Genetics of autism

Genética do autismo

Dear Editor,

We have read with special interest the paper "Genetics of Autism" by Carvalheira et al[1] and we would like to contribute for this important updating work by presenting and discussing some interesting data in this area.

Genome-wide screens have also found two interesting genetic sites of putative autism susceptibility on chromosomes 3p25-p26 and 6q21 with linkage scores higher than 2.0 (highest LOD scores: 3p25-p26 was 2.88,[2] and 6q21 was 2.23[3]). These chromosomal regions also contain candidate genes for autism that belong to cerebral systems supposedly related to the disorder. The chromosome 3p25-p26 contains the oxytocin (OT) receptor gene,[4] and the chromosome 6q21 contains the human glutamate receptor-6 kainate-preferring receptor (GluR6) gene.[5]

OT system has been involved in the sociability abnormalities presented in autism. Animal studies have shown that OT levels affect social behavior in mice. Children with autism present low plasma OT levels, and the ratio of the inactive OT precursor (OT-X) to active OT peptide seems to be significantly higher in children with autism.[6]

The glutamate system may play an important role in the pathophysiology of autism. The GluR6 gene on chromosome 6q21 was associated with autism by linkage disequilibrium and multipoint linkage analysis, and a surveyed autistic population possessed a single amino acid substitution in GluR6 (M867I) in a highly conserved domain of the intracytoplasmic C-terminal region of the protein (this change was found in 8% of autistic subjects and in 4% of controls).[7] Some studies have implicated the marker 155CA-2 in the gamma-aminobutyric acid (GABA) type-A receptor beta3 subunit gene (*GABRB3*), and the metabotropic glutamate receptor gene (*GRM8*) on chromosome 7q31-q33 in the susceptibility for autism.[6] Although apparently contradictory, several evidence suggest the involvement of the glutamate system in the pathophysiology of autism. Symptoms of hypoglutamatergia (defective habituation, impaired attention, a meagre behavioral repertoire and a general behavioral primitivization) simulate the autistic behavior in rodent model study; serotonin receptor 2A (5HT2A) agonists cause behavior similar to autism, perhaps via expression of 5HT2A on glutamatergic-inhibiting GABAergic neurons (intimate interplay between central glutamate and serotonin, notably the serotonin (5-HT) 2A receptor, has been shown by several investigations); an excessive glutamatergic activity is associated with epilepsy, which is highly common in autism (up to a third of patients with autism); the mRNA levels of the excitatory amino acid transporter 1 and glutamate receptor AMPA 1 genes, two members of the glutamate system, were significantly increased, showing an upregulated expression of them in postmortem studies of brain tissue of autistic patients.[6]

These data have shown the importance of chromosomes 3p25-p26 and 6q21 for the investigation of the genetic susceptibility for autism.

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A memantina como terapia adjuvante para os sintomas negativos da esquizofrenia

Memantine as an adjunctive therapy for schizophrenia negative symptoms

Sr. Editor,

Os antipsicóticos atípicos trouxeram uma melhora marcante nos sintomas negativos da esquizofrenia. Entretanto, muitos pacientes permanecem refratários à remissão destes sintomas, fato que piora muito a qualidade de vida e a deterioração psicossocial destes indivíduos. Recentemente, a memantina, um antagonista dos receptores N-metil D-aspartato (NMDA), foi descrita como uma substância neuroprotetora na esquizofrenia;[1] um relato de caso mostrou a efetividade deste fármaco na esquizofrenia catatônica.[2] A seguir, relatamos três casos clínicos sobre a melhora dos sintomas negativos com uso de memantina em pacientes do sexo feminino com diagnóstico de esquizofrenia pelo DSM-IV e uso de antipsicóticos atípicos, em atendimento ambulatorial. Os sintomas foram avaliados através da Escala Breve de Avaliação Psiquiátrica Versão Ancorada (BPRS-A)[3] antes do uso da memantina (T0) e após quatro semanas (T4). Desconhecemos outros relatos semelhantes na literatura até o momento.

Paciente A, 56 anos, em uso de sulpirida 800 mg por dia. Apresentava em T0, predominantemente, retraimento afetivo