ALABAMA PSYCHIATRIC PHYSICIANS ASSOCIATION
A District Branch of the American Psychiatric Association

SPA/APPA 2021 Virtual Meeting Medical Student/Resident Poster Presentation

Abstract 21-2-09

Abstract Title: MicroRNA Correlates of Childhood Maltreatment and Suicidality

Presenting Authors/Affiliation: Matthew Bonds, MS-3: University of Alabama at Birmingham School of Medicine

Additional Authors/Affiliations: Clinton Martin M.D.; Janaki Nimmagadda M.D.; Anupama Yedla M.D.; Richard Shelton M.D.; Yogesh Dwivedi Ph.D.: University of Alabama at Birmingham School of Medicine

Introduction/Background: Early life trauma, especially physical, sexual, or emotional abuse, are strong risk factors for both depression and suicide. However, the precise mechanisms that link abuse with depression and suicide risk are not well understood. One hypothesis is that these environmental events induce chemical modifications of DNA, and that these changes link early life abuse with later development of depression and suicide attempts. However, this has received very little systematic study. Our preliminary data indicate that chemical modification of the DNA sequences for micro RNAs (miRNAs) link early trauma with depression and suicide. Micro RNAs are short regulatory RNAs that are an important mechanism for environmental regulation of RNA and protein expression. These are significantly altered in people with early life trauma, and specific miRNA changes are associated with depression and suicide risk. The overarching hypothesis of this study is that childhood maltreatment can induce long-term chemical modifications of DNA for micro RNAs. The net effect of these changes may lead to long-term cellular (mal)adaptations which may lead to depression and suicide vulnerability in people with a history of childhood maltreatment.

Methods: Our research group has developed a novel method of extracting miRNAs that are specific to neurons, which are contained in small vesicles called exosomes in peripheral blood samples. We have shown that the patterns of miRNA expression are very similar in neuron-specific exosomes and human post-mortem brain samples. This study will recruit participants in three groups – depression with recent serious suicidal ideation or attempt, depressed without recent ideation or attempt, and normal volunteer controls.

Only depressed and suicidal participants will be recruited at Huntsville Hospital. Non-suicidal depressed patients and controls will be recruited at the UAB HRMC. Hospitalized patients will be approached by their respective attending physicians who will serve as co-investigators on the project about participating. People who assent to participation will be contacted by a research staff person. Written informed consent will be obtained prior to any research procedure. A screening interview will be conducted by the research staff person to ensure that inclusion and exclusion criteria are met. However, the remainder of the procedures will be conducted at the UAB HRMC after discharge.

We will also conduct a widely used experimental stressor called the Trier Social Stress Test (TSST). Both depression and suicidality are increased by stressful life events. The TSST is a standardized mildly stressful experience that reliably induces an increase in blood cortisol. We have also shown that the TSST induces changes in miRNA expression that are different in people with a history of childhood maltreatment who are depressed and suicidal. The TSST consists of people presenting a 5-minute speech on any topic of their choosing and then doing some mental arithmetic in front of a panel of two or more observers. Ten ml. blood samples will be obtained at baseline and immediately post-TSST and

15, 30, 60, and 90 minutes after the test. The blood samples will be immediately processed and stored at -80°C. Exosomes will be extracted from the blood plasma samples and miRNA analyzed using an RNA sequencing method. We have conducted hundreds of TSSTs with blood sampling without incidents in a wide range of psychiatric patients and normal volunteer controls.

All data collected in this study will be kept in a HIPAA-compliant REDCAP database for subsequent analysis. The data reported from the study will be done in aggregate and no personally identifiable information will be released.

Results: This is an ongoing study.

Discussion and Conclusion: If successful, this study may lead to reliable, blood-based biomarkers for depression and suicide risk.

References:

1. Penner-Goeke, S., & Binder, E. B. (2019). Epigenetics and depression. Dialogues in clinical neuroscience, 21(4), 397–405. https://doi-org.ezproxy3.lhl.uab.edu/10.31887/DCNS.2019.21.4/ebinder

2. Tavakolizadeh, J., Roshanaei, K., Salmaninejad, A., Yari, R., Nahand, J. S., Sarkarizi, H. K., Mousavi, S. M., Salarinia, R., Rahmati, M., Mousavi, S. F., Mokhtari, R., & Mirzaei, H. (2018). MicroRNAs and exosomes in depression: Potential diagnostic biomarkers. Journal of cellular biochemistry, 119(5), 3783–3797. https://doi-org.ezproxy3.lhl.uab.edu/10.1002/jcb.26599

3. Lopez, Juan Pabloa,b; Kos, Aronb; Turecki, Gustavoa Major depression and its treatment, Current Opinion in Psychiatry: January 2018 - Volume 31 - Issue 1 - p 7-16 doi: 10.1097/YCO.0000000000000379

4. Allen, L., Dwivedi, Y. MicroRNA mediators of early life stress vulnerability to depression and suicidal behavior. Mol Psychiatry 25, 308–320 (2020). https://doi.org/10.1038/s41380-019-0597-8