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Aerobic exercise in pregnancy for prevention of postpartum depression

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ABSTRACT

Introduction: Benefits associated with exercise in pregnancy include lower incidence of diabetes mellitus, and hypertensive disorders, while data on exercise in prevention of postpartum depression are limited.

Objective: The aim of this study was to evaluate whether antenatal exercise decreases the incidence of postpartum depression.

Methods: This was a single-center observational study. Included participants were divided to either exercise or control group. Women in the intervention group were those who performed aerobic exercise during pregnancy, women in the control group were those who did not. Exercise during pregnancy was defined as exercise program including an aerobic exercise program three days per week (60 minutes per session) from the first trimester until at least 30 weeks. Self-reported postpartum depressive symptoms, assessed with the Edinburgh Postnatal Depression Scale (EPDS) 3-months after delivery, was the primary endpoint of the study.

Results: Women who performed aerobic exercise, at least 3 times per week, during pregnancy, had significantly lower risk of gestational diabetes mellitus (11/116 vs 33/123; RR 0.35, 95% CI 0.19 to 0.67; p=0.001); and lower rate of EPDS score ≥12 (17/116 vs 32/123; RR 0.56, 95% CI 0.33 to 0.93; p=0.03). Moreover, those who received EPDS score ≥12, had a lower risk of postpartum depression diagnosis at SCID-5, in case of exercise during pregnancy (5/17 vs 22/32; RR 0.43, 95% CI 0.20 to 0.93; p=0.03).

Conclusions: Among pregnant women, routine aerobic exercise during pregnancy, decreases the incidence of postpartum depression.

INTRODUCTION

Postpartum depression

Epidemiology

Depression is a major public health problem, twice common in women compared to men. Postpartum depression is defined as an episode of major non-psychotic depression that is temporally associated with childbirth, usually with onset within 12 months after delivery (1).

Affects about 1 to 7 women and is associated with significant maternal and perinatal morbidity. A history of major depression is the most important risk factor for developing postpartum depression (2,3). Other risk factors are genetic predisposition, thyroid dysfunction, fear of childbirth, smoking, and maternal age older than 40 years. Predictors of postpartum depression include childcare stress, difficult infant temperament, as well as low self-esteem. No relationship was found for level of education and maternal age, in high-income countries (4). Some studies have found the same prevalence of postpartum depression in different societies (2). However, European and Australian women appear to have lower levels of postpartum depression than women in the United States of America (USA) (5). Women from Asia and South Africa have been identified as being most at risk. The symptoms are similar to symptoms of depression at other times of life, but in addition to low mood, sleep disturbance, change in appetite, diurnal variation in mood, poor concentration,

and irritability, women with postpartum depression also experience guilt about their inability to look after their new baby. For most women, symptoms are transient and relatively mild known as postpartum blues; however, 10–15% of women experience a more disabling and persistent form of mood disturbance (6,7).

Diagnosis

Postpartum depression often remains undiagnosed, although several measures have been studied to detect depressive symptoms in postpartum women. The American Psychiatric Association, in the 2013 diagnostic and statistical manual of mental disorders (DSM-V), amended the name of this condition to peripartum depression and stipulates that the onset of mood disturbance can occur in pregnancy or within four weeks after delivery. The DMS-V classifies peripartum depression as a major depressive disorder. DSM-5 Criteria for major depressive disorder are included in Table 1 (5).

A. Five or more of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either depressed mood or loss of interest or pleasure. Do not include symptoms related to other medical conditions	
1	*Depressed mood most of the day*
2	*Markedly diminished interest or pleasure in almost all activities most of the day*
3	*Significant weigh loss or decrease or increase in appetite nearly every day*
4	*Insomnia or hypersomnia nearly every day*
5	*Psychomotor agitation, or retardation nearly every day*
6	*Fatigue or loss of energy nearly every day*
7	*Feelings of worthlessness or excessive or inappropriate guilt*
8	*Diminished ability to think or concentrate, or indecisiveness, nearly every day*
9	*Recurrent thoughts of death, recurrent suicidal ideation without specific plan, or suicide attempt or a specific plan for committing suicide.*
B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning	
C. The episode is not attributable to the physiological effects of a substance or to another medical condition	

D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder
E. There has never been a manic episode or hypomanic episode.

