Physical activity and individual plasma phospholipid SFAs in pregnancy: a longitudinal study in a multiracial/multiethnic cohort in the United States

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ABSTRACT

Background: Circulating individual SFAs in pregnant females are critical for maternal and fetal health. However, research on identifying their modifiable factors is limited.

Objectives: We aimed to examine the associations of total physical activity (PA) and types of PA with circulating individual SFAs during pregnancy in a multiracial/multiethnic cohort of pregnant females in the United States.

Methods: The study included participants in a nested case–control study ($n = 321$) from the *Eunice Kennedy Shriver* NICHD Fetal Growth Studies–Singleton Cohort. Sampling weights were applied, so the results represented the entire Fetal Growth Cohort. Plasma phospholipid SFAs were measured at 4 visits [10–14 (visit 1), 15–26 (visit 2), 23–31 (visit 3), and 33–39 (visit 4) weeks of gestation] throughout pregnancy. PA of the previous year at visit 1 and since the previous visit at the subsequent visits was assessed using the validated Pregnancy PA Questionnaire. Time-specific and longitudinal associations were examined using multivariable linear and generalized estimating equation models.

Results: Total PA (metabolic equivalent of task-h/wk) was positively associated with circulating heptadecanoic acid (17:0) at visit 1 ($\beta \times 10^3$: 0.07; 95% CI: 0.02, 0.11) and pentadecanoic acid (15:0) at visit 3 ($\beta \times 10^3$: 0.09; 95% CI: 0.03, 0.14) independent of sociodemographic, reproductive, pregnancy, and dietary factors. Across the 4 visits, the positive associations with total PA were consistent for pentadecanoic acid ($\beta \times 10^3$: 0.06; 95% CI: 0.02, 0.10) and heptadecanoic acid ($\beta \times 10^3$: 0.10; 95% CI: 0.06, 0.14). Out of the 4 PA types (i.e., sports/exercise, household/caregiving, transportation, and occupational PA) considered, the magnitude of positive associations was the largest for sports/exercise PA.

Conclusions: Our findings suggest that maternal PA is positively associated with circulating pentadecanoic and heptadecanoic acids. The findings warrant confirmation by future studies. This trial was registered at clinicaltrials.gov as NCT00912132. *Am J Clin Nutr* 2022;116:1729–1737.

Keywords: saturated fatty acids, SFAs, physical activity, PA, pregnant females, maternal exercise, pregnancy health, prospective cohort

Introduction

Circulating SFAs have been recognized to play essential roles in human health for >20 y (1–4). Emerging evidence suggests that individual SFAs may have distinct functions and health effects in the general population (5–10) and pregnant females (11–14). For example, maternal circulating even-chain SFAs [e.g., myristic acid (14:0) and palmitic acid (16:0)] have been associated with increased risks of pregnancy-induced hypertension (11), dyslipidemia, and gestational diabetes mellitus (GDM) (12). In contrast, odd-chain [e.g., pentadecanoic acid (15:0) and heptadecanoic acid (17:0)] or very-long-chain SFAs [e.g., arachidic acid (20:0), behenic acid (22:0), and lignoceric acid (24:0)] have been associated with decreased risks and a favorable cardiometabolic biomarker risk profile (12).

The new findings for distinct health effects of circulating individual SFAs on health indicate an urgent need for research to identify the modifiable determinants of circulating individual SFAs instead of total SFAs. This is particularly critical for pregnant females because the fetus cannot synthesize fatty acids efficiently (15). In addition, the importance of circulating individual SFAs may vary by gestational age (16, 17). However, research on modifiable determinants of circulating individual SFAs for pregnant females is sparse.

