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Thursday

Metabolomic effects of sporadic, genetic and pre-symptomatic frontotemporal dementia

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State of the art
Markers of disease and prognosis would aid stratification for clinical trials and prioritization of targets. Following Murley et al (J Neurol 267, 2228–2238, 2020) we test the hypotheses that (i) there are metabolomic differences between frontotemporal dementia, Progressive Supranuclear Palsy and controls (ii) there are fewer metabolomic differences between the related syndromes of PSP and FTD; and (iii) metabolomic differences emerge prior to symptom onset.
Methodology
269 plasma samples from the PIck's disease and Progressive supranuclear palsy Prevalence and Incidence study (PiPPIN) and Genetic Frontotemporal Dementia Initiative (GENFI) underwent analysis with ultra-performance liquid chromatography and mass spectroscopy. 964 metabolites were assayed from people with prevalent FTD (N=55), PSP (N=60), symptomatic genetic FTD (N=50, MAPT, C9orf72, GRN), presymptomatic carriers (N=50, MAPT, C9orf72, GRN) and controls from each study (PIPPIN N=24, GENFI N=30).
Results
Concentrations were different by t-tests (thresholded $p<0.05$) for 232/964 (24%) of metabolites for sporadic FTD vs controls and 282/964 (29%) for PSP vs controls. Only 99/964 (10%) of metabolites differed between FTD and PSP. 131/964 (17%) of metabolites differed between symptomatic genetic FTD carriers vs presymptomatic carriers
Conclusion
Metabolomic differences are more common than expected by chance in people with PSP and FTD compared to healthy controls. Differences were observed across multiple metabolic pathways. Metabolomic differences were less common in genetic FTD, although procedural or age-related differences between cohorts may contribute. Further work will explore multivariate metabolomic patterns by principal components analysis, and their relationship to cognitive/behavioural profiles and survival.

Conflicts of interest

N/A