Table 1. DMS-V Criteria for major depressive disorders

National and international guidelines recommend women to be screened for peripartum depression using a single tool, such as the Edinburgh Postnatal Depression Scale, or a two-step approach, e.g. the Patient Health Questionnaire-2, followed by a more comprehensive screening test if the initial screen is positive. Women positive for peripartum depression screening, should then be evaluated for different disorders, including bipolar disorder, postpartum psychosis, and suicide risk and referred for emergent psychiatric evaluation when appropriate (6). Table 2 shows common screening tests for peripartum depression. All tests are self-administered.

Test	**Number of items**	**Time to administer (minutes)**	**Sensitivity (%)**	**Specificity (%)**
Edinburgh Postnatal Depression Scale	10	<5	75	76
Patient Health Questionnaire-9	9	<5	75	90
Postpartum depression screening scale	35	5 to 10	91	72

Table 2. Common screening tests for peripartum depression

Symptoms

Peripartum depression usually begins within 1 to 3 months after delivery of the baby. In some women, postpartum blues simply continue and become more severe. In other patients, a period of wellbeing after delivery is followed by a gradual onset of major depression (8). In about 25% of peripartum depression, the large majority of incident symptoms occurs during pregnancy, therefore before delivery (9)

Symptoms similar to major depressive disorder that may be present include depressed mood, loss of interest or pleasure in activities, sleep disturbance, appetite disturbance, loss of energy, feelings of worthlessness or guilt, diminished concentration, irritability, anxiety, and thoughts of suicide (1,10). Most women with peripartum depression may worry excessively about baby health and see themselves as inadequate as mothers (4).

The prevalence of peripartum depression is thought to be approximately 10 to 20% (11). However, the prevalence varies widely across countries (12). Actually, according to several authors, has been proposed that the estimated incidence of 10-20% may be an underestimate of the global problem, given that has been found that this disease is often underdiagnosed (13).

Pathophysiology

The pathophysiological mechanisms implicated in postpartum depression is still a subject of debate (14). The evidence supports a role for neuroendocrine changes, neuroinflammation, neurotransmitter alterations, circuit dysfunction, and the involvement of genetics and epigenetics.

Given the timing of onset of the symptoms, altered levels of reproductive hormones have been studied as candidates for potential biomarkers, including increased level of placental corticotropin releasing hormone (CRH), being a strong predictor of peripartum depression in one study (15). The neuroactive steroid allopregnanolone, a metabolite of progesterone, has also recently been proposed as new biomarkers. Indeed, allopregnanolone has been demonstrated to exert anxiolytic and antidepressant effect (16). There is also evidence for a genetic influence in peripartum depression based on twin and family cohort studies (17). The estrogen receptor alpha gene (ESR1) plays a major role in mediating hormonal changes during the peripartum period, and polymorphisms in this receptor have been associated with severity of postpartum depression (18). Other evidence also linked mutation in different gene, including serotonin transporter (5-HTT), polymorphisms in gene encoding for MAOA, and catechol-O-methyltransferase (COMT), with postpartum depression (14).

Studies on epigenetic modifications in postpartum depression are, finally, emerging. These data point to an interaction between epigenetic modification and neurosteroid levels (Figure 1).

