

Probing the Irritability—Suicidality Nexus

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Suicide is a major public health concern.¹ Although still rare in absolute numbers, suicide is the second cause of death in adolescents and seems to be on the rise.² One of the strongest risk factors for suicide is suicidality (ie, suicide ideation and attempts) alongside depression, substance abuse and, of course, access to lethal means.³⁻⁵ Identifying modifiable early predictors of suicidality and suicide should therefore be a priority for mental health researchers. In this issue of the *Journal*, Orri *et al.* examine whether distinct childhood trajectories of irritability, one of the most common symptoms across psychiatric disorders in youth, are associated with suicidality in adolescence.⁶

Irritability, as defined in the paper and elsewhere,⁷ refers to interindividual differences in proneness to anger. From a clinical point of view, irritability may reach an extent that is impairing, a condition that the *DSM-5* tried to capture when they introduced disruptive mood dysregulation disorder (DMDD). Clearly, it is perfectly normal to be irritable, but the adverse outcomes for those who experience high levels of irritability are well documented.⁸ These include increased rates of depression and anxiety occurring up to 20 years later, as well as worse educational and occupational outcomes.⁷ However, what is the evidence for irritability as a risk for suicidality? Until recently, very little.

About 10 years ago, Pickles and Maughan published their 30-year follow-up findings from the Isle of Wight study showing that irritability was a significant predictor of suicide independently of depression.⁹ The extent of the prediction was fairly substantial, with an odds ratio (OR) close to 2 even after controlling for other potential confounds. More recently, using the same cohort as described in this study, Orri *et al.*¹⁰ also showed that the presence of irritability increased the probability of suicidality.

The new paper by Orri *et al.* makes excellent use of the large Québec Longitudinal Study of Child Development birth cohort to examine the direct and indirect effects of irritability on suicidality. Some of the study's main assets are the longitudinal design, the cross-informant (teacher to self) predictions, and the analytical approach, namely the modeling of irritability trajectories along with the mediation analyses.⁶

A great advantage of the method used in this paper, a type of latent growth modeling, is that it allows for the empirical identification of subpopulations based on the participants' profile of symptoms across time—in this case, their scores on irritability between ages 6 and 12 years. As expected, the authors find that the majority (74.4%) of children belong to a low irritability trajectory; that is, their score remains consistently low across time. However, a substantial proportion are on a rising (13%) and a smaller proportion on a persistent (5%) trajectory; another small fraction of children are on declining trajectory (7%), a childhood-restricted form of irritability. Of these trajectories, the rising one—that is, children whose irritability is on the ascending—showed the strongest association with suicidality. A few numbers serve to emphasize this relationship: membership of the rising class, compared to membership of the low class, made a young person 2.5 times more likely to suffer from suicidality. Specifically, 17% of children in the rising irritability class expressed suicidality compared to 9% in the low class.

The authors then used a mediation analysis to estimate how much of the association between childhood irritability and adolescence suicidality was best accounted for by depression, anxiety, disruptive behaviors, or hyperactivity-impulsivity symptoms in early adolescence. They found that there were two pathways—one direct pathway from irritability to suicidality, and another in which depression intervened. In those children belonging to the rising class, the direct pathway was particularly strong (OR = 2.11), accounting for the lion's share of the association (77%); although there was also some prediction via depression (OR = 1.17). By contrast, in those children whose irritability was persistently increased, any relationship with suicidality was explained by the presence of depression. Importantly, anxiety, disruptive behaviors, and hyperactivity-impulsivity symptoms did not predict suicidality for any of the classes.⁶

Clearly, one of the main insights of this paper is developmental: it appears to be that the rise—rather than the persistence—of irritability is the most important predictor of suicidality above and beyond the presence of depressive

symptoms. However, a few things should be noted when interpreting these findings. First, it was teachers who reported on children's irritability, which is different from most other studies of irritability. In most countries, clinicians do not have access to teacher reports; thus, whether parent or self-reporting of irritability would predict similar outcomes is unclear. Second, although the overall sample size was satisfactory, the absolute numbers of people with suicidality within certain classes were quite low (eg, only seven people in the persistent group). This means that particularly the mediation models, which rely on how many of those seven had depression, may well be underpowered. Also, all the main comparisons presented in the paper were between each class against the low irritability trajectory—for example, the differences between the rising and persistent trajectory were not significant. Finally, the term “suicidality” is a useful heuristic, but hides considerable heterogeneity in its own right. Whereas the authors did not find differences between ideation and attempts, there is, for example, good reason to distinguish nonsuicidal self-harm from attempts at killing oneself.

As any great piece of work, this one too raises new questions about the mechanisms underlying the effects of irritability. A key question is whether irritability is a cause, in and of itself, of suicidality. From a clinical standpoint, this would seem plausible: how often have we clinicians seen patients whose explosive temper precedes acts of aggression to self and others, or at least thoughts about self-harm? In other words, irritability could provide the emotional substrate for suicidality as a proximal risk factor, which would imply that treating irritability could be crucial.

An alternative to this model would be to regard irritability as a statistically significant by-product, but not a causal component of suicidality. It could be, for example, that both suicidality and irritability share risks. Depression, for example, might account both for making an adolescent reach for a razor blade to self-harm and for the anger that this very adolescent may experience. There are, of course other, less parsimonious but still clinically plausible models, for example, a double hit where a risk factor such as depression is more likely to lead to

suicidality in the presence of irritability (an interaction). Finally, even if irritability were not causally involved in suicidality, it could still be a clinically important marker, as it can be associated with other risks that might actually be involved. Yet, designs different from those presented here would be necessary to establish the predictive value of irritability, for example, in clinical settings. Needless to say, disentangling these models might prove be challenging using standard research tools.

Maybe one of the most promising avenues for future research is developing or re-purposing existing treatments for children with irritability. It would be interesting to know whether a treatment for irritability would reduce the probability of suicidal thoughts and self-harm. Appropriately designed, such a treatment study would, at the same time, be an “experiment” about the involvement of irritability in the pathogenesis of suicide.

Taken together, the findings from Orri *et al.* indicate that, at the very least, irritability may signify increased probability for suicidality, and clinicians will want to factor that into their risk assessment. Future research will determine whether irritability's effects are causal or not.

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