EXPOSURE TO ENVIRONMENTAL AND LIFESTYLE FACTORS AND ATTENTION-DEFICIT / HYPERACTIVITY DISORDER IN CHILDREN – A REVIEW OF EPIDEMIOLOGICAL STUDIES

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Abstract
Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders in children. Although the mechanisms that lead to the development of ADHD remain unclear, genetic and environmental factors have been implicated. These include heavy metals and chemical exposures, nutritional and lifestyle/psychosocial factors. The aim of this review was to investigate the association between ADHD or ADHD-related symptoms and widespread environmental factors such as phthalates, bisphenol A (BPA), tobacco smoke, polycyclic aromatic hydrocarbons (PAHs), polyfluoralkyl chemicals (PFCs) and alcohol. Medline, PubMed and Ebsco search was performed to identify the studies which analyze the association of prenatal and postnatal child exposure to environmental toxicants and lifestyle factors and ADHD or ADHD-related symptoms. The review is restricted to human studies published since 2000 in English in peer reviewed journals. Despite much research has been done on the association between environmental risk factors and ADHD or ADHD symptoms, results are not consistent. Most studies in this field, focused on exposure to tobacco smoke, found an association between that exposure and ADHD and ADHD symptoms. On the other hand, the impact of phthalates, BPA, PFCs, PAHs and alcohol is less frequently investigated and does not allow a firm conclusion regarding the association with the outcomes of interest.

Key words: Children, Environmental toxicants, Attention–deficit/hyperactivity disorder, Inattention, Impulsivity

INTRODUCTION
Attention–deficit / hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders in children, with an estimated pooled worldwide prevalence in children and adolescents of 5.3% (95% CI: 5.0–5.6) [1]. When the children are considered alone, the range for prevalence is about 5–10%, whereas when adolescents are considered by themselves, the range is lower (about 2.5–4%) [1,2]. Like many other childhood-onset behavioural disorders, ADHD is diagnosed more frequently in boys than girls [3,4]. Children diagnosed with ADHD are a heterogeneous population sharing common symptoms, including inattention, impulsivity, and, in some cases, hyperactivity, or a combination of
the symptoms. Inattention is identified when child is easily distracted and unable to keep his/her mind on single task for extended periods of time. Impulsivity can be recognized by lack of control or restraint and hyperactivity by child’s constant restlessness. Children with ADHD are at increased risk for conduct disorder, antisocial behaviour and drug abuse later in life [3,5,6]. Although the mechanisms that lead to the development of ADHD remain unclear, genetic and environmental factors have been implicated. These include heavy metals and chemical exposures, nutritional and lifestyle/psychosocial factors.

This paper reviews the literature published since 2000 investigating the association between ADHD or ADHD-related symptoms and widespread environmental factors such as phthalates, bisphenol A (BPA), tobacco smoke, polycyclic aromatic hydrocarbons (PAHs), polyfluoroalkyl chemicals (PFCs) and alcohol.

Criteria for inclusion of studies into the review
Medline, PubMed and Ebsco search was performed to identify the studies which analyze the association of prenatal and postnatal child exposure to widespread environmental toxicants and ADHD or ADHD-related symptoms. Relevant studies were also identified via review of references cited in all published studies. The review is restricted to human studies published since 2000 in English in peer reviewed journals. The following keywords were used to identify relevant papers: ADHD, hyperactivity, inattention, impulsivity, pregnancy, prenatal period, child, environment, environmental exposures, chemicals, lifestyle factors, maternal smoking, passive smoking, PAHs, phthalates, BPA, PFCs and alcohol. For each factor we reviewed:

- study design and population,
- sources of exposure and methods used for its assessment,
- assessment of ADHD or ADHD-related symptoms,
- confounding factors included in analysis,
- the proposed mechanism by which the exposure is linked with ADHD-related neurobehavioural changes.

Out of total 72 articles identified, 40 meet eligibility criteria and have been included in the present review.

PHTHALATES AND ADHD OR ADHD SYMPTOMS
Phthalates are a family of industrial chemicals that have been used for a variety of purposes. They are added to plastics applied in the manufacture of children’s toys and medical devices to make them soft and flexible as well as added to cosmetics as a vehicle for fragrance. Because phthalates are ubiquitous in daily life, the potential consequences of human exposure to phthalates have raised concerns in the general population. Animal studies have also reported that some phthalates might cause hyperactivity similar to the clinical syndrome of ADHD found in children [7].

Several mechanisms of adverse neurodevelopmental outcomes in humans exposed to phthalates are postulated. Phthalates may interfere with the thyroid hormone system [8,9], lipid signal transduction pathways [10], decrease the number of midbrain dopaminergic neurons, reduce tyrosine hydroxylase biosynthetic activity [11] and tyrosine hydroxylase immunoreactivity [12], and exhibit antiandrogenic activity [13]. Phthalates have been shown to cause hyperactivity in rats, possibly through effects on the dopamine system [12,14].

The first studies investigating the relationship between prenatal phthalate exposure and ADHD-related behaviours and ADHD were published by Engel et al. [15,16] and Kim et al. [17] (Table 1). In the study performed among neonates enrolled into a multiethnic birth cohort at the Mount Sinai School of Medicine in New York City, maternal urinary concentrations of phthalate metabolites and neonatal behaviour measured within 5 days of birth were evaluated. There were strong, inverse associations