and self-report Achenbach instruments. Results supported a 3-factor model comprised of irritability (mood change, hot temper, stubborn sullen and irritable), defiant (argues, disobeys home, disobeys school, stubborn sullen and irritable), and hurtful (mean, teases) dimensions. Further, by parent- and self-report, irritability was associated with anxiety, depression, attention problems, and delinquent behavior, whereas defiant and hurtful symptoms were linked to delinquent behavior and subsequent crimes in adulthood.

In one interesting approach, Herzhoff and Tackett (2016) combined CFA and LCA to clarify the dimensions of ODD. They found that Burke et al.'s (2010) 2-factor model fit the data slightly better than several alternative models. In a primary and replication sample, they found a 3-class solution, with low severity (69–75%), defiant (11–28%), and defiant-irritable classes (13–15%); the distinction was a function of irritability symptoms (temper, touchy, angry, spiteful, along with argues). Further, at baseline, both irritability and defiance were consistently associated with high neuroticism and low agreeableness; however, defiance was also consistently associated with low extroversion and conscientiousness. Internalizing problems were positively predicted by irritability and negatively by defiance, whereas externalizing problems were only predicted by defiance. Lastly, in the largest test of the structure of ODD-irritability to date, Burke et al. (2014) used 5 large community datasets (total N = 16,280) to compare the most prominent models of ODD-irritability (touchy-angry-temper and touchy-angry-spiteful), testing 5 hierarchical factor structures for both. In 4 samples, the temper-touchy-angry model of irritability best fit the data. Further, in all 5 data sets, the best-fitting model included both a general ODD factor along with distinct but correlated irritability and oppositional behavior dimensions.

In sum, studies evaluating alternative models of ODD dimensions have generated results that broadly resemble the earlier studies from which the different models originated: the irritability dimension, despite some variation in its composition across studies, has been linked to internalizing problems. The largest and most definitive test (Burke et al., 2014) supported a correlated bifactor model comprised of irritable and defiant dimensions as well as a general ODD factor. With regard to the composition of the irritability symptom cluster, the large majority of research on ODD dimensions—consistent with the earliest models (Stringaris & Goodman, 2009a, 2009b) and the symptom organization in DSM-5 (APA, 2013)—converges to support the conclusion that ODD-irritability in youth is best defined by three symptoms: often touchy and easily annoyed, often angry and resentful, and often losing temper.

3.4. Subsequent applications

Among preschool-age children, network analyses highlight the centrality of the irritable cluster within ODD symptomatology (Smith, Lee, Martel, & Axelrad, 2016). In children with autism spectrum disorder, only the irritable dimension was uniquely and consistently associated with internalizing symptoms, while defiant behavior and vindictiveness both showed associations with externalizing problems (Mandy, Roughan, & Skuse, 2014). In a clinical sample of youth with Tourette's syndrome, ODD-irritability uniquely predicted obsessive-compulsive behaviors, whereas defiant behaviors predicted ADHD symptoms (Thériault et al., 2014). Physiologically, limited evidence suggests that defiant/hurtful behavior, but not irritability, is associated with increased sympathetic skin responses to mild electrical stimuli, a sign of high autonomic reactivity (da Silva et al., 2014). And in a secondary analysis of MTA study data, de la Cruz et al. (2015) found that irritability and defiant behaviors were both stable over time and demonstrated unique contributions to impairment. Moreover, irritability was a stronger predictor of internalizing problems both before and after treatment, while defiant behavior was a stronger predictor of externalizing problems at baseline only.

A few studies have begun to examine genetic and developmental mechanisms underlying ODD symptom dimensions. Among youth with ADHD, subtypes of ODD symptoms were associated with parenting behaviors but not specific genetic markers (Aebi et al., 2015). Interestingly, one study suggests that the association between ADHD and ODD-irritability might be accounted for by a correlated risk factors model, whereas the association between ADHD and ODD-defiance might be understood through a different model emphasizing developmental precursors (Harvey, Breaux, & Lugo-Candelas, 2016). Regarding the irritability dimension in particular, Whelan, Leibenluft, Stringaris, and Barker (2015) found evidence for two developmental pathways from pre−/post-natal maternal depressive symptoms to adolescent depressive symptoms: a temperament/irritability pathway, and an anxiety/mood pathway. Further, irritability mediated the link between harsh parenting in early childhood and subsequent bullying and victimization (Whelan, Kretschmer, & Barker, 2014).

