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**Association Analyses of *Reln* Rs4298437 and Rs6943822 Polymorphisms with Alzheimer's Disease**

A. Fehér<sup>1</sup>, A. Juhász<sup>1</sup>, M. Pákási<sup>1</sup>, J. Kálmán<sup>1</sup>, Z. Janka<sup>1</sup>

<sup>1</sup>Psychiatry, University of Szeged, Szeged, Hungary

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Reelin, an extracellular signaling glycoprotein encoded by the *RELN* gene, plays a significant role in neuronal development and adult synaptic plasticity. Alterations in the expression of Reelin and in Reelin-mediated signaling have been implicated in the pathology of Alzheimer's disease (AD). We examined the possible role of the *RELN* rs4298437 and rs6943822 polymorphisms and their synergistic effect with the Apolipoprotein E (*APOE*)  $\epsilon$ 4 allele in the development of AD.

A total of 365 patients with a clinical diagnosis of probable AD according to NINCDS/ADRDA criteria and 276 elderly, cognitively healthy control individuals were involved in the study. The genetic analyses were performed by PCR-RFLP and TaqMan real-time PCR methods.

The investigated genotype distributions were in Hardy-Weinberg Equilibrium. No significant difference in mean age or in the distribution of genders between cases and controls was found. Comparison of rs4298437 genotype frequencies between AD and control groups showed no statistically significant difference ( $p=0.890$ ). The frequencies of the different rs6943822 genotypes were similar in the two investigated groups ( $p=0.914$ ). The interaction between the *RELN* and *APOE* polymorphisms did not contribute significantly to the logistic regression model ( $p>0.1$ ).

Our study suggests no individual influence of the investigated *RELN* polymorphisms on the risk for developing AD. Given the involvement of Reelin in the *APOE* signaling pathway, a possible interaction of *RELN* and *APOE*  $\epsilon$ 2/ $\epsilon$ 3/ $\epsilon$ 4 polymorphisms in the prediction of AD was assessed, but no epistasis was found. This project was supported by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences.