Suicide Ideas and Attempts in People with a Depressed and/or Anxiety Condition are Linked to Three Key Physiological Stress Systems

Steve Raulerson*

Editorial Office, Journal of Psychological Abnormalities, Brussels, Belgium

Corresponding Author*

Steve Raulerson

Editorial Office, Journal of Psychological Abnormalities,

Brussels, Belgium

E-mail: info@longdom.org

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Perspective

Suicide ideas and attempts are more common in people with depressive and/or anxiety disorders, although the biological underpinnings of this risk are unknown. Dysregulations in physiological stress systems, including the Hypothalamic–Pituitary–Adrenal axis (HPA-axis), immune-inflammatory system, and Autonomous Nerve System (ANS), may add to this risk. However, thus far, findings have been inconsistent or nonexistent. Individual markers and cumulative indices of the HPA-axis (cortisol awakening response and evening cortisol), immune-inflammatory system (C-reactive protein, Interleukin-6 (IL-6) and tumor necrosis factor-α), and the autonomic nervous system (heart rate, respiratory sinus arrhythmia, and pre-ejection period) and the outcomes no Suicide Ideation with Suicide Attempt (SI-SA+), Suicide Ideation without Suicide Attempt (SI+SA-), and (NESDA). After controlling for covariates and repeated testing, high levels of CRP and IL-6 were related with SI-SA+ and SI+SA+, respectively, when compared to non-suicidal individuals. SI+SA+ was also positively related with cumulative immune-inflammatory dysregulations, implying a dose–response relationship. There were no significant links between HPA-axis or ANS indicators and suicide outcomes, nor between immune-inflammatory system markers or cumulative stress system dysregulations and SI+SA-.

Suicide is a severe global public health problem that kills almost 800,000 people each year, and it frequently involves mental health issues. In the general population, a depressive or anxiety condition raises the risk of suicide by twelve and four times, respectively, and comorbid depression and anxiety increases the risk even more than either disorder alone. Although these mental diseases enhance the risk of suicide, they lack specificity because the majority of people will not consider suicide, much alone act on suicidal thoughts by attempting suicide. Suicidal ideas and suicide attempts have their own reasoning and antecedents, according to the ideation-to-action paradigm. As a result, separating these occurrences is necessary for earlier diagnosis and better treatment of high-risk individuals. So far, little attention has been paid to the role of underlying biological systems in the process. According to the Integrated Motivational-Volitional model of suicidal behavior (IMV), a diathesis is a prerequisite for the development of suicidal thoughts and attempts, in addition to stressors and environmental variables. Diathesis can be seen in biological components, among other places. The Hypothalamic–Pituitary–Adrenal axis (HPA-axis), the immune-inflammatory system, and the Autonomous Nerve System (ANS) are all known to have a role in safeguarding the body and assisting it in adapting to acute stress. When these systems are dysregulated, which is commonly the result of allostatic overload from repeated exposure to physically and emotionally stressful events, they can cause health and psychological difficulties. Hyperactivity of the HPA axis, as well as greater levels of immune-inflammatory markers and ANS tone, have all been linked to depression and anxiety disorders. As a result, it's crucial to see if mediators of these stress systems also increase the incidence of suicide ideation and attempts in these individuals. Until recently, just a few researches have attempted to do so.

Dysregulations of the cumulative stress system are frequently linked to worse physical and mental health consequences. Hyperactivity of the ANS and HPA-axis may have an additive negative effect on stress perception, and cumulative indices of dysregulations within and across the stress systems in question have been linked to present sadness and/or anxiety. As a result, various stress system dysregulations are thought to be a more powerful risk factor in suicide outcomes. Several research looked at different stress systems in suicidal individuals at the same time and discovered that dysregulations don't happen in isolation. Patients with suicidal thoughts had lower vagal tone and higher pro-inflammatory cytokine levels than non-suicidal depressed patients, and it was discovered that patients with suicide attempts had greater inflammatory levels and a blunted HPA-axis compared to patients with suicide thoughts and healthy controls. As a result, it's possible that cumulative stress system dysregulations might enhance the risk of suicide by increasing the cognitive, behavioral, and emotional issues linked to stress system dysregulations already discussed.

Overall, the physiological stress mechanisms in issue have a hazy role in suicide processes. This is owing to a small number of studies that typically provide inconsistent results and employ small samples, seldom distinguishing between suicide ideas and attempts, and rarely looking at connections that aren't influenced by mental conditions. Furthermore, no research has looked at accumulated dysregulations within and across stress systems using an integrated approach. As a result, the first goal of this study is to look into the relationship between the HPA-axis (measured by cortisol awakening response and evening cortisol), immune-inflammatory markers (CRP, IL-6, and TNF-), and ANS markers (HR, RSA, and PEP) and suicide ideation and attempts in a large, well-characterized cohort of patients with a depressive and/or anxiety disorder. The second goal is to see if accumulated dysregulations within and across the three stress systems enhance the risk of suicide attempt and ideation.

Despite the use of a large, well-characterized patient cohort, there are certain limitations to consider. First, because causality cannot be deduced from the current cross-sectional investigation, relationships between individual and cumulative inflammatory indicators and suicide attempt groups should be studied longitudinally and/or experimentally. Second, when individuals are asked if they have ever attempted suicide, recollection bias may be an issue. Errors in reporting have been documented. Another drawback of retrospective reporting of factors like suicide thoughts and attempts is the difficulty of documenting state changes in the natural environment in real time prior to their occurrence. Using current technology such as smartphones and wearable devices, ecological momentary assessment can overcome these constraints, and it should be used to explore physiological activity and its involvement in the start of suicidality. So far, this technology has been underused in suicide research, with just a few cases of depressed individuals being studied. Third, the suicide attempt group was not divided into subgroups based on single or many attempts, lethality of suicide attempts, or degree of suicidal ideation since this would result in underpowered subgroups and some of this information was unavailable. According to certain study, risk profiles may vary depending on the aforementioned criteria. Fourth, despite the fact that the immune-inflammatory indicators employed in this study are among the most commonly studied in depression and suicide research, the cytokine profile is restricted. IL-1, IL-2, Interferon-Gamma (IFN)-, IL-4, and IL-10 are all promising cytokines. More research is needed to examine such cytokines and develop detailed biological profiles that account for various suicidal processes as well as their influence on suicidal status outside the presence of mental problems.

Although stress system indicators were unable to distinguish between SI+SA and non-suicidal individuals, the data suggest that dysregulations

of individual and cumulative immune-inflammatory markers are linked to suicide attempts in depressed and/or anxious patients. As a result, immune-inflammatory system dysregulation may have a role in the pathophysiology of suicidal behavior, implying that the benefits of anti-inflammatory therapies on suicidality should be investigated further.

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