ORIGINAL CONTRIBUTION

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Suicidal behaviors and irritability in children and adolescents: a systematic review of the nature and mechanisms of the association

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Abstract

While many psychiatric disorders are associated with an increased risk for suicidal behaviors (SB) in children and adolescents, a few studies have explored the role of clinical symptoms based on a dimensional approach. Irritability is seen as a marker, a general psychopathology, and a symptom of both externalizing and internalizing disorders. In this review, we are interested in determining *whether* and *how* irritability can predict SB in youth. First, we reviewed consistencies and variation in the literature linking irritability to suicidal ideation (SI) and suicide attempt (SA). Second, based on the available models, we proposed specific mechanistic pathways, whereby irritability may modulate the risk for SB. Irritability has been found associated with SB both in cross-sectional and in longitudinal studies. The relation is consistent in different settings (i.e., general population and clinical settings) and across psychiatric disorders. The association is reduced but persists after adjusting for psychiatric disorder, including depression. On one hand, irritability constitutes a risk factor for SI via the onset of internalized disorder. On the other hand, irritable youth may be more prone to attempt suicide when experiencing SI. The measures for irritability were heterogeneous. A limited number of studies were designed to explore the role of mediators and/or moderators. Recognizing irritability in children and adolescents is a key issue with regards to suicide prevention.

Keywords Irritability · Trait anger · Rage · Disruptive mood dysregulation disorder · Emotional dysregulation · Suicidal behavior · Suicidal ideation · Suicide attempt

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Introduction

Suicidal behaviors in youth

Suicide is the second leading cause of death among 10–19 years old in Western countries [1–4]. A better knowledge of the mechanisms leading to suicidal behaviors (SB) in children and adolescents is of major interest for the development of effective therapeutic interventions at these ages [2]. In the vast majority of research, the role of psychopathological factors in the emergence of SB is examined using a categorical approach. Therefore, the impact of each psychiatric disorder is studied separately (e.g., [5, 6]). The limits of categorical models to predict the emergence of SB have been raised in terms of statistical power, clinical needs, and medico-economic reasons [7–9]. For example, we cannot said exactly whether youth with anxiety disorders and those with oppositional defiant disorder (ODD), two conditions associated with an increased risk for SB [4, 6], shared common treatable clinical risk factors. Over the last decades, the use of dimensional view of psychopathology alongside categorical

approaches to model risk factors in suicide research has, therefore, been promoted [2, 10].

Irritability in youth

Irritability is defined as a negative mood characterized by a decreased threshold for experiencing anger in response to frustration, provocation, or threat relative to peers of the same developmental level [11]. It is a diagnostic criterion for several psychiatric disorders in the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5) [12] and a clinical feature of many different psychiatric conditions [13] (Table 1). In general population, there is a gradient of severity of the level of irritability, with those scoring high being more likely to have a significant level of functional impairment and associated psychopathology compared to those scoring low [11]. Irritability in children and adolescents has been regarded as a general psychopathological marker predicting the risk of developing psychiatric disorder. There is now a large amount of studies, showing that irritability predicts the onset of anxiety disorders, dysthymia, and major depressive episode (MDE) in late adolescence and adulthood [14–17].

Preliminary evidence for a link between irritability and suicidal behaviors

Descriptive studies showed that suicide attempts (SA) in children and adolescents are often depicted as a sudden and unplanned behaviors immediately following a frustrating or a stressful event [18, 19] with a few or no preexisting suicidal ideation (SI). Psychological autopsies of children and young adolescents showed that emotional and behavioral disturbances associated with irritability are frequently reported during the period preceding the suicidal act [20–22]. These youths are described by their friends and their family as more "aggressive, mistrustful, and sensitive to criticism" than usual [20], "angry, nervous, and impulsive" [21], or "vulnerable and touchy" [22]. One may think that a suicidal young who experience a high level of irritability are more prone to react in a disproportionate way to situations elicited by emotional stressors (e.g., frustration; perceived threat) and then to manifest impulsive SA.

Aims

In a first section, we examine the association between irritability as a risk factor, and SB, as an outcome in children and adolescents. Attention has been paid to document the validity, consistency, and specificity of the association between irritability and SB. In particular, we sought to determine whether the association between irritability and SB was truly independent from the onset of a psychiatric disorder. Four

types of research are presented here (in separate sections): studies conducted in community-based samples, studies conducted in inpatient samples with various disorders, studies conducted in a group of patients with a specific psychiatric disorder, and studies conducted in a sample of youth with clinical constructs related to irritability. The following hypotheses are examined: (1) a positive association exists between irritability and SB both cross-sectionally and longitudinally; (2) the positive association between irritability and SB is consistent in different settings (i.e., in clinical and community-based samples) and across psychiatric disorders; (3) the association between irritability and SB is reduced but remains positive and significant while taking into account the association with comorbid psychiatric disorders.

It is worth noting that irritability was used in the literature with a heterogeneous range of definitions with imprecise limits [11–13, 23–27]. In this review, we used the definition developed by Leibenluft [11]. To have a comprehensive approach, we also included in the review studies exploring the relation between SB and clinical constructs related to irritability. This ad-hoc category encompasses the clinical symptoms that refer to the observable consequences of irritability at the emotional level (e.g., expressed anger) or at the behavioral level (e.g., impulsive, reactive, and hostile aggressive behavior). Table 1 presents the definition of these terms, clinical examples, and the rationale for the inclusion in the study.

In a second section, developmental models for SB will be examined to determine how irritability modulates this risk. It is expected that irritability affects SB at different levels through development. A general framework synthesizing the reviewed models will be proposed enlightening more specific mechanistic pathways, whereby irritability influences SB.

Methods

Search method for identification of studies

Relevant articles for this study were obtained through PubMed, Medline, PsychINFO, PsychINDEXplus, and Dissertation Abstracts. Each database was searched from January 1990 to July 2017. Considering the exploratory approach of this study, a wide definition of irritability that encompassed clinically related constructs was used (Table 1). In this study and in line with Posner's classification [28], SB encompassed SI and SA, and completed suicide (CS), but not non-suicidal self-injury (NSSI).