Physical activity (PA), either acute or regular, plays an essential role in lipid metabolism and is well known for its influence on circulating concentrations of HDL, LDL, TG, and total FFAs in both nonpregnant (18–21) and pregnant females (22–24). For individual SFAs, PA has been associated with circulating or skeletal muscle palmitic acid and stearic acid (18:0) in a small observational study (25) and an interventional study (26) in males. In pregnant females, a few studies, including 1 of our works, have reported the associations of PA with total FFAs and individual unsaturated fatty acids such as linoleic acid (18:2n–6) and γ-linolenic acid (18:3n–6) (24, 27–29). However, the associations between PA and circulating individual SFAs in pregnant females have not yet been investigated. Because pregnancy is a period with dynamic changes in lipid metabolism, including accumulation of maternal fat depots and hyperlipidemia (30), the objective of the current study was to examine the time-specific and longitudinal associations of total and types of PA (i.e., sports/exercise, household/caregiving, transportation, and occupational PA) with the total and individual plasma phospholipid SFAs during pregnancy.

Methods

Study population and design

The study participants were selected from the *Eunice Kennedy Shriver* NICHD Fetal Growth Studies–Singleton Cohort (NCT00912132), a multicenter, multiracial/multiethnic, prospective cohort for low-risk, singleton pregnant females (31). Between 2009 and 2013, 2802 racially/ethnically diverse pregnant females aged 18–40 y without hypertension, diabetes, renal/autoimmune disease, psychiatric disorder, cancer, or HIV/AIDS were enrolled during early pregnancy from 12 clinical sites across the United States.

The current study utilized data from 321 pregnant females who had individual plasma phospholipid SFAs quantified in a nested GDM case–control study (GDM cases: $n = 104$, controls: $n = 214$). This study was approved by the institutional review boards of all participating sites, with all participants submitting a written informed consent.

PA

PA was scheduled to be assessed at 8–13, 16–22, 24–29, and 34–37 weeks of gestation, but the actual time windows were 10–14 (visit 1), 15–26 (visit 2), 23–31 (visit 3), and 33–39 (visit 4) weeks of gestation. PA was assessed using the validated Pregnancy PA Questionnaire (PPAQ) (32), which was also validated in females with obesity and GDM (33, 34). PA of the previous year was assessed at visit 1, and PA since the previous visit was assessed at the subsequent visits. Time spent in each activity (h/wk) was multiplied by the associated intensity [in metabolic equivalent of tasks (METs)] to derive the weekly energy expenditure. Activities of light intensity and above (METs $\geq$1.5) were summed to calculate total PA (MET-h/wk) (32, 35). PA by types (i.e., sports/exercise, household/caregiving, transportation, and occupational PA) was also calculated using an established method (32).

Plasma phospholipid SFAs

Blood samples were collected at each visit without within-participant overlaps. Biomarkers were measured among all GDM cases ($n = 107$) at all visits, all controls ($n = 214$) at visits 1 and 2, and only half of the controls ($n = 107$) at visits 3 and 4 to gain cost efficiency. To account for this study design, sampling weights were derived for pregnant females at visits 1 and 2 and visits 3 and 4 separately. For the nonfasting samples, the mean $\pm$ SD hours since the last meal were 3.7 $\pm$ 3.9 h at visit 1, 3.2 $\pm$ 4.0 h at visit 3, and 2.9 $\pm$ 3.7 h at visit 4. For the fasting sample at visit 2, the mean $\pm$ SD hours since the last meal were 11.8 $\pm$ 3.5 h. Plasma phospholipid SFAs were measured via a Hewlett Packard 5890 GC system with flame ionization detection and a previously published extraction method (36). The plasma phospholipid fraction includes mainly phosphatidylcholine and phosphatidylethanolamine, and a small amount of sphingomyelin and lysolecithin (or lysophosphatidylcholine). Individual plasma phospholipid SFAs were measured as proportions of plasma total phospholipid fatty acids. With relative levels >0.05%, individual plasma phospholipid SFAs consist of even-chain myristic acid, palmitic acid, stearic acid, arachidic acid, behenic acid, and lignoceric acid, as well as odd-chain pentadecanoic acid and heptadecanoic acid. During pregnancy, palmitic acid and behenic acid had a positive trajectory, whereas pentadecanoic acid, heptadecanoic acid, stearic acid, and lignoceric acid had a negative trajectory (37). Myristic acid and arachidic acid stayed stable (37).

