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Effects of Exercise during Pregnancy on Pediatric Heart Measures

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Abstract

Our previous research has shown regular maternal exercise during pregnancy influences fetal cardiac development by decreasing fetal heart rate and increasing fetal heart rate variability. Whether maternal exercise promotes chronic cardiac adaptations in offspring is not known. We hypothesized that children of mothers who exercised during pregnancy would display improved cardiac function through infancy and into early childhood. An ultrasound database was queried for normal pediatric ultrasounds obtained 1 month to 7 years after birth. Mothers (n=25; 30.3 + 5.5 y of age) of cases extracted from the database completed a self-report survey to ascertain exercise behavior during the 3rd trimester. Mothers performed between 120 and 5730 minutes of exercise (M = 1449 + 14 min). Overall, minutes of exercise were not significantly correlated with any cardiac measures. However, after controlling for child's age, minutes of exercise were negatively associated with left ventricular end systolic and diastolic dimensions ($p<0.05$) and left ventricular end systolic volume relative to body surface area ($p<0.05$). Further, minutes of exercise were positively associated with left ventricular ejection fraction ($p<0.05$). These results suggest exercise during late pregnancy has a significant effect on offspring heart function into early childhood independent of physiologic increases in anatomical heart size.

Introduction

Various types of regular physical activity improve heart health and decrease risk of cardiovascular disease. For example, physical training improves cardiac efficiency as evidenced by lower resting heart rates (HR) in trained men and women [1]. Echocardiographic findings also demonstrate cardiospecific adaptations to exercise. These findings can be seen in adults, elderly, and even in children who are regularly active. Pregnant women who engage in the current recommended amount of exercise (150 minutes/week of moderate, aerobic activity) also achieve health benefits [2,3].

With so many known benefits and cardiac adaptations to exercise in various populations, researchers have recently begun to focus on potential adaptations of the fetus in response to their mothers' exercise. We previously reported that regular, aerobic exercise during pregnancy was associated with lower fetal HR and higher heart rate variability (HRV). HRV is a useful, noninvasive tool to assess cardiac autonomic function) at rest [4-6]. Further, we found that these cardiac parameter changes persisted into the first month of life in the offspring [7].

Reduced HRV in adults is associated with a number of cardiovascular risk factors and disease states, such as diabetes [8], obesity [9] and hypertension [10] and is a known predictor of mortality after myocardial infarct [11,12]. In the developing fetus and infant, metrics of HRV help describe the degree of integration between central and peripheral nervous systems. Moreover, the association of autonomic function and fetal behaviors are the earliest precursors to newborn behavioral regulation [13]. For example, HRV serves as an index of attention regulation in newborns [14], orientation in neonates [15], and early life information processing [16].

While it is known that maternal exercise improves fetal and newborn cardiac autonomic nervous system development, it is not known if these effects persist into early childhood. Evidence is needed to further confirm the chronic adaptive nature of fetal cardiac changes. We hypothesized that exercise during pregnancy promotes sustained improvements in measurements of childhood heart function, independent from anatomical changes.

Methods

Participants

TOAD software was used to query a database for normal echocardiograms as noted by pediatric cardiologists, indication for echocardiograms were murmurs found to be benign. The search was restricted to children between one day and seven years of age at the time of the exam, healthy, from a singleton pregnancy, and who had normal echocardiograms as denoted by pediatric cardiologists' notes.

In order to mail them the survey material, the names and contact information for mothers of children selected were obtained from the database. Questionnaires were sent between January 2012 and August 2012 to 200 women. Three monthly reminders were sent to women who did not respond 30 days after being sent the questionnaire. By the close of the study in December 2012, 70 mothers had returned questionnaires; however, two could not be matched with children's data. From the remainder (n=68), 43 reported no leisure-time physical activity (LTPA) during pregnancy. While our main focus was to determine the influence of exercise during pregnancy on childhood heart measures, we focused on those cases with some type of activity and excluded cases with zero value of activity; this also normalized the distribution of maternal exercise LTPA. The remaining 25 completed questionnaires were entered into a database and then merged with their child's ultrasound data.