We used the following search terms: "Disruptive mood dysregulation disorder" OR "Severe mood dysregulation" OR "Irritability" OR "Anger" OR "Temper outburst" OR "Impulsive aggression" OR "Reactive aggression" OR

Table 1 Terminology and definitions of the main terms used in the systematic review

	Irritability and related constructs		
	Definitions	Examples	Comments
Irritability	*Traditional definition* "Propensity to react with anger, grouchiness or tantrum disproportionate to the situations" [25] *DSM-5 definition* "Persistent anger, a tendency to respond to events with angry outbursts or blaming others, an exaggerated sense of frustration over minor matters" [12] *Working definition* "A negative mood characterized by a decreased threshold for experiencing anger in response to frustration, provocation or threat relative to peers at the same developmental level" based on [11, 13] *Definition based on physiology* "Irritability is a mood of partial physiological agitation characterized by an increased sensitivity to sensory stimuli and a non-cognitively mediated lowered threshold for responding with anger and/or aggression to typically less vexing stimuli; it is caused by factors that directly affect physiology and/or biology such as hunger, lack of sleep, pain, and fatigue" [24]	"I have been feeling ready to explode" "I have been rather sensitive" "He/she is easily frustrated" "I am easily annoyed by others"	Irritability is defined as a propensity and not as an observable behavior The definition provided by Toohey and Di Giuseppe [24] is based on items which are not overlapped with related construct such as aggression and anger
Anger	Anger is an observable consequence of irritability at the emotional level Anger is a negative emotional state that may include increased physiological arousal. It is often elicited by frustration, provocation, or threat [11] When a person is irritable, anger will be triggered by a lowered threshold, with a higher frequency, a higher intensity, and a longer duration of angry responses	"I feel anger out of proportion" "I have been feeling mad"	Anger can occur without being associated with irritability (i.e., cognitively mediated anger for example when one be witness of serious social injustice, or when one being offended) The negative emotional states associated with irritability (e.g., anger) may or may not be outwardly expressed

Table 1 (continued)

	Irritability and related constructs		
	Definitions	Examples	Comments
Impulsive, reactive and/or hostile aggression	Impulsive, reactive and hostile aggressive behaviors are observable consequences of irritability at the behavioral leve Impulsive aggression is usually conceived as thoughtless (automatic, fast, and without consideration of consequences) and affect laden [25]. The distinction between impulsive and premeditated aggression is based on whether the behaviors is planned Reactive aggressive behaviors are elicited by highly emotional situations (such as frustration or perceived threat). It is a response to a prior provocation [26]. The distinction between reactive and proactive aggression is based on the presence or absence of an emotion trigger for the behavior Hostile (also referred as affective) aggression having the ultimate motive of harming the target without other indirect goal [27]. The distinction between hostile and instrumental aggression is based on whether the primary goal of the behavior is to harm the victim or to gain some benefit for the perpetrator	"He/she has been so enraged that he/she has hit someone" "Does he/she get into arguments?" "Does he/she raise his/her voice in anger?" "Sometimes I shout, hit and kick and let off steam" "Sometimes I really want to pick a fight"	Such distinctions are not exclusive and the same behavior can have multiple components [27] Impulsive, reactive and hostile aggressive behaviors are typically conceived in overlapping ways. Such subtypes of aggressive behavior were all used to refer to non-premeditated aggressive behaviors elicited by highly emotional situations (such as frustration, provocation or perceived threat) by contrast to premeditated/proactive/instrumental aggressive behavior These subtypes of aggressive behaviors have been found associated with irritability. However, only a minority of youths with irritability manifest reactive aggressive behaviors (<12%) [13]
Tantrums	Tantrums (also referred as temper outbursts) are observable consequences of irritability at the behavioral level It is an intense uncontrollable outburst of anger expressed through cursing, kicking, hitting, biting, screaming, rolling on the ground, and destruction of property	"I feel like losing my temper at people" "Often have temper outbursts I cannot control"	
	Categorical approach		
DMDD	The disorder is characterized by severe recurrent temper outbursts in response to common stressors. The syndrome is characterized by the following criteria [12] The temper outburst are manifest verbally and/or behaviorally, such as in the form of verbal rages, or physical aggression towards people or property (Criteria A1). The reaction is grossly out of proportion in intensity or duration to the situation or provocation and the responses are inconsistent with the developmental level (Criteria A2). The temper outbursts occur, on average, three or more times per week (Criteria B) The mood between temper outbursts is persistently negative (irritable, angry, and/or sad) nearly every day (Criteria C1) and the negative mood is observable by others (e.g., parents, teachers, and peers) (Criteria C2) Criteria A–C have been present for at least 12 months. Throughout that time, the person has never been without the symptoms of Criteria A–C for more than 3 months at a time (Criteria D). The temper outbursts and/or negative mood are present in at least two settings (at home, at school, or with peers) and must be severe in at least one setting (Criteria E). Chronological age is at least 6 years (or equivalent developmental level) (Criteria F). The onset is before age 10 years (Criteria G)		

Table 1 (continued)

