2021 Best Research Poster Award

Barwon Health

DEAKIN UNIVERSITY

Cerebrospinal fluid biomarker model comprising of next generation biomarkers enables stage-specific accurate diagnosis of Alzheimer's disease

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INTRODUCTION

- Approximately 75% cases of Alzheimer's disease (AD) remain undiagnosed, given the lack of accurate, clinically and economically compliant diagnosis. Therefore, there is a need of an accurate and feasible stage-specific diagnosis of AD.
- Given that AD is a disease of multiple pathologies, an accurate stage-specific diagnosis can be made by developing diagnostic models comprising biomarkers specific to individual pathologies.

OBJECTIVES

To assess the combined diagnostic potential of next generation cerebrospinal fluid (CSF) biomarkers associated with different aspects of AD:

- **Neurodegeneration:** neurofilament light (NfL), visinin like protein 1 (VILIP-1) and fatty acid binding protein 3 (FABP3)
- **Synaptic dysfunction:** neurogranin, growth-associated protein 43 (GAP-43) and synaptosomal-associated protein 25 (SNAP-25, peptide B)
- **Neuroinflammation:** YKL-40
- **Core CSF biomarkers:** amyloid-β (Aβ)42, total tau (T-tau) and phosphorylated tau (P-tau)

METHOD

This study included 127 participants from the Australian Imaging, Biomarkers and lifestyle study of ageing (AIBL, healthy controls n=106 and AD n=21).

Biomarker levels in CSF samples were measured via:

- Enzyme-linked immunosorbent assay (NfL, VILIP-1, YKL-40, neurogranin, GAP-43, Aβ42, T-tau, P-tau)
- Electrochemiluminescent assay (FABP3)
- Immunoprecipitation mass spectrometry (SNAP-25)

Logistic regression analyses and receiver operating characteristic (ROC) curve analyses were used to generate and test the diagnostic accuracy of biomarker models for diagnosing AD, as well as presence of preclinical AD pathology/pathological change amongst healthy controls.

RESULTS

- The model comprising of all 10 biomarkers identified AD with an area under the ROC curve **[AUC] of 0.97** (Fig. 1).

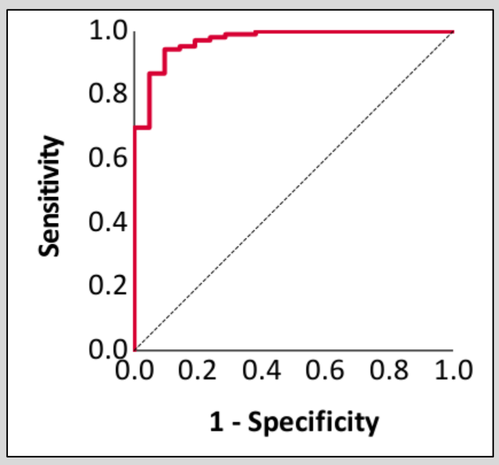

Fig. 1 ROC curve for AD vs healthy controls
AUC 0.97 (CI 0.94 – 1.00)*
Sensitivity 94%#
Specificity 91%#

*p<0.001; #cut-off 0.68, computed using Youden Index

- Cases of preclinical AD/preclinical AD pathological change were identified among healthy controls using the biomarker guided classification (amyloid-β+, P-tau+ and T-tau±; A+T+/N±; n=32) and normal AD biomarkers (A-T-N-; n=57).
- The model with 4 biomarkers (FABP3, neurogranin, GAP-43, SNAP-25) identified preclinical AD/pathological change among healthy controls with an **AUC of 0.82** (Fig. 2).

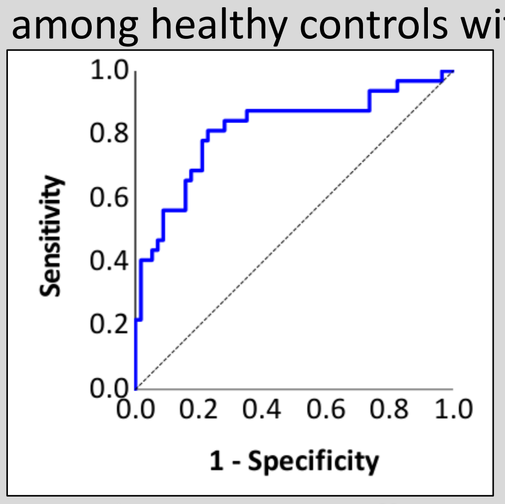

Fig. 2 ROC curve for preclinical AD/preclinical AD pathological change vs normal AD biomarkers
AUC 0.82 (CI 0.72 – 0.92)*
Sensitivity 81%#
Specificity 77%#

*p<0.001; #cut-off 0.35, computed using Youden Index

DISCUSSION

Given that AD is a disease of multiple pathologies an accurate diagnosis of AD could be made via a biomarker model comprising CSF biomarkers associated with various AD specific pathological changes. The model that identified preclinical AD comprised biomarkers of lipid dyshomeostasis and synaptic dysfunction, indicating a disruption of these pathologies in early stages of the disease.

CONCLUSION

An accurate diagnosis of AD and preclinical AD can be made using a combination of biomarkers pertaining to stage-specific pathophysiological changes in AD.

REFERENCES & ACKNOWLEDGEMENTS

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