IDENTIFICATION OF BLOOD BIOMARKERS FOR EARLY DIAGNOSIS OF ALZHEIMER'S DISEASE THROUGH NMR SPECTROSCOPY

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Introdcution

Alzheimer's disease (AD) is the leading cause of dementia in late adult life and current biomarkers for early detection of subject at risk of AD have limited accuracy and reliability. In order to identify new biomarkers that could be useful for early and accurate diagnosis of AD, we measured, trough NMR spectroscopy, plasma levels of several metabolites in different groups of subjects: AD patients; subjects at risk of AD, namely with mild cognitive impairment (MCI) or subjects memory complaint (SMC); healthy subjects (HS).

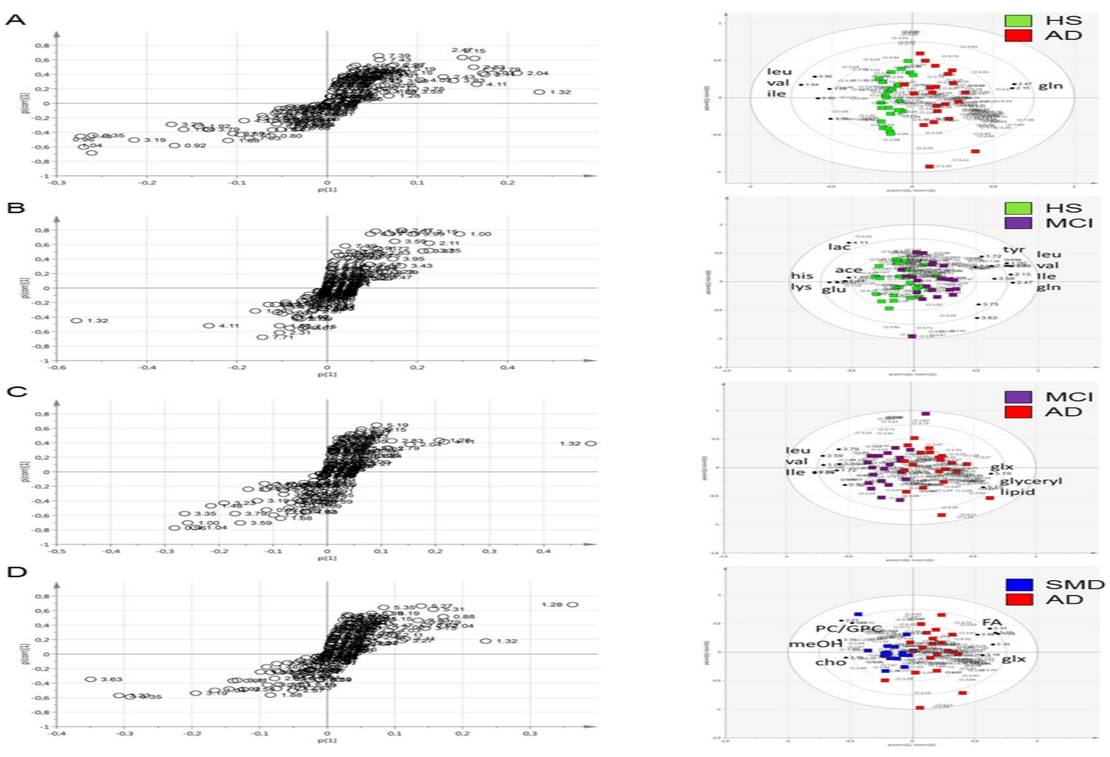

Figure 1- *S-plot and the corresponding bi-plot representing respectively the pcorr and the co-chart of loadings with samples and covariance for each single class model of the Training Set.*

Results

The panel composed of glutamine, histidine, glucose, methanol, tyrosine, valine and unsaturated fatty acids is capable of discriminating HS group from MCI or AD, MCI from AD, and SMC from AD, with a sensitivity ranging from 88% to 95%. Pathway analysis showed that glutamine (p=6.02×10-11; impact=0.29), alanine, aspartate and glutamate (p=5.45×10-9; impact=0.21) and histidine (p=2.47×10-5; impact=0.14) metabolisms were the most relevant networks.

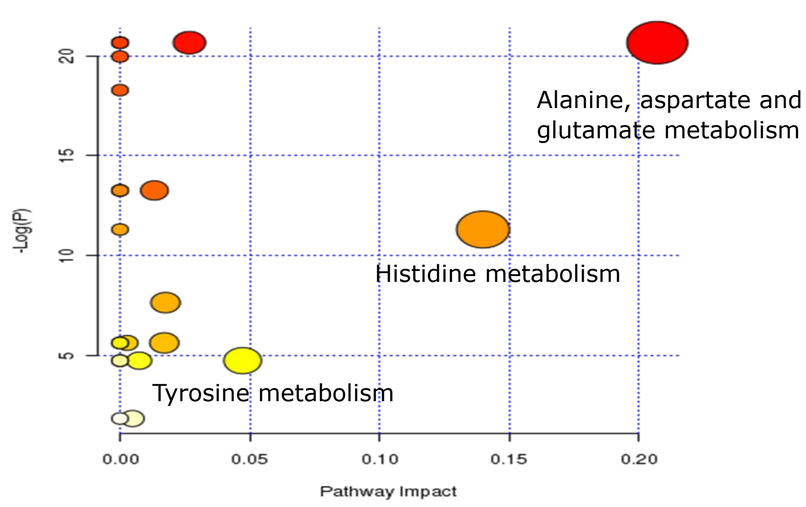

Figure 2- *Pathway analysis overview showing the altered metabolic pathways associated with blood markers derived from discriminant class analysis.*

Materials and methods

171 participants were recruited and divided into four groups according to their clinical profile: 40 with probable AD, 40 with amnestic MCI, 40 with SMC and 51 cognitively HS.
High resolution-NMR spectra were acquired from serum samples of all participants and metabolite signals were accurately identified. Then, a multivariate statistical data analysis and a receiver operating-characteristic (ROC) curves analysis were carried out. Relevant metabolites, highlighted from the statistical models, were addressed to pathway analysis.

