Exploring the effect of adducins genetic variability on cognition in schizophrenia


BACKGROUND

Neuropsychological deficits are recognized as cardinal features of schizophrenia and represent suitable endophenotypes for genetic studies. Cognitive impairment shows an heterogeneous profile among patients that can partially be explained by individual genetic variability, as pointed out by several association studies analyzing polymorphisms of putative genes regulating neurotransmission, mainly dopaminergic and serotonergic. Recently there is growing interest also in genes codifying for structural proteins involved in stability, morphology and thus plasticity of synapses, suggested to play a role in neurophysiologic and behavioral alterations observed in psychiatric and neurodegenerative conditions. Among these, adducins family cytoskeleton proteins appear of interest, as they are constituents of dendritic spines and growth cones of neurons and modulate synaptic strength through a variety of mechanisms. Adducins are heterodimeric proteins ubiquitously expressed in three differentiated forms (α, β, γ) encoded by three genes (ADD1, ADD2, ADD3). Genetic manipulation and inter-individual variability at this level are reported to affect neuronal connections and underlying behavioral performances. β-adducin KO mice show an impairment of long-term potentiation (LTP) and long-term depression (LTD) in the hippocampus, associated with deficits in learning and motor performances [1]. Phenotypic analysis of α-adducin KO worms demonstrated that the gene is required for consolidation of synaptic plasticity and influences short and long-term memory. Moreover genotype-phenotype correlations revealed a significant association of ADD1 genotype on episodic memory measures in humans [2].

AIM

This study aims to explore the possible effect of genetic polymorphisms belonging to adducins (ADD1, ADD2, ADD3) on neuropsychological performances in a sample of patients with schizophrenia, a disease characterized by frontal brain regions dysfunction and core cognitive impairment.

METHODS:

• 290 patients with diagnosis of schizophrenia, (DSM-IV, APA1994) were enrolled in the study

RESULTS:

Table 1. Demographic, clinical and neuropsychological characteristics

<table>
<thead>
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<th>Mean</th>
<th>S.D.</th>
<th>Mean</th>
<th>S.D.</th>
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<td>PANSSNEG</td>
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<td>10.38</td>
<td>30.72</td>
</tr>
</tbody>
</table>

Fig.1: Interaction effect of ADD1 & ADD3

Fig.2: Interaction effect of ADD1 & ADD3

Fig.3: Interaction effect of EADD1 & ADD2 & ADD3

DISCUSSION

Our results confirm a previously reported effect of genetic variability of adducins, specifically β-adducin, in memory performances and suggest that different forms may interact influencing also other cognitive domains, probably through control of synaptic plasticity. Although the specific underlying mechanism is still largely unknown, these observations support a putative role of adducins in the study of pathophysiology of schizophrenia.

REFERENCES


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