Stress, Trauma, and Risk for Attempted and Completed Suicide

In the literature, several stress-related constructs have been linked to suicidal behaviors. These include stressful life events, trauma, or early life adversity, often defined as childhood abuse and neglect.

The strength and consistency of the stress-suicidal behavior (SB) association differs by the characteristics of the stressor: type (eg, assaultive vs nonassaultive); chronicity; severity; and timing of occurrence (ie, during early development). The salience of specific stressors may differ at certain points over the course of development. There is also individual variation in trauma vulnerability, as well as psychological and physiological responses following stressors and trauma. Psychiatric disorders, aggression/impulsivity, and acute substance abuse are influential in the stress-SB association as possible common causes, mediators or moderators of the relationship. Social, cultural, and community contextual factors are also important in this association. Approaches to identify causal mechanisms in the pathway to SB, and to prevent suicide, differ by the characteristics of the stressor as well as an individual’s response to the stressor.

HEURISTIC AND PREDICTIVE MODELS OF SUICIDAL BEHAVIOR

Heuristic Model

Acute stressors are often conceptualized in heuristic and predictive models of suicide risk as precipitants or “triggers,” whereas chronic stressors are often conceptualized as part of a diathesis.1,2 A heuristic model for suicide prevention introduced in 1999 by Shaffer and Craft1 proposes that, to die by suicide, a psychiatric or behavioral condition, such as a mood disorder, substance abuse, and/or aggressive/impulsive traits, must be present. Within this context, suicide may be preceded by a stressful event (eg, being in trouble at school or with the law, or the loss of a relationship). This pathway is relatively common and, in most instances, does not lead to suicide. Certain contextual factors make suicide less likely and include: living in a setting with a strong taboo against suicide; having available support or the presence of others; and not having access to lethal means.
Predictive Model

The stress-diathesis model of suicidal behavior,2 developed and tested among patients with mood disorders, conceptualizes the onset of a depressive episode as a stressor, that when linked with a diathesis or predisposition, increases risk for SB. The serotonergic, noradrenergic,3,4 and hypothalamic-pituitary-adrenal (HPA) axis systems have been implicated in the diathesis for SB via severe anxiety or agitation, impulsive aggression, and higher suicide intent.5-7 Heightened cortisol response to stress has been reported to be a promising endophenotype that may help in the identification of genes for SB.8

EPGENETIC MECHANISMS IN THE STRESS-SUICIDE LINK

Epigenetics investigates how the environment regulates the genome on the molecular level.9 Some level of stress and adversity builds resilience when tolerable and, in the context of social support, facilitates coping and an adaptive response. Epigenetic changes in response to early stress and adversity allow the individual to adapt the function of their genes to the environment in which they live. Under harsh conditions, and to increase their chances for survival, people adapt to be more vigilant and actively prepared to combat risks they might face. The long-term health costs associated with these “adaptations” can be seen in terms of increased vulnerability to stress and stress-related disorders.10

In 2009, McGowan and colleagues11 found that DNA methylation levels at the NR3C1 gene resulted in lower glucocorticoid receptor (GR) expression in brains of suicide victims with a history of childhood abuse as compared with suicide victims and fatal accident death controls, both without child abuse. Changes in GR expression are closely linked with early life adversity, in this case childhood abuse. The McGowan study is the first in humans to show the relationship between the social environment and brain epigenetic changes and is consistent with the animal literature.11

Investigators have found that epigenetic gene alteration is reversible by pharmacological and possibly cognitive forms of intervention.12 Studies of rats have shown that depressive-like behaviors and increased methylation in GR sites are observed in rat pups reared by mothers who provided less nurturing in the form of licking and grooming. Transferring care of these pups to more nurturing mothers during critical developmental windows resulted in decreased methylation at previously hypermethylated sites and restored normal function.

The hope is that once epigenetic pathways are identified, it will be possible to prevent or therapeutically intervene to reverse the emergence of associated disorders later in life. By understanding how early life experiences underlie epigenetic programming of behaviors, appropriate interventions can be developed.13

The strength of the association between stress/trauma and SB differs by the type and characteristics of the stressor as well as an individual’s response to the stressor.

