Causes of attention-deficit/hyperactivity disorder (ADHD)

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Abstract

In this paper we aimed to discuss about a controversial topic: the causes of attention-deficit/hyperactivity disorder. To achieve this objective we made a synthesis of the most relevant research. The etiology is discussed in the literature in the field of genetics; the exact causes have not been yet fully elucidated. ADHD seems to come from a combination of several genetic and environmental factors that alter brain developing.

Keywords: *ADHD, environmental factors, genetic factors, executive functions, epidemiological factors, adults, childhood*

I. INTRODUCTION

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Approximately 80% of children enrolled in school in the first grade during 2002 were affected by ADHD in the US and between 30 and 65% are assumed to have behavioral disorders during adolescence (Arnsten, 2006; Rutter, 2011).

In the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, the symptoms occurred in ADHD were limited to those associated with cognitive (attention deficit) and behavioral (hyperactivity/impulsivity) deficits, while deficient emotional self-regulation, a relevant source of morbidity, was left out.

According to the American Psychiatric Association (2013), there are three types of ADHD:

1. Combined/mixed subtype: This subtype can be used if six (or more) symptoms of inattention and six (or more) symptoms of hyperactivity-impulsivity have persisted for at least 6 months. Most children with ADHD have mixed type.
2. ADHD Predominantly Inattention: Six or more of these symptoms must be present for at least 6 months, be inconsistent with the child's developmental level, and have a negative effect on their social and academic activities. In order to be endorsed, the following must occur:

a. Fails to pay close attention to details
b. Has trouble sustaining attention
c. Doesn't seem to listen when spoken to directly
d. Fails to follow through on instructions and fails to finish schoolwork or chores
e. Has trouble getting organized
f. Avoids or dislikes doing things that require sustained focus/thinking
g. Loses things frequently
h. Easily distracted by other things
i. Forgets things

3. ADHD Predominantly Hyperactivity and Impulsivity: six or more of these symptoms must be present for at least 6 months, be inconsistent with the child's developmental level, and have a negative effect on their social and academic activities. In order to be endorsed, the following must occur:

a) Fidgets with hands/feet or squirms in chair
b) Frequently leaves chair when seating is expected
c) Runs or climbs excessively
d) Trouble playing/engaging in activities quietly
e) Acts “on the go” and as if “driven by a motor”
f) Talks excessively
g) Blurts out answers before questions are completed

h) Trouble waiting or taking turns

i) Interrupts or intrudes on what others are doing.

Specify if:

- Mild: Six or only slightly more symptoms are endorsed and impairment in social or school functioning is minor
- Moderate: Symptoms or impairment is between mild and severe
- Severe: Many symptoms are above required, 6 are endorsed and/or symptoms are severe; impairment in social or school functioning is severe (American Psychiatric Association, 2013).

II. ATTENTION DEFICIT/HYPERACTIVITY DISORDER - ETIOLOGY IN CHILDHOOD

The etiology is discussed in the literature in the field of genetics, its exact causes have not yet been fully elucidated. ADHD seems to come from a combination of several genetic and environmental factors that alter the developing brain, resulting in structural and functional abnormalities (Schuch, Utsumi, Costa, Kulikowski, & Muszkat, 2015).

There are epidemiological studies in which it is alleged that ADHD is a disorder of neural development, characterized by a pattern of behavior that could affect the performance of people diagnosed in the social, educational and professional environments.

The main objectives of this type of research are genes encoding the dopamine components of the dopaminergic, noradrenergic and serotonergic system. Dopamine is a catecholamine neurotransmitter involved in controlling movement, in learning, mood, emotion, cognition, sleep and memory. It is a natural precursor of norepinephrine and epinephrine, of the catecholamine with stimulating action on the central nervous system (Purper-Ouakil, Ramoz, Lepagnol-Bestel, Gorwood, & Simonneau, 2011).

Dopaminergic disorders are associated with several neuropsychiatric disorders. Dopamine active transporter 1 (DAT1, also known as SLC6A3) was firstly investigated because the protein carrier is involved in the modulation of the effects of stimulating drugs commonly used to treat ADHD. Dopamine receptors, particularly DRD4 and DRD5, are also strongly associated with the development of ADHD (Ptacek, Kuželová, & Stefano, 2011).

There have been few studies of the molecular genes related to the noradrenergic system. Such studies have focused mainly on the gene encoding of the dopamine-beta-hydroxylase (DβH), which catalyze the degradation of dopamine into norepinephrine, with direct effects on the overall level of dopamine in the brain. Serotonergic system may also participate in the

etiology of ADHD, in particular serotonin receptor (HTR1B) and transporter genes (SCL6A4) (Banaschewski Becker Scherag, Franke & Coghill, 2010; Akutagava-Martins et al., 2014).