	Categorical approach
SMD	This research syndrome has been operationalized by Leibenluft's research team [11] in view of conducting studies on youths with chronic, severe, persistent irritability
	Diagnostic criteria are similar to DMDD except for (1) the presence of hyperarousal (defined by at least three of the following: insomnia, agitation, distractibility, racing thoughts or flight of ideas, pressure speech or intrusiveness) and (2) the age of onset before age 12
	A vast majority of youth with SMD also meets criteria for DMDD [12] (e.g., 97% in the study conducted by Deveney 95% in the study by Stoddard et al.)
CBCL-DP	Category defined as two or more standard deviations away from the mean on the Child Behavior Checklist (CBCL) subscales of anxiety/depression, aggression, and attention subscales [33–37]
	This category initially known as CBCL-Juvenile Bipolar Disorder profile was further relabeled CBCL-DP
Criterion for other psychiatric disorder	According to DSM-5 [12]
	"Irritability" is a diagnostic criterion for Generalized Anxiety Disorder, Substance Withdrawal
	"Irritable mood" is diagnostic criterion for Major Depressive Episode, Bipolar Disorder, and Oppositional Defiant Disorder
	"Irritable behavior" is a diagnostic criterion for Post-traumatic Stress Disorder and Acute Stress Disorder
Suicidality terminology based on Columbia Classification Algorithm of Suicide Assessment [33]	
Suicidal behavior	Nonfatal suicidal thoughts and attempt
Suicidal ideation	Passive thoughts about wanting to be dead or active thoughts about killing oneself, not accompanied by preparatory behavior
Suicidal attempt	A potentially self-injurious behavior, associated with at least some intent to die, as a result of the act
Suicide	A self-injurious behavior that resulted in fatality and was associated with at least some intent to die as a result of the act

DMDD Disruptive Mood Dysregulation Disorder, *SMD* Severe mood dysregulation, *CBCL-DP* Child Behavior Checklist-Dysregulation Profile

"Hostile aggression" AND "Suicidal behavior" OR "Suicidal ideation" OR "Suicidal attempt" OR "Completed suicide". We excluded studies on NNSI. Only studies conducted in subjects younger than 18 years old were included. In addition, we handed searched reference lists of identified articles and pertinent reviews for additional studies. References from the reviewed articles were also screened to find more articles of interest. In particular, we look for psychiatric disorder in which irritability is common or part of the defining criteria, i.e., oppositional defiant disorder [ODD], anxiety disorders, depressive disorders, bipolar disorders, post-traumatic stress disorders, acute stress disorder, and substance withdrawal. The authors independently screened potential studies, after reading the full article, for inclusion in the review, and the results were collated.

Results

The systematic review yielded 148 hits; 82 hits could be excluded based on the information in the title or abstract. The full texts of 66 hits were critically reviewed. Finally, 27 studies were included in this systematic review: eight were community-based studies, eight were clinical studies conducted in youth with different types of psychiatric disorders, eight were conducted in youth with a specific psychiatric disorder (depressive disorder $n = 4$, bipolar disorder

$n = 2$, ODD $n = 2$), and three other studies examined the relation between SB and hostile/impulsive/reactive aggressive behaviors. Among the studies reviewed 19 were cross-sectional and eight adopted a longitudinal design (Fig. 1).

Nature of the association between irritability and suicidal behaviors

Community-based studies

Pickles et al. [29] examined the relationship between irritability and the risk of developing psychopathology based on the longitudinal data from the Isle of Wight study in a 35-year follow-up study ($N = 2226$, 14–15 years old at baseline in 1968). At baseline, 19.1% of boys and 23.9% of girls were rated by their parents as displaying significant irritability (based on frequency, severity, and duration of youth 'symptoms assessed on one item). Irritability appeared a significant risk factor for SB in adulthood beyond associations with other adult disorders. Three cross-sectional studies examined the relationship between anger and SB in school-based adolescent samples [30–32]. All studies found that students, who self-reported higher levels of anger, were more likely to report SI, while the association with SA was mitigated.

In four studies [33–37], the Child Behavior Check List (CBCL) was used to define a class of youth with severe

Fig. 1 PRISMA flow chart
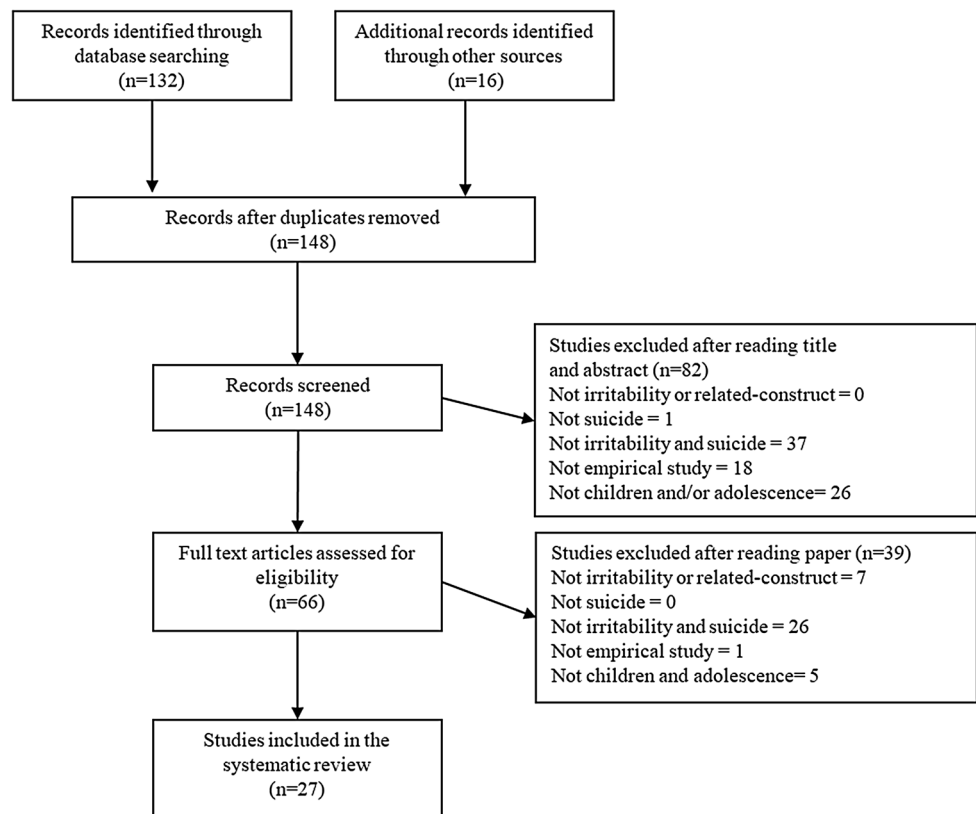
affective and behavioral dysregulation symptoms. Two cross-sectional studies showed that youth with the CBCL-DP are more likely to report SB compared to the rest of the population [33, 34]. Althoff et al. [33] found that youth whose mother reported a CBCL-DP were 25–36 times more likely to endorse the two items measuring SB in the CBCL compared to the class without psychopathology. They also noted that although the CBCL-DP accounts for only 4–5% of the total sample, these children accounted for 20–25% of the endorsement of SB. Volk and Todd [34] showed that past SI and SA were more likely to be reported by parents of youth with CBCL-JBD compared to the rest of the population. The likelihood that subjects with CBCL-JBD planned to take their own life over the past months was 16 times higher than for those who did not meet the CBCL-JBD profile.

