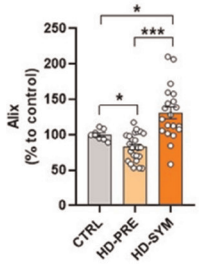


Figure 1

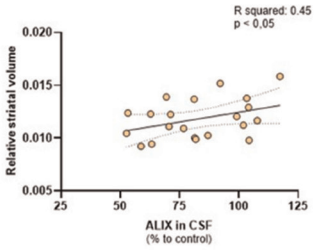


Figure 2

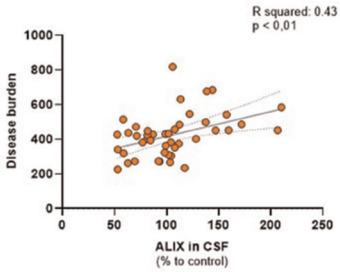


Figure 3

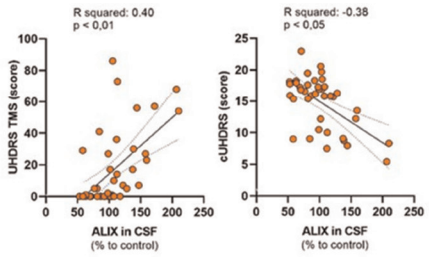


Figure 4

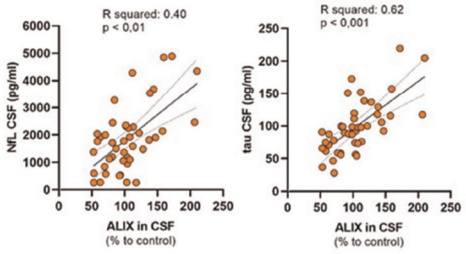


Figure 5

**Abstract D016 Figure 1–5** (1) The level of Alix in CSF is lower in pre-symptomatic HD compared to controls and increases in symptomatic HD patients; (2) CSF Alix levels in presymptomatic HD mutation carriers positively correlate with striatal volume; (3) Alix in CSF correlate with disease burden score in HD. (4) Alix levels in CSF correlate with standardized clinical scales for HD. (5) Alix levels in CSF correlate with CSF biomarkers of neuronal cell damage

tau (r=0.62, p<0.001) and neurofilament light chain (r=0.40, p<0.01) (figure 5).

**Conclusions** Our findings suggest Alix as a potential peripheral biomarker for HD progression, warranting further exploration into its roles in HD pathogenesis.

## D017 CHARACTERISING NEUROFILAMENT LIGHT PROTEIN AS A TRANSLATIONAL BIOMARKER IN HUNTINGTON'S DISEASE

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10.1136/jnnp-2024-EHDN.91

**Background** Neurofilament light protein (NfL) has emerged as a promising biomarker candidate. Detectable in CSF and blood, NfL correlates with HD severity and provides an ongoing measure of neuronal damage, suggesting multiple potential utilities: stratification and enrichment, as a prognostic biomarker, and as a safety biomarker.

**Aims** Evaluate NfL's multiple utilities as a translational biomarker of HD using human cell models and patient biofluid data.

**Methods** Biofluid NfL was modelled in vitro using iPSC-derived medium spiny neurons from HD patients and controls. NfL release was quantified via immunoassay of the culture media, and pathophysiology was characterised using immunocytochemistry (ICC). Different therapeutic interventions were performed to assess safety biomarker utility. NfL natural history will be characterised throughout HD via retrospective analysis of patient biofluid from multiple observational cohorts (TRACK/TrackOn-HD, PREDICT-HD, HD-CSF, HD-YAS). NfL data will be collated and harmonised using conversion models for assay calibration and blood collection tube type (generated from a subcohort with matched LiHep, EDTA and CPT collections). NfL will be analysed in the resulting pan-study dataset across HD-ISS stages and against clinical and MRI outcomes using mixed-effects models.

**Results** In cell models, media NfL concentration correlated with neuronal damage, and NfL was detectable via ICC; further characterisation ongoing. In patient biofluids, NfL measurements were elevated in LiHep samples, and EDTA/CPT data were adjusted accordingly. Ongoing work focuses on completing the harmonisation pipeline and downstream analyses.

**Conclusions** Comprehensive evaluation of NfL's multiple translational roles through utilisation of cell models and patient data could facilitate therapeutic development in HD.

## D018 MULTIMODAL ANALYSIS OF MUTANT HUNTINGTIN, NFL, AND MRI CORRELATIONS IN HUNTINGTON'S DISEASE

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10.1136/jnnp-2024-EHDN.92

**Objective** This study aims to investigate correlations between mHtt and NfL levels and MRI findings in individuals at different stages of HD, including presymptomatic and symptomatic individuals.

**Background** Biomarkers in Huntington's disease (HD) are crucial for understanding disease progression and developing effective therapies. Cerebrospinal fluid (CSF) biomarkers like neurofilament light chain (NfL) are sensitive indicators of