With respect to the peer context, Evans, Pederson, Fite, Blossom, and Cooley (2016) found that ODD-irritability was uniquely associated with

physical victimization, depressive symptoms, and reactive aggression, whereas ODD-defiance was linked to proactive aggression and hyperactive-impulsive symptoms; both dimensions were linked to physical and relational aggression, relational victimization, and peer rejection. Similarly, Barker and Salekin (2012) found that irritability was stable and predictive of peer victimization, which was then linked to internalizing problems and callous-unemotional traits in childhood and adolescence. When Déry et al. (2016) examined outcomes of ODD dimensions among a sample of school-age children with conduct problems, irritability was associated with higher levels of depression and anxiety 2 years later while defiance in girls and hurtfulness in boys predicted lower depression scores; however, these associations were all modest in effect size, highlighting the overlap between ODD dimensions. Similarly, Leadbeater and Ames (2016) were not able to examine distinct outcomes of irritability and defiance could not be examined due to their multicollinearity. Nonetheless, adolescents with high or increasing levels of overall ODD symptoms exhibited poorer academic and occupational functioning in young adulthood.

3.5. Conclusions regarding ODD dimensions

Evidence from over three dozen studies now suggests that ODD symptoms comprise at least two major dimensions: irritability, linked to concurrent and subsequent internalizing difficulties, and defiance, linked to concurrent and subsequent externalizing difficulties. Indeed, research provides the strongest support for an irritable dimension, moderate support for a defiant dimension, and weak support for a hurtful dimension (see Table 2). It should be emphasized, however, that these findings do not support cleaving ODD into distinct subtypes or disorders; rather, ODD items include heterogeneous variability that is accounted for by a general ODD factor, as well as dimensions of irritability and defiant behavior. In retrospect, the above-reviewed research on ODD appears to have had very little influence on DSM-5 diagnostic criteria for ODD; the 8 symptoms were retained from DSM-IV and simply rearranged per Stringaris and Goodman's (2009b) 3-dimensional model. These changes are effectively inconsequential, both for the diagnosis itself (i.e., no new subtypes, specifiers, or changes to the definition) and for the population to whom it is given (i.e., no changes in diagnostic threshold or prevalence). As this review demonstrates, the body of evidence supporting the irritability dimension of ODD has grown rapidly, even in the short period of time since DSM-5 was developed. Thus, the evidence seems sufficient to influence the formulation of ODD in ICD-11 in one way or another.

4. Evaluating the options for youth irritability in ICD-11

Taken together, the research on SMD, DMDD, and dimensions of ODD demonstrates that youth irritability poses a challenge for diagnostic classification systems. The literatures on SMD/DMDD and ODD dimensions evolved largely independently of one another, with few efforts toward integration (e.g., Vidal-Ribas et al., 2016). Consequently, two bodies of evidence have emerged, with different conclusions and implications, and no studies have investigated SMD, DMDD, and ODD-irritability in relation to one another. In the interest of integration, we have adopted a "both/and" approach to the literature rather than an "either/or" approach. The research reviewed above does not clearly support the findings of one body of research over that of the other, and the question at hand is not which typology should be established as a distinct disorder and which should be ignored. While there are important differences between DMDD and ODD-irritability (e.g., severity, frequency, pervasiveness), these may be artifacts of their different histories and purposes, and probably do not reflect natural boundaries in child psychopathology.

Children with SMD or DMDD and those with ODD-irritability share marked similarities in their persistent irritability and temper outbursts, in their concurrent associated difficulties, and in their longitudinal course and outcomes. Accordingly, these two literatures may be interpreted, with caution, as a confluence of evidence, as two diagnostic constructs approximating very similar clinical phenomena, or perhaps converging

interpretations of a single phenomenon. From that perspective, it seems that the conclusion best supported by the evidence is that there exists a clinically significant population of children, not explicitly delineated by existing nosologies, characterized by severe irritability, anger, and temper outbursts in childhood, usually associated with ODD and a greater risk for depressive and anxiety disorders. This broad view of irritability entails a number of alternatives to be considered for ICD-11.