Two longitudinal studies showed that CBCL-DP predicted a higher risk of developing SI [36] and SA [35, 36]. Althoff et al. [35] examined the outcomes of youth with CBCL-DP in a 14-year follow-up study based on 13 birth cohorts in a Dutch population. The association between CBCL-DP profile and the onset of suicidal thoughts or behavior did not reach significance after controlling for psychopathology, OR = 3.30 [0.83–13.06]. The authors concluded this association is overshadowed by the stronger relation between the current suicidality and current anxiety and mood disorders. Alternatively, they suggested that the associations between the CBCL-DP and suicidality could not be as strong in adulthood as they are in childhood. Finally, Holtmann et al. [36] found that young adults with a higher CBCL-DP score in childhood were at increased risk for suicidality at age 19. In contrast to prior study, the prediction remains significant after adjustment for parental education, family income, impairment, and psychiatric disorders at baseline (Table 2).

Clinical studies conducted in youth with different types of psychiatric disorders

Table 3 details the eight clinical studies that explored the relation between irritability and SB in youth with different types of psychiatric disorders [37–45]. The association between irritability and SB varies significantly according to the samples studied, the measure of irritability or related constructs, and whether results are controlled for other psychiatric symptoms. Among the 225 youths consequently admitted in a psychiatric unit, Goldston et al. [41] showed that those who had presented SA did not differ in terms of level of anger trait compared to those without a history of SA. However, the authors reported that the level of anger differed between those with a single SA and those with multiple SA. This finding has been replicated later in a group of youth inpatients using a similar measure of anger trait [42]. The view of irritability as a trans-diagnostic risk factor

for SI has been endorsed in a recent cross-sectional study conducted in 322 adolescent inpatients [43]. The authors noted that the level of irritability was positively associated with SI after controlling for gender, depressive symptoms, substance use disorders, disruptive behavior disorders, and post-traumatic stress disorders. However, association was significant only for self- but not for parent-reported irritability. One recent study showed that the relation between self-report levels of anger was higher for prepubertal children with recent SA, compared to those with SI [44]. Daniel et al. [45] examined the relationship between the course of anger and the risk for SA among a group of adolescents, discharged from an inpatient psychiatric unit and followed for a 13-year period. The authors noted that the presence of trait anger and anger expressed outwardly continued to be associated with SA, irrespective of diagnoses of major depression and/or substance use disorders for the boys. An increase of one standard deviation of the mean of the anger out State-Trait Anger Expression Inventory (STAXI) subscore was associated with a 34% increased risk for an SA during the period of follow-up. For women, low trait anger or low anger expression increased the risk for SA only when they were depressed. Mbekou et al. [37] found that, among inpatient youth seeking treatment for mood symptoms, those with the CBCL-DP profile presented more severe SI when compared to those without the profile.

Association across different psychiatric disorders

Among the literature devoted to the identification of clinical features predicting SB in youth with psychiatric disorders, very few studies examined the heterogeneity at a symptom level for a specific disorder.

Internalized disorders Two studies showed that bipolar youth with mixed features (during which patient experiences irritability rather than elated mood) are more likely to have a history of SA compared to those without mixed features [46, 47]. Findings about depression are more inconsistent. Myers et al. [39] found that the presence of an angry mood among youth aged 7–17 with a MDE predicted later suicidality in a 3-year follow-up study. Greening et al. [48] noted that depressed youth who scored higher on reactive aggression reported more SB in a sample of consecutively admitted inpatient youth over 18 months (N = 223); however, the association remains significant only for girls after adjusting for depressive symptoms. Stringaris et al. [17] used data from the Great Smoky Mountain Study to examine the relation between irritability, anhedonia, and a variety of clinical and functional outcomes in a community-based sample of youth with depressive symptoms. They found that depressed youth with predominant irritability did not differ from those with predominant anhedonia in regards with

Table 2 Relation between suicidal behaviors and irritability in community-based studies

