

CAUSATIVE FACTORS FOR ADHD

PERINATAL RISK FACTORS

Investigators at Seoul National Hospital, and other centers in Seoul, Korea, studied the genetic, perinatal, and developmental risk factors in 147 children, ages 6 to 15 years, diagnosed with ADHD. Compared to a healthy control group of 502 children without ADHD, the ADHD-Combined subtype children showed more severe externalizing symptoms, more deficits in a continuous performance test, and were more likely to have comorbid disorders. Risk factors for both ADD-Inattentive and ADHD-Combined subtypes included maternal stress during pregnancy, postpartum depression, and changes in the primary caretaker during first 3 years. The ADD-I group was less likely to have received prenatal check-ups and more likely to have had postnatal medical illness than the ADHD-C group. The genotype frequencies of the dopamine transporter (DAT1) and serotonin transporter-linked polymorphisms were the same for the two subtypes. The inattentive subtype, ADD-I, differs from the combined subtype, ADHD-C, in having less severe symptoms, less comorbidity, and fewer environmental risk factors. (Park S, Cho SC, Kim JW, et al. Differential perinatal risk factors in children with attention-deficit/hyperactivity disorder by subtype. **Psychiatry Res** 2014 May 28).

COMMENTARY. In addition to the genetic factor, acquired environmental causes may contribute to the etiology of ADHD and these are classified according to the time of their occurrence: 1) *pregnancy- and birth-related (pre- and perinatal) risk factors*, and 2) *childhood (postnatal) illnesses*. Nutritional and dietary factors also play a role; of the numerous environmental causes listed, a deficiency of omega-3 fatty acid and treatment with supplemental fatty acid are receiving most attention [1][2].

Treatment is occasionally determined by etiological environmental factors (e.g. thyroid, dietary), but usually a correction of deficient catecholamine metabolism using methylphenidate or amphetamine medication is the primary aim of treatment. Variability of response to medication may be explained by the occurrence and variability of environmental etiological factors. Gene-environment interaction is increasingly recognized as an important mechanism in the etiology and development of ADHD [3]. In therapy of ADHD, a combination of stimulant medication and supplemental omega-3 fatty acid may provide a better response than stimulant alone [4].

In previous clinical and animal studies, patients with the highest levels of motor activity were more likely to respond to methylphenidate therapy [5][6]. In addition, the most active patients had the highest number of neurological soft-sign abnormalities, and in animals rendered hyperactive by prefrontal cerebral lesions, the more severe brain damage [5]. It is not surprising that the ADHD-C patient group in the Korean study [7] have more severe symptoms compared to the ADD-I subtype, greater comorbidity, and more evidence of environmental etiologic factors.

References.

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ROLE OF THYROID STIMULATING HORMONE RECEPTOR IN ADHD

Investigators from Meijo and Nagoya Universities, Nagoya, Japan, studied the role for thyroid stimulating hormone receptor (TSHR) in TSHR knockout mice with phenotypes of ADHD such as hyperactivity, impulsiveness, and impairment of short-term memory. Administration of methylphenidate reversed impulsiveness, aggression and object recognition memory impairment. Monoaminergic changes in the brain, including an increase in the ratio of homovanillic acid/dopamine, were accompanied by an increase in the expression of noradrenaline transporter in the frontal cortex. These changes were attributed to the loss of the TSH-TSHR pathway, suggesting a novel role for TSHR in behavioral and neurological phenotypes of ADHD. (Mouri A, et al. Thyrotropin receptor knockout changes monoaminergic neuronal system and produces methylphenidate-sensitive emotional and cognitive dysfunction. *Psychoneuroendocrinology* 2014 Jun 24;48C:147-161).

COMMENTARY. Dysregulation of TSH and its receptor TSHR is implicated in the pathophysiology of ADHD, and ADHD is reported in association with resistance to thyroid hormone, a disease caused by a mutation in the thyroid hormone receptor B (TRB) gene. Investigators at the National Institutes of Health, Bethesda, MD, evaluated the presence and severity of ADHD in 18 families with a history of generalized resistance to thyroid hormone. Among the children, 19 of 27 subjects resistant to thyroid hormone (70%) and 5 of 25 unaffected subjects (20%) met criteria for ADHD ($P < 0.001$). The odds of having ADHD were 3.2 times higher for affected male subjects than for affected females and were 2.7 times higher for unaffected male subjects than for unaffected female subjects. The mean symptom score was 2.5 times higher in the affected group than in the unaffected group (7.0 vs 2.8, $P < 0.001$). The frequency of other psychiatric diagnoses was similar in the two groups. In this study sample, ADHD is strongly associated with generalized resistance to thyroid hormone [1]. In a later Australian study, the prevalence of thyroid hormone abnormalities in children with ADHD attending the State Child Development Centre in Perth was 2.3%, and none had generalized resistance to thyroid hormone [2]. Routine screening for thyroid hormone abnormalities in children with ADHD is supported by the NIH study but not by the Australian study. We recommend screening of patients with a family history of thyroid dysfunction [3].

References.

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