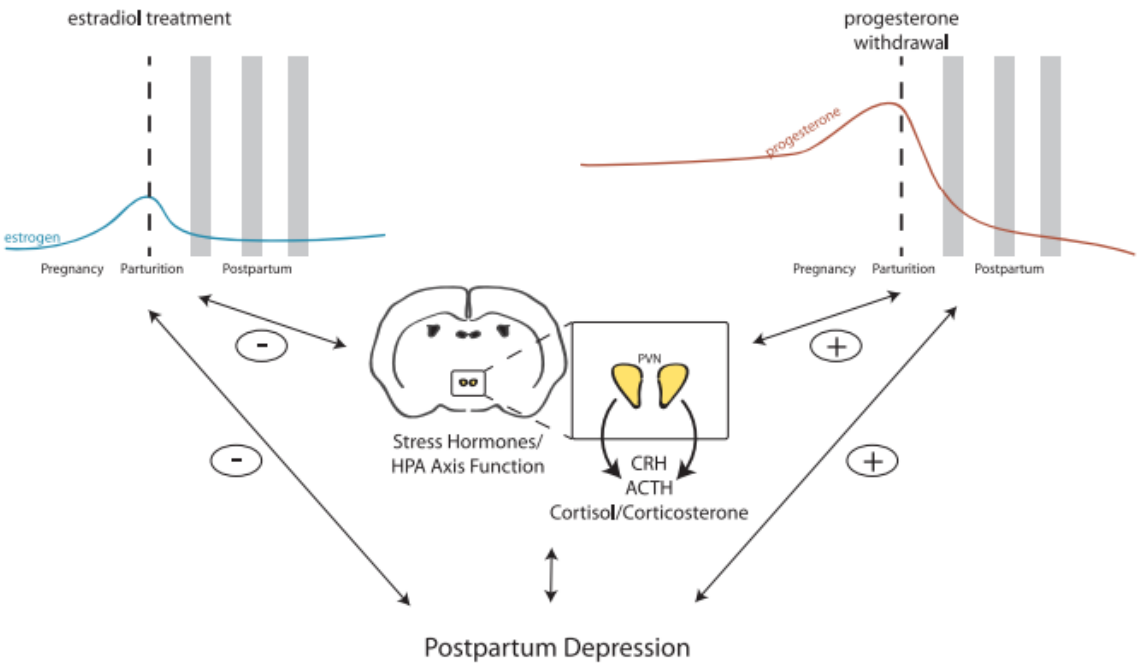

Figure 1. Crosstalk between the HPG and HPA axes in postpartum depression. Adapted from: Payne JL, Maguire J. Pathophysiological mechanisms implicated in postpartum depression. Front Neuroendocrinol. 2019 Jan;52:165-180. doi: 10.1016/j.yfrne.2018.12.001. Epub 2018 Dec 12. PMID: 30552910; PMCID: PMC6370514. (14)

Stress hormones and inflammation are correlated to postpartum depression. Indeed, there are changes in neuroinflammatory markers throughout normal pregnancy. Disruption in these peripartum changes may contribute to peripartum depression (14) (Figure 2)

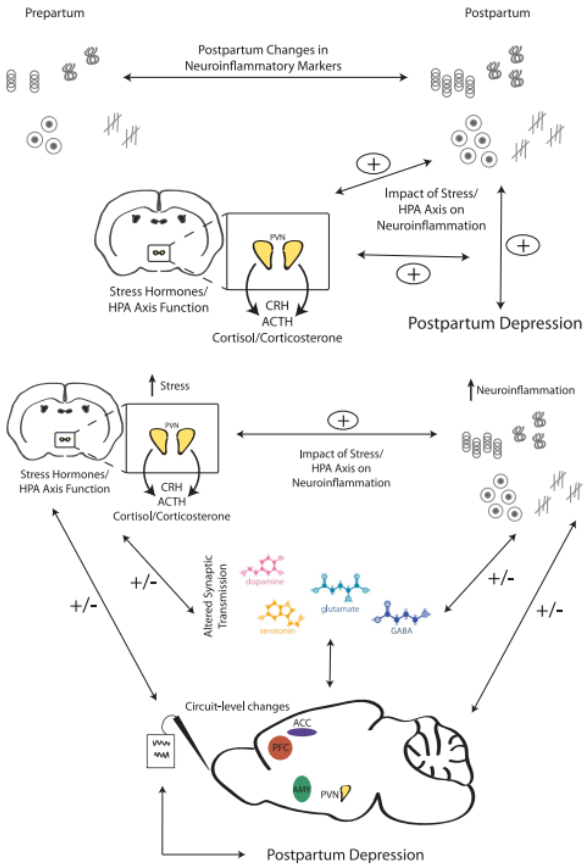

Figure 2. Stress hormones and inflammation are correlated to postpartum depression. Adapted from: Payne JL, Maguire J. Pathophysiological mechanisms implicated in postpartum depression. Front Neuroendocrinol. 2019 Jan;52:165-180.