Physical activity questionnaire

From the list of normal pediatric echocardiograms, we sent a questionnaire, a letter explaining the study, and a self-addressed return

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envelope to mothers. Instructions included with the questionnaire asked mothers to choose from a list and/or write in the LTPA that they participated in during pregnancy [17]. Participants provided frequency (days/week), duration (minutes/session), and intensity for each month of pregnancy and the three months prior to becoming pregnant. The Modifiable Activity Questionnaire (MAQ) was used to assess all LTPA performed during pregnancy. This questionnaire has been validated as a tool for use with pregnant and post-partum women [17]; since pregnancy represents a unique time in a woman's life, this questionnaire is also found to be a reliable historical recall up to 6 years postpartum of physical activity during pregnancy and pregnancy weight gain [17]. Based on the researchers' previous findings demonstrating an association between maternal duration (in minutes) of 3rd trimester LTPA and fetal/infant heart outcomes, the same measurement and procedures were used [5,6]. The primary exercise variable used in our analyses was the total duration of all LTPA performed during the 3rd trimester. Total minutes/3rd trimester was derived by multiplying the total number of sessions of third trimester LTPA and the self-reported average duration (minutes) of a session, and then adding the sum across all LTPA [5,6].

Included in this questionnaire were demographic questions about prior pregnancies, the use of substances and supplements during pregnancy, pregnancy complications, number of previous pregnancies, age, education, and pre-pregnancy height and weight. The education variable was categorical and consisted of women with and without a bachelor's degree or higher. Pre-pregnancy body mass index (BMI) was calculated using the formula [weight (kg) ÷ height (m^2)].

Ultrasound measures

As a retrospective study, all heart measurements were acquired from pediatric cardiologists' as routine patient care and thus not biased to the study question or participation. Demographic recordings were child's age, height, and weight at time of exam. All pediatric values were indexed by body surface area (BSA) based on the Mosteller formula for children [18]. Cardiovascular measures from recorded ultrasounds were left ventricular end diastolic dimension and left ventricular end-systolic dimension. Based on these values, left ventricular end-diastolic volume, end-systolic volume, left ventricular mass, and ejection fraction were calculated. Left ventricular mass was indexed to the child's height as well.

Statistical analyses

Maternal continuous demographic variable and the children's heart measure distributions were approximately normal. The Pearson Product Moment correlation procedure was used to assess bivariate relationships between maternal variables and children's ultrasound heart measures. Multiple regression analyses were then performed. In these analyses, pediatric heart measures were regressed (in separate models) on maternal age and minute/3rd trimester of LTPA which were the only maternal variables significantly related with at least one child heart measure in the bivariate analyses. The level of significance was set a priori at alpha < 0.05 and all statistical analyses were performed using the Statistical Package for Social Sciences (SPSS version 17.1, Chicago, 2009).

Results

Participant demographics

All women. The 25 mothers who engaged in LTPA during their 3rd trimester of pregnancy were between 30 and 42 years of age at the time of giving birth, non-smokers with no history of alcohol or drug use, and well-educated with 66.7% having at least a bachelor's degree (Table 1). Forty-four percent had a BMI over 25 suggesting they were overweight or obese prior to becoming pregnant. Their total LTPA within the third trimester ranged between 120 and 5730 min. The children ranged in age from less than one month to seven years (Table 1). All of the pediatric heart measures examined in this study show a considerable degree of variance but were within the normal range for age (Table 2).

Infant heart correlations with maternal activity (Table 3)

A significant and positive correlation was found between minute/3rd trimester of LTPA and left ventricular ejection fraction ($P<0.05$). There were no significant correlations between maternal LTPA and left ventricular end systolic dimension, stroke volume relative to BSA, end systolic and diastolic volumes relative to BSA, and left ventricle mass index (corrected for height). The child's age, but not maternal BMI or education level, was significantly negatively related with all the child heart measures except ejection fraction.

Multiple regression analyses

Provided in Table 4 are the results of the analyses where each pediatric heart measure (in separate models) was regressed on the child's age in years and total minutes of maternal LTPA performed in the 3rd trimester. After considering the effects of the child's age, maternal LTPA duration still accounted for a significant portion of the variance in left ventricular ejection fraction, left ventricular end systolic and diastolic dimensions and end systolic and diastolic volumes (relative to BSA). Children whose mothers engaged in more

Table 1: Demographics for Mother:Child pairs.

Measurement	Mean (or % where denoted)	SD (if applicable)
3rd Trimester LTPA Duration (min)	1449	1468
Mother's Age when pregnant (yrs)	30.3	5.5
Child's current age (yrs)	2.4	2.5
Maternal pre-pregnancy BMI	26.3	7.0
College degree or higher	66.7%	

Maternal physical activities had intensity classifications as 1=low, 2=moderate, 3=high intensity.

