EDITORIAL

What Makes a Useful "Predictor" of Risk for Suicide Attempt?

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There is now robust evidence that children as young as preschool-aged can express suicidal ideation, and even engage in behavior that can be understood as suicide attempts.[1,2]

Related article

Young children who express suicidal ideation or exhibit suicidal behaviors have a more accurate understanding of death than their nonsuicidal peers,[3] and early suicidal ideation/behavior predicts ongoing suicidal ideation/behavior into school age and in some cases adolescence.[4] However, it is still not clear whether the risk factors and variables associated with suicidal ideation/behavior in early adolescence are the same as those later in adolescence or adulthood. To help address this question, Lee et al[5] used the large-scale Adolescent Brain and Cognitive Development study data to generate a very important and informative set of analyses examining whether polygenic risk scores (PRSs) for adult suicide are associated with childhood suicidal ideation and/or attempts, whether this relationship is independent from associations with PRSs for depression and attention-deficit/hyperactivity disorder (ADHD), and what mental health or behavioral factors might mediate the association between adult suicide PRSs and child suicide ideation or behaviors. There were several crucial findings from this study. First, PRSs for adult suicide were associated with child suicide attempts, but not ideation. Second, this association with adult suicide PRSs was over and above shared variance with PRSs for depression and ADHD. Third, this association was mediated in part through a variety of parent-reported behaviors, including increased aggression, attention problems, rule-breaking behavior, social problems, and somatic complaints, as well as depressed mood. Fourth, adult suicide PRSs in a data-driven analysis added unique information, along with a number of other risk factors, for estimating child suicide attempt.

The first of these findings—that adult suicide PRSs were associated with suicide attempt but not ideation—is key as the quest to predict which individuals with ideation also engage in attempts has been challenging. Suicidal ideation may be a more nonspecific indicator of distress and the majority of individuals who experience suicidal ideation will not go on to engage in suicide attempts. It has proven challenging in many past studies to identify unique factors associated with attempts beyond prior suicidality or psychiatric hospitalization. Nonetheless, a number of recent studies have had some success in predicting suicide attempts among adolescents using electronic medical record data[6] or a combination of self-report and medical record data in adults.[7] These analyses using PRSs add to the literature suggesting that it is possible to distinguish those with suicidal ideation from those who go on to engage in attempts, which will be crucial for practical implementation of risk prediction in clinical or nonclinical settings. Further, finding that PRSs based on adult suicide behavior were associated with early adolescent suicide attempts adds to the literature suggesting that there is continuity in the potential causes of suicidal ideation and behavior across the life span.

It was also important that Lee et al found that the association with adult suicide PRSs was independent of associations with PRSs for depression and ADHD. This is consistent with literature indicating that suicide attempts do not always occur in the context of depression and suggests that there are additional pathways of genetic risk for suicide attempts that may be dissociable from pathways that contribute to depression and other forms of mental illness. Lee et al provide some evidence that a range of parent-reported behaviors indicative of temperament or mental health characteristics were potentially part of a pathway by which genetics may confer risk for suicidal behavior. Notably, their results did not identify impulsivity as part of this pathway based on parent-report measures of impulsivity, though attentional problems were identified. A number of studies have identified increased impulsivity as a potential factor distinguishing suicide attempt from ideation,[8] though not all studies support this distinction. Critically, Lee et al did not examine any measures of child report, though early adolescence is a time when parent and child reports of a range of experiences are known to diverge. This is especially important given that the Lee et al analyses focused on variables associated with youth-reported suicide behaviors, yet 88% of 9- to 10-year-olds in the sample who reported suicide attempts lacked parental concordance.[1] Thus, it will be critical in future work to examine child- as well as parent-reported mental health and temperament/personality measures to further elucidate the pathways by which polygenic risk for suicide operates. In the ABCD Study, there are many youth-report measures that could be examined, including negative urgency as a form of impulsivity that has distinguished suicide attempt from ideation in prior work.[9]

In their logistic regression analyses, Lee et al found that adult suicide PRSs were one of several features that contributed unique variance in the association with child suicide attempts. This led them to suggest that it may be useful to incorporate genetic data into the identification of youth at risk for suicide attempts. However, these findings raise questions about what criteria we should be using when trying to identify which types of factors would have practical utility in identifying at-risk children or adolescents. It is true that the adult suicide PRSs contributed independent variance, as did major

depressive disorder PRSs; a number of socioeconomic (SES) indicators (single-parent household, lack of caretaker college education) and parent-reported child psychopathology measures also contributed. Importantly, the highest odds ratios for variables included in the regression analysis were for the 2 SES variables (single-parent household, 2.2 [95% CI, 1.24-3.88] and lack of caretaker college education, 1.78 [95% CI, 1.01-3.15]), higher than either PRSs (suicide attempts, 1.4 [95% CI, 1.08-1.82] and major depressive disorder, 1.34 [95% CI, 1.01-1.78]) or child characteristics (anxious depression, 1.3 [95% CI, 1.04-1.63], high-intensity pleasure/surgency, 1.41 [95% CI, 1.09-1.81], and depressive mood, 1.47 [95% CI, 1.1-1.96]). While the 95% CIs are overlapping, the finding that SES indicators had the highest odds ratios echoes previous research on predictors of adolescent suicide attempt, which also found that SES-related measures contributed important predictive utility.[10] Thus, the work of Lee et al highlights the potential utility of using polygenic risk to understand pathways to suicide attempt; it also highlights the crucial importance of understanding the environmental factors that may also shape child suicide behavior. Further, Lee et al only examined main effects in terms of prediction of suicide attempt. It is critical that future work explore the interactions between different classes of risk factors, such as whether PRSs have greater or lesser potential predictive utility for child/adolescent suicide behavior in youth from higher or lower SES backgrounds. This kind of investigation would not only allow improved understanding of polygenic risk and youth suicide attempts, but for whom PRSs are effective potential predictors. Along these lines, it will be important to continue efforts to generate PRSs based on more diverse ancestral populations to better capture the full range of variability in genetic, environmental, and behavioral characteristics of youth. The current analyses could only examine youth with western European ancestry, leaving a gap in our understanding of the utility of these features in predicting suicide attempt risk among youth with different racial and ethnic identities.

Taken together, incorporating children's report of symptoms, interactive environmental terms, and more diverse samples of youth hold promise for extending the impact of the important work by Lee et al demonstrating the potential predictive validity of polygenic risk in early adolescent suicide. With further investigation incorporating a diversity of demographic, environmental, and psychopathology variables, Lee and colleagues' important work may serve as the foundation for improved prediction of suicide attempt in early adolescence.

ARTICLE INFORMATION

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