4.1. Considering DMDD for ICD-11

The most obvious option for incorporating irritability/anger into ICD-11 is that which has already been established in DSM-5: a freestanding diagnosis like DMDD. The rationale for DMDD has been presented elsewhere (DSM-5 Childhood and Adolescent Disorders Work Group, 2010; Leibenluft, 2011), with limited empirical examination (reviewed above). The introduction of DMDD was received with some critical response from the professional community (e.g., Axelson, 2013; Axelson et al., 2011; Parens et al., 2010; Raven & Parry, 2012) and in popular press publications (e.g., Dobbs, 2012; Frances, 2013). Indeed, the limitations of the SMD/DMDD literature (noted in part 1 of this review) raise several concerns about including DMDD in ICD-11. Broadly, these problems relate to the scientific foundation as well as clinical implications for assessment, diagnosis, and treatment; these are discussed below.

4.1.1. The scientific underpinnings of DMDD

Conclusions from the SMD/DMDD research must be drawn in light of the original studies' objectives and limitations. SMD was created to investigate its relation to pediatric BD (Leibenluft et al., 2003; Leibenluft, 2011). While the studies reviewed above suggest some divergence from BD, they do not support the construct validity of SMD or DMDD (Axelson et al., 2011). In fact, these studies were never intended to validate SMD as a syndrome, but rather to clarify the diagnosis of BD in children (Leibenluft, 2011; Leibenluft & Rich, 2011). Proponents of DMDD acknowledge this problem (DSM-5 Child and Adolescent Work Group, 2010; Leibenluft, 2011). Despite the insufficiency of extant research, the DSM-5 Child and Adolescent Work Group (2010) argued that DMDD should be included in order to help a nosologically "homeless" population in need of treatment and facilitate further research on DMDD. Closer examination reveals the circularity of this argument: (a) if DMDD is valid, it should be added to DSM-5; (b) further research is needed to establish its validity; (c) adding DMDD to DSM-5 would facilitate further research; (d) therefore, it should be added to DSM-5. It seems that a new diagnosis was added to DSM-5 both *because of* and *in spite of* the insufficiency of the evidence.

With respect to methodological limitations, much of the laboratory-based research on SMD was generated by a single research group (i.e., without independent replication), using relatively small samples that appear to show some overlap across studies. Further, the samples appear to have very little sociodemographic diversity, comprised primarily of white U.S. adolescents. This raises concerns about generalizability (e.g., to other ages, racial/ethnic backgrounds, cultures, countries) as well as the utility of SMD and DMDD. Moreover, the paucity of international research on SMD or DMDD is extremely problematic when it comes to fulfilling the global public health priorities of ICD-11 (Reed, 2010). Many SMD studies have yielded mixed results from extensive analyses, only some of which correct for multiple comparisons; thus, findings include relatively few robust, between-group differences which are not plausibly due to chance. More generally, it is premature to know how to interpret these kinds of findings with respect to the validation of a syndrome or disorder. Indeed, such findings have been remarkably inconsistent with respect to the pathophysiology of long-established disorders (Insel et al., 2010).

Additional problems lie in the inconsistencies in measuring SMD and DMDD, and in the fundamental differences between these two diagnostic constructs. For example, the definition of SMD was based on three core features (outbursts, negative mood, and hyperarousal) whereas the DMDD criteria omit hyperarousal. Further, the creation of DMDD

involved relaxing several of the exclusion criteria for SMD, including allowing several concurrent diagnoses and low cognitive ability. To our knowledge, the effects of these changes have still not been tested empirically. To the extent that SMD represents a different construct, its relations to DMDD are tenuous and evidence regarding SMD should not be generalized to DMDD. Unfortunately, there is still very little research on "DMDD proper."

4.1.2. Potential clinical implications of DMDD

The defining features of DMDD (severe irritability and temper outbursts) are characterized by high prevalence in community populations (e.g., Copeland et al., 2013) and low diagnostic specificity in clinical populations (e.g., Axelson et al., 2011). Thus, meeting criteria for DMDD is primarily a matter of demonstrating sufficient duration, frequency, and impairment of symptoms across settings (APA, 2013), as well as the diagnostician's ability to accurately assess these criteria (Axelson, 2013). Popular media outlets have taken particular issue on this problem of threshold, raising concern that the new diagnosis might entail pathologizing normal temper tantrums and irritability, in turn leading to increased prevalence in childhood diagnoses (Dobbs, 2012; Frances, 2013). These concerns do not appear to hold up when the full DMDD criteria are applied to existing datasets (e.g., Copeland et al., 2013), but usage of the diagnosis in real-world settings remains unclear.

