***Biomarkers in the HPA Axis and Inflammatory Pathways for Suicidal Behavior in Youth***

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Suicidal behavior is the most serious sequela of psychiatric disorders; yet, our ability to predict who goes on to attempt suicide is limited. Studies find no association between clinicians’ prediction for a patient and their actual suicidal behavior. Thus, it is critical to identify objective biological signatures for suicidal behavior. We conducted a study to identify biological markers that differentiate inpatients admitted for suicide attempt (SA) from inpatients admitted for suicidal ideation and no prior history of attempt (SI) and healthy controls. We find the severity of suicidal ideation to be the only clinical characteristic that was significantly different between SA and SI in a clinical setting. However, SA and SI were significantly different on several biological markers in the HPA axis and inflammatory pathways. Inpatients admitted for SA had lower hair cortisol concentrations (HCC) compared to those admitted for SI and healthy controls. HCC provides a retrospective assessment of cortisol levels over the past few months and thus in our study, prior to attempt. These results are the first to show that blunted HPA axis activity precedes attempt. In addition, lower HCC were associated with increased lethality of the attempt within attempters. Suicide attempters also differed by their lower GR mRNA and increased inflammation as measured by C-Reactive Protein and TNF-amRNA. These results shed light on the importance of combining biological measures with already existing clinical measures to better identify those at highest risk for suicidal behavior. Indeed, combining these biological measures with clinical measures in our study achieved better performance in differentiating suicide attempters compared to the model including clinical measures only.