INCREASED VULNERABILITY IN CRITICAL DEVELOPMENTAL PERIODS

Although epigenetic adaptations occur at any point over an organism’s life course, it has been hypothesized that there are critical developmental periods associated with increased sensitivity to long-term remodeling of behavior.14 Stress response systems attempt to maintain homeostasis in the time of adverse environmental challenges.15 Abuse or neglect early in life can be biologically embedded leading to alterations of the stress-response systems.16 How genetic factors can buffer and augment the effects of early life trauma is not well-known.17 It could be that, while environmental factors can affect the development of emotional behavior, the duration and timing of sensitive periods are determined by genetic factors that vary across individuals.17

HETEROGENEITY IN VULNERABILITY

Zhang and colleagues10 point out that only about 20% to 30% of those who experience high magnitude traumatic events, such as rape, develop posttraumatic stress disorder (PTSD);19 yet many cases of PTSD arise from events that may not commonly be considered traumatic by the general population.19 This heterogeneity suggests underlying individual differences in vulnerability may moderate the stress-behavior associations.

Wilcox and colleagues20 investigated the effect of exposure to traumatic events on subsequent suicide attempts, separating trauma-exposed people who developed PTSD — a subset of less than 10% of those exposed to traumatic events — from trauma-exposed people who did not. PTSD was an independent predictor of suicide attempt, whereas exposure to traumatic events without PTSD was not associated with a later attempt. These results point to the need to base risk estimates of SB on data that include individual response to the trauma.

Psychological autopsy studies that gather data from surviving family members and close friends after a suicide suggest that acute stressors may lead to extreme agitation or anticipatory anxiety, and that suicide is a way to avoid this feeling.1 Nock and colleagues,21 using data from 21 countries participating in the World Mental Health Surveys, found that after controlling for psychiatric comorbidity, lifetime psychiatric disorders char-
characterized by anxiety (especially PTSD) and poor impulse control emerged as the strongest predictors of which people with suicide ideation would make suicide plans and attempts; these were especially useful in the prediction of unplanned attempts.

MEDIATORS AND MODERATORS

Mediating and moderating factors in the association between stress and suicide could involve the following domains: individual demographic (e.g., age, gender/sex, and ethnicity); biological (genetic and epigenetic); psychological (temperament, onset of mood and anxiety disorders); and social (social support and community connectedness). Specific subtypes or endophenotypes, defined by early-onset mixed-mood and anxiety states or impulsive aggression, could characterize specific trauma-SB pathways.

Recent studies have identified several genes (such as FKBP5, CRHBP, and CRHR1) that appear to moderate the effects of psychosocial stressors, such as child abuse, on risk for suicide attempt.

The precise mechanism of how such interactions in humans is not known, but preclinical work on epigenetics shows complex interactions between genes and stressful experiences, with environmental influences causing changes in gene expression leading to increased glucocorticoid secretion as well as stress-related behavioral outcomes.

It is also possible that, in the context of vulnerability for diathesis, social connectedness could protect against aberrant stress responses characterized by fatal or nonfatal SBs. With a rich history dating back to Emile Durkheim, social variables are among the most robust protective factors for SB (e.g., social support).

CONCLUSION

Aggression, self-control, or the ability to self-regulate may be common etiological factors influenced by stress and trauma exposure in the pathway to SB (as well as an important target for intervention). There appear to be individual differences in response to trauma, which could imply individual thresholds based upon psychiatric status, as well as genetic and epigenetic influences. Work in this area is critical to our ability to identify mechanisms and prevent suicide.

It is possible that individual response to chronic and acute stress is a malleable risk factor for SB. Appropriate identification of psychiatric symptoms and treatment of the underlying psychiatric condition may make a suicide attempt much less likely in the event of a stressful life event. Exposure to early life adversity, as well as the recent occurrence of assaultive violence within the context of a major psychiatric disorder, may be important elements of suicide risk assessment.

REFERENCES