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Short Communication

Association between maternal smoking during gestation and offspring objectively-measured physical activity behavior during adolescence

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ABSTRACT

Background: Although inconclusive, previous work demonstrates an association between maternal smoking and offspring cardiovascular-related biomarkers. Whether maternal smoking is associated with offspring cardiovascular-related behaviors (e.g., physical activity) has yet to be examined, which was this study's purpose. **Methods:** Data from the 2003-2006 National Health and Nutrition Examination Survey was examined. Adolescent participants (N=1,033; 12-15 yrs) completed a survey assessing their biological mother's smoking behavior during gestation and also wore an accelerometer for up to 7 days. Three mutually exclusive groups were created, including Group 1) mother did not smoke during participants pregnancy; Group 2) mother smoked during entire pregnancy; and Group 3) mother quit smoking during pregnancy. **Results:** After adjustments, moderate-to-vigorous physical activity was not different in adolescents who belonged to Group 2 vs. 1 (RR = 1.12; 95% CI: 0.94-1.34; P=0.18) or Group 3 vs. 1 (RR = 0.96; 95% CI: 0.75-1.22; P=0.74). **Conclusions:** Maternal smoking was not associated with their offspring's physical activity during adolescence.

KEY WORDS: Accelerometry; Epidemiology; Gestational smoking; Physical Activity

INTRODUCTION

Exposure to maternal smoking is associated with various health consequences in the offspring, including intrauterine growth restriction, low birth weight, preterm birth, and neonatal morbidity[1,2].Research has also demonstrated that maternal smoking is associated with health outcomes (e.g., obesity and metabolic disorders) of their offspring later in life (e.g., childhood to adulthood)[3]. This observation of maternal smoking on offspring health later in life is biologically plausible given the emerging research, for example, demonstrating an impact of maternal nicotine exposure on fetal programming of vascular oxidative stress in adult offspring, via augmented angiotensin II-induced vasoconstriction and impaired endothelium-dependent NO-mediated vasodilatation[4]. Notably, such oxidative stress may precipitate the development of various chronic diseases, such as metabolic syndrome[5].

Numerous studies have demonstrated that maternal smoking is associated with child overweight/obesity[6,7]. To illustrate this, a recent review on maternal smoking status and offspring health found an association with overweight/obesity to be present in 34 out of 42 evaluated studies.[3] There is some evidence to suggest that even passive exposure to smoke (i.e., secondhand smoke) may be associated increased risk of obesity among adolescent offspring, independent of birth weight[8,9]. Given the relatively well-established (abovementioned) association between maternal smoking and child weight status, additional work has begun to evaluate the association of maternal smoking with other health outcomes. While significant associations have undoubtedly been observed between maternal smoking and non-obesity health-related outcomes in offspring[6,10], these associations are much less explored than the maternal smoking-offspring weight status relationship and the collective results remain equivocal[3].

The link between maternal smoking and offspring blood pressure, cholesterol, risk for diabetes types I and II, and metabolic syndrome is largely unclear[3,11-13], with observed significant associations often being attenuated after covariate adjustment[10,11,14]. When considering the influence of offspring gender, a recent study found that maternal smoking was significantly associated with a reduced risk for metabolic syndrome among sons, but not daughters[6]. This study also observed greater correlations between maternal BMI with daughters' BMI (as compared to sons) and paternal BMI with sons' BMI (as compared to daughters). Similarly, with regards to parental gender, no association between paternal smoking and waist circumference was noted, in contrast with significant associations between maternal smoking and waist circumference. The authors indicate that the aforementioned gender differences may suggest some epigenetic effects[6,15] (e.g., offspring waist circumference may be mediated by exposure

