Ali Jawaid

MUSE ACE

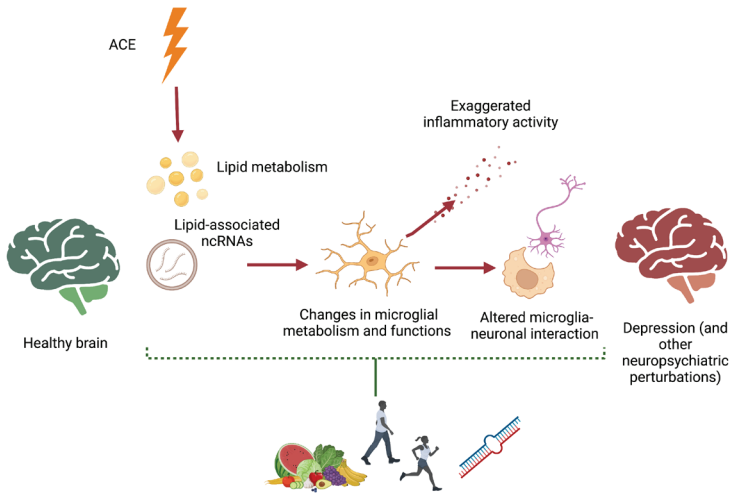
Metabolic Underpinnings of Susceptibility to Adverse Childhood Experiences

Project Coordinator:
Ali Jawaid, Nencki Institute of Experimental Biology, Warsaw, Poland

Project Partners:
Rosa Paolicelli, University of Lausanne, Lausanne, Switzerland

Anthony Hannan, The Florey Institute of Neuroscience and Mental Health, Melbourne, Australia

Exposure to adverse conditions during childhood can severely impact our mental health as adults. We now know that eating unhealthy diet or lack of physical activity can further accentuate the harmful effects of childhood adversity, whereas some other factors like exercise are protective. We believe that this is due to the fats present in our blood, which determine the vulnerability to the impact of adverse childhood experiences (ACE) on adult mental health. Our previous studies on children that were exposed to forced separation from their mothers revealed that those who developed depression after this traumatic experience had specific changes in blood fats. Our recent research indicates that such changes in blood fats have the possibility to impact the immune cells in the brain known as microglia. Thus, it is plausible that microglia serve as the bridge between changes in blood fats and the long-term psychological effects of ACE. To test this hypothesis, we plan to feed laboratory mice a fat-enriched diet after exposing them to early life stress. We will then study their microglial functions. Then to test whether microglia are related to mental disturbances after ACE, we will deplete these cells in the brain of mice fed on either regular or fat-enriched diet. Furthermore, we will also stimulate lab-grown human brain tissue-like structures with the blood samples from different populations that have been exposed to ACE. Finally, we will check if improving good fats in the blood through dietary supplements will enhance resilience to the mental disturbances after ACE.



Adverse childhood experiences (ACE) lead to changes in peripheral lipids and lipid-associated ncRNAs (including specific miRNAs) that distinctly or collectively converge to alter microglial metabolism and functions. Modifications in microglial inflammatory and phagocytic properties alter microglia-neuronal interactions via induction of inflammation and/or impaired synaptic remodeling. Sustained changes in microglial functions via ACE-induced alterations of peripheral lipids manifest as neuropsychiatric disease, such as depression and associated affective disorders. Preclinical validation of this hypothesis could pave the way for new modalities to enhance resilience against the long-term behavioral sequelae to ACE via manipulation of peripheral lipids through life-style modifications and/or dietary supplements, as well as targeted miRNA therapeutics.