

Using Event-Related Potentials to Improve Our Prediction of Suicide Risk

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At this point, the statistics are all too well known. Rates of suicide rose by approximately 34% between 1999 and 2017, exhibiting an almost perfectly linear year-to-year increase [$r = .97$ (1)]. Suicide is now the second leading cause of death among individuals 10 to 34 years of age, the fourth leading cause of death among individuals 35 to 54 years of age, and the tenth leading cause of death across all age groups (1). We tend to habituate to information we see over and over so that it no longer shocks us. But this is shocking. And unacceptable. What is perhaps equally shocking is that despite the hundreds of millions of dollars spent on suicide research in the last few decades by federal and private agencies, our ability to accurately predict risk for suicide attempts and deaths has not noticeably improved in the last 50 years (2).

The majority of research on suicide risk has focused on a circumscribed set of putative risk factors that are almost entirely composed of self-report (e.g., hopelessness, symptoms, and diagnoses), demographic (e.g., age, sex, race/ethnicity, and income), and historical (e.g., history of previous self-injury or treatment) measures (2). These are problematic for at least three reasons. First, although these factors are often statistically significant predictors of risk for future suicidal behaviors, they exhibit poor diagnostic accuracy. Specifically, although they exhibit reasonable specificity (correctly classifying true negatives), this may be largely due to the low base rate of suicidal behavior in the samples, and the levels of sensitivity (identifying true positives) exhibited by these predictors is low (2). Second, although demographic and historical factors (e.g., sex, age, history of mental illness, or previous attempts) may tell us something about lifetime risk for suicide attempts or deaths, these factors do little to improve the prediction of individual risk and even less for helping determine individuals who are at imminent risk. Third, self-report measures are problematic because they require individuals to accurately report suicide-related processes. This necessitates an adequate awareness of, and accurate memory for, these processes, which may not always be realistic. Self-report measures also require a willingness to share this information; however, there are many situations in which an individual may wish to minimize reports of any potential risk (e.g., to avoid or end involuntary hospitalization).

What is urgently needed in the field of suicide research is a focus on novel markers of risk—ideally, markers that do not rely upon a person's self-report and that are modifiable so that they can be targeted to reduce future risk. In this issue of *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, Albanese *et al.* (3) provide an important contribution in this regard by using event-related potentials (ERPs) within the

context of a modified go/no-go task to examine whether two aspects of inhibitory control—conflict detection (indexed by N2) and motor inhibition (indexed by P3 and behavioral responses)—could help differentiate currently suicidal adults with and without a history of at least one previous suicide attempt. Albanese *et al.* (3) found that the two groups differed in conflict detection but not in motor inhibition. Specifically, those with a history of attempting suicide exhibited a smaller differentiation in N2 amplitude to go versus no-go trials, which was driven primarily by a larger N2 response to no-go trials, compared with ideators with no history of suicide attempt. As Albanese *et al.* (3) point out, this suggests that those with a history of attempting suicide are characterized specifically by deficits in detecting when inhibition is required rather than in motor inhibition itself.

The study exhibited several clear strengths, including the focus on ERP markers of neural activity, which allow the temporal resolution necessary to examine fine-grained differences in cognitive processes such as inhibitory control. Indeed, the N2 differences only emerged in analyses based on latent waveforms derived from temporospatial principal components analysis and were not observed based on the raw N2 waveforms. Although this finding requires replication, one would expect the principal components analysis-derived results to be stronger because principal components analysis can isolate the component of interest from other neural processes that may overlap in time and scalp location. The study also adds to recent efforts to take a Research Domain Criteria approach to understand suicide risk, which have thus far focused primarily on negative valence systems (4), by focusing specifically on a construct within the cognitive systems domain. Another key strength is the comparison group in this study, which did not differ from the suicide attempt group in terms of severity of current suicidal ideation or presence of current diagnoses (i.e., depressive disorders, posttraumatic stress disorder, or substance use disorders). This is important because it suggests that the observed differences in N2 may have been due to participants' history of suicide attempts specifically rather than to several other factors that can impact conflict detection and that are often confounded with attempt history.

ERPs, and electroencephalography more generally, represent powerful tools for examining a wide variety of neural processes, including processes that span each of the domains within the Research Domain Criteria. The benefits of ERP/electroencephalography over other imaging approaches include its low cost, high level of temporal precision, and its increasing flexibility of use for ambulatory assessments,

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including outside the laboratory (5). Given this, ERP/electroencephalography measures of neural activity have the potential to significantly advance our understanding and prediction of suicide risk.

Albanese *et al.*'s study (3) represents a significant addition to a growing body of research evaluating neural and performance-based markers of suicide risk. For example, there is growing evidence from cross-sectional and prospective studies for the predictive utility of individuals' implicit attitudes toward death/self-injury stimuli (6). In our own research, we have focused on ERP indices of reward processing deficits as a marker of suicide risk (7). The goal of this line of research is to improve the field's ability to determine who is at greatest risk for making a fatal or nonfatal suicide attempt within a specific time frame so that we can provide more targeted interventions for those who are at greatest risk. To do this, research is needed that tells us not only who is at risk but also why they are at risk (i.e., which specific factors can be targeted to reduce risk) and when they are at risk (i.e., how imminent is the risk). We should keep in mind an important point made by Franklin *et al.* (2) in their recent review: given the base rate of deaths from suicide [0.014/100 people in 2017 (1)], even a risk factor that increases the odds of suicide by 1000% (odds ratio = 10) would still indicate minimal absolute risk. To be clinically useful, Franklin *et al.* (2) argue that odds ratios need to be in the hundreds or thousands. This cannot be accomplished by examining individual predictors in isolation.

ERP indices, therefore, are likely to be key predictors within a larger, multipronged assessment approach. To maximize sensitivity and specificity in predicting risk, this approach will also likely include performance-based tasks (6), ecological momentary assessments, and passive data collection (8) along with more traditional assessments, including self-reports and medical records, with overall risk algorithms generated across indices using machine learning approaches. Indeed, machine learning approaches have already demonstrated utility in improving risk prediction (9), including the short-term prediction of risk (10), which is likely to be of greatest benefit to clinicians. The current study by Albanese *et al.* (3) provides promising initial data on a key marker of risk that could be included in these risk algorithms.

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