Annals of General Hospital Psychiatry

Poster presentation

Molecular genetics of neurodevelopment and treatment response in psychosis

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from International Society on Brain and Behaviour: 1st International Congress on Brain and Behaviour
Hyatt Regency Hotel, Thessaloniki, Greece, 20–23 November, 2003

Published: 23 December 2003 Received: 1 November 2003

Annals of General Hospital Psychiatry 2003, **2**(Suppl 1):S131

This article is available from: http://www.general-hospital-psychiatry.com/content/2/S1/S131

Background

There is evidence for neurodevelopmental aberrations in both schizophrenia and bipolar disorder. We have studied the genes for synaptosomal associated protein of 25 kilodaltons (SNAP-25) and the brain derived neurotrophic factor (BDNF), that are known to be involved in normal brain development. SNAP-25 expression is associated with regions of high synaptic plasticity and is required for axonal elongation. A strain of mouse designated coloboma possessing a 2 cM deletion encompassing the Snap-25 gene exhibits hyperactivity, delayed development, and abnormalities in dopaminergic, serotonergic, and glutamatergic transmission. Additionally, several studies have suggested a direct involvement of SNAP-25 in schizophrenia etiology based upon altered levels of brain and CSF expression. Furthermore, our group (Wong et al., 2003) have observed SNAP-25 expression to be significantly altered in rats treated with the antipsychotic medication haloperidol, versus controls. We examined transmission of alleles at three single nucleotide polymorphisms in the SNAP-25 gene in more than 100 schizophrenia triad families and found evidence of a haplotype related to the disease (Klempan et al., 2002).

Material and Methods

We then went further to examine SNAP-25 in antipsychotic drug response, investigating a sample of 61 schizophrenia patients who had undergone an antipsychotic drug clinical trial.

Results

ANOVA-based analysis of SNAP-25 genotypes against mean change in the PANSS scores (14 week) for this sample is significant for two of the three genetic variants (DdeI: *F = 0.147, p = 0.703; MnlI: *F = 5.586, p = 0.008;TaiI: *F = 5.525, p = 0.008).

Discussion

It may be that SNAP-25 gene variation alters the course of neurodevelopment in individuals who go on to have schizophrenia, or it may influence the synaptogenic role that SNAP-25 plays in adult humans. Another gene of neuro-developmental interest is the BDNF. We have shown that BDNF plays an important role in risk for bipolar mood disorder (Neves-Pereira et al., 2002), child onset depression (Strauss et al., 2002) and possibly in schizophrenia (Muglia et al., 2003). We are currently dissecting the phenotype in these disorders to test whether BDNF is involved more specifically in mood, psychotic symptoms, early onset, cognition, or drug response. Overall, the genetic prediction of these major psychiatric disorders is moving closer to clinical application.