Genomic research provides clues into PTSD

A psychiatrist at Emory University and her colleagues used gene expression analysis to study the biological mechanisms underlying PTSD and comorbid depression.

Clinical data is a rich source of genetic and gene expression information

The Grady Trauma Project is revolutionizing the way we think about PTSD. Ten years’ worth of data from the hospital’s Emergency Department serves as the basis for new research inquiries into both the psychological and biological factors underlying the PTSD phenotype. Researchers like Wingo hope that with a new understanding of predictive factors, they will be able to develop more effective early interventions and improve long-term outcomes for sufferers of this tragic disorder.

The Grady Trauma Project provided Wingo and her collaborators with data from a cohort of 6,863 at-risk inner city participants, among which the observed PTSD rate was 28.4 percent. It’s a highly complex data set that has been used by researchers in a number of different fields through the years. Wingo’s work draws on both genetic and gene expression information to understand those biological mechanisms that underlie psychological resilience. In recent years, Wingo has sought to identify the genetic signatures of PTSD based on a genome-wide differential gene expression survey of PTSD with comorbid depression.

Her target? DICER1, an enzyme that generates mature microRNAs in the blood and brain. “DICER1 is especially interesting because
it’s implicated in other mechanisms in the body like DNA repair and microRNA generation,” Wingo says. Though PTSD affects the brain, it’s difficult to obtain sufficient brain data. As a result, she has had to find an alternative approach. “The most significant challenge I’ve encountered;” she says, “is studying gene expression in the blood – as opposed to in the brain.”

The “QC pipeline,” as she calls it, in JMP Genomics helps to identify data quality issues and pinpoint outliers that should be removed prior to analysis. The basic expression workflow also permits investigators to look at samples after applying statistical normalization. And quality control results can be visualized in interactive graphics.

Wingo also relies on JMP Genomics to conduct differential gene expression analysis with the software’s microarray capabilities. In addition to detailed statistics on each gene, JMP Genomics provides dynamic visualizations that quickly pointed Wingo to genes with interesting expression patterns.

An important step in furthering our understanding of PTSD’s biological mechanisms

Ultimately, Wingo and her colleagues observed that DICER1 expression in the blood of patients with PTSD was significantly lower than levels observed in control groups. Wingo and colleagues were then able to link lower blood DICER1 expression to increased activity in the amygdala in the face of fearful stimuli - one of the primary correlates for PTSD. Importantly, her findings make the case that the enzyme DICER1 is involved in the molecular mechanisms of PTSD with co-morbid depression.

“It’s an initial step to try and understand all the biological mechanisms of PTSD. And we need more follow-up studies,” she says. But these findings are promising: “The mechanism that we found in the blood - that is, the DICER1 and microRNA expression pathway - is very similar to what other researchers have found in the brain of stressed mice.”

Solution

Aliza Wingo, MD, of Emory University and colleagues used JMP® Genomics to look at data from the Grady Trauma Project, examining genome-wide differential gene expression profiles in the blood.

Results

Wingo and her colleagues found that the enzyme DICER1 may be involved in biological pathways underlying PTSD.