to exogenous free radicals during pregnancy)[16]. In addition to the need for future research to continue the examination of physiological outcomes as they relate to maternal smoking, a particular area that has yet to be explored is whether maternal smoking is associated with offspring physical activity *behavior*, which was this study's purpose. Such an association is conceivable given that, for example, maternal smoking has been associated with parameters (e.g., weight status and hypertension) known to influence physical activity behavior[17]. Contributing additional plausibility to a potential maternal smoking-offspring physical activity relationship, physical activity participation is well understood to positively correlate with cardiorespiratory fitness,[18] which was recently shown to independently associate with maternal smoking[19]. Additionally, maternal behaviors besides smoking have been associated with numerous behavior-related outcomes in offspring. For instance, a high-fat diet among mothers has been shown to associate with certain social behaviors, cognitive functioning, and elevated risk of mental health disorders within offspring[20]. With regards to behavior programming, high-fat diet and obesity are postulated to modify certain neurotransmitter signaling pathways (e.g., the serotonergic and dopaminergic systems), possibly via increased exposure to circulating proinflammatory cytokines, hormones, and nutrients[21,22]. Considering that smoking is known to induce proinflammatory cytokine release,[23] it seems plausible that maternal smoking may similarly alter neurotransmitter signaling, ultimately influencing offspring behavior (e.g., physical activity participation)[24]. Within the context of the present study's examined outcome, a recent animal study demonstrated that maternal exercise during pregnancy was associated with physical activity in adult mice[25]. Taken together, the previous examples of maternal behavior-offspring behavior relationships provide further justification and plausibility for the current study.

METHODS

Study Design

Data were restricted to the 2003-2006 NHANES cycles because these are the only present cycles with objectively-measured physical activity data (i.e., accelerometry). The NHANES is an ongoing survey conducted by the Centers for Disease Control and Prevention that uses a representative sample of non-institutionalized United States civilians selected by a complex, multistage, stratified, clustered probability design. The multistage design consists of 4 stages, including the identification of counties, segments (city blocks), random selection of households within the segments, and random selection of individuals within the households. In the 2003-2006 cycle, participants were sampled across 15 different geographic areas across the U.S. during each 2-year cycle. Participants were interviewed in their homes and then subsequently examined in a mobile examination center (MEC) by NHANES personnel. NHANES study procedures were approved by the National Center for Health Statistics ethics review board, with informed consent obtained from all participants prior to data collection.

Study Participants

Among the eligible sample, 1,746 adolescent (12-15 yrs) participants provided data on all the study variables when not considering the physical activity data. This included 1,469 (mother did not smoke during pregnancy), 177 (mother smoked during entire pregnancy), and 100 (mother quit smoking during pregnancy) participants. After excluding those with missing/insufficient (described below) physical activity data, 1,033 adolescent participants remained, which constituted the analytic sample. As noted below, the analytic sample size for the three respective groups was 873, 112, and 48. Notably, we did not excluded participants based on weight status or other parameters, but as described below, such parameters were considered as covariates in our analytic models.

Assessment of Maternal Smoking

During a home interview, participants were asked, "*Did your biological mother smoke at any time while she was pregnant with you?*"; and "*At any time during pregnancy, did your biological mother quit or refrain from smoking for the rest of the pregnancy?*" Based on these responses, 3 mutually exclusive groups were created, including 1) mother did not smoke while pregnant with the participant; 2) mother smoked during entire pregnancy; and 3) mother quit smoking during pregnancy.

Assessment of Physical Activity

The 2003-2006 NHANES participants were asked to wear an ActiGraph 7164 accelerometer during all activities, except water-based activities and while sleeping. Prior to the participant's examination, accelerometers were initialized to collect data in one minute time periods. The output of an accelerometer is *activity counts*, which are proportional to measured acceleration. The ActiGraph 7164 accelerometer measures accelerations in the vertical axis using a piezoelectric plate. The accelerometer output is digitized using an analog-to-digital converter, and once digitized, the signal passes through a digital filter that detects accelerations ranging from 0.05 to 2.00 g in magnitude with frequency responses ranging from 0.25 to 2.5 Hz to filter motion outside normal human movement. The filtered signal is then rectified and summed over a pre-determined epoch period. After the activity count is sorted into an epoch, it is stored in the internal memory and then the integrator is reset to zero.

