COMMUNICOME PROTEINS IN CSF AND PLASMA THAT MODEL CSF BIOMARKERS FOR ALZHEIMER’S DISEASE CAN CLASSIFY DISEASE

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Introduction: Cells use hundreds of secreted proteins to communicate with each other within or across tissues. This subset of the proteome, called the communicome, can be quantified non-invasively in plasma or other fluids over the course of a neurological disease and may provide information about pathophysiological processes.

Aims: To identify proteins in CSF and blood whose levels are associated with levels of Aβ and tau in CSF, predict disease, and thus point to disturbed biological pathways in AD.

Methods: We used the levels of 91 communicome proteins in plasma of 118 healthy non-demented controls (NDC) and 78 AD patients as well as in CSF of 18 NDC and 25 AD patients to model with a variable selection method the CSF marker levels of AD pathology total tau, phosphorylated tau (p-tau₁₈₁), and Aβ1-42. The results of these models were validated in classification analysis.

Results: Seven CSF communicome proteins plus APOE4 status outperformed the accepted ratio of Aβ1-42 /p-tau₁₈₁ to classify AD (AUC 0.93 vs 0.86, respectively). Up to 15 communication factors in plasma together with age and APOE4 status classified AD close to or as effectively as CSF Aβ1-42 or tau levels in a training and an independent test set. Correlation networks between these selected CSF or plasma communication factors showed prominent changes in their connectivity in AD patients compared with NDC.

Conclusion: AD CSF biomarkers are associated with CSF and plasma communicome proteins. Sets of these proteins can help in diagnosing AD and may provide insight in the disease process.