Study	Setting	Population	Assessment of SB	Outcomes	Comments
Cross-sectional studies					
Althoff et al. [33]	Community sample Twin pairs	4% of girls and 5% of boys of the total sample (N=7124) with CBCL-JBP Age: min 3, max 12	CBCL items Maternal report	Youths with CBCL-JBP are more likely to report SB (SI or SA) in the last 6 months OR: 25–36	No control on psychiatric comorbidities
Volk et al. [34]	Community sample Twin pairs	33% of the total sample (N=1346) with CBCL-JBP Age: mean 11.7	MAGIC parental report	Youths with CBCL-JBP are more likely to report: a lifetime history of SI (OR=4.42) and SA (OR=6.8) SI in the last month (OR=16.9)	Associations remain significant while controlling for current psychiatric disorder Data come from a population-based sample, originally over-selected for DSM-IV inattentive ADHD
Park et al. [30]	Korean school-based sample	63% of the total sample (N=18,752) classified with high risk for SI Age: mean 14.5, min 12, max 19	19-item self-report questionnaire (Scale for Suicidal Ideation, SAS)	Youths with high risk for SI (SAS > 6) show higher levels of state anger, trait anger at the STAXI	Association is comparable in males and females, but no control on other environmental risk factors
Zhang et al. [31]	Chinese school-based sample	Total sample (N=14,537) divided in seven class according to the score at the Buss and Warren's Aggression Questionnaire Age: mean 15.1, min 10, max 18	Four self-reported questions	Positive association between anger trait and SI (OR=2.12) Negative association between anger trait and SA (OR=0.24)	Associations remain significant while controlling for socio-demographic and various environmental risk factors
Sigfusdottir et al. [32]	Icelandic school-based sample	Total sample (N=9,085) Anger measured with five questions drawn from the anger-hostility dimension of SCL-90, Age: min 16, max 19	Three self-reported questions	Positive association between anger and SI only (r=.23 for males, r=.18 for females) Positive association between anger and SA (r=.23 for males, r=.25 for females)	Structural equation modeling showed that depressed mood, but not anger, mediates the relation between sexual abuse and SI; while anger, but not depressed mood mediates the relation between sexual abuse and SA
Longitudinal studies					
Pickles et al. [29]	Community sample Isle of Wight Follow-up=35 years	24% of girls and 19% of boys of the total sample (N=2226) rated by their parents as having severe irritability on SADS Age: min 14, max 15	Ad-hoc five-point suicidality scale	Parent-reported significant irritability at age 14 predicted the presence of SI and/or SA at age 45 (OR: 3.2)	Association remains significant while controlling for adult psychopathology

Table 2 (continued)

Study	Setting	Population	Assessment of SB	Outcomes	Comments
Althoff et al. [35]	Community sample ZHLS, Follow-up = 14 years	4% of the total sample (N=1580) with CBCL-DP, Age: mean 9.9, min 4, max 16	ASR, Self-report	Youths with CBCL-DP are more likely to report SA in adulthood (OR: 3.30)	No control on psychiatric comorbidities; The questions from the ASR encompassed non-suicidal self-injurious behavior
Holtmann [36]	Community sample MSCR, Follow-up = 19 years	CBCL-DP studied as a dimensional score (N=384)	BDI item (SI), MEL item (SA)	The CBCL-DP score at baseline predict at age 19 SI ($\beta=0.03$) and SA ($\beta=0.04$)	Associations remain significant while controlling for current psychiatric disorder at age 8

SADS the Schedule for Affective Disorders and Schizophrenia Lifetime version, *CBCL-DP* Child Behavior Checklist-Dysregulation Profile, *ZHLS* The Zuid-Holland Longitudinal Study, *SA* suicide attempt, *SB* suicidal behavior, *SC* suicide completion, *SI* suicidal ideation, *ASR* Adult Self-Report, *MAGIC* The Missouri Assessment for Genetics Interview for Children, *MSCR* the Mannheim Study of Children at Risk, *BDI* Beck Depression Inventory, *MEL* the Munich Events List

SB. Comparable findings were found by Horesh et al. [49] in a clinical sample. The team compared the risk of SB in a group of inpatient adolescent with an MDE and a group with BPD. In the subjects with BPD, impulsiveness and aggression correlated significantly and positively with SB, but the association was not observed in the group of adolescents with MDE. No specific data were found for DMDD, anxiety disorders, acute stress disorder, or post-traumatic stress disorder.

Externalized disorders Aebi et al. [50] found that the irritable dimension but not the defiant/vindictive dimension of ODD symptoms predicted SB in a sample of 158 detained male adolescents. The authors used Latent Class Analysis to identify distinct subtypes of adolescent offenders according to their ODD symptom profiles: no-ODD subtype, severe ODD subtype, and two moderate ODD subtypes with either defiant or irritable symptoms. Youth with an irritable subtype of ODD were 12 times more likely to have current SB compared to those without ODD; this subtype was associated with anxiety but not mood disorder. Okado and Bierman [51] followed a sample of 317 children with the early externalizing problems from school entry (ages 5–7) to late adolescence (ages 17–19). Using Latent Class Analyses, they identified a group of subjects (6.5% of the total sample) who combined elevated reactive anger, dysphoric mood, and suicidal thoughts.

Association with reactive, hostile, impulsive–aggressive behaviors

In addition to the study conducted by Greening et al. [48] among depressed youth mentioned above, three studies have examined the presence of aggressive behaviors in relation to SB in children and/or adolescents [52–54]. Conner et al. [53] found that reactive aggression was linked to SI among prepubertal and adolescent youth after controlling for disruptive behavior disorders. Fite et al. [52] found that reactive, but not proactive aggression, was related to increased SB in a young psychiatric population ($N = 105$). However, the authors did not control findings for depressive symptoms. In a 1-year follow-up community-based study conducted in 359 American adolescents, McKeown et al. [54] showed that a high level of impulsive aggression at baseline was associated with a higher likelihood of suicidal plan at follow-up ($OR = 2.3$, in multivariate analysis), but not SI or SA.

Different developmental pathways from irritability to suicidal behaviors

Three models to link irritability and SB can be distinguished where irritability is successively regarded as a predisposing factor, as a developmental factor, and as a precipitating

Table 3 Relation between suicidal behaviors and irritability in clinical studies conducted in youths with different types of psychiatric disorders