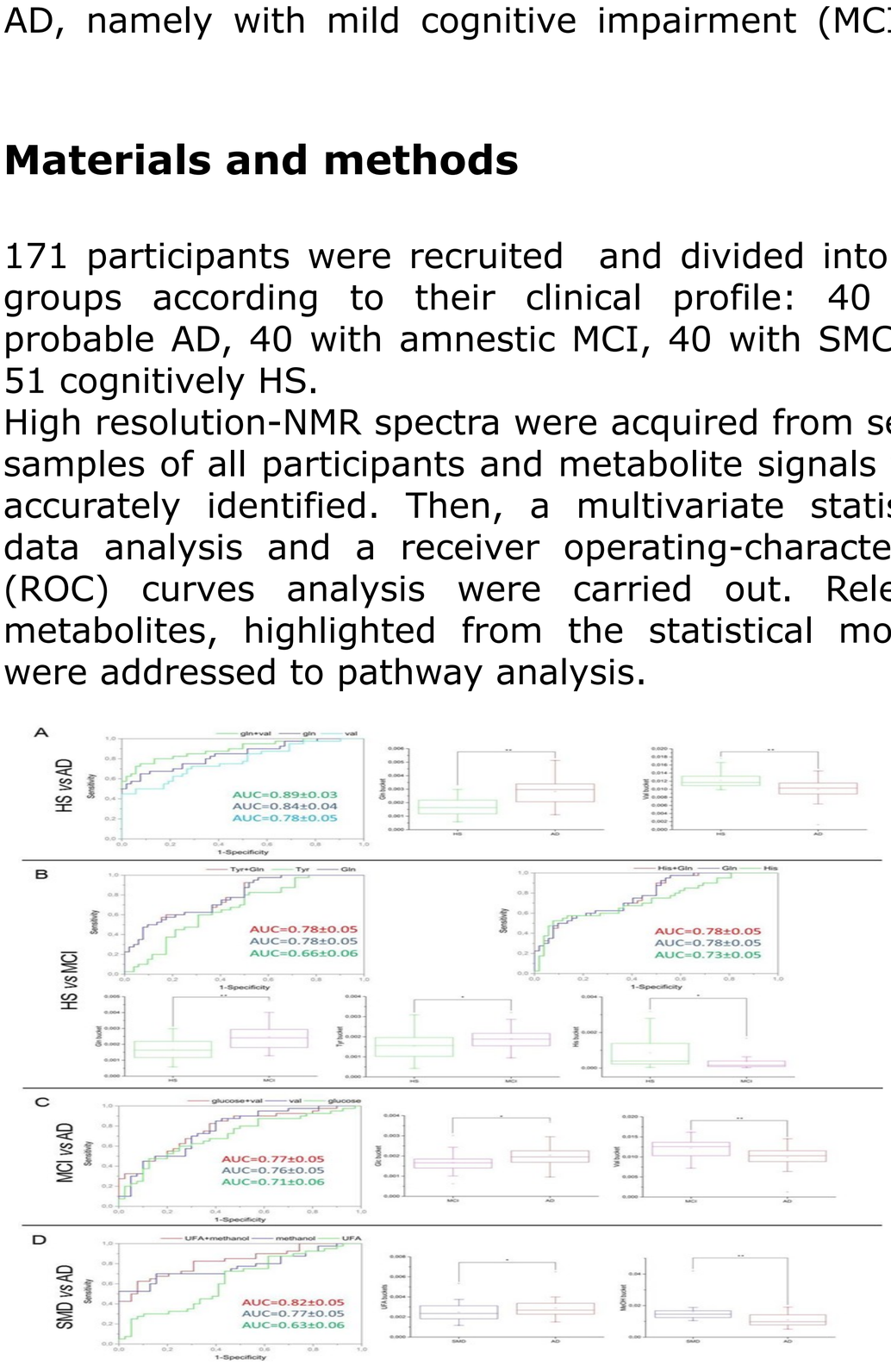

Figure 2*-Simple and multiple logistic regression of selected variables for each discriminating model: A) HS vs AD; B) HS vs MCI; C) MCI vs AD; D) SMD vs AD. Receiver operating characteristic (ROC) curve and the corresponding area under the curve (AUC) of each classifier are reported together with the Student's t-Test*

Conclusion

The metabolic panel including glutamine, histidine, glucose, methanol, tyrosine, valine and unsaturated fatty acids could be an useful biomarker for early diagnosis of AD. However, even if the number of analyzed samples is large, further validation in longitudinal studies is necessary before application to clinical practice. The altered metabolic pathways could provide new therapeutic targets.

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