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Invited Commentary | Substance Use and Addiction

Association of Smoking During Pregnancy With Compromised Brain Development in Offspring

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The study by Zou et al[1] provides new insights into the association between maternal smoking during pregnancy and offspring brain development in preadolescence. The study is part of the Generation R Study, a prospective population-based cohort study in Rotterdam, the Netherlands. The present study included a total of 2704 singleton children, of whom 2102 (77.7%) were unexposed, 364 (13.5%) were exposed throughout pregnancy, and 238 (8.8%) were exposed only during the early stages of pregnancy. Participating children underwent magnetic resonance imaging assessment of the brain at a mean (SD) age of 10.1 (0.6) years. Exposure to smoking throughout pregnancy was associated with lower total brain volume, lower cerebral gray matter volume, lower cerebral white matter volume, smaller surface area, and less gyrification compared with no exposure.

The fetal brain is sensitive to the effects of smoking during pregnancy.[2] The neurotoxic effects of smoking are supported by withdrawal symptoms seen in newborns exposed to smoking.[2] In addition, smoking exposure has been linked with a significant range of neurobehavioral challenges during the first year of life.[3] Smoking exposure has been linked with smaller head circumference at birth, reflecting the size of the brain of the newborn.[2] The study by Zou et al[1] provides evidence that persistent exposure to maternal smoking during pregnancy might affect brain morphology 10 years later. It is noteworthy that 285 of the 364 exposed children (78.3%) had been exposed to fewer than 10 cigarettes per day.[1] Thus, only reducing the number of smoked cigarettes per day may not provide protection against the harmful effects of smoking during pregnancy.

A previous review by Bublitz and Stroud[4] showed that smoking exposure during pregnancy also has long-lasting adverse effects on brain function among adolescents assessed with functional magnetic resonance imaging. Those investigators found a lack of coordination across a large and diverse set of brain regions, including frontal, temporal, and parietal lobes and cerebellum during information and auditory processing among exposed children. The smoking exposure–related variations in brain development could translate to later maladjustment and mental health problems among adolescents.[4]

Many of the mechanisms whereby smoking during pregnancy may affect brain development and later mental health are epigenetic in nature.[5] Smoking exposure is one of the most significant environmental factors associated with DNA methylation alterations. Thus, Zou et al[1] further studied whether previously identified smoking-associated DNA methylation patterns at birth mediated the observed associations. Variance in DNA methylation was indexed using a methylation risk score of 5643 5′-C-phosphate-G-3′ (CpG) sites rather than smoking-related CpG sites at an individual level. The neonatal DNA methylation risk score did not mediate the association between prenatal exposure to maternal smoking and brain morphology. Studies considering epigenetic pathways as a causal mechanism are only beginning to emerge,[5] and the study by Zou et al[1] is one of the first on smoking and brain development. Thus, more research is needed on this topic.

Zou et al[1] showed that children exposed to smoking only in the first trimester showed no differences in brain morphology compared with unexposed children. Thus, most of the harmful effects of smoking on brain development can be avoided if smoking cessation occurs as soon as possible during pregnancy. This finding is encouraging and emphasizes the importance of smoking cessation during pregnancy. It is important to exploit such information when encouraging pregnant women to quit smoking.

The biological mechanisms behind the potential effects of smoking exposure at the molecular level remain unclear. Nicotine is known to be responsible for many of the harms of smoking.[6] There is undisputed information on the harmful effects of nicotine in animal experiments, in which nicotine acts as a neuroteratogen.[7] Information on the effect of nicotine itself on fetal brain development is urgently needed because of the epidemic of new nicotine products, such as increasing use of electronic nicotine delivery systems. Convincing data on the fetal toxicity of nicotine are available[6,7]; thus, there is no reason to wait for the results of epidemiological studies on the effects of nicotine itself. All efforts should be made to help pregnant women quit smoking as well as to stop the use of all other nicotine-containing products before pregnancy or as early as possible during pregnancy.

In summary, maternal smoking during pregnancy may exert long-lasting adverse effects on the brain development of offspring. The plausible role of nicotine must be considered owing to the increasing use of nontobacco products that contain nicotine. The goal should not only be smoke-free but also nicotine-free pregnancy, which would allow optimal brain development of offspring.

ARTICLE INFORMATION

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