Study	Setting	Population	Assessment of SB	Outcomes	Comments
Cross-sectional studies					
Brent et al. [40]	Inpatient psychiatry unit	37 subjects who report SA in the last year and 29 psychiatric control Age: min 13, max 19 Irritability measured with the Buss–Durkee Hostility Inventory (BDHI)	Suicidality: Beck Suicidal Intent Scale Lethality: the risk Rescue Rating Scale	No difference between completers and controls on the BDHI subscales and history of assaultive behavior	No control on psychiatric comorbidities
Goldston et al. [41]	Inpatient consecutively admitted in psychiatric unit over 3-years	27 subjects with single SA, 32 subjects with multiple SA, 126 subjects with SI without SA, and 40 subjects without SI/SA Age: mean 14.8, min 12, max 18 Irritability measured with the State-Trait Anger Expression Inventory (STAXI)	Interview Schedule for Children (ISC) by mental health professionals	No difference between groups in terms of state anger Subjects with multiple SA have higher level of trait anger compared to other groups SI without SA no significant difference with controls in terms of level of state or trait anger	No control on psychiatric comorbidities
Esposito et al. [42]	Inpatient consecutively admitted in psychiatric unit or ED immediately after a SA	74 subjects with single SA, 47 subjects with multiple SA Age: mean 15, min 12, max 18 Irritability measured with the State-Trait Anger Expression Inventory (STAXI) and Regulation of Affect and Impulses (RAI)	SA evaluated by medical team in ED	Subjects with multiple SA have higher level of STAXI score and RAI compared to subjects with single SA	Associations remain significant while controlling for mood disorders, and then depressive symptoms
Mbekou et al. [42]	Outpatient patients seeking treatment for mood problems in a specialized unit	397 subjects, 150 with the CBCL-DP profile Age: mean 14.1, min 6, max 18 Irritability measured with the CBCL-DP	SI evaluated with one item of the CBCL parental form	Subjects with the CBCL-DP profile are three times more likely to present with SI compared to subjects without the CBCL-DP profile	No control on psychiatric comorbidities Only parent-report measures
Bodzy et al. [44]	Inpatient consecutively admitted in psychiatric unit	70 subjects with SI, 59 subjects with recent SA Age: mean 9.9, min 7, max 12 Irritability measured with the Children's Inventory of Anger (CHIA)	SA evaluated in the medical chart SI: self-report questionnaire, the Child–Adolescent Suicidal Potential Index	Subjects with recent SA have higher level of CHIA total score compared to subjects with SI	No control on psychiatric comorbidities Age and gender did not moderate the association Only self-report measures

Table 3 (continued)

Study	Setting	Population	Assessment of SB	Outcomes	Comments
Frazier et al. [43]	Inpatient consecutively admitted in psychiatric unit or ED over 1 year	391 subjects Age: mean 14.9, min 12, max 18 Irritability measure with the K-SADS-MRS	Suicide Probability Scale	Positive association between adolescent-rated irritability and SI, but not for parent-rated irritability	Associations remain significant while controlling for gender, depressive, substance use, oppositional defiant, conduct, and post-traumatic stress disorders No measure of SA
Longitudinal studies					
Daniel et al. [45]	Consecutive discharge from an inpatient psychiatry Unit over four year Follow-up = 13 years	180 subjects Age: min 12, max 19 Anger measured with the STAXI	SA: Interview Schedule for Children, a semi-structured interview SC: Social Security Death Index	Higher anger trait predicts an increased likelihood of SA among males (OR = 1.34)	The onset of an episode of major depression moderates the relation between trait or state anger and SA in females but not in males
Other designs					
Withers et al. [38]	Retrospective chart review	173 inpatient consecutively admitted in psychiatric unit over 4-years Age: mean 17, min 10, max 20	Medical and paramedical chart	The most prominent mood characteristic just prior to the attempt was reported to be intense anger (42% male and 29.8% female)	No non-SA control group ACE: NR FH: NR

factor. Table 4 details the clinical correlates and the consequences for preventive interventions for each of these assumptions. Some of the information presented here are based on reviewed empirical data (upper column 2, Table 4), while the others are more theory-driven hypotheses (upper column 3, 4, Table 4) and presented to highlight future research strategies.

Predisposing factor

The first model posits that emotional dysregulation that encompassed irritability and mood lability is a psychological trait that predisposes to SB. Mann et al. [55] suggested that this trait is underpinned at a neurobiological level by a dysfunction in the serotoninergic system that predispose youth to impulsive–aggressive behaviors. While this assumption has been documented in adolescents in several longitudinal studies [18, 54, 56], empirical demonstration in prepubertal children is lacking.

The model has largely been supported by familial studies. A cross-sectional study shows that, among subjects who attempted or completed suicide, a higher level of impulsive aggression was associated with greater family aggregation of SB [57]. Brent et al. [58] compared the offspring of three mood disorder proband groups: parents with SA with siblings with SA ($n=19$), parents with SA with siblings without SA ($n=73$), and parents without SA with siblings without SA ($n=73$). They noted that the familial loading for SA affected rates of transmission as well as age at onset of SA, and that this effect was mediated by the familial transmission of impulsive aggression. The same team also showed that impulsivity mediated the impact of other risk factors such as parental history of sexual abuse [59].

The highest level of evidence for a co-segregation of SB and irritability in family comes from longitudinal studies conducted in offspring of adults who attempted/committed suicide. Melhem et al. [60] examined the risk of SA in the Pittsburgh cohort of offspring with parent mood disorders ($N=365$ offspring, $M=20.2\pm9.0$ years). During the 2-year follow-up period, 5.4% of them attempted suicide. Self-reported impulsive aggression in offspring was an independent predictor of an earlier time to, and greater hazard of an SA event. By contrast, Brent et al. [61] presented contradictory finings. The research, conducted in offspring of parents with mood disorders who were followed up for a mean of 5.6 years, showed that the impact of impulsive aggression on the onset of SA was largely mediated by the onset of mood disorders.

The assumption that impulsive aggression contributes to suicidal risk in at-risk population suggests that the assessment and management of impulsive aggression may also help to reduce early onset SB in children and adolescents. Limitations of this model should be discussed. First, the overlap between irritability and SB is far from complete: many youth with severe irritability do not exhibit SB; and this model does not account for the vast majority of youth without irritable mood who commit SB. Second, empirical evidence for the role of impulsive aggression in the intergenerational transmission of SB is derived from cross-sectional studies or longitudinal studies with short period of follow-up leading to multiple possible confounding biases. For example, McGirr et al. [62] used pathway analysis to show that familial aggregation of SB was mediated by impulsive–aggressive behavior. Comparable mediation models using longitudinal data with assessment of SB in childhood will be of main interest to document causality, especially whether or not irritability precedes the onset of psychopathology associated with SB. Third, whether it is worth targeting impulsive aggression to reduce suicidal risk in youth whose family presented neither mood disorder nor SB is less clear as findings are based on at-risk probands of adults with mood disorders. Fourth, the association between impulsive aggression trait and SB may also reflect the role of environmental risk factors affecting the familial transmission of SB, such as poor attachment bond or history of sexual abuse [59].

