



Alexander Niculescu

SUMMARY AND COMMENT | PSYCHIATRY

ON THE HORIZON

September 6, 2017

Genetic Testing May Improve Suicide Risk Prediction

Peter Roy-Byrne, MD reviewing Niculescu AB et al. Mol Psychiatry 2017 Sep.

A group of genes expressed in blood may, when combined with clinical data, help predict both generic and even person-specific risk for suicide.

Suicide, an extraordinarily difficult public health problem, is challenging to predict due to its low frequency and large number of social and psychological risk factors. These researchers conducted a complex, multistep genetics study.

Using a powerful within-subjects study design, they identified large changes in gene expression (biomarkers from blood assays) associated with large changes in suicidal ideation over time in 66 individuals with various diagnoses and identified suicidal-ideation subtypes (psychotic, anxious, depressed, and mixed). Genetic findings were “prioritized” by agreement with genes previously linked to suicide and were validated in 45 people who had died by violent suicide.

The 12 most consistently predictive biomarkers and 148 promising biomarkers were then validated in 226 individuals with various diagnoses. Biomarkers were associated with suicidal ideation and hospitalization for suicidality, both universally (predictions, 90% and 77%, respectively) and within patient subtypes and, more personally, based on symptoms and individual history (with special focus on ~50 men with bipolar disorder). “Universal” gene predictors were involved in neurogenesis, programmed cell death, inflammation, and insulin signaling. Some person-specific genes were modulated by suicide and depression treatments (lithium, clozapine, omega-3 polyunsaturated fatty acids) and by other compounds that might provide leads for antisuicide drug development. The combination of symptom and life history data with genetic expression best predicted suicide risk.

COMMENT

Because patients' suicide risks change over time, these authors could conduct a powerful within-subject longitudinal analysis, identify gene-expression changes associated with changing suicidality levels, and rely on the relatively reliable phenotype for suicide — yielding results much superior to those in genetic studies of psychiatric diagnosis or treatment outcome for predicting suicide risk. Linkage of these genes with familiar suicide risk factors (e.g., social isolation and anxiety symptom severity) and with effective suicidality treatments (lithium and clozapine) reinforce the validity of this approach and these preliminary findings.

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Disclosures for Peter Roy-Byrne, MD at time of publication

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