THE HARTWELL FOUNDATION

2019 Individual Biomedical Research Award

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Adolescent Depression: Illness Severity and Treatment Effects in Digitally Acquired Brain Electrical Activity

Major Depressive Disorder (MDD) is a clinical psychiatric condition and a common cause of adolescent suicide. In the last decade, more children age 10-19 have died from suicide than from cancer, heart disease, birth defects, lung disease and influenza combined. Unfortunately, accurate diagnosis of MDD in adolescents is so challenging that it may take up to a year to confirm. In contrast to other childhood illness, there are no standardized objective laboratory tests or technologies for the diagnosis of MDD, but rather simply a clinical interview and evaluation by a child psychiatrist. The biologic causes of MDD are not fully understood but are related to dysregulated dynamic neurologic processes in the brain. For example, early childhood denotes a time for rapid growth in the number and strength in neuronal connections or synapses. Adolescence marks a period of re-organization and pruning of these connections — reducing the overall number of neuronal connections. The process of "pruning" is influenced by genes, environment, physical health and other factors that contribute to the types and strength of neural connections in the adolescent and adult brain, which however, do not appear similar until about age 25. Clearly, an analytical biomarker for MDD would improve insight into the functional neurologic disorder that gives rise to depression but also provide for a means to early diagnosis and treatment. To address this unmet need, Molly proposes to use neuroimaging focused on analysis of digitally acquired brain electrical activity (electroencephalography or EEG). In EEG, voltage fluctuations resulting from ionic current created by the activity of neurons that contribute to spatially distributed sub-networks are recorded as oscillations at a variety of frequencies, some of which are characteristic and known to be associated with different states of brain function. When processed with computer software using a specialized algorithm developed with her collaborators, she discovered abnormal patterns of EEG activity in adolescents diagnosed with MDD that reflect a disruption in synchronous electrical activity (coherence) at the level of a resting-state network (default mode network). Compared with healthy controls, youth with MDD showed decreased coherence (reflecting reduced network connectivity) and no differences in power in any major frequency band. She proposes to confirm whether such quantitative changes in EEG brain connectivity (qEEG) may be a useful diagnostic biomarker to assess condition severity and a means to distinguish healthy versus clinically depressed adolescents. If successful, qEEG will provide the means to discern those individuals responding to treatment before traditional clinical interview measures, an extremely important consideration since it can take several weeks for antidepressant drugs to reduce symptoms. In this way, the use of qEEG for managing MDD could help guide personalized precision medicine for a highly vulnerable group of children.