The differential diagnosis of DMDD presents further challenges. Beyond DSM-5, there is little guidance for appropriate assessment methods and tools such as multi-informant rating scales and diagnostic interviews. Irritability and temper outbursts are common across a range of disorders, and there are no truly unique features of DMDD. Thus, DMDD would become part of the differential diagnosis for any youth who are irritable, moody, reactive, or aggressive (Axelson et al., 2011). Rates of comorbidity are extremely high with ODD, depression, and ADHD, among other disorders. Thus, even though the creation of DMDD might not cause an increase in the number of children with mental disorder diagnoses, it would most likely increase the number of diagnoses assigned to many individual children.

The results of the DSM-5 field trials (Regier et al., 2013) do little to dispel concerns about diagnostic difficulties, and secondary analyses of existing data have yielded mixed findings. For example, results suggest relatively low prevalence and reasonable comorbidities in community samples (Copeland et al., 2013), but higher prevalence, poor longitudinal stability, and enormous rates of comorbidity in various clinical samples (e.g., Axelson et al., 2012; Margulies et al., 2012). In short, whether an irritable child receives a diagnosis of DMDD may depend in large measure upon when, where, and from whom clinical services are received, including the assessment techniques and judgment of the clinician.

The decision to place DMDD within DSM-5's Depressive Disorders section has key implications of its own. First, a central principle of the ICD-11 formative studies (e.g., Reed, Roberts, et al., 2013) is that when diagnostic categories are arranged in a manner that "fits" with clinicians' working taxonomies of mental disorders, the result is a classification system that is more intuitive, reliable, and easier to use during clinical encounters (Keeley et al., 2016; Reed, 2010). The placement of DMDD within the Depressive Disorders section is therefore notable because it discounts the strong association between DMDD and behavioral disorders (ADHD and ODD) in favor of its relatively weaker association with depressed mood, posing problems for clinical utility. It has been argued that this will help highlight the irritable mood component of DMDD for treatment purposes (Leibenluft, 2011), but this move seems unnecessary because irritability is already represented in the diagnostic features of ODD. It is also conceptually inconsistent because mood disorders emphasize episodic problems, whereas DMDD is by definition a non-episodic problem (APA, 2013). Second, and perhaps more importantly, treating DMDD as a Depressive Disorder—and withholding a diagnosis of ODD, per DSM-5 hierarchical rules—may lead clinicians to conceptualize these youth as having a mood disorder rather than a behavior disorder. For primary care providers and pediatricians, treating DMDD as a mood disorder and removing the ODD label may both decrease referrals for behavioral interventions that are well-established (e.g., parent management training) and increase the administration of psychotropic medications such as antidepressants, antipsychotics, and mood stabilizers, for which evidence is limited.

Indeed, there are currently no well-validated psychiatric or psychosocial treatments for the new disorder (Stringaris & Taylor, 2015; Tourian et al., 2015). Moreover, there exists little guidance regarding selection among possible treatments, or knowledge about potential for side effects or iatrogenic effects. Most extant recommendations are based on inductive extrapolations from what is known about treatments for clinically similar problems and disorders (e.g., aggression, ODD, ADHD, mood disorders; Baweja, Mayes, et al., 2016; Leibenluft, 2011; Tourian et al., 2015; Sukhodolsky, Smith, et al., 2016). Recently, evidence has begun to accumulate regarding psychosocial and psychotropic interventions for SMD and DMDD (e.g., Baweja, Belin, et al., 2016; de la Cruz et al., 2015; Kim & Boylan, 2016; Krieger et al., 2011; Stoddard et al., 2016; Waxmonsky et al., 2008, 2013). Until this evidence base matures, however, many clinicians are left with a diagnosis that they can assign but do not know how to treat. Thus, even if DMDD helps curb the misdiagnosis of pediatric BD and accurately identifies a population in need of services, the new diagnostic category may open the door for further off-label usage of psychotropic medication in children (Axelson et al., 2011; Parens et al., 2010), and create a new target for pharmaceutical development, with unknown implications for harm/benefit potential (Raven & Parry, 2012).