Environmental factors associated with ADHD, epidemiological, include psychosocial adversity, maternal mental illness, domestic violence, stress, smoking and alcohol consumption in prenatal and childhood. In a longitudinal study conducted in Brazil by Pires and his colleagues, it was tried to correlate family environment and pregnancy diagnosis of ADHD in children and symptoms described by various informants (mothers and teachers). These authors found that family dysfunction, lack of social support for mothers, traumatic life events and disagreements during pregnancy were associated with ADHD (Pires da Silva, & de Assis, 2013).

Exposure to tobacco smoke prenatal and/or childhood could be extremely harmful to the neurodevelopment of the child. It induces changes that alter the dynamics of cells, triggering a cascade of risk factors that affect the neurotoxic sensory processing unwholesome action of neuronal nicotinic acetylcholine receptors (nAChRs) by exposure to nicotine modulates synaptic plasticity in early childhood; most likely endogenous influences; cholinergic transmission and modifies the cell, physiological processes and behavioral courses in critical periods of development processes (Heath, Horst & Picciotto, 2010).

Studies on ADHD have identified some interactions between smoke exposure during prenatal and variants specific genotypic, particularly affecting DAT1, DRD4 and sub acetylcholine receptor alpha-4 (CHRNA4) (Becker, El-Faddagh, Schmidt, Esser, & Laucht , 2008). For example, children with two copies of a DAT polymorphism had a higher risk of ADHD when they also had exposure to prenatal maternal smoking (Kahn, Khoury, Nichols, & Lanphear, 2003).

Some evidence suggests that prenatal exposure to alcohol causes pathological changes that increase the risk of ADHD, mainly due to the effect of alcohol on modulating the expression transport system of catecholamines. Kim et al. found that prenatal exposure to ethanol in significant concentrations physiologically induced phenotypes of hyperactive behavior, inattentiveness and impulsiveness in rats and their offspring are associated with increased protein expression DAT and cuts ties of methyl CpG 2 (MeCP2), protein being expressed in the prefrontal cortex and striatum (Kim et al., 2013).

Neuro-imaging studies indicates that ADHD is a result of an operation in the anatomical abnormalities and a connectivity in the fronto-striatal line, frontal-temporal, fronto-parietal and/or fronto-striatal-parietal-cerebellar circuits. In addition to the circuits mentioned, structures and specific areas of the brain have also received attention, and include among others, the prefrontal cortex, previously caudate cingulate cortex, globus pallidus, parietal regions, temporal regions, corpus callosum, splenium, vermis of the cerebellum and cerebrum (Weyandt, Swentosky, & Gudmundsdottir, 2013).

Neuropsychological studies detected functional changes in neural networks in the brain areas specific issues related to executive functions (Rubia, 2011; O'Brien, Dowell, Mostofsky, Denckla, & Mahone, 2010). Executive functions represent a set of abilities that help the person adapt their behavior to the context in which they are (Schuch et al., 2015). Weyandt et al. (2013) have suggested that executive dysfunction is the headline deficit in ADHD.

III. ATTENTION DEFICIT/HYPERACTIVITY DISORDER - ETIOLOGY IN ADULTS

In approximately 5% of people diagnosed in childhood with ADHD, this diagnosis is also maintained during adulthood (Bonvicini, Faraone, & Scassellati, 2016). In recent years, genome-wide molecular genetic studies in adult form of attention deficit/hyperactivity led to the identification of LPHN3 and CDH13 as novel genes associated with ADHD across the lifespan. LPHN3 was associated with ADHD in a large sample of children and adults, and subsequently replicated in an independent adult form of ADHD sample (Martinez, Muenke, & Arcos-Burgos, 2011; Arcos-Burgos et al., 2010).

Bonvicini, Faraone, & Scassellati (2016) have discovered a significant role of BAIAP2 and DHA in the etiology of ADHD exclusively in adults. The DHA was associated with hyperactivity in adults with ADHD, and BAIAP2 is expressed at higher levels in the left human cerebral cortex and participates in neuronal proliferation, survival and maturation (Ribasés et al., 2009). This association was found for ADHD in adults, but not in children, suggesting a distinct genetic load between persistent and remitting ADHD (Ribasés Ramos-Quiroga, Hervás, Bosch, Bielsa, Gastaminza, & Bayés, 2009).

IV. CONCLUSIONS

Unquestionably, ADHD is a complex disorder (which affects men more than women) and there is no simple explanation despite a significant amount of research, which try to isolate the causes of this disorder (Thapar, Cooper, Eyre & Langley, 2013). None of the studies led to the identification of genes significantly related to the occurrence of ADHD, but rather explains small part of their contribution to the occurrence of this disorder (Weyandt, Swentosky, & Gudmundsdottir, 2013). ADHD seems to come from a combination of several genetic and environmental factors that alter brain developing, resulting in structural and functional abnormalities (Schuch, Utsumi, Costa Kulikowski, & Muszkat, 2015).

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