# 45 - Molecular associations (Schizophrenia and Bip

# Molecular associations (Schizophrenia and Bipolar disorder)

© SPMM Course Other implicated chromosomes –  Chr 18 - nearly 4 loci, affective disorders in general;? parent of origin effect)  Chr 21q - both in scz and BPAD.  An X-chromosomal locus to BPAD has been suggested on the basis of the cosegregation of BPAD in some families with color blindness, the glucose-6-phosphate dehydrogenase deficiency, and the coagulation factor IX deficiency. In an extended Finnish pedigree, Xq24-q27.1 was demonstrated to segregate with bipolar disorder.  Low activity allele in COMT gene may be associated with rapid cycling.  Serotonin transporter gene (hSERT) and 5HT2A gene may be associated with modest statistical significance in Seasonal Affective Disorder.

Unipolar depression (MDD)  Age-adjusted risk of MDD to first-degree relatives: 5-30%, relative risk 1.1-4.0. MZ Twin concordance for MDD: 40%. DZ Twin concordance for MDD: 11%. Heritability: Unclear (~20-80%); meta-analysis reports 31-42%. (Data from NCHPEG Empric Risk Data: Retrieved from www.nchpeg.org )  Early onset and recurrent episodes likely increase risks to first-degree relatives. Recurrence risks for unipolar depression could be 50 percent or higher for probands with early-onset and recurrent episodes. While the definition of “early onset” is not entirely clear, research suggests that family members of probands who had onset before age 25-30 years have the highest risk; relatives of probands with onset between ages 25-40 years have an intermediate risk; and relatives of probands with onset after age 40 years have a risk that is only slightly increased over the population risk Schizoaffective disorder  The risk to first-degree relatives for ANY psychiatric disorder is higher in SA disorder than any other psychiatric disorder. The extent of heritability is unclear, although likely in the range of schizophrenia.  Relatives have a higher rate of schizoaffective illness, schizophrenia and bipolar disorder.  The rate of bipolar disorder is high if proband has a schizoaffective-manic presentation. The rate of schizophrenia is high if proband has schizoaffective-depressive presentation. In depressive subtype no elevation in

bipolar risk has been noted in a large cohort (Andreasen 1987).

Molecular associations (Schizophrenia and Bipolar disorder)  G72: The function of G72 (also sometimes referred to as DAOA) may be to, oxidize serine, a potent activator of glutamate transmission via a modulatory site on the NMDA (n-methyl-d-aspartate) receptor. Inadequate DAOA function might be hypothesized to lead to problems in modulating the glutamate signal in areas of the brain such as the prefrontal cortex. A new suggestion is that the major role of G72 may be in maintaining neuronal structure.  Brain-Derived Neurotrophic Factor (BDNF): Several studies have shown that antidepressant administration is associated with increased central BDNF levels in experimental animals, and administration of BDNF itself has been associated with the antidepressant-like activity. Depression has Shared genes – BPAD and Schizophrenia DAO & BDNF – seen more in mood disorders than schizophrenia DISC 1 & NRG – shared with schizophrenia; seen in schizoaffective disorder Dysbindin – seen more in schizophrenia than mood disorders CREB1 (chr2) – unipolar depression

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