Covariates

Data on sociodemographic, anthropometric, reproductive, and lifestyle factors, pregnancy characteristics, and pregnancy complications were obtained from structured questionnaires or extracted from medical records. Covariates were preselected potential confounders, including age (y), race/ethnicity (i.e., Asian/Pacific Islander, Hispanic, non-Hispanic black, non-Hispanic white), education (i.e., high school or less, Associate, Bachelor's or higher), married/living with a partner (i.e., yes,

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Supplemental Figure 1 and Supplemental Tables 1–5 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/ajcn/.

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Abbreviations used: AHEI, Alternative Healthy Eating Index; ASA24, Automated Self-Administered 24-Hour dietary recall; GDM, gestational diabetes mellitus; GEE, generalized estimating equation; MET, metabolic equivalent of task; PA, physical activity; PPAQ, Pregnancy Physical Activity Questionnaire.

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TABLE 1 Weighted characteristics of pregnant females in the NICHD Fetal Growth Studies–Singleton Cohort[1]

Weighted characteristics	$n = 321$
Sociodemographic, anthropometric, reproductive, and lifestyle factors at visit 1	
Age, y	28.2 ± 0.3
Race/ethnicity	
Asian/Pacific Islander	78 (18.5%)
Hispanic	123 (27.2%)
Non-Hispanic black	45 (23.3%)
Non-Hispanic white	75 (31.0%)
Prepregnancy BMI, kg/m^2	25.7 ± 0.3
Prepregnancy BMI status (kg/m^2)	
Normal (<25.0)	156 (51.7%)
Overweight (25.0–29.9)	99 (33.1%)
Obese (>30.0)	66 (15.2%)
Born in the United States	182 (68.5%)
Education	
High school or less	148 (45.5%)
Associate	50 (14.7%)
Bachelor's or higher	123 (39.8%)
Insurance	
Medicaid, other	108 (35.4%)
Private or managed care	211 (64.6%)
Married/living with a partner	259 (72.9%)
Nulliparity	144 (51.1%)
Smoked 6 mo prepregnancy	5 (0.7%)
Consumed alcoholic beverages 3 mo prepregnancy	198 (63.7%)
Dietary intakes[2] ($n = 191$)	
Total energy, kcal/d	2176.0 ± 70.0
AHEI	44.1 ± 0.7
Pregnancy characteristics and pregnancy complications	
Gestational weight gain at delivery, kg	12.3 ± 17.8
Institute of Medicine gestational weight gain category at delivery	
Inadequate	96 (31.1%)
Adequate	100 (28.6%)
Excessive	125 (40.3%)
Gestational hypertension	7 (1.3%)
Pre-eclampsia	11 (2.2%)
Gestational diabetes mellitus	107 (3.9%)

[1]Values are *n* (weighted percentage) for categoric variables and weighted mean ± weighted SE for continuous variables. Sampling weights were applied to represent the entire NICHD Fetal Growth Studies–Singleton Cohort. AHEI, Alternative Healthy Eating Index.

[2]Dietary intakes were available among 198 females who completed the FFQs at visit 1; 7 females with implausible total energy intake (i.e., <600 or >6000 kcal/d) were excluded.

no), nulliparity (i.e., yes, no), prepregnancy BMI (in kg/m^2), and the Alternative Healthy Eating Index (AHEI). Race/ethnicity groups were self-identified at visit 1. The prepregnancy BMI was calculated using height measured and self-reported prepregnancy weight at visit 1. Habitual dietary intakes for the last 3 mo were measured via a validated FFQ at visit 1 and via the validated Automated Self-Administered 24-Hour dietary recall (ASA24) at the subsequent visits (38–40). The AHEI excluding alcohol was derived based on a validated method (41). Higher AHEI was associated with lower risks of major chronic diseases such as diabetes, cardiovascular diseases, and cancers (41). The AHEI was used as an indicator for overall dietary quality and as a potential confounder in the analyses.

