Inflammation Biomarker Discovery in Parkinson's Disease and Multiple System Atrophy

Anna Santaella[1,2,3], H. Bea Kuiperij[1,2], Bas R. Bloem[1,3], Anouke van Rumund[1], Rianne A.J. Esselink[1,3], Alain J. van Gool[2], Marcel M. Verbeek[1,2,3]

[1]Department of Neurology, Radboud University Medical Center, and Donders Institute for Brain, Cognition and Behaviour, Nijmegen, The Netherlands
[2]Department of Laboratory Medicine, Radboud University Medical Center, Nijmegen, The Netherlands
[3]Parkinson Center Nijmegen, Radboud University Medical Center, Nijmegen, The Netherlands

INTRODUCTION

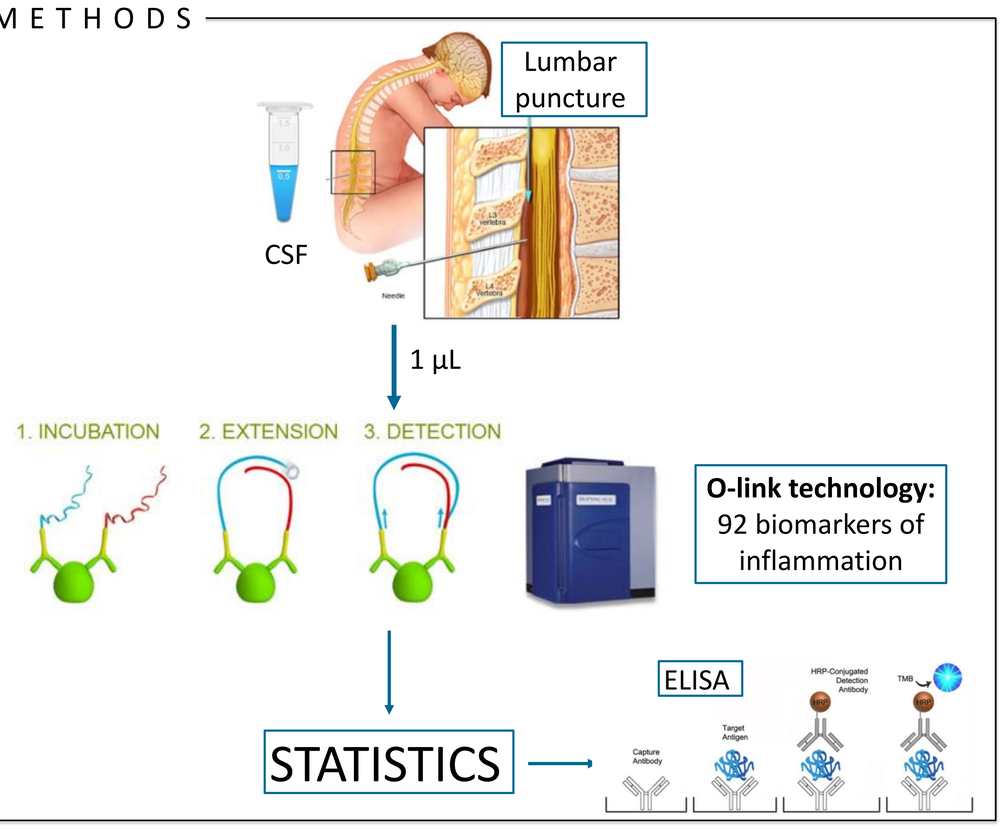
Parkinson's disease (PD) and atypical PD (aPD), such as Multiple System Atrophy (MSA) and Vascular Parkinsonism (VP) are neurodegenerative diseases primarily characterized by motor dysfunction. PD and aPD are difficult to discriminate from each other and show different response to treatment and prognosis. Thus, reliable biomarkers capable to distinguish between the two conditions are needed. Because inflammation plays a role in neurodegeneration, we aim to identify and validate biomarkers of inflammation in cerebrospinal fluid (CSF) to differentiate diseases and to establish prognosis.

DESIGN

COHORT

Using O-link technology, we analyzed 92 biomarkers of inflammation in CSF of 44 PD, 14 MSA, 9 VP, 7 PD/VP patients and 25 controls. Patients underwent UPDRS, ICARS, MMSE and Hoehn and Yahr (HY) score assessment at baseline and after 3-years follow-up.

METHODS



DATA ANALYSIS

Statistical analysis were performed in IBM SPSS Statistics 22 (Armonk, NY, USA). Pair-wise Kruskal-Wallis Test with multiple comparisons was used for analysis of patients characteristics and chi^2 test for gender analysis. Proteins that were detected in more than 35% of the samples were analyzed using ANOVA with Games-Howel post-hoc test after a rank transformation with age as a covariant to determine differences in protein level expression. Spearman's test with bootstrapping between proteins and disease progression was used to analyze correlations.

ACKNOWLEDGEMENT

Marie Skłodowska-Curie Actions

This project has been funded by the European Union Horizon 2020 Programme (H2020-MSCA-ITN-2015) under the Marie Skłodowska-Curie Innovative Training Networks and Grant Agreement No. 676408.

