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Neuroscience and Biobehavioral Reviews 30 (2006) 24–41
NEUROSCIENCE AND BIOBEHAVIORAL REVIEWS
www.elsevier.com/locate/neubiorev

Review

Maternal smoking, drinking or cannabis use during pregnancy and neurobehavioral and cognitive functioning in human offspring

Anja C. Huizink*, Eduard J.H. Mulder

Erasmus Medical Center, Department of Child and Adolescent Psychiatry, P.O. Box 2060, 3000 CB Rotterdam, The Netherlands

Received 29 April 2004; revised 16 February 2005; accepted 18 April 2005

Abstract

Teratological investigations have demonstrated that agents that are relatively harmless to the mother may have significant negative consequences to the fetus. Among these agents, prenatal alcohol, nicotine or cannabis exposure have been related to adverse offspring outcomes. Although there is a relatively extensive body of literature that has focused upon birth and behavioral outcomes in newborns and infants after prenatal exposure to maternal smoking, drinking and, to a lesser extent, cannabis use, information on neurobehavioral and cognitive teratogenic findings beyond these early ages is still quite limited. Furthermore, most studies have focused on prenatal exposure to heavy levels of smoking, drinking or cannabis use. Few recent studies have paid attention to low or moderate levels of exposure to these substances. This review endeavors to provide an overview of such studies, and includes animal findings and potential mechanisms that may explain the mostly subtle effects found on neurobehavioral and cognitive outcomes. It is concluded that prenatal exposure to either maternal smoking, alcohol or cannabis use is related to some common neurobehavioral and cognitive outcomes, including symptoms of ADHD (inattention, impulsivity), increased externalizing behavior, decreased general cognitive functioning, and deficits in learning and memory tasks.

Keywords: Prenatal; Exposure; Alcohol; Nicotine; Cannabis; Neurobehavioral Deficits; Cognitive deficits

Contents

1. Background and theoretical framework . . . 25
2. Perturbations in neurodevelopment . . . 25
3. Methodological issues . . . 26
   3.1. Study design . . . 26
   3.2. Measurement of exposure variables . . . 26
   3.3. Outcome measures . . . 27
   3.4. Statistical issues . . . 27
   3.5. Interpretation of results . . . 28
4. Smoking during human pregnancy . . . 28
   4.1. Neurobehavioral outcomes related to prenatal maternal smoking . . . 28
   4.2. Cognitive function after prenatal maternal smoking . . . 29
   4.3. Prenatal smoking effects in animal pregnancy . . . 30
   4.4. Mechanisms related to prenatal smoking and offspring outcomes . . . 30
5. Alcohol use during human pregnancy . . . 31
   5.1. Neurobehavioral effects of prenatal (moderate) maternal drinking . . . 31
   5.2. Cognitive function after prenatal maternal drinking . . . 32

* Corresponding author. Tel.: +31 10 4637072; fax: +31 10 4637006.
E-mail address: a.c.huizink@erasmusmc.nl (A.C. Huizink).

0149-7634/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.neubiorev.2005.04.005

5.3. Alcohol effects in animal pregnancy . . . 32
5.4. Mechanisms related to prenatal maternal drinking and offspring outcomes . . . 33
6. Cannabis use in human pregnancy . . . 34
6.1. Neurobehavioral outcomes after prenatal cannabis exposure . . . 34
6.2. Cognitive function after prenatal cannabis exposure . . . 34
6.3. Cannabis effects in animal pregnancy . . . 35
6.4. Mechanisms related to prenatal cannabis use and offspring outcomes . . . 35
7. Discussion . . . 35
References . . . 37

1. Background and theoretical framework

Studies of behavioral and cognitive effects of in-pregnancy exposures, such as stress and undernutrition, often treat prenatal substance use as a confounding variable without addressing the role of these lifestyle factors, such as smoking, drinking, or cannabis use, on the offspring as a direct or interactive agent. However, drug abuse during pregnancy has also been related to postnatal consequences, manifested as alterations in behavior and cognition.

Research into these mostly subtle associations between prenatal smoking, drinking or cannabis use and offspring outcome utilizes the concepts and methods of behavioral teratology (Vorhees, 1989). The identification of the fetal alcohol syndrome (FAS) in the 1970s was an important milestone in bringing the value of the behavioral teratological approach to human studies. Since the description of FAS, there has been a dramatic increase in the number of research reports examining the neurobehavioral and cognitive consequences in young babies who have been exposed to a myriad of drugs during prenatal development (Fried, 2002).

Over the years, teratological investigators have demonstrated that agents that are relatively harmless to the mother may have significant negative consequences to the fetus (Annau and Eccles, 1986). Vorhees (1989) has modified and extended general teratological principles to research in behavioral teratology, resulting in two major postulates (Fried, 1998): (1) vulnerability of the central nervous system (CNS) to injury extends throughout the fetal, neonatal periods and beyond the infancy stage, including all aspects of nervous system development (e.g. neurogenesis, neuronal differentiation, arborization, synaptogenesis, functional synaptic organization, myelination, gliogenesis, glial migration and differentiation), and (2) the most frequent manifestation of injury to the developing CNS does not result in nervous system malformations but rather in functional abnormalities that may not be detectable at birth.

Substances that are most frequently used by pregnant women include nicotine, alcohol, and cannabis. Although there is a relatively extensive body of literature that has focused upon birth and behavioral outcomes in newborns and infants after prenatal exposure to maternal smoking, drinking and, to a lesser extent, cannabis use, information on neurobehavioral and cognitive teratogenic findings beyond these early ages is still quite limited. Furthermore, most studies have focused on prenatal exposure to heavy levels of smoking, drinking or cannabis use, whereas only few recent studies have paid attention to low or moderate levels of exposure to these substances. This review summarizes the studies that have addressed the possible association of low to moderate levels of maternal smoking, drinking or cannabis use during pregnancy with neurobehavioral and cognitive outcomes in the human offspring. This review aims to examine (1) whether in particular low to moderate prenatal exposure to maternal smoking, drinking or cannabis use results in common or specific neurobehavioral and cognitive outcomes in the human offspring, and (2) which mechanisms may account for the relationship between prenatal substance exposure and neurobehavioral and cognitive outcomes in offspring. To address the second aim, some findings from animal studies are included as well, because they may increase our insight into the possible mechanisms underlying the potential harmful effects of maternal smoking, drinking or cannabis use during pregnancy on later offspring behavior and cognition. Furthermore, the use of animal models permits control of environmental factors, which may become critical to validate findings in humans. However, when generalizing the results of animal models to humans there are some caveats. For instance, the species differ in the timing of brain maturation. It is important to scale developmental processes in animals to those in humans, and it is particularly important to take into account differences in the stage of brain development at the time of birth (Huizink et al., 2004). Besides, species differences in vulnerability to substances can exist (Goodlett and Horn, 2001).

2. Perturbations in neurodevelopment

During fetal development, every area, system, and circuit of the brain has its growth spurts. If the area does not fully develop in those assigned periods, the developing brain does not compensate; the area is left with a deficit. Genetic expression moves on to develop the next scheduled area (Watson et al., 1999). Thus, the timing of the perturbation in neurodevelopment may be critical in determining if a neurobehavioral or cognitive deficit results, and the timing