Transcript:
50 million people currently live with dementia; this stark statistic highlights the global urgency of further research into this area. We know that genetic and environmental/lifestyle risk factors play a role in the development of dementia, and that these extend from early life, with factors such as cognitive ability in childhood showing remarkable enduring impact. Previous research has also highlighted a period before diagnosis where disease mechanisms are accumulating, presenting as a great opportunity to intervene, but how do we identify individuals in this period?

Well, using studies that have followed individuals over a long period, we can identify early indicators such as biological markers preceding diagnosis, for which metabolites present as a promising candidates. Metabolites, such as fatty acids and amino acids, are the products of biological events and are influenced by both genetic and environmental factors, providing a unique snapshot into the health status of the individual. They are also easily accessible and potentially modifiable, demonstrating potential for clinical use.

We aimed to investigate whether metabolites could be valuable markers of early changes relevant to dementia and evaluate whether these associations are influenced by life course factors. This work could help reveal early disease mechanisms, identify those at risk and guide interventions.

To do this, we used the 1946 British birth cohort study; a large, well-characterised cohort with rare information ranging from early life to other life course measures such as diet and exercise. We then measured all metabolites able to be captured (roughly 1000 metabolites) in 1800 participants in late midlife and looked at whether they were associated with several measures relevant to early dementia. Examples of these measures include brain scans and cognitive tests measured at the same time point as well as 5-9 years later. To capture the effects of metabolites and the relationships between them, we used multiple analytical designs to identify single metabolites, metabolite pathways (such as glucose metabolism) and groups of similarly expressed metabolites that were associated with our outcomes. Integrating these analyses, we honed in on the most important metabolites that are likely to be key drivers in these pathways and groups. Finally, we looked at biological functions to understand potential disease mechanisms.

Once we identified these metabolites and metabolite groups, we explored whether any associations were related to life course factors. In this regard, we identified some metabolites, such as a particular class of lipids, that appear to be entirely explained by early life education, suggesting a potential mechanism by which these early influences may embed biologically. We also identified a group that were independent of all known risk factors, and honed in on a highly influential metabolite, indicating a candidate for further study.

We will next seek to understand whether these relationships are also disease causing using statistical genetics techniques. If this is the case, then they may be useful for diagnosis and intervention. Finally, we will interrogate whether our findings are able to accurately predict individuals that go on to experience dementia; this will further establish whether they may show utility as markers of early dementia.