P02-214

# POSSIBLE INVOLVEMENT OF THE CALRETICULIN GENE IN THE EVOLUTION OF COGNITION IN HUMANS

T. Farokhashtiani[1], A. Mirabzadeh[2], M. Ohadi[1]
[1]Genetics Research Center, [2]Department of Psychiatry, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

The chromosomal region, 19p 13.2, has been suggested to be linked with schizoaffective disorder (Hamshere et al. 2005). This region harbors the calreticulin gene, protein encoded by which is an endoplasmic Ca+2-binding molecular chaperone. Development-dependent, tissue-specific expression of this gene in the gray matter coincides with the expression of psychoses phenotypes. We have recently reported instances of mutations within the core promoter (-48 G>C, -205 C>T) and coding sequence [exon 5 (c: 682 C>T, pro228ser)] of the gene in schizoaffective disorder. In view of the mounting evidence on the genetic overlap in the psychiatric spectrum, we investigated this gene in 386 patients afflicted with schizophrenia, schizoaffective disorder , major affective disorder and 600 controls by PCR/SSCA. We found that a unique mutation within the core promoter of the gene, located at a conserved genomic block, co-occurring with four cases of psychoses including schizophrenia, schizoaffective disorder and bipolar disorder type I. This unique mutation reverts the human promoter sequence to the ancestral types observed in chimpanzee, rhesus Macaque and mouse, implying that the genomic block harboring this nucleotide may be involved in the evolution of human-specific higher-order functions of the brain (i.e. cognition), that are ubiquitously impaired in psychoses. Our findings propose that calreticulin is not only a promising candidate in the spectrum of psychoses, but also, a gene that may be important in the process of human-unique higher-level functions of the brain.

https://doi.org/10.1016/S0924-9338(11)72515-9 Published online by Cambridge University Press