4.2. A proposed subtype for ICD-11: ODD with chronic irritability/anger

Based on the above considerations, the approach for ICD-11 requires a more conservative solution than an independent diagnostic category for irritability and temper outbursts. At the same time, however, the evidence reviewed above seems too compelling to allow childhood irritability/anger to be entirely omitted from ICD-11. Nor should it be relegated to a separate list of syndromes in need of further research, as this would not serve the global public health priorities of ICD-11. Instead, we argue that the most rational solution is to create a new subtype, *ODD with chronic irritability/anger* (see Appendix).

4.2.1. Relations to ODD-irritability and DMDD

For ICD-11 to serve its clinical and statistical purposes, each diagnosis, including subtypes and qualifiers, must be supported by evidence for its validity and utility. Because the proposed subtype is derived from the two bodies of evidence reviewed above, its relations to the ODD dimensions and to DMDD must be clearly delineated and justified. With respect to the ODD dimensions literature, the strongest and most consistent evidence supports the inclusion of an irritable/angry subcomponent of ODD (see Table 2). There is strong, though slightly less, evidence for the validity of a defiant dimension, and greater variability in how it has been defined. Evidence for a possible third dimension (hurtful) is even more limited.

The evidence shows that a large majority of those diagnosed with DMDD would also have at least one other diagnosis. ODD and ADHD were the most common comorbidities—typically between 70% and 100%—in clinical and community samples (e.g., Althoff et al., 2016; Axelson et al., 2012; Copeland et al., 2013; Freeman et al., 2016; Margulies et al., 2012). These estimates suggest that DMDD identifies very few youth who would not have already received at least one other diagnosis, calling into question the argument of "diagnostically homeless" youth. Consequently, the question of where to place severe irritability becomes a question of which of the existing categories demonstrates the greatest degree of qualitative and quantitative overlap with ODD. Comorbidity rates show ADHD and ODD are approximately equivalent in terms of quantitative overlap. The nature of the angry/irritable clinical presentation and the long-term clinical outcomes

reviewed above are qualitatively consistent with the picture of ODD. Therefore, ODD seems to provide the most rational nosological home for an irritability/anger subtype.

4.2.2. Rationale behind the proposed formulation

The general ICD-11 proposal for ODD (see Appendix) is based on a monothetic definition of the disorder as well as a 2-factor model. The monothetic definition is consistent with previous formulations of ODD (APA, 1994, 2013; WHO, 1993), which have been extensively studied over the past two decades. Within that framework, a 2-factor model presents irritability and defiant behavior as two separate but correlated clusters of ODD symptoms. This formulation is broadly consistent with the findings of ODD dimension studies (Table 2), and particularly accordant with the bifactor model incorporating both broad ODD and narrow dimensions of irritability and oppositional behavior (Burke et al., 2014). While the monothetic definition is reflected in the diagnostic code and intended to maintain the unified construct of ODD, the 2-factor framework is intended to facilitate a clinical conceptualization that does not inappropriately homogenize children with ODD.

Because irritability/anger represents both a dimension of ODD and a more severe syndrome of SMD or DMDD, both of these formulations are reflected in the current proposal. The more severe pattern of chronic irritability/anger represents a specific subcategory of ODD. While its clinical picture is similar to the irritability dimension of ODD, the subtype requires a greater level of severity and impairment than the definition of ODD. Thus, separate definitions and diagnostic guidelines are needed to delineate ODD *with* versus *without* chronic irritability/anger. In essence, this framework constitutes a synthesis of the irritability dimension of ODD and a more severe form of irritability, anger, and outbursts akin to DMDD.

The subtype proposal is preferred to a separate diagnostic category for several reasons. First, this solution does not permit the diagnosis of anyone who would not already have received a diagnosis. At the same time, it is likely to capture approximately 80% of youth who would otherwise receive DMDD and seek clinical services (Axelson et al., 2012; Freeman et al., 2016; Leibenluft, 2011; Margulies et al., 2012). Second, it highlights important subdimensions within ODD, which might otherwise be missed by clinicians accustomed to diagnosing child behavioral disorders but not affective disorders, or vice versa. In these regards, the diagnosis is likely to increase clinical identification of those who warrant a separate form or tier of clinical care, while precluding the inappropriate diagnosis of normal tantrums and irritability. Third, compared to adding a freestanding diagnosis, adding a subtype may convey less risk for reification and the problems associated with it (Hyman, 2010). Fourth, adding a subtype to an existing and relatively common disorder is less likely to attract stigma toward children and parents affected by the diagnosis.

