

Chem 412 Seminar

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Julian Buss

Genetic Linkage of Dopamine Transporter (DAT1) Gene and Dopamine Receptor D4 (DRD4) Gene to Attention Deficit-Hyperactivity Disorder

Inattention and hyperactivity/impulsivity are hallmarks of attention-deficit hyperactivity disorder. ADHD is a common neurobehavioral disorder afflicting 5-10% of children and adolescents, with around 30-50% of cases persisting into adulthood. Genetic linkage studies coupled with family-based patient studies have identified several polymorphisms, defined by variable numbers of tandem repeats (VNTR), linking dopamine transporter (DAT1) gene and dopamine receptor (DRD4) gene to this comorbid disorder. The DAT1 susceptibility gene is defined by a 40-bp sequence repeated 10 times on chromosome 5p15.3 and the DRD4 susceptibility gene is identified by a 48-bp sequence repeated 7 times on chromosome 11p15.5. Diagnosis of this disorder is based on standardized assessment testing via DSM-IV or DSM-III diagnostic criteria. Treatment after diagnosis typically consists of prescription stimulant medications that act on the dopamine pathway (dopamine agonists). Studies have shown that amphetamine treatments act on the DAT1 gene product to assist in the re-uptake of dopamine to presynaptic terminals. Mutated DRD4 receptors show sub-sensitivity to dopamine and have lower binding affinities due to the 7 VNTRs located in exon-III. Neurobehavioral studies are a relatively hot and new topic and many studies are being conducted in this area.

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