Table 2: Cardiovascular measures of children.

Measurement	Mean	SD
Left Ventricle End Systolic Dimension (mm)	17.6	5.4
Left Ventricle End Diastolic Dimension (mm)	27.8	8.3
Left Ventricle Ejection Fraction (%)	67	5
End Systolic Volume- relative to BSA (mL)	21.0	11.8
End Diastolic Volume- relative to BSA(mL)	63.6	36.0
Stroke Volume- relative to BSA (mL)	42.6	24.6
Left Ventricle Mass Index- corrected for height (mm)	46.7	17.1

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Table 3: Pearson correlations of children's cardiovascular measures and maternal LTPA.

Measurement	LTPA (min/3rd trimester)	Child's age (y)	Maternal BMI	Maternal Education Level§
Left Ventricle End Systolic Dimension	-0.32	0.81**	0.06	0.10
Left Ventricle End Diastolic Dimension	-0.25	0.82**	-0.01	0.11
Left Ventricle Ejection Fraction	0.44*	-0.13	-0.21	0.01
End Systolic Volume (relative to BSA)	-0.22	0.84**	0.07	0.08
End Diastolic Volume (relative to BSA)	-0.29	0.85**	-0.01	0.10
Stroke Volume (relative to BSA)	-0.19	0.82**	-0.05	0.10
Left Ventricle Mass Index (corrected for height)	-0.09	-0.55**	-0.01	-0.03

*=p<0.05; **=p<0.001; §=Maternal Education Level (0 = hs or less; 1 = bachelors or higher) Abbreviations: LTPA: Leisure-Time Physical Activity; hs: High School; BSA: Body Surface Area; min: Minutes

Table 4: Associations between LTPA (min/3rd trimester) and Children's Cardiovascular Measures after controlling for the child's age.

Measurement	LTPA (min/3rd trimester)	
	Standardized Beta	Adjusted R^{2a}
Left Ventricle End Systolic Dimension	-0.257*	0.791
Left Ventricle End Diastolic Dimension	-0.185*	0.820
Left Ventricle Ejection Fraction	0.440*	0.122
End Systolic Volume (relative to BSA)	-0.231*	0.822
End Diastolic Volume (relative to BSA)	-0.160	0.825
Stroke Volume (relative to BSA)	-0.124	0.806
Left Ventricle Mass Index (corrected for height)	-0.142	0.284

p<0.05; [a]includes independent variables child's age in years and maternal LTPA duration.

minutes of LTPA during their 3rd trimester of pregnancy had greater ejection from smaller heart dimensions and lower heart volumes, regardless of child age (p<0.05). Stroke volume relative to BSA and left ventricular mass index corrected for height were not significantly affected by maternal LTPA.

Discussion

Our current study focused on determining if there was a relationship with mother's level of physical activity while pregnant and left ventricle (LV) functional measures of her offspring. We found a significant, positive association between duration of 3rd trimester maternal LTPA and pediatric left ventricular ejection fraction, and a negative association with LV dimensions and volumes in age-adjusted data. The findings support our hypothesis that exercise during pregnancy promotes improved functional heart measurements into early childhood.

Research in adults has found differences in resting LV dimensions in those who are exercise-trained relative to controls, without significant differences in ejection fraction [19,20]. Similarly, studies comparing swim-trained children (between 7-14 years of age) to non-trained controls found increased LV dimensions without changes in ejection fraction at rest [21-23]. These cardiac adaptations to exercise training are associated with lower heart rate at rest, and increased stroke volume to maintain resting cardiac output. A trained heart will exhibit lower heart rate at a given work load, increased stroke volume and cardiac output, and increased efficiency at maximal workloads. These changes are attributed to improved autonomic control as well as increased cardiac contractility, via the Frank-Starling mechanism. These physical cardiac adaptations allow the heart to function more efficiently.

The left ventricular ejection fraction (LVEF) was larger in children of mothers who engaged in more LTPA during the 3rd trimester, even though these children did not have an increase in heart dimensions or volumes. It appears that children of mothers who engaged in more LTPA during the 3rd trimester had more efficient heart contractility, as evidenced by higher ejection fractions despite reduced heart dimensions and volumes. Children of mothers who engaged in lower levels of LTPA did not receive the benefit of cardiac efficiency and therefore compensated by increasing dimensions and volumes. Since many of our participants were overweight or obese prior to becoming pregnant, it is important to note that physical activity during pregnancy improves offspring heart function regardless of her fitness level prior to pregnancy. This point has significant public health implications for our increasing obesity and cardiovascular epidemic in US adults and children [24].

