

ROLE OF COPY NUMBER VARIANTS IN ADHD

Investigators from Brazil determined if copy number variants (CNVs) in glutamate metabotropic receptor genes (GRM) were overrepresented in 1038 individuals with ADHD compared to 1057 subjects without ADHD. No significant difference in the total number of CNVs was found in the two population samples ($P=0.326$). The presence of CNVs was associated with lower IQ scores in ADHD samples ($P=0.026$) but not in the sample without ADHD. CNVs in GRM5 were associated with anxiety disorders in ADHD cases ($P=0.002$), but not in subjects without ADHD. CNVs in the glutamatergic genes were associated with cognitive and clinical characteristics of ADHD. (Akutagava-Martins GC, et al. Glutamatergic copy number variants and their role in attention-deficit/hyperactivity disorder. *Am J Med Genet B Neuropsychiatr Genet* 2014 Jul 2).

COMMENTARY. The results of this study suggest a role for glutamate in ADHD. In an investigation of the association between metabotropic glutamate receptor subtype 7-gene polymorphism and treatment response to methylphenidate, children with the G/A genotype had a more pronounced response rate than children with the G/G genotype [1].

References.

1. Park S, et al. *J Child Adolesc Psychopharmacol.* 2014 May;24(4):223-7.

DIAGNOSTIC CRITERIA FOR ADHD

IMPACT OF THE DSM-5 CRITERIA ON PREVALENCE OF ADHD

Investigators at the National Institute of Mental Health, Bethesda, MD, compared the prevalence and clinical correlates of DSM-IV-TR versus DSM-5-defined ADHD and subtypes in a nationally representative sample of US youth based on age-of-onset criterion. Extension of the age-of-onset criterion from 7 to 12 years led to an increase in the prevalence rate of ADHD from 7.38% (DSM-IV-TR) to 10.84% (DSM-5). Severity of ADHD and patterns of comorbidity were not changed by the later age-of-onset, but the group with later age of onset was more likely to be from lower income and ethnic minority families. (Vande Voort JL, He JP, Jameson ND, Merikangas KR. Impact of the DSM-5 attention-deficit/hyperactivity disorder age-of-onset criterion in the US Adolescent population. *J Am Acad Child Adolesc Psychiatry* 2014 Jul;53(7):736-44).

COMMENTARY. The DSM-5 edition released in May 2013 replaces the DSM-IV-TR edition and the changes are as follows: symptoms can now occur by age 12 rather than by age 6, and for adults and adolescents age 17 or older, only 5 symptoms are needed instead of the 6 needed for younger children.

Unchanged is the requirement that symptoms must be present for at least 6 months and they are inappropriate for developmental level; several symptoms were present before age 12 years; several symptoms are present in two or more settings (e.g., at home, school or work; with friends or relatives; in other activities); symptoms interfere with or reduce the quality of social, school, or work; and the symptoms are not better

explained by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, or a personality disorder. A patient may have both ADHD and ASD. Symptoms are now referred to as “presentations”: Combined, predominantly inattentive, and predominantly hyperactive-impulsive presentations.

References.

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders : DSM-5. 5th Ed. Arlington, VA: American Psychiatric Association; 2013:947.

BIOLOGICAL MARKERS IN DIAGNOSIS OF ADHD

BIOLOGICALLY BASED NOSOLOGY FOR ADHD

Investigators at Oregon Health and Science University and other centers attempt to refine subtyping of childhood ADHD by using biologically based behavioral temperament types. Groups were validated using 3 external validators: cardiac measures of respiratory sinus arrhythmia, CNS functioning via functional MRI, and clinical outcomes at 1-year follow-up. Three novel types of ADHD were recognized: mild (normative emotion regulation), surgent (extreme levels of positive approach-motivation), and irritable (extreme levels of negative emotionality, anger, and poor soothability). These types were stable over time and showed unique patterns of cardiac physiological response, resting-state functional brain connectivity, and clinical outcomes. This biologically informed temperament-based typology is thought to provide a superior description of heterogeneity in the ADHD population than any current classification. (Karalunas, et al. Subtyping attention-deficit/hyperactivity disorder using temperament dimensions: toward biologically based nosologic criteria. **JAMA Psychiatry** 2014 Jul 9).

COMMENTARY. The use of a combination of biological markers may help to reduce heterogeneity and to identify homogeneous phenotypes of ADHD. A consensus report of the World Federation of Societies of Biological Psychiatry (WFSBP) task force on biological markers and the World Federation of ADHD determined in 2012 that no reliable ADHD biomarker had been described to date, but some promising candidates (e.g. olfactory sensitivity, substantial echogenicity) exist. The development of ADHD markers is hindered by sample heterogeneity due to etiological and phenotypic complexity and age-dependent co-morbidities [1].

References.

1. Thome J, et al. World J Biol Psychiatry. 2012 Jul;13(5):379-400.

EEG THETA/BETA RATIO IN DIAGNOSIS OF ADHD

Investigators at the Research Institute Brainclinics, Nijmegen, Netherlands, conducted a meta-analysis on the Theta/Beta ratio (TBR) during Eyes Open from location Cz (the electrode halfway between the inion and the nasion) in the EEG of children/adolescents 6-18 years of age with and without ADHD. In nine studies identified with a total of 1253 subjects with and 517 without ADHD, the grand-mean effect size (ES) of the TBR decreased from 0.75 to 0.62 with increasing age, explained by an