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RESIST-D

Reward-stress interactions as neural substrate for resilience and vulnerability in mental health: A translational large-scale project

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While the association between the experience of early life stress (ELS), that is, stressful events related to different forms of child abuse or neglect, and heightened risk of mental health problems, in particular depression, is well-established, the reasons for divergent outcomes remain unclear, as does the understanding of age-related variations in the onset of depression. Depression is one of the most frequent mental health problems, yet it remains difficult to treat; and little is known about the etiology of late-life depression. We focus here on the neurobehavioral responses to rewards and to acute stress as key neurobiological mechanisms underlying the risk of developing depressive symptoms at different ages after ELS. The project is divided into five work packages, encompassing preclinical models (WP1), human studies on individuals exposed to ELS across different age groups (WP2) using functional magnetic resonance imaging (fMRI) and electroencephalogram (EEG) measures, investigations in currently depressed participants (WP3), computational analysis of brain networks (WP4), and the creation of a Fair, Accessible, Interoperable, and Reusable (FAIR) database for large-scale analyses (WP5). We aim to identify biomarkers and adopt a transdiagnostic and dimensional approach to depression. The emphasis on a developmental, lifetime perspective may significantly advance the understanding of depression at different ages, with potential implications for clinical use. The creation of a FAIR database specific for ELS available in open-access after the end of project will be an important deliverable of this project.

Overall, by studying the mechanisms that determine why some people develop PTSD and others do not, we hope to highlight new therapeutic targets and better, more effective, treatments for PTSD and similar conditions that develop in individuals exposed to deleterious life events.