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Posters
P41- Genome-wide association in a cohort of Alzheimer’s patients from Iberia: an exploratory analysis with common variants

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Aims/Context: The polygenic form of Alzheimer’s disease (AD) is complex and late-onset (LOAD, after 65 years old) with heritability ranging from 25% to 80%. APOE ε4 remains the strongest genetic risk factor for AD. Almost 40 other genetic variants have been identified, although current findings account for only 31% of LOAD heritability. Currently, known AD markers cannot explain the majority of genetic variance and are not helpful for predicting or diagnosing the disease (aside from APOE ε4). We aimed at performing an exploratory association analysis in a cohort of LOAD patients from Northern Portugal and Spain. Methods: DNA was extracted from saliva and buccal swab samples and genotyped with Axiom Spain Biobank Array. This analysis comprised 128 LOAD patients from North Portugal (n=55) and from the Spanish autonomous community of Castile and León (n=73) with a clinical diagnosis of AD. In addition, 59 controls (individuals over 65 years old with no signs of dementia) from both regions were also analyzed. Using PLINK we implemented a genotypic additive model including 4 principal components, sex and age as covariates. Results: Excluding known APOE risk variants, SNPs were selected for p-values below 10-4 to evaluate the performance of the model, taking into account the small sample size (which prevents us from drawing significant results at the genome-wide correction threshold, 5.0e-08). We found nominal significance for other variants previously associated with AD or in relevant molecular pathways for the disease. Namely, rs3773341 (p-value=6.98e-06) and rs2046210 (p-value=6.5e-06), the most significant variants assuming logistic regression, are within the makorin ring finger protein 2 (MKRN2, which is involved in neurogenesis) and near the estrogen receptor (ESR1), respectively. Conclusions: These results suggest that our model is being correctly implemented. Increasing the sample size with more patients and controls from Iberia will likely yield significant results.