Finally, it is in the interest of child and adolescent mental health that a new diagnosis not be received with substantial controversy among professional communities and the public. The history of DMDD illustrates this point. Some clinicians may refuse to give the diagnosis at all, while others may over-apply it. And if clinicians are publicly uncertain about the validity of a childhood disorder, then parents, youth, teachers, and families have reason for skepticism toward the diagnosis and, perhaps by extension, the clinicians who give it. All things being equal, it would appear that it is better to err on the side of less change rather than more. The diagnosis of ODD with chronic irritability/anger appears to best reflect the current evidence and maximize clinical utility while minimizing potential for harm.

5. Conclusions and future directions

Recent findings underscore both the importance and the challenges in the assessment, diagnosis, and classification of youth irritability. After reviewing the research on SMD/DMDD and ODD dimensions, the available evidence supports the inclusion of a chronic irritability/anger subtype for ODD in ICD-11. It should be reiterated that irritability is also a diagnostic requirement or associated feature of over a dozen other disorders and problems, most of which can affect children and adolescents. Research is needed to better understand the etiology and mechanisms of irritability in youth, both within and across diagnostic categories. Consistent with recent initiatives in mental health research (Insel et al., 2010), various methods and paradigms spanning multiple levels of analysis should be explored. These avenues may include neuroimaging, behavioral assessment, frustrative non-reward, reward prediction error, emotion regulation, and attention and language (Meyers et al., 2016; Sukhodolsky, Wyk, et al., 2016).

Additionally, there is a need for further longitudinal and behavioral research, with a particular focus on the multi-informant assessments. Low correlations among parent, youth self-report, and other informant ratings of child and adolescent mental health are well-documented (De Los Reyes et al., 2015; Youngstrom et al., 2015). For this reason, studies examining parent-report in childhood as a predictor of self-reported outcomes during adolescence or adulthood (as is the case with much of the literature reviewed above) are problematic, and might yield different results if multiple informants were incorporated at all time points. Clinically, it is critical to utilize multi-informant assessment, involving parents, youth, teachers, and clinical judgment with respect to behavior across settings, because this can have significant implications for what diagnosis is assigned and what intervention is delivered.

Lastly, it is critical to study irritability among culturally, ethnically, and linguistically diverse populations. This is necessary for any classification system to possibly aid in mental health diagnosis and treatment around the globe. Intervention research, in turn, must also advance evidence for the treatment of severe irritability. However, effective treatment is predicated upon the validity of the condition being treated and the reliability of its measurement. Thus, research is greatly needed to advance the basic understanding and assessment of irritability in diverse populations of children and adolescents.

While we advance these recommendations for ICD-11 based on our review of the evidence, we also acknowledge that the validity, reliability, and clinical utility of diagnostic constructs are elusive targets to be pursued by researchers and clinicians. For that reason, mental health professionals, including those who work with children and adolescents, are contributing to the ICD-11 development process through avenues such as field studies and online public comment forums (Keeley et al., 2016). By incorporating feedback from the global mental health community, we hope that these revisions may improve the diagnostic classification of irritability and advance our knowledge and treatment of youth behavioral and emotional difficulties.

interpretation of the literature, and subsequent revisions of the manuscript. All authors approved the final manuscript.

Conflict of Interest

Acknowledgements

Appendix

Proposed definition and diagnostic guidelines for Oppositional Defiant Disorder in ICD-11

The following are draft versions of ICD-11 definitions and diagnostic guidelines and will be further revised based on the results of field testing and further review and comment. Current draft definitions for ODD and other proposed ICD-11 diagnostic categories can be found on the ICD-11 beta platform (http://apps.who.int/classifications/icd11/browse/l-m/en). Mental health or primary care professionals who are members of WHO's Global Clinical Practice Network (GCPN) may also review and provide comments on complete field testing versions of the diagnostic guidelines. To register for the GCPN, visit https://gcp.network.

