Measurement of CSF hypothalamic peptides in frontotemporal dementia

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Introduction

Frontotemporal dementia (FTD) is a progressive, neurodegenerative disorder with clinical and pathological heterogeneity. The main clinical FTD phenotypes are behavioural variant FTD (bvFTD), semantic dementia (SD) and progressive nonfluent aphasia (PNFA). One of the key clinical characteristics of bvFTD is disturbance in eating behaviour, which can be helpful in diagnosing bvFTD and differentiating it from Alzheimer's disease (AD) (Piguet et al, 2011; Bocchetta et al, 2015).

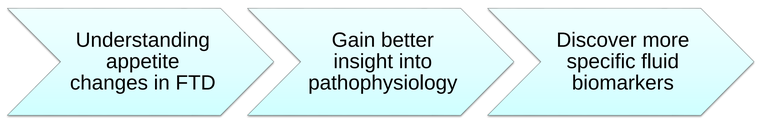


Figure 1: Flowchart of the study aim.

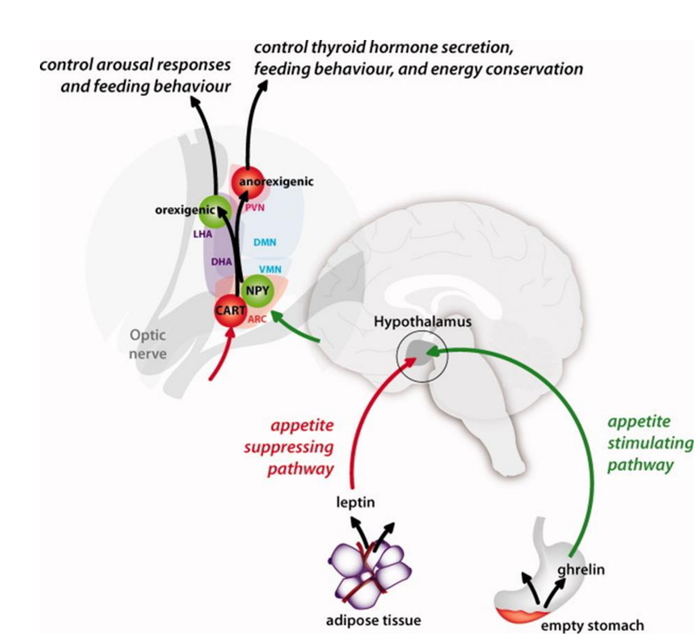


Figure 2: Appetite-controlling central and peripheral pathways. Adapted from Piguet et al, 2011.

Methods

A peptide multiplex panel of 13 hypothalamic and 9 peripheral appetite regulating peptides was developed on a liquid chromatography coupled tandem mass spectrometry platform. Concentrations were measured in the CSF of the three main clinical FTD phenotypes (bvFTD n=9, SD n=9, PNFA n=4) as well as AD (n=4) and healthy controls (n=6) and compared using non-parametric statistical tests.

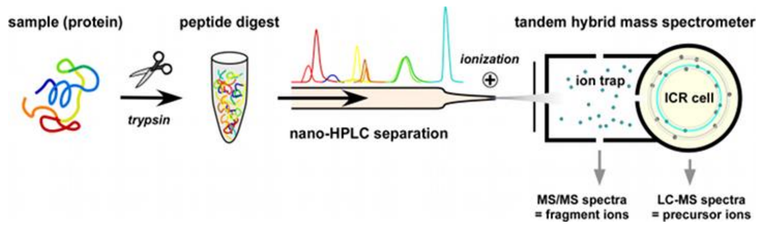
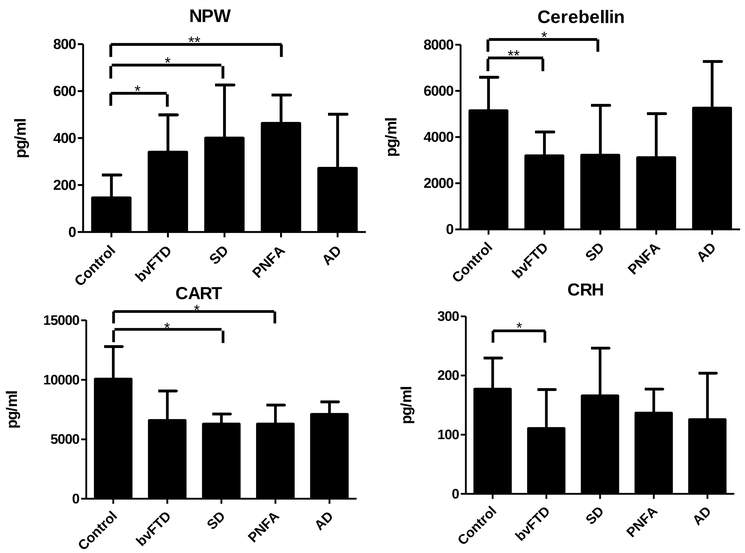
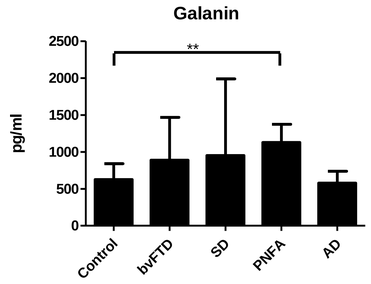


Figure 3: Schematic diagram of methodology, samples were digested using trypsin prior to HPLC separation and subsequent ionization and analysis using a mass spectrometry platform (Fakler, 2017).

Results



Results cont.



In five of the hypothalamic peptides a significant difference between controls and at least one of the FTD groups ($p<0.05$) was observed.

Figure 4: Results of proteomic multiplex assay of peptides quantified in CSF. Peptide concentrations (mean ±SD) of 5 sample groups.

Conclusion

This pilot study shows changes in concentration of a substantial proportion of the hypothalamic peptides within the CSF in the FTD groups compared to controls. Further exploration on a larger clinically defined cohort will enable understanding of the differences in hypothalamic peptides in FTD and investigate whether such a panel could be used as a biomarker in FTD disease diagnosis, prognosis or stratification.

References

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Bocchetta, M., Gordon, E., Manning, E., Barnes, J., Cash, D. M., Espak, M., … Rohrer, J. D. (2015). Detailed volumetric analysis of the hypothalamus in behavioral variant frontotemporal dementia. *Journal of Neurology*, *262*(12), 2635–2642.

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