Developmental factor

The second model holds that youth with irritability are at high risk for SB via the onset of psychopathology. This model has been largely generated on the basis of longitudinal studies showing that irritability in childhood predicts the onset of anxiety and depression in adolescence and young adulthood [14–17]. This model is at least partly supported by the current review as all the studies showed that the association between irritability and SB is reduced when the association with comorbid psychopathology is considered. This model also predicts that the association between externalized disorder and SB is largely driven by the presence of irritable mood, although strong evidence on this point is lacking due to the paucity of data.

There is a consensus among most authors that the combination of poor emotional regulation strategies and low motor inhibition dramatically raise the risk of SB in children and adolescents [18, 54, 56]. Returning to irritability, it is worth noting that the dimension is strongly associated with both internalized and externalized disorders in clinical samples in four cross-sectional and longitudinal studies with a short period of follow-up [63], and comparable findings are reported in community-based samples [11]. This model predicts that the co-occurrence of internalized and externalized symptoms in youth with severe irritability has a synergic effect on suicidal risk, and would place them at higher risk of SB compared to those with internalized or externalized disorders alone.

Table 4 Three models to explore the relation between irritability and suicidal behaviors

	General assumptions	Empirical evidence		Expected results in further research			Putative implications for preventive intervention programs	
		Strength of the relation between irritability and suicidality	Effect of adjustment f associated psychopathology	Risk factors for irritability and SB	Clinical courses of irritability and SB	Mediation analyses in longitudinal studies		Benefits of treating irritability on SB risks
Model 1 Predisposing factor	Severe irritability is a clinical endophenotype for suicidality	High for SI and for SA	Reduced but persisting relation [e.g., 60]	Shared genetic and environmental risk factors between irritability and SB	Distinct clinical course for irritability and SB at the individual level	Irritability fully mediates the relation between pre-existing risk factors for SB and the onset of SB	Subjects with high-level of irritability are at-risk of SB	Moderate
Model 2 Developmental factor	Severe irritability is risk factor for SB via the onset of psychopathology	Moderate for SI and for SA	The association vanishes [e.g., 61]	Distinct genetic and environmental risk factors for irritability and SB	Similar but dissociable clinical course for irritability and SB at the individual level	Psychopathology fully mediates the relation between irritability and SB	No benefit	Low (via a reduced likelihood to develop psychopathology) Impact on SI and SA
Model 3 Precipitating factor	Severe irritability is a risk of transition from SI to SA	Moderate for SI but High for SA	Reduced but persisting relation for SA [e.g., 43]	Distinct genetic and environmental risk factors for irritability and SI, but common with SA (in particular multiple SA)	Associated clinical course of irritability and SA at the individual level	Irritability mediate the relation between SI and SA	Subjects with high-level of irritability are at-risk of SA	High (reduced the risk of presenting SB in youths with other risks factor, in particular SI) No impact on SI

Precipitating factor

The third model holds that youth with irritability are at high risk of presenting SA, not via an increased level of suicidal thoughts, but, because they are more prone to SB while experiencing SI. In line with the Turecki and Brent's model [2], it can be hypothesized that the combination of behavioral disinhibition and oversensitivity to stress in irritable youth accelerate the transition from SI to SA. This model has much in common with the concept of "acquired capability" for SB, which is regarded as a factor that predisposes to SA independently from the presence of SI [64].

This model is supported by three types of findings. First, the transmission of aggression and SA, but not SI, are related, whereas the familial transmission of SI seems to co-occur with mood disorder [65]. Second, irritability seems to be associated with the recurrence of SB, as shown in the studies comparing youths with single and repeated SA [41, 42]. Third, psychological autopsy studies in adolescents and young adults showed that, in a substantial amount of cases, the SA is not a premeditated act but rather an explosive behavior in immediate response to a frustrating or stressful life experience with few or no pre-existing SI [18, 19].

Asarnow et al. [66] examined coping styles and self-perception in 8–13-year-old suicidal inpatient children. They found that suicidal children, though not necessarily depressed children, generated less active coping style to regulate their affective and behavioral responses to stressful life events, with a high rate of physically aggressive coping strategies for solving interpersonal difficulties. The combination of poor socio-emotional regulation strategies and low self-esteem would put these youth at a very high risk of SB independently of the presence of depressed mood.

Discussion

Association between irritability and SB

First, irritability was associated with SB both in cross-sectional and in longitudinal studies (hypothesis 1). Second, the relation was consistent in different settings (i.e., in general population and in clinical settings) and across psychiatric disorders (hypothesis 2). Third, this relation persisted even after adjusting for psychiatric disorders, in particular depression (hypothesis 3). These findings support the view that the association exists along a continuum of irritability, and does not only concern the proportion of youths with the highest level of irritability and who are very likely to present a comorbid psychiatric disorder [63]. This is important as concerns were raised that the association between irritability and poor functional outcome might be an artefact due to the association with psychiatric disorder [67].

The contribution of irritability to SB among youths with externalized behaviors was shown in the study conducted by Aebi et al. [50]. Surprisingly, no studies have examined the relation between Attention Deficit Hyperactivity Disorder (ADHD) and SB at a symptom level in children and adolescents. The previous reports noted that the relation between ADHD and suicidality would mainly be indirect and mediated by the onset of psychiatric comorbidities, in particular conduct disorder and substance abuse [5, 68]. While irritability is not a DSM-5 diagnostic criterion for ADHD, emotional dysregulation is seen as a common feature of the disorder [69]. Future studies should help to determine whether the mediation effect of conduct disorder and substance use on the relation between ADHD and SB is not better explained by the presence of irritability or by the new DMDD concept. If this is true, it could inform screening and preventive procedures for SB in youths with externalized disorders.