RESULTS

PATIENT CHARACHTERISTICS

	Controls	MSA	PD	VaP	PD/VaP	p value
N	25	14	44	9	7	
Age (at inclusion)	64.46 ± 10.31	61.65 ± 8	57.84 ± 10.11	69.46 ± 9.03	70.22 ± 5.14	0.003
Gender (men/female)	11/14	8/5	28/16	7/2	6/1	0.289
Follow-up (years)	N.A.	3 ± 0	3 ± 0	3 ± 0	3 ± 0	1
Disease Progression						
HY score	N.A.	n = 10	n = 41	n = 6	n = 5	0.002
		0.40 ± 0.31	0.1 ± 0.21	0.50 ± 0.28	0.03 ± 0.25	
UPDRS score	N.A.	n = 5	n = 38	n = 4	n = 5	0.955
		1.60 ± 2.29	0.89 ± 5.32	1.92 ± 1.83	1.20 ± 4.35	
ICARS score	N.A.	n = 5	n = 32	n = 3	n = 5	0.024
		1.07 ± 1.32	0.23 ± 1.25	3.22 ± 4.74	-1.73 ± 1.66	
MMSE score	N.A.	n = 5	n = 34	n = 4	n = 5	0.461
		-0.6 ± 0.28	-0.25 ± 0.82	-0.42 ± 0.83	-0.47 ± 1.71	

BIOMARKERS FOR DIAGNOSIS

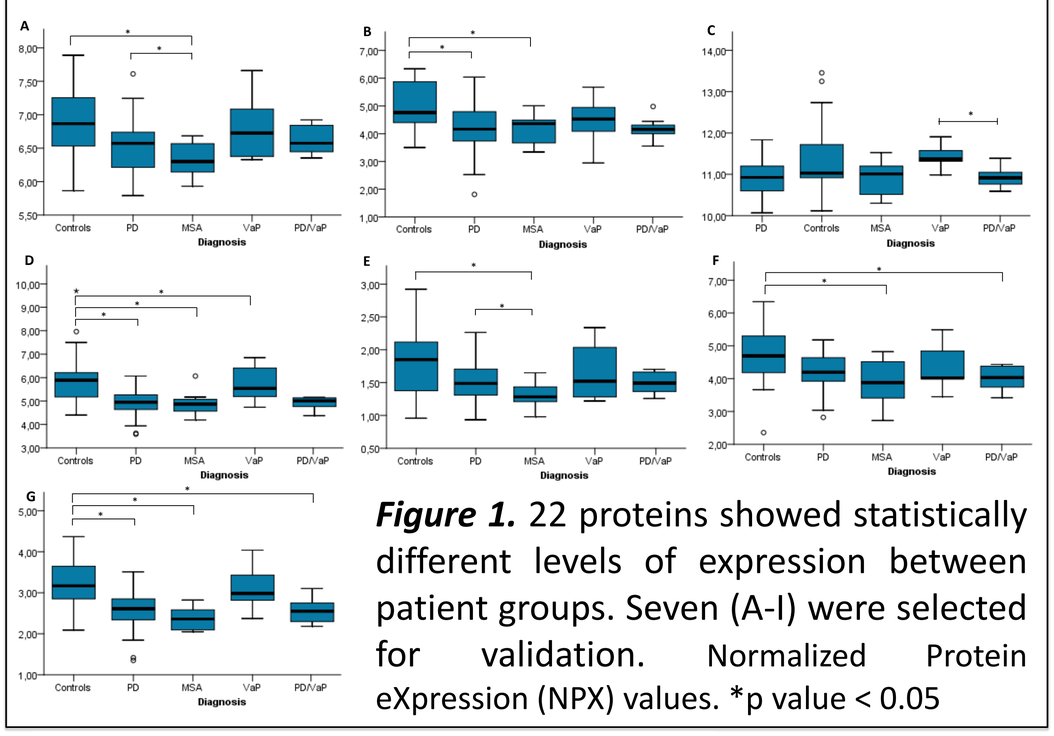


Figure 1. 22 proteins showed statistically different levels of expression between patient groups. Seven (A-I) were selected for validation. Normalized Protein eXpression (NPX) values. *p value < 0.05

BIOMARKERS FOR PROGNOSIS

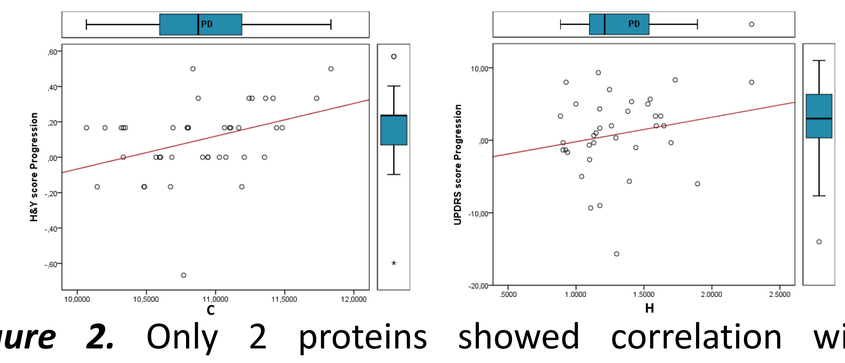


Figure 2. Only 2 proteins showed correlation with PD progression. Rho > 0.500; p value < 0.05

ELISA

Above LOD	Below LOD
F	A
C	E
B	G
H	D

Figure 3. 7 proteins were selected to be validated through ELISA. Only 4 proteins were detected in CSF above the ELISA limit of detection (LOD).

CONCLUSIONS

- Inflammatory proteins in CSF could be promising biomarkers to distinguish PD from MSA and controls from PD or aPD.
- CSF inflammatory proteins do not seem to be associated with disease progression.
- Concentrations of inflammatory proteins in CSF are low.
- O-link technology is more sensitive than colorimetric ELISA.

FUTURE STUDIES

- Validation of biomarkers using ELISA technique.

Anna.Santaella@radboudumc.nl

brain mattrain

DONDERS INSTITUTE

Institute for Health Sciences
Radboudumc