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The role of Phospholipids in Neurodegeneration

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Abstract: Introduction: Disturbances in phospholipid metabolism have been linked to the risk of dementia. However, data on how phospholipid disturbances change across the different dementias and their relationships to brain function and structural changes are lacking. This study aimed to elucidate the role of plasma phospholipids in neurodegenerative disorders associated with dementia in the Ontario Neurodegenerative Research Initiative (ONDRI) cohort. Methods: Plasma phospholipid species were quantified using LC-MS/MS in 520 individuals diagnosed with Mild Cognitive Impairment (MCI), Alzheimer's Disease (AD), Vascular Dementia (VD), Parkinson's Disease (PD), or Frontotemporal Dementia (FTD), and compared to controls. Cognitive function was assessed, and structural brain changes were evaluated via 3.0T MRI. Adjusted linear regression models analyzed phospholipid differences among groups and their corresponding clinical characteristics. Results: Significantly lower phospholipids and higher lysophospholipids were found in individuals diagnosed with MCI, AD, VD, PD and FTD, compared to controls. Significant positive associations were found between Lysophospholipids and phospholipids and brain atrophy, as well as hippocampal volume, in individuals with MCI and dementia. Conclusions: This study identifies novel phospholipid signatures specific to different forms of neurodegeneration, highlighting distinct underlying pathophysiological processes. These signatures may serve as potential biomarkers for early diagnosis and improve diagnostic accuracy for neurodegenerative diseases.