Draft definitions for Oppositional Defiant Disorder

Oppositional Defiant Disorder: Oppositional Defiant Disorder is a persistent pattern (e.g., 6 months or more) of markedly defiant, disobedient, provocative or spiteful behavior that occurs more frequently than is typically observed in individuals of comparable age and developmental level and that is not restricted to interaction with siblings. Oppositional Defiant Disorder may be manifest in prevailing, persistent angry or irritable mood, often accompanied by severe temper outbursts or in headstrong, argumentative and defiant behavior. The behavior pattern is of sufficient severity to result in significant impairment in personal, family, social, educational, occupational or other important areas of functioning.

Oppositional Defiant Disorder with chronic irritability-anger: A form of Oppositional Defiant Disorder characterized by prevailing, persistent angry or irritable mood. The negative mood is often accompanied by regularly occurring severe temper outbursts that are grossly out of proportion in intensity or duration to the provocation.

Oppositional Defiant Disorder without chronic irritability-anger: A form of Oppositional Defiant Disorder that is not characterized by prevailing, persistent, angry or irritable mood, but does feature headstrong, argumentative, and defiant behavior.

Draft diagnostic guidelines for Oppositional Defiant Disorder

Essential features.

- A pattern of markedly noncompliant, defiant, and disobedient behavior that is atypical for individuals of comparable age and developmental level. Specific behaviors include arguing with adults or other authority figures, or actively defying or refusing to comply with their requests, directives, or rules. The pattern of noncompliance is often accompanied by other social and emotional difficulties (e.g., irritability/anger, blaming others; see Additional features).
- The behavior pattern has persisted for an extended period of time (e.g., 6 months or more).
- The behavior pattern is of sufficient severity to result in significant impairment in personal, family, social, educational or other important areas of functioning.
- The severity and frequency of the behaviors must be clearly outside the normal range of behavior for an individual of the same age and gender in his or her socio-cultural context.
- The oppositional behaviors are not better explained by relational problems between the individual and a particular authority figure toward whom he/she is behaving defiantly. Examples may include parents, teachers, or supervisors who act antagonistically or place unreasonable demands on the individual.

Additional features.

- The pattern of noncompliant behavior may include:
  o Extreme irritability and anger (e.g., being touchy or easily annoyed, losing temper, angry outbursts, being angry and resentful).
  o Persistent difficulty getting along with others (e.g., deliberately annoying others, blaming others for mistakes or misbehaviour).
  o Provocative, spiteful, or vindictive behavior.

- Frequently, the oppositional defiant features have a provocative quality so that individuals initiate confrontations and may be seen as excessively rude and uncooperative.
- Oppositional Defiant Disorder sometimes co-occurs with limited prosocial emotions. When assessing for Oppositional Defiant Disorder, the clinician should also assess for limited prosocial emotions (see below), and assign the appropriate qualifier.
- Interactions with authority figures that form the basis for a diagnosis of Oppositional-Defiant Disorder are generally quite frequent in younger children (e.g., 3 to 5 years of age), in which closer supervision and directive interactions are normative. As children grow older, direct demands by authority figures often become less frequent. A diagnosis is not precluded based on low frequency if the behavior characterizes most interactions with authority figures.
- Although often identified through parental report of noncompliant behavior, the negative and antagonistic aspects of Oppositional Defiant Disorder exert much broader negative influence on interactions with others. Oppositional Defiant Disorder is associated with peer rejection and interpersonal discord through the school years and into adulthood.
- Adults with Oppositional Defiant Disorder continue to experience conflictual relationships with parents and family members and have generally poorer social support networks. This affects the number and quality of their friendships and romantic relationships. They typically struggle to function with supervisors and coworkers in the workplace.

Subtypes of Oppositional Defiant Disorder.

Two subtypes of Oppositional Defiant Disorder can be specified in individuals who meet the diagnostic requirements described above.

- *Oppositional Defiant Disorder with chronic irritability-anger.* This subtype is characterized by prevailing, persistent angry or irritable mood, including often being 'touchy' or easily annoyed, that is characteristic of the individual's functioning nearly every day and is observable across multiple settings or domains of functioning (e.g., home, school, social relationships) and is not restricted to the individual's relationship with his/her parents or guardians. The negative mood is often accompanied by regularly occurring severe temper outbursts that are grossly out of proportion in intensity or duration to the provocation.

- *Oppositional Defiant Disorder without chronic irritability-anger.* This subtype refers to presentations of Oppositional Defiant Disorder not characterized by prevailing, persistent angry or irritable mood.

Boundaries with other disorders and with normality.