Statistical analyses

Because females with GDM were overrepresented in the nested case–control study, sampling weights were derived and applied to all analyses to ensure the study results represented the entire NICHD Fetal Growth Studies–Singleton Cohort (42). In the weighted sample, 4% of pregnant females had GDM, whereas in the unweighted sample, 33% of them had GDM. At each visit, multiple comparisons were addressed using the conservative Bonferroni correction method to avoid false-positive findings. Overall statistical significance was defined as P value < 0.05. After the Bonferroni correction, statistical significance was defined as P value < 0.006 [0.05/9 (total SFA and 8 individual SFAs)]. All regression models were adjusted for the preselected potential confounders, including age (y), race/ethnicity, education, marital status, nulliparity, prepregnancy BMI, and the AHEI. All analyses were conducted using SAS software, version 9.4 (SAS Institute).

Unweighted *n* (weighted percentage) for categoric variables and weighted mean ± SE for continuous variables were described for sociodemographic, anthropometric, reproductive,

TABLE 2 PA and plasma phospholipid SFAs at visit 1 of pregnant females in the NICHD Fetal Growth Studies—Singleton Cohort[1]

	$n = 321$
Total PA, MET-h/wk	325.5 ± 170.9
Household/caregiving PA	125.1 ± 80.7
Occupational PA	117.6 ± 111.0
Transportation PA	33.5 ± 31.7
Sports/exercise PA	14.1 ± 14.3
Other PA	35.4 ± 22.5
Total SFAs, % of plasma total phospholipid fatty acids	42.7% ± 1.9%
Odd-chain SFAs	
Pentadecanoic acid (15:0)	0.2% ± 0.1%
Heptadecanoic acid (17:0)	0.4% ± 0.1%
Even-chain SFAs	
Myristic acid (14:0)	0.3% ± 0.1%
Palmitic acid (16:0)	27.2% ± 1.6%
Stearic acid (18:0)	12.8% ± 1.2%
Arachidic acid (20:0)	0.3% ± 0.1%
Behenic acid (22:0)	0.8% ± 0.3%
Lignoceric acid (24:0)	0.6% ± 0.2%

[1] Values are weighted means ± SEs. Sampling weights were applied to represent the entire NICHD Fetal Growth Studies–Singleton Cohort. Visit 1 measured PA of the previous year. MET, metabolic equivalent of task; PA, physical activity.

and lifestyle factors at visit 1. Pregnancy characteristics and complications, including gestational weight gain, gestational hypertension, pre-eclampsia, and GDM, were described. Unweighted *n* (%) for categoric variables and unweighted mean ± SD for continuous variables were described and compared between females with and without GDM. PA and plasma phospholipid SFA profiles at visit 1 were also described.

For the primary analyses, time-specific associations of total PA with total and individual plasma phospholipid SFAs were examined separately at each visit using weighted multivariable linear models with robust variance estimation to illustrate the associations at different time points during pregnancy (i.e., PA of the previous year with SFAs at visit 1, PA since the previous visit with SFAs at the subsequent visits). When the direction of associations at different visits was the same, weighted generalized estimating equation (GEE) models with unstructured correlation structures and robust variance estimation were performed to improve statistical power. Associations of types of PA (i.e., sports/exercise, household/caregiving, transportation, and occupational PA) with total and individual plasma phospholipid SFAs were also examined.

