



The PSP Association's International Medical Workshop 7th July 2009

ABSTRACT

Title of Talk: Quantification of CSF Proteins as Biomarkers for Neurodegenerative Diseases

Part 1: Speaker(s) details	
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Part 2: Abstract (Maximum 400 words) Please make your abstract easy to understand as it will appear on our website and will be read by people with PSP and their carers who are not scientists but who will want to understand your work and what it means for them.

Many fundamental decisions in medical practice outside the field of neurodegeneration are based on objective laboratory biomarkers.

Since cerebrospinal fluid (CSF) is in direct contact with the central nervous system, it is obvious that any changes in biochemical composition of brain parenchyma should be predominantly reflected in the CSF. In fact, the permeation of brain-derived proteins is prioritized to the diffusion of blood proteins into CSF. Lumbar puncture is an easy procedure, with low incidence of complications. But due to the invasive character the development of a biomarker in more accessible body fluid is highly wanted.

Our hypothesis states that human body fluids reflect the metabolism of neuronal proteins in neurodegenerative diseases [like Parkinson disease (PD), Progressive Supranuclear Palsy (PSP) and Dementia with Lewy Bodies (DLB)]. We postulate that quantification of these markers in human fluids will aid the diagnostic accuracy in Tauopathies and Synucleinopathies.

The concentration of CSF total and phosphorylated tau protein has been explored in PSP by commercially available enzyme-linked immunosorbent assay (ELISA). There no alteration of the levels between PSP and other neurodegenerative diseases was seen (Arai et al., 1997; Urakami et al., 2001 and 2002). After the detection of tau protein fragments in brain species, the quantification of tau forms in CSF by Western/Immunoblot (after immunoprecipitation) has been established by Borroni et al. 2008 und 2009). There the ratio of 33kDa/55kDa tau forms revealed decreased levels in CSF of PSP patients compared to other neurodegenerative diseases (Borroni et al., 2009). This finding looks promising but has not yet been validated by an independent group and needs further characterization.

For potential biomarkers for neurodegenerative diseases specific and highly sensitive high-throughput assays need to be developed. One example for such an assay is the development of a highly sensitive and alpha-synuclein-specific enzyme-linked immunoadsorbent assay (ELISA) for the direct quantification of lower picomolar amounts of alpha-synuclein using 96- and 384-well plates loading 200 or 50µl un-concentrated CSF (Mollenhauer et al., 2008). Several independent cohorts showed a decrease of CSF alpha-synuclein in Synucleinopathies [PD, DLB, multiple system atrophy (MSA)] compared to Alzheimer disease and neurological controls (Mollenhauer et al., 2008 and Mollenhauer et al., *in press*).

Further potential markers for neurodegenerative diseases in CSF and blood need to be detected including the development of assays for the quantification of these markers. In future laboratory testing may help to asses the diagnosis of Tauopathies and Synucleinopathies.