Activity counts per minute of ≥ 2020 used to denote moderate-to-vigorous physical activity (MVPA) intensity[26]. Nonwear was defined by a period of a minimum of 60 consecutive minutes of zero activity

counts, with the allowance of 1-2 minutes of activity counts between 0 and 100.[26] For the analyses described here, only those participants with at least 4 days with 10 or more hours per day of monitoring data were included in the analyses.[26]

Statistical Analyses

Negative binomial regression was used to examine the association between material smoking status and MVPA, as MVPA time is an outcome variable expressed in integral minutes and was positively skewed. Coefficients from negative binomial models are expressed as rate ratios (RR), reflecting the relative rate of events (i.e. MVPA) associated with specific model elements over a specific period of time (i.e. day). Statistical significance was established as $P<0.05$.

A series of negative binomial regression models were computed, which included:

Model 1: Unadjusted model

Model 2: Age-adjusted

Model 3: Adjusted for age, gender, race-ethnicity and income-to-poverty ratio

Model 4: Adjusted for age, gender, race-ethnicity, income-to-poverty ratio, and offspring self-reported birthweight

Model 5: Adjusted for age, gender, race-ethnicity, income-to-poverty ratio, offspring self-reported birthweight, and measured body mass index

Model 6: Adjusted for age, gender, race-ethnicity, income-to-poverty ratio, offspring self-reported birthweight, measured body mass index and serum-assessed cotinine

Model 7: Same as model 6, but delimited to those with a low birth weight (<5.51 lbs)

Model 8: Same as model 6, but delimited to those with above the low birth weight cut-point (≥ 5.51 lbs)

RESULTS

Sociodemographic characteristics of the adolescent sample are shown in Table 1. Among the 48 participants whose mother quit smoking during pregnancy, 33 (69%) quit within the first 3 months of gestation.

In the following results:

Group 1: Mother did not smoke during pregnancy (referent)

Group 2: Mother smoked during entire pregnancy

Group 3: Mother quit smoking during pregnancy

As shown below, there was no association between maternal smoking status and offspring physical activity for any of the regression models.

Model 1: Unadjusted

MVPA was not different in adolescents who belonged to Group 2 vs. 1 (RR = 1.04; 95% CI: 0.86-1.24; P=0.66) or Group 3 vs. 1 (RR = 1.05; 95% CI: 0.79-1.39; P=0.72).

Model 2: Age-adjusted

MVPA was not different in adolescents who belonged to Group 2 vs. 1 (RR = 1.05; 95% CI: 0.86-1.28; P=0.60) or Group 3 vs. 1 (RR = 1.00; 95% CI: 0.79-1.25; P=0.98).

Model 3: Adjusted for age, gender, race-ethnicity and income-to-poverty ratio

MVPA was not different in adolescents who belonged to Group 2 vs. 1 (RR = 1.12; 95% CI: 0.92-1.36; P=0.23) or Group 3 vs. 1 (RR = 0.96; 95% CI: 0.76-1.22; P=0.78).

Model 4: Adjusted for age, gender, race-ethnicity, income-to-poverty ratio, and offspring self-reported birthweight

MVPA was not different in adolescents who belonged to Group 2 vs. 1 (RR = 1.12; 95% CI: 0.92-1.37; P=0.21) or Group 3 vs. 1 (RR = 0.97; 95% CI: 0.76-1.23; P=0.80).

Model 5: Adjusted for age, gender, race-ethnicity, income-

Table 1. Study variable characteristics of the adolescent sample (mean/proportion [SE]), 2003-2006 NHANES.

Variable	Mother Did Not Smoking During Pregnancy (N=873)	Mother Smoked During Entire Pregnancy (N=112)	Mother Quit Smoking During Pregnancy (N=48)
Age, yrs	13.5 (0.1)	13.6 (0.1)	13.5 (0.2)
% Male	53.6	49.3	64.5
% White	61.3	78.2	75.1
MVPA, min/day	33.8 (1.7)	35.0 (2.4)	35.4 (5.1)
Poverty Score	2.8 (0.1)	2.0 (0.1)	2.5 (0.2)
Birthweight, lbs	7.5 (0.1)	7.2 (0.2)	7.4 (0.2)
BMI, kg/m2	22.0 (0.2)	22.2 (0.5)	22.7 (1.4)
Cotinine, ng/mL	1.4 (0.5)	12.5 (9.6)	25.1 (12.8)

BMI, Body mass index
MVPA, Moderate-to-vigorous physical activity
Cotinine was measured in the serum using an isotope dilution-high performance liquid chromatography/atmospheric pressure chemical ionization tandem mass spectrometry.

to-poverty ratio, offspring self-reported birthweight, and measured body mass index

MVPA was not different in adolescents who belonged to Group 2 vs. 1 (RR = 1.13; 95% CI: 0.94-1.36; P=0.17) or Group 3 vs. 1 (RR = 0.98; 95% CI: 0.77-1.24; P=0.88).