- *Boundary with normality and with Anxiety and Fear-Related Disorders:* Irritability, anger, and noncompliance are sometimes associated with anxiety, and this should be taken into account when considering this diagnosis. For example, children may exhibit angry outbursts when presented with a task or situations that make them feel anxious (e.g., going to school and separating from parents). If the defiant behaviors only occur when triggered by a situation or stimulus that elicits anxiety, fear, or panic—regardless of whether or not the individual meets the requirements for an anxiety disorder— Oppositional Defiant Disorder should not be diagnosed.
- *Boundary with Attention Deficit-Hyperactivity Disorder:* Individuals with Attention Deficit Hyperactivity Disorder often have difficulty following directions, complying with rules, and gettting along with others. When these disruptive behaviors can be accounted for primarily by symptoms of inattention and/or hyperactivity-impulsivity (e.g., failure to follow long and complicated directions, difficulty remaining seated or staying on-task when asked), Oppositional Defiant Disorder should not be diagnosed and a diagnosis of Attention Deficit Hyperactivity Disorder should be assigned instead. For Oppositional Defiant Disorder to be diagnosed, the pattern of noncompliance must be characterized by deliberate disobedience, beyond problems with attention and behavioral inhibition. Both diagnoses may be given if the full diagnostic requirements are met for each.
- *Boundary with Conduct-Dissocial Disorder:* The behavior problems associated with Oppositional Defiant Disorder are largely characterized by interpersonal conflict with authority figures and difficulty getting along with others. By contrast, Conduct-Dissocial Disorder is characterized by a repetitive and persistent pattern of more severe and dissocial behavior in which the basic rights of others or major age-appropriate social or cultural norms, rules, or laws are violated (e.g., aggression toward people or animals, destruction of property, deceitfulness or theft, serious violations of rules). However, individuals with Conduct-Dissocial Disorder often demonstrate a range or history of behavior problems that may include the interpersonal difficulties characteristic of Oppositional Defiant Disorder. Both diagnoses may be given if the full diagnostic requirements are met for each.
- *Boundary with Intermittent Explosive Disorder:* Regularly occurring severe temper outbursts that are grossly out of proportion in intensity or duration to the provocation may occur in the context of Oppositional Defiant Disorder with chronic irritability-anger. In such cases, an additional diagnosis of Intermittent Explosive Disorder should not be applied.
- *Boundary with Autism Spectrum Disorder:* Noncompliant and other disruptive behaviors characteristic of Oppositional Defiant Disorder should be distinguished from behavior problems that are common among individuals with Autism Spectrum Disorder. The key difference is that, in Autism Spectrum Disorder, disruptive behaviors are often associated with a trigger (e.g., sudden change in routine, aversive sensory stimulation), or the noncompliance is related to the symptoms of that disorder (e.g., social communication deficits, restricted, repetitive, inflexible patterns of behavior, sensory sensitivities) rather than reflecting a desire to be provocative or spiteful. Individuals with Oppositional Defiant Disorder do not typically exhibit the social communication deficits and restricted, repetitive, and inflexible patterns of behavior, interests, or activities that are characteristic of Oppositional Defiant Disorder. However, both diagnoses may be assigned if the full diagnostic requirements for each are met.

- *Boundary with Mood Disorders:* It is common, particularly in children and adolescents, for patterns of noncompliance and symptoms of irritability/anger to arise as part of a mood disorder. Specifically, noncompliance may result from a number of depressive symptoms (e.g., diminished interest or pleasure in activities, difficulty concentrating, hopelessness, psychomotor retardation, reduced energy). During manic or hypomanic episodes, individuals are less likely to follow rules and comply with directions. Oppositional Defiant Disorder is often comorbid with mood disorders, and irritability/anger can be a common symptom across these disorders. When the behavioral problems occur primarily in the context of mood episodes, a separate diagnosis of Oppositional Defiant Disorder should not be assigned. However, both diagnoses may be given if the full diagnostic requirements are met for each.
- *Boundary with Disorders due to Substance Use:* If the individual's pattern of defiance is limited to the use of substances in violation of the rules or directives of others, or if the noncompliance is exclusively related to the use or effects of a substance, Oppositional Defiant Disorder should not be diagnosed. Disorders due to Substance Use and Conduct-Dissocial Disorder should be considered instead.

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