Current Suicidal Ideation and its Relationships with Heart Rate Variability and Inflammatory Markers among Depressed Patients

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DEAR EDITOR

Major depressive disorder (MDD) is a significant public health issue worldwide, giving rise to long-term disability and disease burden and economic burden [1,2]. This mental disorder is also associated with high risk of committing suicide because around 4% of patients with MDD end their life by suicide [3]. Recent evidence indicates that inflammation might be involved in the development of MDD [4-6]. For example, the expression of inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) is elevated in the blood of depressed patients [7-11]. Of the two markers, recent meta-analyses particularly emphasized the higher CRP levels in patients with MDD compared to non-depressed controls [4,12]. However, depressed patients have not demonstrated elevated inflammation in all studies [13,14]. It is possible that inflammation may be elevated in only a subset of depressed patients [13,15,16].

If this is the case, an add-on treatment with an anti-inflammatory medication might be beneficial for the subgroup of depressed patients who show signs of inflammation [17,18]. Therefore, research clarifying the relationship between specific depressive symptoms (or a specific subtype/subgroup of depression) and inflammation is imperative.

There is also accumulating evidence suggesting a role of inflammation in the pathophysiology of suicidality. The relationship between inflammation and suicidality may be bidirectional. For example, patients receiving pro-inflammatory cytokines for the treatment of medical disorders demonstrated increased suicidal ideation [19,20]. Some characteristics of suicidal depression (e.g., pessimism and hopelessness) [21,22] and perceived psychological stress [23,24] may have inflammation-promoting effects in suicidal patients. All these findings prompted investigations into whether levels of inflammation were particularly high in suicidal depressed patients. Several studies found suicide attempters display higher levels of inflammation than non-suicidal depressed patients [25,26]. However, greater severity of depression and the medical damage caused by suicide attempts could account for such elevated inflammation in suicide attempters. Studies linking suicidal ideation with inflammation are not similarly confounded. A recent study demonstrated that MDD patients with high levels of suicidal ideation still had significantly higher inflammation than those with lower suicidal ideation after adjusting for depression severity and suicide attempts [27]. However, the study enrolled patients taking anti-inflammatory medications, antidepressant or other psychotropic medications, all of which could have influenced levels of inflammation [28]. Studies on physically healthy unmedicated MDD patients without a history of suicidal attempts are necessary to better examine the true relationship between suicidal ideation and inflammation. In addition, the biological mechanisms linking suicidal ideation with inflammation also remain to be elucidated.

Growing evidence indicates a link between suicidality and vagally mediated cardiovascular functioning [29,30]. Heart rate variability (HRV) refers to the complex beat-to-beat variation in heart rate produced by the interplay of sympathetic and parasympathetic (vagal) neural activity at the sinus node of the heart. High HRV reflects a healthy regulation system that is able to respond to environmental demands [31]. Contrarily, low HRV is an indicator of autonomic inflexibility [32] and a predictor of poor health status [33]. A recent study in a nonclinical sample demonstrated a negative correlation between vagally mediated HRV and lifetime suicide ideation [34]. The result implied that low vagally mediated HRV, which reflects reduced inhibitory control capacity [35], may represent a risk factor for suicidality. For depressed patients, results regarding the relationships between suicidality and HRV are conflicting, such as no association [36], positive [37] and negative correlation [38,39]. However, some of these studies have been hampered by the confounding effects of psychotropic drugs and any neurological damage caused by suicide attempts. We are aware of only 1 study recruiting MDD patients who are physically healthy and did neither take any medication nor reported lifetime suicide attempts. The study showed that suicidal ideation is negatively
associated with HRV, in particular vagally mediated HRV [40].

As specialists in cardiac autonomic dysregulation in depression, our research team members are interested in the differences in inflammatory markers and HRV between unmedicated, equally depressed patients with and without suicidal ideation (SI). Taken the above-mentioned literature into account, we hypothesized that depressed patients with SI would have higher levels of inflammation and lower HRV than those without SI. We also hypothesized that in depressed patients with SI, there are meaningful correlations between SI and inflammatory markers and between SI and HRV. Future studies are required to verify these hypotheses.

Regards,

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REFERENCES


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