Model 6: Adjusted for age, gender, race-ethnicity, income-to-poverty ratio, offspring self-reported birthweight, measured body mass index and serum-assessed cotinine

MVPA was not different in adolescents who belonged to Group 2 vs. 1 (RR = 1.12; 95% CI: 0.94-1.34; P=0.18) or Group 3 vs. 1 (RR = 0.96; 95% CI: 0.75-1.22; P=0.74).

Model 7: Same as model 6, but delimited to those with a low birth weight (<5.51 lbs)

MVPA was not different in adolescents who belonged to Group 2 vs. 1 (RR = 1.10; 95% CI: 0.66-1.85; P=0.67) or Group 3 vs. 1 (RR = 1.57; 95% CI: 0.69-3.54; P=0.25).

Model 8: Same as model 6, but delimited to those with above the low birth weight cut-point (≥ 5.51 lbs)

MVPA was not different in adolescents who belonged to Group 2 vs. 1 (RR = 1.12; 95% CI: 0.95-1.32; P=0.14) or Group 3 vs. 1 (RR = 0.96; 95% CI: 0.75-1.24; P=0.80).

DISCUSSION

The main finding of this study was that maternal smoking was not associated with their adolescent offspring's objectively-measured physical activity behavior. Possible reasons for this null finding may be due to methodological limitations inherent in retrospective cohort study designs. For example, limitations in recall may have been present, in that adolescents may not have known the true extent to which their parents engaged in smoking behavior during gestation. Additionally, we cannot discount any potential social desirability bias, and, like most epidemiological studies, a limitation is the possible residual or unmeasured confounding. However, given the null findings, the latter likely places a minimal role in this study. Further, the majority (69%) of mothers who quit smoking during gestation did so during the first trimester, which may have attenuated the detrimental effects of smoking. Another possibility for the null findings may be related to the relatively small sample size for those who smoked during the entire pregnancy (n=112) or who quit smoking during gestation (n=48). However, this latter speculation may be less of a concern as a post-hoc achieved power analysis indicated reasonable statistical power. For example, when comparing MVPA levels between Group 1 and Group 3, and based on a calculated effect size d of 0.42 (based on the mean/sd MVPA values across these groups), an alpha error probability of 0.05, and the respective sample sizes of 873 and 48, the calculated statistical power (1-β error probability) was 0.81. When comparing Group 1 to Group 2, the calculated statistical power was 0.99. Another explanation is the possibility that there is indeed no real relationship between maternal smoking and offspring physical activity behavior during adolescence. However, another consideration for the null findings may be that we were unable to assess the potential moderating effects of genetic predisposition on the association between maternal smoking and physical activity behavior. The genetic predisposition for Alzheimer's Disease, for example, is characterized in part by apolipoprotein E carrier status[27]. There is evidence to suggest that the cognitive benefits of physical activity are significantly better among older adult noncarriers of apoplipoprotien E.[28] When applied to the present study paradigm, it seems conceivable that some offspring may be more genetically susceptible to the negative health consequences of maternal smoking.

In conclusion, maternal smoking was not associated with offspring physical activity behavior during adolescents. Given the paucity of research on this topic, future related research is encouraged. Similar to the present study, future work employing an objective measure of physical activity (with multiple time point assessments) and a representative sample is warranted. However, prospective work on this topic is particularly encouraged that tracks the physical activity behavior of their offspring over time. Before such work is started, however, additional retrospective and cross-sectional studies are needed to provide a stronger justification for the time and allocation resources needed for prospective work on this topic.

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DECLARATION OF INTERESTS

All authors declare no conflicts of interest.

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