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Methyldopa, an agonist of presynaptic alpha-2 adrenergic receptors, prevents neurons from releasing norepinephrine and, consequently, inhibits the sympathetic nervous system (19,20). Methyldopa significantly raises the level of vascular endothelial growth factor (VEGF), which is both an angiogenic factor and a neurotrophic agent. Although neuronal function alteration is probably more complex, VEGF dysfunctions neurogenesis and the functioning of sustained neurons by decreasing serotonin concentration and catecholamine levels due to this property. These changes characterize the neurotrophic depression model. Methyldopa reduces cerebral blood flow by impairing baroreceptor signaling pathways and decreasing sympathetic system stimulation. Impaired neuronal function, cognitive decline, and depression are all consequences of decreased cerebral blood flow, particularly in the orbitofrontal cortex (19,20) (Figure 3).

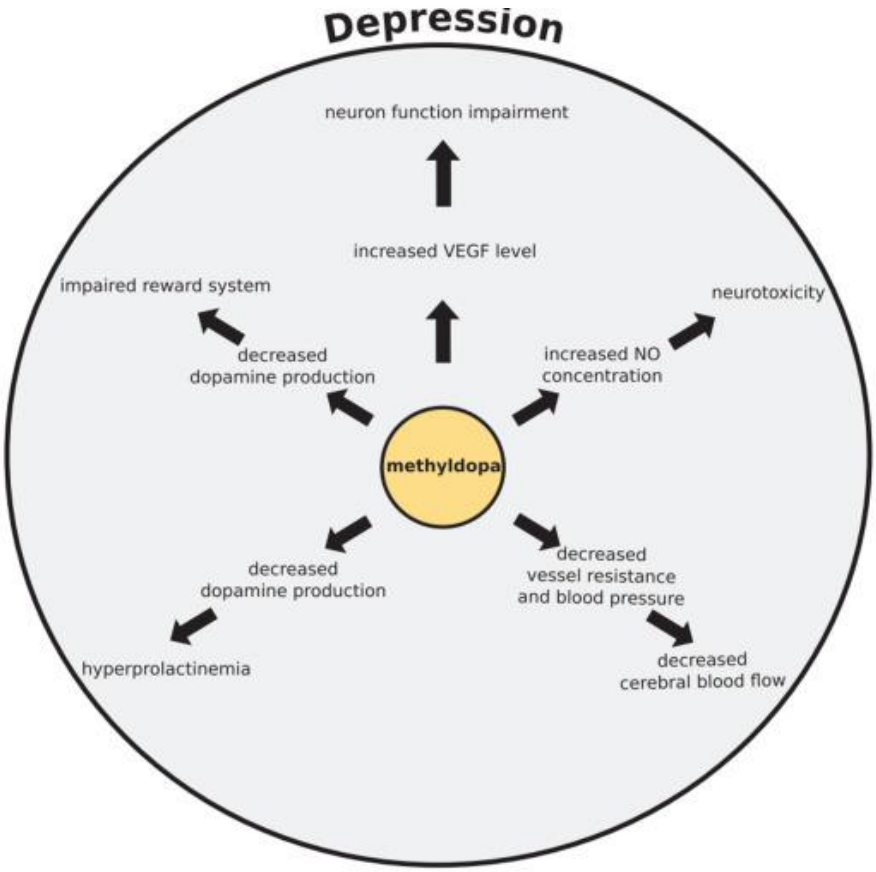

Figure 3. Mechanism of depression induction by methyldopa. Adapted from: Wiciński M, Malinowski B, Puk O, Socha M, Słupski M. Methyldopa as an inductor of postpartum depression and maternal blues: A review. Biomed Pharmacother. 2020 Jul;127:110196. doi: 10.1016/j.biopha.2020.110196. Epub 2020 May 12. PMID: 32413670. (20)

Treatment

Treatment of postpartum depression include pharmacologic and non-pharmacologic approaches (21). Non-pharmacological strategies offer the promise of efficacy without the complexity concerns regarding fetal or neonatal exposure to pharmacological agents. For example, psychotherapy is usually considered the first-line treatment for mild peripartum depression (21).

Regarding the pharmacologic approach, SSRIs are the gold standard treatment for peripartum depression, and are superior to other antidepressants in terms of efficacy and safety. Paroxetine and sertraline are the SSRIs of choice during breastfeeding (22). More evidence is available on the use of SSRIs during breastfeeding than other antidepressant groups and limited data show encouraging outcomes when considering longer term effects on infants. However, they all have relatively long half-lives. Other approaches include SNRI, and brexanolone (22,23). Recently, some new GABAkines (zuranolone and brexanolone) have been administrated to patients with major depressive disorder (MDD) or postpartum depression in randomized controlled trials (24). Nowadays, brexanlone has become the first drug approved by the FDA specifically intended to treat peripartum depression (24). Figure 4 summarize the most common pharmacologic approach used for postpartum depression.

