

Impact of Pesticides on Beta-Amyloid Peptide Accumulation in Alzheimer's Disease: Investigating Short-Chain Fatty Acids' Protective Effects.

Late-onset neuropathologies, such as Alzheimer's disease (AD), are experiencing increasing prevalence, and current prospects for solutions remain limited, necessitating a thorough exploration of underlying factors. Dysbiosis, or imbalance in the gut microbiota, has emerged as a promising area of research in understanding mechanisms related to AD. This dysbiosis could be influenced by diet and other environmental factors, such as pesticide exposure. Pesticides, especially those used in agriculture, are known for their ability to traverse biological barriers, such as the intestinal barrier (IB) and the blood-brain barrier (BBB), and to interfere with the normal functioning of the gastrointestinal system and the brain by playing a role in inflammation and the formation of amyloid plaques corresponding to the accumulation of β -amyloid peptide ($A\beta$) both in the gut and the brain. This is an intriguing hypothesis that has not yet been thoroughly explored. The aim of this thesis project is to characterize *in vitro* the impacts of a cocktail of pesticides on the metabolism and clearance of $A\beta$ peptide at the level of the IB and BBB. We will also investigate how short-chain fatty acids could significantly mitigate the observed dysfunctions both at the intestinal and cerebral levels.