

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



UK Dementia
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INTRODUCTION

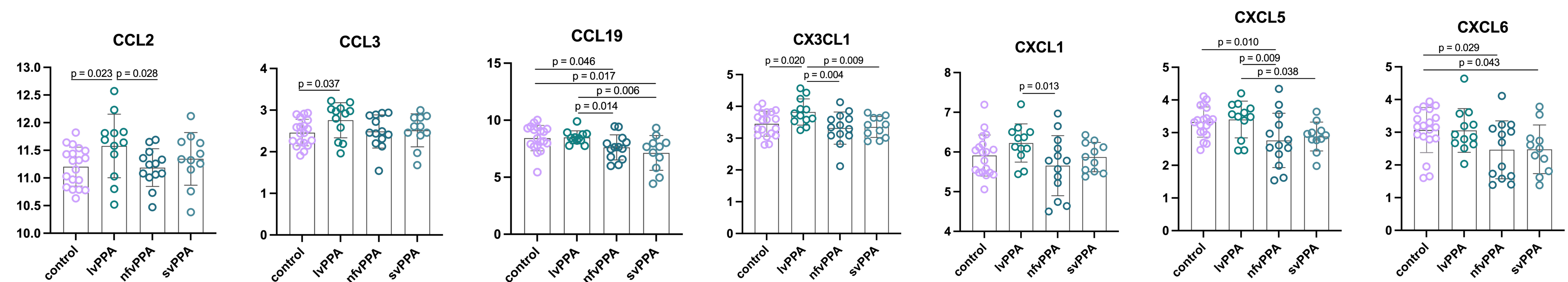
- The primary progressive aphasia (PPA) are a group of degenerative disorders presenting with language impairment. Each variant of PPA is characteristically associated with a different pathological form:
 - nonfluent variant (nfvPPA) with FTLD-tau.
 - semantic variant (svPPA) with FTLD-TDP.
 - logopenic 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

- 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.

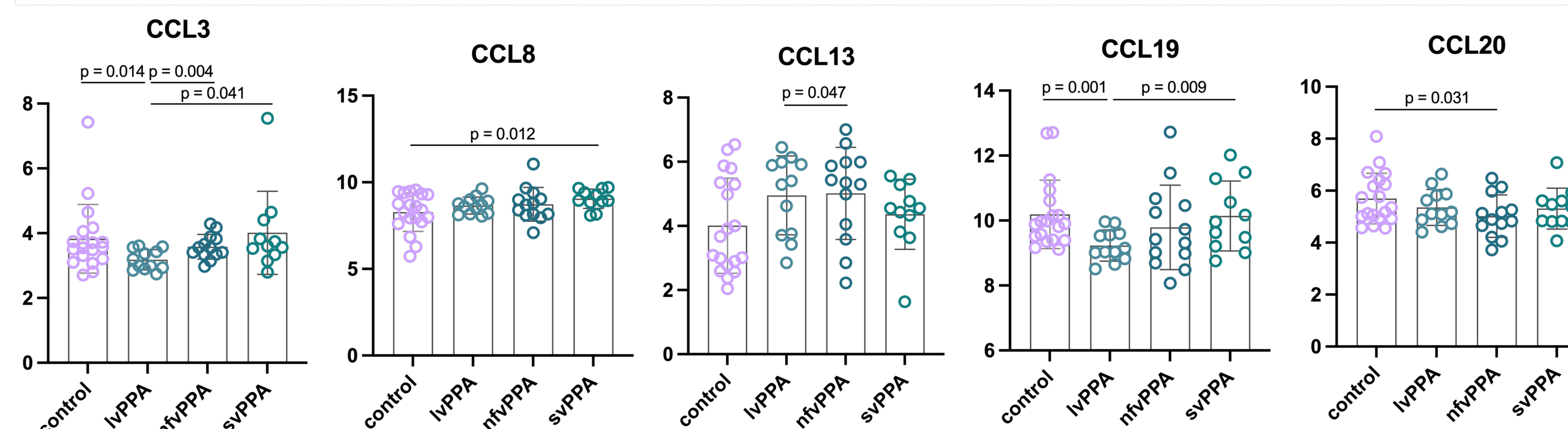
RESULTS

- In CSF:
 - CCL2, CCL3 and CX3CL1 were increased in lvPPA compared with controls, as well as compared with nfvPPA for CCL2 and both nfvPPA and svPPA for CX3CL1. CX3CL1 was significantly correlated with CSF total tau concentrations in the controls and each of the PPA groups.
 - CCL19 and CXCL6 were decreased in both svPPA and nfvPPA compared with controls and lvPPA.
 - CXCL5 was decreased in the nfvPPA group with a borderline significant decrease in svPPA.
 - CXCL1 was also increased in lvPPA compared with nfvPPA but not the other groups.



Levels of chemokines in cerebrospinal fluid. Concentrations expressed in Normalized Protein expression (NPX). p-values indicated for each significant paired group difference.

- Few correlations were seen between chemokine levels in CSF and plasma in either the controls or PPA groups.
- In plasma:
 - CCL3 and CCL19 were decreased in lvPPA compared with controls and svPPA, as well as compared with nfvPPA for CCL3.
 - CCL8 was increased in svPPA when compared with controls.
 - CCL13 was increased in nfvPPA when compared with lvPPA.
 - CCL20 was decreased in nfvPPA when compared with controls.



Levels of chemokines in plasma. Concentrations expressed in Normalized Protein expression (NPX). p-values indicated for each significant paired group difference.

CONCLUSION

Differential alteration of chemokines across the PPA variants is seen in both CSF and plasma. Importantly, these results suggest a role for neuroinflammation in these poorly understood sporadic disorders, and therefore also a potential future therapeutic target.