ANALYSIS OF PLATELET MEMBRANE BETA-SECRETASE ACTIVITY AS A POTENTIAL BIOMARKER FOR THE DIAGNOSIS OF ALZHEIMER'S DISEASE

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Background: β-Secretase activity is the rate-limiting proteolytic step in Aβ peptide production from amyloid precursor protein (APP). We previously reported a significant increase in platelet membrane β-secretase activity in Alzheimer’s disease (AD) patients compared to controls¹. Preliminary statistical analysis of this measure indicated potential utility as a plasma biomarker for AD.

Aims: To determine if platelet membrane β-secretase activity enhances prediction of AD when compared against, or included in statistical models alongside, additional clinical information.

Methods: Binary logistic regression models were constructed from multiple combinations of variables including age, apolipoprotein E (ApoE) genotype and platelet membrane cholesterol, with and without the inclusion of β-secretase activity.

Results: Using data for 164 AD patients and 163 controls, platelet membrane β-secretase activity was the single best predictor of AD status (Scaled Brier score (SBS) 7.34), consistently enhancing discrimination between AD and control groups when included in multiple regression models. Maximal discrimination was delivered by a complex model incorporating all considered variables and their interactions (SBS 21.7, sensitivity 73.8%, specificity 68.1%).

Conclusions: The most complex statistical models improved AD prediction at the expense of transferability to other populations. Balanced selection of simplified models improves applicability to other datasets. The sensitivity and specificity of platelet membrane β-secretase activity in predicting AD status is currently insufficient for use as a stand-alone diagnostic biomarker. A potential limitation of this work relates to the small numbers of individuals studied, with further analysis of a larger dataset warranted.