Göteborg, 2019

Neurofilaments as biomarkers of neuronal damage

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Karl Isaksson, Medicinaregatan 16A, den fredagen den 18 oktober, klockan 09:00

av Fani Pujol Calderón

Fakultetsopponent:
Gerry Shaw, Professor Emeritus
University of Florida, USA

Avhandlingen baseras på följande delarbeten

I. Gaetani L, Höglund K, Parnetti L, **Pujol-Calderón F**, Becker B, Eusebi P, Sarchielli P, Calabresi P, Di Filippo M, Zetterberg H, Blennow K. *A new enzyme-linked immunosorbent assay for neurofilament light in cerebrospinal fluid: analytical validation and clinical evaluation*. Alzheimer's research & therapy. 2018;10(1):8.

II. **Pujol-Calderón F**, Portelius E, Zetterberg H, Blennow K, Rosengren LE, Höglund K. *Neurofilament changes in serum and cerebrospinal fluid after acute ischemic stroke.* Neuroscience letters. 2019; 698:58-63.

III. Wilke C, **Pujol-Calderón F**, Barro C, Stransky E, Blennow K, Michalak Z, Deuschle C, Jeromin A, Zetterberg H, Schüle R, Höglund K, Kuhle J, Synofzik M. *Correlations between serum and CSF pNfH levels in ALS, FTD and controls: a comparison of three analytical approaches.* Clinical Chemistry and Laboratory Medicine. 2019 [Epub ahead of print].

IV. **Pujol-Calderón F**, Zetterberg H, Portelius E, Löwhagen Hendén P, Rentzos A, Karlsson JE, Höglund K, Blennow K, Rosengren LE. *Prediction of outcome after endovascular embolectomy in anterior circulation stroke using biomarkers.* (Manuscript).

V. Behzadi A*, **Pujol-Calderón F*,** Tjust AE, Wuolikainen A, Höglund K, Forsberg K, Portelius E, Blennow K, Zetterberg H, Andersen PM. *Neurofilament light and heavy can differentiate ALS patients from commonly encountered diagnostic mimics.* (Manuscript).

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR NEUROVETENKAP OCH FYSIOLOGY

GÖTEBORGS UNIVERSITET

Göteborg, 2019

Neurofilaments as biomarkers of neuronal damage

Fani Pujol Calderón

Department of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, Sahlgrenska akademin, Göteborgs universitet, Sverige, 2019.

Abstract

Different neurodegenerative diseases have overlapping symptomatology and pathology and have thus become a challenge to modern medicine to achieve a correct diagnosis. The aim of the thesis was to evaluate the use of neurofilaments as biomarkers of neuronal damage by testing their ability to discriminate between different neurodegenerative diseases as well as assessing whether higher neurofilments predict a poorer clinical outcome in ischemic stroke.

For these purposes, we developed two new Enzyme-Linked ImmunoSorbent Assays (ELISAs) for the quantification of neurofilament light (NFL) and phosphorylated neurofilament heavy (pNFH) in cerebrospinal fluid (CSF).

The new NFL and pNFH ELISAs presented good analytical performance and both NFL and pNFH concentrations were valid across different analytical approaches. CSF-NFL concentrations were significantly higher in inflammatory demyelinating diseases and Alzheimer's disease when compared to Parkinson's disease or controls. In ischemic stroke, both CSF and blood NFL and pNFH reflected the temporal dynamics of post ischemic damage of axons. Finally, both CSF-NFL and CSF-pNFH were increased in amyotrophic lateral sclerosis (ALS) compared to other neurological conditions mimicking ALS and controls.

Both NFL and pNFH proved to be sensitive and reliable biomarkers of neuronal damage. These findings support the use of neurofilaments as disease intensity markers and suggest that both NFL and pNFH can be useful laboratory tests in the diagnostic work-up of patients with suspected neurodegenerative diseases.

Keywords: neurofilaments, biomarker, neurodegenerative diseases, stroke, cerebrospinal fluid, blood.

ISBN 978-91-7833-550-3 (PRINT)
ISBN 978-91-7833-551-0 (PDF)

http://hdl.handle.net/2077/60776