Developmental pathways from irritability to SB

The findings stress the different pathways by which irritability impacts SB. The three models described in Table 4 differ in terms of the etiological factors, the clinical course, and the therapeutic opportunities. The current evidence is insufficient to choose decisively among these models, partly because a few studies have been designed to specifically address this question, and partly because it is likely that several mechanisms occur simultaneously. It can be thought that the high risk for SB found in youths with irritability might result from the synergic effect due to the association between internalized symptoms (that make them more liable to experience SI) and externalized symptoms (that make them more prone to SA when experiencing SI) (see Fig. 2). Therefore, the two categories of "planned" and 'impulsive' SA presented in the introduction could reflect two extreme cases of the dominance of one pathway on the other. Youths with persistent severe irritability would have a higher risk for SA directly following the "impulsive–reactive aggressive" pathway to SA (in orange in the figure 2). In addition, as mentioned in the introduction, irritable youth are also at high risk of developing anxiety and depressive disorders [13, 23]. Therefore, these youths would have a higher risk for SA indirectly, i.e., through the "internalized" pathway to SA via an increased level of SI (in blue in the figure 2). While this framework can be regarded as largely speculative, it generates testable hypotheses that can stimulate future research. Future studies should document the temporal association between irritability, psychopathology, and SB to address this question.
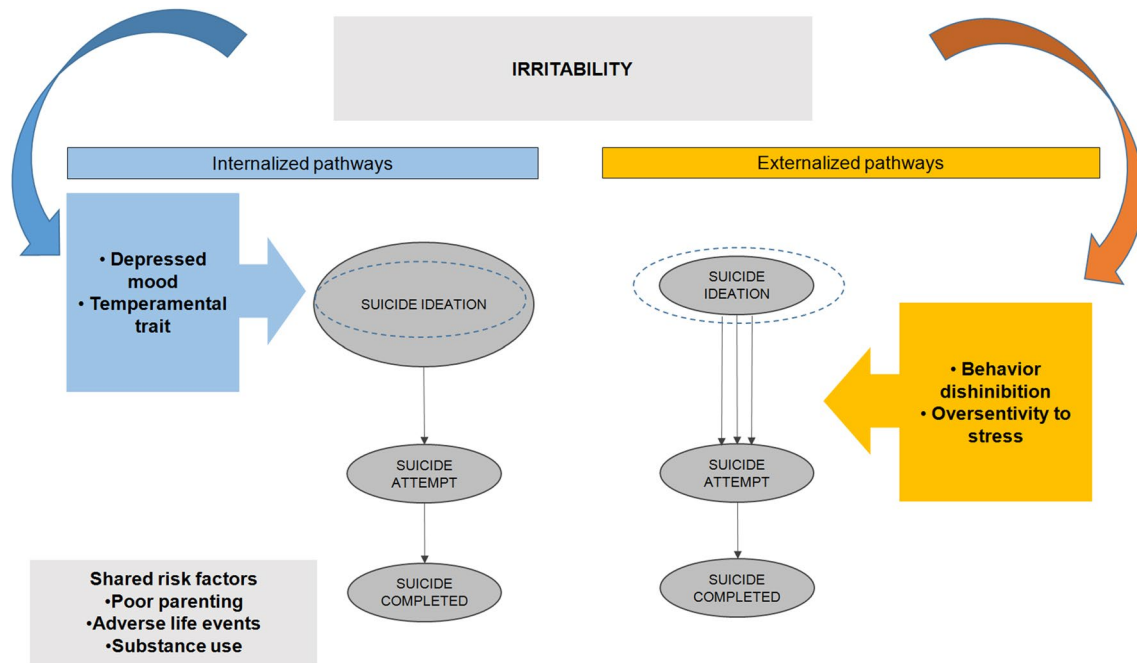
Fig. 2 Different pathways from irritability to suicidal behaviors. Note: this model endorses the view of associated but distinct vulnerability to SI and SA. Distinction was made between a developmental pathway predicting the occurrence of SI in childhood or adolescence and another pathway associated with an increased transition rate to SA when experiencing SI

Limitations

The current findings are limited by the lack of studies available. The vast majority of studies included in this review have cross-sectional designs, which further limit the possible conclusions. This should draw the attention of the researchers that, in the future, more studies are needed with a longitudinal design.

In addition, similar to the previous reviews [24, 70, 71], the measurement methods for both irritability and suicidality in the studies reviewed were very different that preclude direct comparisons between studies.

Clinical/research implications and conclusion

The results of this review have implications for clinical practice. First, the association between irritability and SB suggests that assessments of suicidality in adolescents with DMDD and externalized disorders should be promoted in clinical settings as it is for internalizing disorders. Second, as effective treatment for severe irritability exists [70, 71], the thorough assessment and treatment of irritability in suicidal adolescents could facilitate recovery and favourable therapeutic outcomes. In this vein, one study showed that impulsive–aggressive behaviors were associated with SA only in the group of adolescents who were not being treated with antidepressants [72]. Third, the presence of severe irritability in youth with other serious mental health problems (e.g., depressive disorders, ADHD, and borderline personality traits) might indicate increased vulnerability to SB and would deserve a special attention during routine care.

Regarding further research longitudinal studies with repeated multi-informant assessments of psychopathology, irritability and SB would be of great value to perform pathways analysis and help us testing competing hypotheses. Person-centered method such as Latent Class Growth Analysis could be used to identify specific groups of patients with poor prognosis. Finally, our review supports the need to consider SI and SA as two distinct outcomes when studying the association between irritability and suicidality in children and adolescents.

In conclusion, our systematic research supports the recognition of irritability as a transnosological risk factor for SB. The current literature represents promising first steps to better understand the mediators between psychopathology and SB. A great deal of work is still necessary to clarify the underlying mechanisms.

Compliance with ethical standards

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