Several sensitivity analyses were performed to examine the robustness of the study results. First, gestational weight gains were in addition adjusted in the models. Second, hours since the last meal for blood collections were in addition adjusted in the models. Third, carbohydrate and SFA intakes were in addition adjusted in the models. Fourth, total fatty acid intakes were in addition adjusted in the models. Fifth, missing values for the AHEI (30%) were imputed using the multiple imputation method (means at each visit were used in the primary analyses). In addition, associations between maternal complications and PA were examined. Finally, models were performed among females without GDM at visit 3 and visit 4.

Results

Participants' characteristics

The study participants (**Supplemental Figure 1**) had a mean ± SE age of 28.2 ± 0.3 y at visit 1 and were racially/ethnically diverse: 18.5% Asian or Pacific Islander, 27.2% Hispanic, 23.3% non-Hispanic black, and 31.0% non-Hispanic white. Among all participants, 48.3% were overweight or obese (prepregnancy BMI ≥ 25.0) (**Table 1**). For females with GDM, the mean ± SD age was 30.5 ± 5.7 y at visit 1, and 66.4% were overweight or obese prepregnancy. Compared with females without GDM, females with GDM were more likely to be overweight or obese prepregnancy, have smoked in the 6 mo prepregnancy, have lower AHEI scores, and have pre-eclampsia, but they were less likely to have Bachelor's or higher degrees. Among females with GDM, 61.2% received lifestyle consulting, 11.2% received insulin, 16.8% received oral medications (i.e., Metformin or Glyburide) as treatment, and 26.2% received unknown treatment (**Supplemental Table 1**).

The mean ± SE total PA was 325.5 ± 170.9 MET-h/wk at visit 1. By PA types, the mean ± SE household/caregiving PA was 125.1 ± 80.7, occupational PA was 117.6 ± 111.0, transportation PA was 33.5 ± 31.7, and sports/exercise PA was 14.1 ± 14.3 MET-h/wk. Total PA and types of PA decreased during pregnancy. Plasma phospholipid SFAs accounted for (mean ± SE) 42.7% ± 1.9% of the plasma total phospholipid fatty acids at visit 1. Among individual plasma phospholipid SFAs, even-chain palmitic acid was the most abundant, followed by even-chain stearic acid. The proportions of individual plasma phospholipids did not change much during pregnancy (**Table 2**).

Time-specific and longitudinal associations of PA with plasma phospholipid SFAs

Positive associations between total PA and plasma total phospholipid SFAs were found at visit 3 ($\beta \times 10^3$: 3.07; 95% CI: 1.53, 4.61; $P < 0.001$) and visit 4 ($\beta \times 10^3$: 2.29; 95% CI: 0.74, 3.84; $P = 0.004$), after adjusting for age, race/ethnicity, education, married/living with a partner, nulliparity, prepregnancy BMI, and the AHEI, and correction of multiple testing. When individual plasma phospholipid SFAs were examined, total PA was only positively associated with heptadecanoic acid at visit 1 ($\beta \times 10^3$: 0.07; 95% CI: 0.02, 0.11; $P = 0.005$) and pentadecanoic acid at visit 3 ($\beta \times 10^3$: 0.09; 95% CI: 0.03, 0.14; $P = 0.002$) after adjusting for the preselected covariates and correction of multiple testing (**Table 3**). In the sensitivity analyses, most findings stayed robust (**Supplemental Tables 2–5**). The longitudinal associations of total PA with pentadecanoic acid ($\beta \times 10^3$: 0.06; 95% CI: 0.02, 0.10; $P < 0.001$) and heptadecanoic acid ($\beta \times 10^3$: 0.10; 95% CI: 0.06, 0.14; $P < 0.001$) estimated using GEE models were consistent with the time-specific positive associations after adjusting for the preselected covariates and correction of multiple testing.