Although previous findings by May et al. [5,6] have shown lower heart rates in fetuses and infants exposed to maternal exercise in utero, the lack of similarities in the current findings can be explained by the timing of the exercise stimuli. For example, young male rats that exercised had no significant differences in heart weights, capillary:fiber ratio, or diffusion distance of the heart muscle relative to control rats [25]. However, male rats exposed to maternal exercise in utero have similar heart weight (absolute and relative), but significantly higher capillary:fiber ratio and decreased diffusion distance [26]. Based on prenatal and postnatal exposure to exercise, Parizkova [27] suggests prenatal exposure has a greater impact than postnatal on the microstructure of the cardiac muscle of offspring. This is relevant because it's showing that our findings are congruent with existing literature [25-27]. Our paper discusses findings relevant to changes in the structure of the heart (LVEF), and so this responds to changes in microstructure and other 'micro' changes in the heart.

Additionally, the effects of physical activity vary in different periods of life, and are not the same in individual tissues [28-30]. In the developing organism, physical activity tends to coincide with periods of growth. It is easier to induce structural and physiologic change in an organism that is actively growing and developing, as the cells are more sensitive to surrounding stimuli [31,32]. The age of our sample population is by design quite young and well within this developmental phase. With this in mind, our findings are most likely due to the active growth of the developing cardiac myocytes, rather than a change in the myocardium as a whole [31-35].

This current data combined with our previous findings of a lower heart rate in fetuses and infants exposed to maternal exercise further supports the Barker hypothesis of prenatal programming. These findings have exciting health implications. Exercise-related benefits generally are present only with continual participation in

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activity, whereas our current data suggest that prenatal exposure to maternal exercise may have lasting cardiovascular health implications independent of the child's participation in physical activity. Therefore, regardless of the whether the child participates in physical activity or not, they may have long-term cardioprotection from prenatal exposure to exercise.

Primary care providers frequently recommend exercise to their patients for a myriad of reasons, with varying levels of patient compliance. One recommended model for improving compliance involves utilizing motivational interviewing and recognizing stages of change [36]. Patients who are not currently exercising are often in the "precontemplation" stage of change, and educating the patient about the benefits of a healthy lifestyle can be beneficial in motivating the patient to begin exercise [37]. While some mothers are aware of the benefits of physical activity for their own health, the added benefit to the fetus is not taught. This information may increase the desire and compliance of physical activity in pregnant women. Additionally, the benefit of maternal exercise to the fetus included mothers who were overweight or obese; this could encourage mothers who believe that exercise would only be beneficial if they achieved a normal BMI. Lastly, the average amount of LTPA performed was below the recommended national guidelines, but still had a significant impact on childhood cardiovascular function [38]. This too will likely encourage mothers who may have thought an exercise regimen to be beyond their ability or time constraints.

Limitations

The results of this study should be interpreted with regards to its limitations. Although the modifiable physical activity questionnaire has been validated for assessing physical activity in pregnant women [39] multiple years after the birth of the child, questionnaires by nature are vulnerable to recall bias that could influence estimations of physical activity levels [40]. Additionally, we did have a mother or a seven-year old participate in the study; although, this is a year older than the validation of the questionnaire, the findings did not differ when the child's data was excluded. Second, the population of women was fairly small and educated, however, since the sample was taken from a large metropolitan area, the participants do represent a diverse background. Third, there was a wide range of reported activity levels among the active women, and the average of this population fell below the recommended activity guidelines. With this in mind, further analyses will be done with the very sedentary group of women during pregnancy and this relationship with pediatric heart function. Finally, although this was not a randomized controlled trial, the secondary analysis adjusting for maternal factors and pediatric age strengthen confidence in the current findings.

Summary

Although the average intensity and time is less than the recommended guidelines by the ACOG (American Congress of Obstetrics and Gynecology website), these results are exciting and suggest physical activity during pregnancy is correlated with improved heart function of children. Though further research is warranted, these findings support the prenatal programming hypothesis and warrant further controlled study. Given the current data regarding the benefits of physical activity during pregnancy, it is essential to develop focused health initiatives targeting the gestational period. In light of the fact that cardiovascular disease is the leading cause of death of Americans, research should be done to determine if maternal exercise has a long-term cardioprotective function in children.

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