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Causal Modeling of Prenatal Smoking Effects

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Introduction

Maternal smoking during pregnancy (SDP) is associated with increased risk for various offspring developmental problems, included pregnancy-related problems,[1] cognitive deficits,[2] unhealthy physical traits,[3] and later social and behavioural difficulties.[4] Research over the past two decades has focused on understanding the mechanisms through which SDP influences development. Most research has suggested that fetal exposure to the chemicals in cigarettes specifically causes developmental problems.[1,4] But, maternal SDP does not occur in isolation; SDP is correlated with many risks that may influence both maternal SDP and cause problems in the offspring. Questions, therefore, remain about the degree to which maternal SDP actually causes developmental problems in offspring or whether maternal SDP is a marker for other causal influences. A number of recent studies have used advanced methodological designs[5-6] to rigorously test alternative explanations for the association between SDP and developmental outcomes.[7]

Subject

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Social science research should play a large role in directing public policy initiatives, especially those targeting families, by identifying modifiable causal risk factors for developmental problems.[8-12] When research identifies modifiable causal risk factors, interventions can help reduce exposure to those risks. If, in contrast, basic research rules out a causal inference from a putative risk factor, then subsequent research can identify the true causal influences and open up the possibility of new and more successful interventions.[7] Rigorous research on maternal SDP, therefore, will help influence public policy decisions by identifying true causal risk factors.

Problems

The problems with examining the causal effects of maternal SDP stem from the difficulties researchers have studying risk factors that cannot be experimentally manipulated. Because random assignment in human populations is the only scientific method that permits researchers to make definitive causal inferences, researchers must rely on alternative research designs to help rule out all plausible alternative explanations for the associations between risk factors and outcomes.[5,8-9] As such, research on SDP must take into consideration correlated environmental factors. Women who smoke while pregnant are more likely to use other substances while pregnant, use and abuse substances after pregnancy, have psychological problems, receive less education, and live in poorer neighbourhoods, to name a few examples.[2] And, research must take into consideration the role of possible confounding genetic factors. Because behaviour genetic research has found that genetic factors influence maternal SDP,[13-14] genetic factors that are passed down from parents to their children could account for the increased risk of problems in offspring exposed to SDP.

Research Context

Most research has suggested that SDP causes problems during pregnancy and psychosocial problems.[1,4] The association between SDP and offspring problems are (a) generally robust to the use of statistical controls for measured risks that are correlated SDP, (b) found across various studies, and (c) generally consistent with basic research on SDP conducted in animals.[15] But, questions remain about the generalizability of findings from animal studies to humans and the ability of the existing human research to adequately account for all possible alternative environmental and genetic explanations.[4,13,16-18]

Key Research Questions

The key research questions concern the degree to which SDP (a) specifically causes later developmental problems or (b) is merely a marker for other risk factors that cause later developmental problems. If maternal SDP does not have a causal influence on developmental problems, subsequent research will need to specify the correlated risk factors that are responsible for the increased problems found in offspring exposed to SDP. Such questions require researchers to use many different research designs, especially *quasi-experimental designs*, methods that can pull apart risk factors that typically co-occur.[5-6]

Recent Research Results

Researchers recently have used a number of quasi-experimental designs to study maternal SDP.[7] A number of studies have used the sibling-comparison design, the comparison of siblings who were differentially exposed to SDP.[19-21] Researchers also have utilized the children of twins approach,[13,22] a comparison of differentially exposed offspring of adult twins. Some studies have used a novel *in vitro* fertilization (IVF) cross-fostering design[23] that include offspring who are not genetically related to their birth mother. Each of the designs help account for genetic factors passed down from parents to children, as well as environment confounds.

Recent sibling comparison, children of twins, and IVF cross-fostering studies have found that SDP is independently associated with adverse birth outcomes, such as early gestational age/preterm birth and low birth weight.[1,7,13,24-25] A recent sibling comparison study also found that SDP is independently associated with increased risk for infant mortality.[26] The results are consistent with a specific causal association because the designs helped account for correlated genetic and environmental factors that could otherwise explain the associations between SDP and pregnancy-related problems.

A number of recent quasi-experimental studies strongly suggest SDP does not cause later cognitive and psychosocial problems, however. Sibling comparison studies of offspring childhood conduct problems,[24,27] adult criminality,[28] intellectual abilities,[29-30] academic achievement[31] and adolescent obesity[3] found that family background factors (genetic and/or environmental factors shared by siblings) account for the association between SDP and each trait. These findings also are consistent with recent results from IVF cross-fostering studies of childhood conduct problems[25] and attention-deficit/hyperactivity disorder,[32] as well as a children of twins study of offspring ADHD problems.[33] The findings strongly suggest that risk factors that are correlated with SDP cause these later developmental problems, not the *teratogenic* effects of SDP.

Research Gaps

Most of the quasi-experimental studies on SDP have been based on large epidemiological studies, which have not used precise measurement of SDP or developmental outcomes. Future research, thus, will need to use combine rigorous quasi-experimental methods with more precise assessments. Because the recent quasi-experimental research on the association between SDP and later psychosocial development is not consistent with findings from animal studies[15] more translational research is necessary to better understand the discrepancies between the two research approaches. And, most of the quasi-experimental research only has ruled out a causal influence of SDP on later cognitive and psychosocial outcomes; future research will need to identify the true causal influences. Finally, most of the quasi-experimental research has focused on understanding the main effect of SDP on development. There is also a great need to explore whether particular individuals are more susceptible to the effects of SDP.[34]

Conclusions

Research focused on identifying the causal processes through which SDP influences offspring development needs to use methods that can delineate possible teratogenic effects of SDP from correlated environmental and genetic factors. Research using various quasi-experimental designs suggests that maternal SDP is independently associated with pregnancy-related problems, such as shortened gestational age and low birth weight. Because the results have been replicated in numerous samples and with various research methods, each with their own strengths and weaknesses, a strong causal inference can be drawn with respect to these outcomes. One sibling comparison study, which will need to be replicated, also found that SDP is robustly associated with increased risk for infant mortality. The statistical association between SDP and later developmental difficulties, such as behavioural and academic problems, however, do not appear to be due to the specific effects of maternal SDP on the developing fetus. Rather, environmental and genetic factors that are correlated with maternal SDP are responsible for the increased risk of later problems in offspring exposed to maternal SDP.

Implications for Parents, Services and Policy

First and foremost, the results of the recent research on SDP emphasize that the reduction of maternal SDP remains a major public health priority. Again, recent studies strongly suggest that SDP causes increased pregnancy-related problems and (perhaps) infant mortality. Pregnant

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women, as well as women of childbearing age who are sexually active, should strive to reduce or eliminate their smoking. Service providers and policy makers should help implement empirically supported smoking cessation programs in these populations.

Second, the recent research on SDP emphasizes the need for policy makers and service providers to understand how social science research can and should direct policy initiatives.[8-9] In particular, the recent research suggests that reducing maternal SDP probably will not reduce many of the later problems that have been associated with SDP. Maternal SDP is correlated with many risks, and the recent findings from quasi-experimental designs strongly suggest that comprehensive interventions with pregnant women and young families, which target multiple risk factors,[35] are required to help offspring of women who smoke during pregnancy.

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