When further examining PA by types (i.e., sports/exercise, transportation, caregiving/household, and occupational PA) using GEE models, the positive association of PA and pentadecanoic acid was observed only for household/caregiving PA ($\beta \times 10^3$: 0.13; 95% CI: 0.04, 0.22; $P = 0.005$). The positive association of PA and heptadecanoic acid was observed for sports/exercise

TABLE 3 Time-specific prospective associations of total PA (MET-h/wk) with plasma phospholipid SFAs in the NICHD Fetal Growth Studies—Singleton Cohort[1]

	Visit 1 (10–14 GW) ($n = 321$)			Visit 2 (15–26 GW) ($n = 321$)			Visit 3 (23–31 GW) ($n = 214$)			Visit 4 (31–39 GW) ($n = 214$)		
	$\beta \times 10^3$	95% CI	*P* value	$\beta \times 10^3$	95% CI	*P* value	$\beta \times 10^3$	95% CI	*P* value	$\beta \times 10^3$	95% CI	*P* value
Total SFAs	0.34	(−0.97, 1.64)	0.61	0.92	(−0.43, 2.26)	0.18	3.07	(1.53, 4.61)	<0.001*	2.29	(0.74, 3.84)	0.004*
Odd-chain SFAs												
Pentadecanoic acid (15:0)	0.03	(−0.02, 0.07)	0.22	0.002	(−0.04, 0.04)	0.91	0.09	(0.03, 0.14)	0.002*	0.06	(0.01, 0.11)	0.03
Heptadecanoic acid (17:0)	0.07	(0.02, 0.11)	0.005*	0.05	(0.004, 0.10)	0.03	0.02	(−0.04, 0.08)	0.47	0.07	(0.02, 0.12)	0.01
Even-chain SFAs												
Myristic acid (14:0)	−0.04	(−0.09, 0.02)	0.19	−0.03	(−0.08, 0.02)	0.30	0.01	(−0.06, 0.08)	0.76	0.03	(−0.04, 0.10)	0.38
Palmitic acid (16:0)	−0.38	(−1.51, 0.76)	0.52	0.63	(−0.58, 1.84)	0.31	1.85	(0.46, 3.25)	0.01	0.94	(−0.39, 2.28)	0.16
Stearic acid (18:0)	0.64	(−0.13, 1.40)	0.10	0.18	(−0.47, 0.83)	0.59	0.93	(0.04, 1.82)	0.04	0.78	(−0.09, 1.64)	0.08
Arachidic acid (20:0)	−0.01	(−0.08, 0.05)	0.69	0.02	(−0.01, 0.05)	0.14	0.03	(−0.06, 0.11)	0.50	0.03	(−0.06, 0.13)	0.49
Behenic acid (22:0)	0.05	(−0.15, 0.26)	0.61	0.09	(0.02, 0.16)	0.01	0.12	(−0.18, 0.42)	0.42	0.36	(0.04, 0.67)	0.03
Lignoceric acid (24:0)	−0.02	(−0.15, 0.11)	0.76	−0.03	(−0.13, 0.06)	0.48	0.02	(−0.15, 0.19)	0.84	0.02	(−0.14, 0.18)	0.83

[1]Visit 1 measured PA in the previous year, and the subsequent visits measured PA since the previous visit. Plasma phospholipid SFAs were measured as percentage of plasma total phospholipid fatty acids. Multivariate models with robust variance estimation were adjusted for age (y), race/ethnicity, education, marital status, nulliparity, prepregnancy BMI (kg/m^2), and the AHEI. Missing values for the AHEI were imputed by means at each visit. Sampling weights were applied to represent the entire NICHD Fetal Growth Studies–Singleton Cohort. AHEI, Alternative Healthy Eating Index; GW, gestational week; MET, metabolic equivalent of task; PA, physical activity.

*P value is significant after Bonferroni correction at the overall α level of 0.05 at each visit (i.e., P value < 0.006).

PA ($\beta \times 10^3$: 0.65; 95% CI: 0.19, 1.11; $P = 0.005$) and occupational PA ($\beta \times 10^3$: 0.13; 95% CI: 0.06, 0.20; $P < 0.001$). No associations were found for transportation PA after adjusting for the preselected covariates and correction of multiple testing (**Table 4**).

