Better Measurement for Improved Diagnosis and Management of Alzheimer’s Disease: EMPIR Neuromet Project Update

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Introduction
Neurodegenerative diseases (NDD) are incurable debilitating disorders. Alzheimer’s (AD) and Parkinson’s (PD) are the most common NDD. Early diagnosis is essential for successful treatment, but no early diagnosis method is currently accepted. Measurement variability of cerebrospinal fluid (CSF) biomarkers currently used in diagnosis is high and requires lumbar puncture with potential side effects. Improved anxiety and stress management are within the top 10 patient priorities.

Output and objectives
Early stage diagnosis
Improved Diagnosis & Disease Progression Monitoring
Targeted New Therapies
Patient Treatment & Management

Supporting measurement requirements

Objective 1
Clinical characteristics during sample collection
Validation of improved minimal invasive and non-invasive methods

Objective 2 & 3
Accurate quantification of biomarkers
Development of patient centred outcome measures (PCOMs)

Objective 4

Objective 5

Objective 6
Multimodal statistical analysis

α-synuclein reference method
Primary calibrators: Recombinant protein characterised by LC-MS/MS and amino acid analysis.
Candidate Reference Methods: A LC-MS/MS-based quantification method has been developed for α-synuclein in CSF and saliva. Following validation methods will be applied to AD and PD patient samples (α-synuclein).

Tau reference method
Validation of method in CSF and primary calibrator on-going. To be applied to AD cohort samples.

MRI-MRS
Proton MR spectroscopy (7T) and imaging is being used to provide anatomical, functional, and metabolic information with the final aim to improve sensitivity, resolution and delineation for volume, connectivity, and metabolite quantification and to define protocols for the transfer to clinical 3T scanners.

MRI and MRS protocols
Blood tests

Biomarkers

Statistical analysis and PCOMs
Improved cognitive assessment protocols are currently being developed and their use assessed on published and cohort data.

MRI-MRS protocols

7 Tesla scanner

Anatomical Imaging
MR Spectroscopy in the PCC

Statistical analysis and PCOMs

Biomarkers

For minimally invasive biomarker measurements a novel immunoassay standard addition approach was developed that overcomes matrix interference. The developed method negates the requirement for calibrant diluent and is applicable to a wide range of endogenous analytes.