I38 The Brains of Suicides by Violent Methods Reveal a Distinct Biology

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Learning Overview: After attending this presentation, attendees will understand how the distinct state of mind associated with suicide by violent means may relate to a more salient biology that can be observed postmortem in brain tissue.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by offering a novel key to suicide biology derived by behavior analysis.

Suicide is the tenth leading cause of death for all age groups combined and is on the rise across the United States, according to recent reports by the Centers for Disease Control and Prevention (CDC). As suicidal ideation is a limited predictor of outcome, recent research has turned to the detection of "more objective" biological markers (i.e., genetic marks) for the development of prevention approaches. This may be especially relevant for suicides by violent means, since features of impulsive aggression represent a better predictor of self-destructive acting out, a strong behavioral endophenotype, as well as a valuable research target, being associated with higher prevalence and lethality. In this regard, in completed suicides, the biology underlying the choice of a violent method should represent a more precise feature to target to detect genetic signatures for the behavior at large. Of note, in searching for suicide biomarkers, most studies do not address the relevance of the means adopted, hence they do not consider the possibility of a method-specific frame of mind that ultimately generates the behavior.

Previous discovery findings and further replication suggest that differences in Dorso-Later Prefrontal Cortex (DLPFC) expression of a human-specific non-coding RNA (lincRNA) may influence emotional regulation, aggressive behavior, and suicide by violent means. In the present study, RNA-sequencing (RNA-seq) data from postmortem human brain (228 Caucasian patients; adults) were examined to validate, at a genome-wide level of significance, association of the lincRNA specifically with suicide by violent means and to detect further candidates potentially related to the same signal.

Attribution of suicidal method was determined blind to the postmortem RNA-seq data. Cause and manner of death and contributory causes or medical conditions related to death were obtained from medical examiner documents. The choice of a specific method likely reflects the interplay of multiple determinants, including the availability of a particular suicidal means. However, at the individual level, preferences toward one or the other group appear to influence the ultimate pattern of choices. Cases in which manner of death was pending or not determined at the time of the curation and suicidal samples with ambiguous, or indefinable means of suicide, regarding the level of violence employed, were excluded. Among the remaining suicides, most deaths distinctly fell within the violent or non-violent category. When this was not obvious, an in-depth behavioral assessment was obtained using detailed narrative summaries based on all available sources of historical information, including interviews with next of kin. The differential expression analysis was conducted on all features, including genes, exons, junctions, and expressed regions data, correcting for diagnosis, sex, age, and qSVs, a measure of RNA integrity. A gene-set enrichment analysis was also performed on the top-list differentially expressed features. At $P_{FDR-corr.} \leq 0.05$, minimal signal (i.e., ~10 expressed regions) arose when comparing non-suicide with suicide (all types of method); differentially expressed features further decreased when looking only at suicide by non-violent means. However, comparison between non-suicides and suicides specifically by violent means produced a remarkably greater list of features (i.e., over 1,400 expressed regions). These results validate, at a genome-wide level of significance, previous findings and suggest the engagement of specific signaling and cellular type. These results confirm that classifying suicide by method is key in revealing the underlying different biology.

Brain, Suicide, RNA-Seq