Discussion

In this prospective and longitudinal study with PA and plasma phospholipid SFAs measured at 4 visits across pregnancy, we observed positive associations of total PA (MET-h/wk) with the plasma phospholipids pentadecanoic acid and heptadecanoic acid, independent of sociodemographic, reproductive, pregnancy, and dietary factors. The positive associations of total PA with the plasma phospholipids pentadecanoic acid and heptadecanoic acid were likely related to sports/exercise PA. The findings are consistent with our hypothesis that PA, particularly sports/exercise PA, is a modifiable determinant of circulating individual SFAs. Given that odd-chain pentadecanoic acid and heptadecanoic acid have been linked with a lower risk of GDM and beneficial effects on insulin and lipid homeostasis (12), SFAs could play a role in explaining the potential beneficial effects of PA on cardiometabolic health in pregnant females.

The overall positive associations between total and types of PA and individual plasma phospholipid SFAs during pregnancy are biologically possible. PA has been well recognized for regulating lipid metabolism in both nonpregnant and pregnant females (24, 43–47). In human experiments using stable isotope tracer, plasma phospholipid fatty acid concentrations usually decrease at the beginning of exercise owing to enhanced clearance by skeletal muscle (48). Then, circulating fatty acids gradually increase owing to accelerated lipolysis (49). No previous studies have examined the associations of PA with circulating individual SFAs during pregnancy. In a randomized controlled trial of an aerobic exercise intervention (i.e., a maximum of 5 sessions of 40-min aerobic exercise at 20–35 weeks of gestation) among 84 pregnant females in New Zealand, circulating total FFA at 35 weeks of gestation was lower in the intervention group than in the control group (28). However, this study did not measure the circulating individual fatty acids as relative proportions, and thus the results cannot be directly compared with the current study. The associations of PA with individual circulating fatty acids as relative proportions are likely different from the associations with total FFAs (50–53).

Habitual PA may stimulate the lipolysis of particular fatty acids at different time windows during pregnancy, which may be driven by specific requirements of the fetus. It is well documented that the fetus requires more fatty acids for its development during mid-to-late pregnancy (54–58). However, the exact biological mechanisms for the positive associations of total PA and types of PA with the plasma phospholipids pentadecanoic acid and heptadecanoic acid may be complicated. Some studies have suggested that circulating pentadecanoic acid and heptadecanoic acid are associated with lower risks of diabetes (59–62) and cardiovascular diseases (6, 63–65) in the general population. Among pregnant females, circulating pentadecanoic acid and heptadecanoic acid were inversely

TABLE 4 Longitudinal associations of types of PA (MET-h/wk) with plasma phospholipid SFAs in the NICHD Fetal Growth Studies—Singleton Cohort[1]

	Sports/exercise PA			Household/caregiving PA			Transportation PA			Occupational PA		
	$\beta \times 10^3$	95% CI	*P* value	$\beta \times 10^3$	95% CI	*P* value	$\beta \times 10^3$	95% CI	*P* value	$\beta \times 10^3$	95% CI	*P* value
Pentadecanoic acid (15:0)	0.54	(−0.07, 1.16)	0.08	0.13	(0.04, 0.22)	0.005*	0.12	(−0.07, 0.30)	0.21	0.06	(0.004, 0.11)	0.03
Heptadecanoic acid (17:0)	0.65	(0.19, 1.11)	0.005*	0.14	(0.004, 0.28)	0.04	0.24	(−0.18, 0.67)	0.26	0.13	(0.06, 0.20)	0.0004*

[1] $n = 214$. Visit 1 measured PA of the previous year, and the subsequent visits measured PA since the previous visit. Plasma phospholipid SFAs were measured as percentage of plasma total phospholipid fatty acids. Generalized estimating equation models with unstructured correlation structures and robust variance estimation were adjusted for age (y), race/ethnicity, education, marital status, nulliparity, prepregnancy BMI (kg/m^2), and the AHEI. Missing values for the AHEI were imputed by means at each visit. Sampling weights were applied to represent the entire NICHD Fetal Growth Studies–Singleton Cohort. AHEI, Alternative Healthy Eating Index; MET, metabolic equivalent of task; PA, physical activity.

