

Differential chemokine changes are seen in the different variants of primary progressive aphasia

Aitana Sogorb-Esteve^{1,2}, Henrik Zetterberg^{1,3,4}, Jonathan D Rohrer^{1,2}.

¹UK Dementia Research Institute at University College London, UCL Queen Square Institute of Neurology, London, UK ²Dementia Research Centre, Department of Neurodegenerative Disease, UCL Queen Square Institute of Neurology, London, UK ³Clinical Neurochemistry Laboratory, Sahlgrenska University Hospital, Mölndal, Sweden ⁴Department of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, the Sahlgrenska Academy at the University of Gothenburg, Mölndal, Sweden



Introduction

Primary progressive aphasias (PPA) are degenerative disorders presenting with language impairment.

Each variant of PPA is characteristically associated with a different pathological form:

- nonfluent variant (nfvPPA with FTLD).
- semantic variant (svPPA) with FTLD.
- logopenic variant (lvPPA) with AD.

Previous studies have suggested a role for inflammation in these disorders, and so we aimed to investigate the concentrations of a panel of chemokines in cerebrospinal fluid (CSF) and plasma samples from individuals with PPA as well as healthy controls.

Methods

A total of 55 participants were recruited to the study: 11 with svPPA, 13 with nfvPPA, 12 with lvPPA, 19 age-matched controls.

CSF and plasma samples from all participants were assessed using the Olink® Proximity Extension Assay inflammatory panel.

The chemokines included in the panel are:

CCL2 (MCP-1), CCL3 (MIP-1a), CCL4, CCL7 (MCP-3), CCL8 (MCP-2), CCL11, CCL13 (MCP-4), CCL19, CCL20, CCL23, CCL25, CCL28, CX3CL1, CXCL1, CXCL5, CXCL6, CXCL8 (IL-8), CXCL9, CXCL10, and CXCL11.

Results

Few changes were seen in plasma and levels in plasma and CSF didn't correlate, therefore all results focus in CSF.

- In the CSF, CCL3 and CX3CL1 concentrations were increased in lvPPA compared with controls.
- CCL19 and CXCL5 concentrations were decreased in both svPPA and nfvPPA compared with controls.
- CXCL6 showed a decrease only in svPPA when compared with the controls.
- CCL3 and CXCL1, upregulated in lvPPA, are correlated with both t-tau and ptau levels, being CX3CL1 highly significant for both.
- CCL19, CXCL5 and CXCL6, decreased in the other variants of PPA, showed a positive correlation as well with both t-tau and p-tau.

chemokine	Aβ42		T-tau		P-tau	
CCL3	r=0.035	p-value=0.840	r=0.392	p-value=0.018*	r=0.399	p-value=0.016*
CCL4	r=0.051	p-value=0.769	r=0.344	p-value=0.040*	r=0.281	p-value=0.097
CCL19	r=-0.093	p-value=0.591	r=0.492	p-value=0.002*	r=0.562	p-value=0.0004***
CCL20	r=-0.057	p-value=0.742	r=0.348	p-value=0.038*	r=0.322	p-value=0.055
CX3CL1	r=0.025	p-value=0.883	r=0.724	p-value<0.0001****	r=0.718	p-value=<0.0001****
CXCL1	r=-0.059	p-value=0.733	r=0.423	p-value=0.010*	r=0.353	p-value=0.035*
CXCL5	r=0.031	p-value=0.860	r=0.431	p-value=0.009**	r=0.464	p-value=0.004**
CXCL6	r=0.012	p-value=0.947	r=0.416	p-value=0.012*	r=0.435	p-value=0.008**
CXCL8	r=-0.034	p-value=0.842	r=0.333	p-value=0.047*	r=0.323	p-value=0.055

Table: correlations of chemokines with Aβ42, t-tau and p-tau.

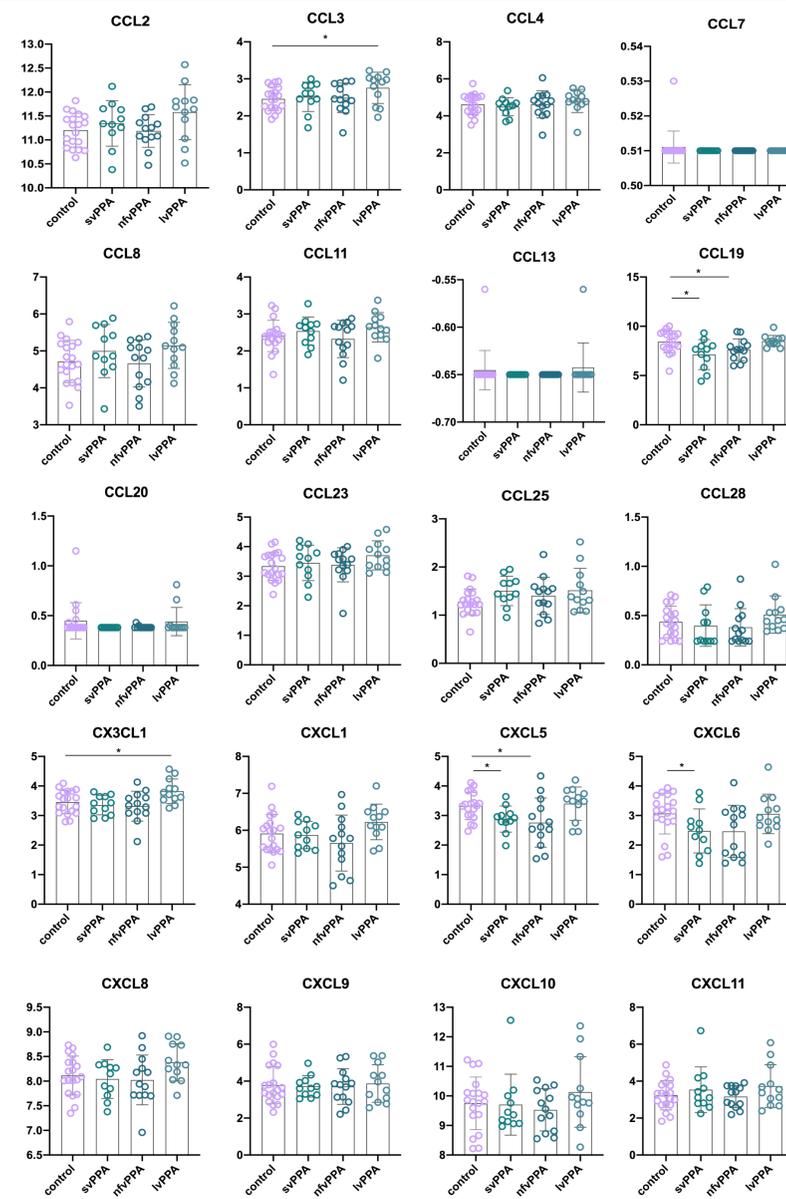


Figure: Levels of chemokines in cerebrospinal fluid. Concentrations expressed in Normalized Protein eXpression (NPX). p-values indicated in Results section.

Conclusions

- There are abnormal chemokine concentrations in the CSF of people with PPA, suggesting involvement of inflammation in the pathogenesis of these conditions.
- There is differential involvement of chemokines between lvPPA (an atypical form of AD) and both svPPA and nfvPPA (both non-Alzheimer, FTLD disorders), revealing the complexity of the inflammatory response in PPA.