CANDIDATE GENES ASSOCIATED WITH PSYCHOSIS IN ALZHEIMER’S DISEASE

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Alzheimer’s disease (AD) is a chronic, devastating, heritable, irreversible progressive neurodegenerative disease characterized with rapid decline in memories and other cognitive functions. It can be subdivided into AD with early or late onset. Only 5% of all AD cases are early-onset or familial AD, occurring in age 30-60, caused by the mutations in the presenilin 1 and 2 and the amyloid precursor protein (APP) genes. In contrast, late onset AD is frequent, develops after age 60, its etiology is still not clear, but is assumed to be precipitated by the complex interactions between a combination of genetic, environmental, and lifestyle factors. Numerous risk genes, with small effects, affect the risk for developing late-onset AD. The є4 allele of the apolipoprotein E (APOE) gene is the most replicated genetic risk for late-onset AD.

Patients with late-onset AD have a great risk of developing psychosis, and almost 50 % of patients develop psychotic symptoms. Patients with AD complicated with psychosis have more rapid cognitive decline, and they experience more behavioral disturbances such as agitation and aggression, and also more depressive symptoms. All these symptoms lead to earlier institutionalization of patients, worse outcome, increased mortality, higher costs for society and exacerbate the burden for caregivers and families. Delusions occur in 36%, misidentification delusions in 25% and hallucinations in 18% of patients. It is assumed that psychotic AD is heritable, since this type of AD aggregates within families.

Although there are a lot of inconsistent and inconclusive findings, the results from the candidate genes and genome-wise association studies have suggested that polymorphisms in the APOE, serotonin 2A and 2C, alpha 7 nicotinic acetylcholine and dopamine 1 and 3 receptors, serotonin transporter, catechol-O-methyl-transferase, oligodentrocyte lineage transcription factor 2, G720/G30 (DAOA-D-amino acid oxidase activator), interleukin 1beta gene promoter, untranslated region of the prion like protein gene, brain derived neurotrophic factor, neuroregulin 1, serine/threonine kinase 11, visinin-like 1, and visinin-like protein-1 might be associated with the risk of psychosis in AD. However, no single gene or polymorphism is definitely associated with the risk of psychosis in AD (De-Michelle et al., 2010 and 2014; Murray et al., 2014).

References:

DeMichele-Sweet MA, Sweet RA (2010) Genetics of psychosis in Alzheimer’s disease: a review. J Alzheimers Dis 19: 761–780

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