* *P* value is significant after Bonferroni correction at the overall α level of 0.05 at each visit (i.e., *P* value < 0.006).

associated with GDM risk in the Fetal Growth Studies–Singleton Cohort (12). In addition, pentadecanoic acid was positively correlated with circulating HDL, whereas heptadecanoic acid was negatively correlated with circulating HOMA-IR, glucose, insulin, C-peptide, leptin, and triglycerides, and positively correlated with adiponectin and HDL (12). Thus, circulating pentadecanoic acid and heptadecanoic acid may have beneficial impacts on insulin and lipid homeostasis. It is unclear whether the observed positive associations of PA with circulating pentadecanoic acid and heptadecanoic acid could play a role in explaining the potential benefits of PA on cardiometabolic health.

The magnitude of the positive associations with plasma phospholipid SFAs was the most considerable for sports/exercise PA, although it only accounted for a small proportion of total PA. Compared with other PA types, sports/exercise PA had beneficial effects on lipid metabolism, probably due to its intensity and duration (45, 66–68). When designing potential interventions for PA, the influence of PA types may need to be considered.

The current study has several unique strengths. First, this prospective study was based on longitudinal data of 8 individual plasma phospholipid SFAs at 4 visits throughout pregnancy. It allowed the analysis of temporal associations between PA and plasma phospholipid individual SFAs at various time windows during pregnancy. Second, this study included geographically and racially/ethnically diverse pregnant females in the United States, increasing the generalizability of the findings. Finally, potential confounders, including detailed dietary intakes at multiple time points, were collected and adjusted for in the analyses.

A few potential limitations of this study are worth pointing out. First, this study was observational by design. Although we have carefully controlled for potential confounders, residual confounding cannot be completely ruled out. Second, PA was self-reported using the PPAQ. Regardless, the PPAQ had robust reproducibility and modest validity against accelerometer data among pregnant females (32), aligning with other standard PA questionnaires (69, 70). In addition, fasting blood samples were only available at visit 2. However, previous studies, including work from us, have shown that plasma phospholipid fatty acid concentrations are not sensitive to fasting status (27, 71). In the current study, additional adjustment for hours since the last meal at each visit did not change the main findings, as shown in the sensitivity analysis. Lastly, the semiquantitative dietary intake FFQ was used at visit 1, whereas the quantitative ASA24 was used at the subsequent visits to derive the AHEI. Nevertheless, the FFQ and ASA24 have been used to derive the AHEI in epidemiologic studies (40, 72).

In conclusion, in the current study in racially/ethnically diverse pregnant females, total PA was positively associated with the plasma phospholipids pentadecanoic acid and heptadecanoic acid. Such associations are likely related to sports/exercise PA. These findings suggest that PA, particularly sports/exercise PA, may be a lifestyle factor that could be modified to optimize the plasma phospholipid SFA profile during pregnancy.

The authors' responsibilities were as follows—XL, LC, and CZ: designed the research and had primary responsibility for the final content; CZ: supervised data collection and obtained funding; NLW and MYT: led the laboratory testing; SKZ, YZ, MLR, JW, NLW, and MYT: contributed to data interpretation; XL, LC, ZF, TX, and JD: analyzed data or performed statistical analysis; XL and LC: wrote the paper; and all authors: revised and edited the manuscript and read and approved the final manuscript.

Data availability

The data, along with a set of guidelines for researchers applying for the data, will be posted to a data-sharing site, NICHD Data and Specimen Hub (DASH) [https://dash.nichd.nih.gov/].

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