Commentary

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Toward Identifying Neurocognitive Processes That Confer Suicidal Behavior

Mary E. McNamara, Mackenzie Zisser, and Christopher G. Beevers

Death by suicide is a pressing public health concern, particularly among adolescents. Understanding how and for whom suicidal ideation (SI) transitions into suicidal behavior is a critical area of research, and adolescents are an important population for study given the increase in SI around this time period (1).

In the current issue of *Biological Psychiatry: Global Open Science*, Allison *et al.* (2) report interesting work with exciting implications for future research on adolescent suicide. A primary finding from this cross-sectional study is that a neurophysiological waveform, known as P2, generated early (i.e., approximately 200 ms after stimulus onset) during self-referent processing of positive and negative adjectives, differentiates individuals with SI who have attempted suicide (n = 26) from those who have not (n = 30). Allison *et al.* propose several considerations for future research in this area, which we expand on below.

As Allison *et al.* (2) allude to in their excellent discussion, more work is needed that links the P2 waveform during self-referent processing to suicide attempts (SAs). They propose an intriguing possibility that an enhanced P2 waveform leads to a "feelings triggering action" phenomenon. In this model, early attention orienting and arousal in response to emotional and self-referential features of stimuli generates negative affect. The individual then attempts to discharge the build-up of affect through behavior (i.e., feelings triggering action). It would be fascinating to evaluate whether enhanced P2 amplitudes precede emotion-related impulsivity (negative urgency). Notably, other work has linked error-related negativity, a negative deflection in the event-related potential waveform that occurs within 100 ms after making an error, to negative urgency (3). If alterations in the P2 waveform also precede negative urgency, it seems possible that effects in the Allison *et al.* (2) study could have been even stronger if people with comorbid diagnoses that are characteristically impulsive (e.g., history of mania, substance use, or head injury) were included in the sample. Nevertheless, early controlled attention may contribute to negative urgency, which in turn could serve to trigger suicidal behavior. Much more research, perhaps with transdiagnostic samples, is needed to test this and other exciting putative etiological mechanisms.

More work is also needed to determine the optimal lag between the assessment of the P2 waveform, SI, negative urgency, and the transition to suicidal behavior (4). The P2 waveform generated in response to self-referent stimuli is presumably a somewhat stable trait, but the precise time intervals between the other aspects of the model remain to be determined. Correctly specifying the time windows (minutes, hours, days, weeks) will be critical to capturing what is likely a dynamic process from SI to action. Study assessment schedules are often selected based on tradition/superstition instead of a strong theoretical or empirical understanding of how cognitive processes give rise to risk for suicidal behavior. Future work using intensive assessment schedules (e.g., repeated assessments within a day across many days) among high-risk adolescents might be useful for determining the optimal assessment lags between key constructs that give rise to suicidal behavior (5).

In addition, Allison *et al.* (2) made thoughtful design decisions by recruiting a sample with current SI that included those who had also attempted suicide in the past and those who had not. As Schwartz and Susser (6) describe, to tease apart key features of psychopathology, the comparison groups should have the same inclusion and exclusion criteria, differing only on the feature of interest (in this instance, SAs). We applaud the authors for the steps they took toward this end. However, we invite future work to consider even tighter comparisons.

First, while the SI and SA groups did not differ on depression severity or total SI severity, the SA group did have higher levels of ideation on two subscales: past-week plans and past-month plans. Thus, those with an SA in the past year may also have stronger levels of recent, active SI (at least across some facets). Similarly, although all members of the SA group had an SA in the past year, they could also have other attempts in their lifetime. The SI group did not have a recent or lifetime history of SAs. Thus, it may be hard to precisely pinpoint whether group differences are being driven by suicidal behavior in the distant or recent past. Future studies might try to recruit a sample with similar levels of SI across dimensions and possibly ensure that recruitment is restricted to people with only one previous SA (alternatively, allow for lifetime attempts across groups and let past-year attempts be the sole differing feature between the two). Admittedly, we know how difficult this could be given that past SAs and current SI are often correlated.

If such a distinction were possible, it could greatly help with the development of etiological models. For instance, if the P2 waveform in response to self-referent processing is more trait-like, we might expect differences between groups that differ in presence or absence of a lifetime SA (making sure that current SI was the same across groups). Conversely, if the P2 waveform response is conceptualized as more state-like, a study might recruit adolescents with and without more recent SAs (e.g., within the past year), again equating current SI and requiring all participants to have no lifetime SAs beyond the past year. Such a recruitment strategy would be challenging and would require a relatively large population from which to draw. One possible solution is to monitor recruitment in real time and dynamically adjust recruitment so that the groups do not vary on key characteristics, such as current SI and lifetime

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attempts, by the end of the study. Our group adopted a similar approach, where we aimed to recruit a sample of adults with normally distributed depression severity, which required that we carefully monitor recruitment in real time and oversample individuals with elevated symptoms of depression (7).

Finally, we also wanted to note the careful attention paid to modeling the behavioral data from the self-referent processing task. The authors used the drift diffusion model (8) to estimate self-referent processing of positive and negative adjectives. This computational model allows for the isolation of decision making from other cognitive processes (response bias, starting point, etc.). We believe that this is an important but neglected approach to modeling reaction time data in psychopathology research. There is a growing appreciation that behavioral tasks using more traditional scoring approaches (e.g., difference scores) may lack sufficient psychometric characteristics for these scoring approaches to be highly reliable (9). Applying computational models to two-choice reaction time data, as done in the current study, is an important step toward developing more robust behavioral assessments of processes that may have important etiological roles in psychopathology.

In sum, Allison *et al.* (2) make a compelling contribution to this nascent literature and their study has many strengths, including both behavioral and neuropsychological correlates of suicide risk, and a well-designed comparison group to help identify which of these correlates might be specific to adolescents with SAs. We hope that future research will build upon these strengths and incorporate the additional considerations we have described above.

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From the Department of Psychology and Institute for Mental Health Research, The University of Texas at Austin, Austin, Texas.

Address correspondence to Christopher G. Beevers, Ph.D., at beevers@utexas.edu.

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