Antidepressant Therapy for PPD

Drug	Dosage	Side Effects	Use During Breast-Feeding
		SSRIs	
Sertraline	50-200 mg/day	Headache, nausea, insomnia, sexual dysfunction, dizziness, tremor	No AEs reported
Paroxetine	20-60 mg/day	Same as sertraline	No AEs reported
Fluoxetine	20-80 mg/day	Same as sertraline	Drug, active metabolites have long elimination half-lives; crying, sleep disturbance, vomiting, watery stools in exposed infants; monitor infant blood levels at 6 wk to rule out accumulation
Fluvoxamine	100-300 mg/day	Same as sertraline	No AEs reported
Citalopram	20-40 mg/day	Somnolence, insomnia, nausea, diaphoresis, agitation	Sleep disturbances possible in nursing infants
		SNRIs	
Venlafaxine	75-300 mg/day	Headache, dizziness, insomnia, nausea, nervousness, sustained HT	Undetectable/low serum levels of drug; metabolites usually measurable; levels similar to adult levels in some infants
Duloxetine	40-60 mg/day	Nausea, dizziness, headache, insomnia, diarrhea, dry mouth	Unknown
		TCAs	
Nortriptyline	75-150 mg/day	Dry mouth, blurred vision, sedation, constipation, OH, weight gain	No AEs reported
Imipramine	50-300 mg/day (outpatients: max 150 mg/day)	Same as nortriptyline	Unknown
Desipramine	75-300 mg/day	Same as nortriptyline	No AEs reported
Amitriptyline	50-300 mg/day (outpatients: max 150 mg/day)	Same as nortriptyline	Unknown
		Other	
Bupropion	150-450 mg/day	Headache, nausea, insomnia, agitation	Unknown
Nefazodone	300-600 mg/day	OH, dry mouth, nausea, somnolence	No published data on serum levels in infants; sedation, poor feeding in premature infants
Mirtazapine	15-45 mg/day	Somnolence, dry mouth, weight gain, increased cholesterol/TG levels	Unknown

PPD: postpartum depression; SSRI: selective serotonin reuptake inhibitor; AE: adverse event; SNRI: serotonin norepinephrine reuptake inhibitor; HT: hypertension; TCA: tricyclic antidepressant; OH: orthostatic hypertension; max: maximum; TG: triglyceride.

Figure 4. Antidepressant therapy for postpartum depression

Exercise in pregnancy

Introduction

Regular physical activity in all phases of life, including pregnancy promotes health benefits. Pregnancy is an ideal time for maintaining or adopting a healthy lifestyle. According to the American College of Obstetricians and Gynecologists (ACOG), physical activity and aerobic exercise in pregnancy are associated with minimal risks and several benefits (25) (Table 3), including include lower incidence of gestational diabetes mellitus, gestational hypertensive disorders, preterm delivery, and cesarean section (4)

Lower incidence of	Higher incidence of
Gestational weight gain	Vaginal delivery
Diabetes mellitus	Maternal satisfaction
Hypertensive disorders	
Preterm birth	
Cesarean delivery	
Birthweight and macrosomia	

Table 3. Benefits of exercise in pregnancy according to the American College of Obstetricians and Gynecologists

There are more than 50 randomized trials published on exercise in pregnancy, and several meta-analyses (26). According to Berghella and Saccone, pregnant women should at least exercise 30 min per session, three times per week.

Characteristics of a safe and effective exercise regimen in pregnancy includes aerobic exercise starting in the early first trimester until delivery, with an intensity of 60% of age-predicted maximum maternal hearth rate (Table 4).

When to start	<12 weeks
Duration of session	30-60 min
Times per week	3-4 up to daily
Intensity of exercise	<60—80% of age-predicted maximum maternal hearth rate
Self-reported intensity of exercise	12-14 on Borg scale
Supervision of exercise	Preferred, if available
When to end	Until delivery, or at least 34 weeks

Table 4. Characteristics of a safe and effective exercise regimen in pregnancy

Benefits of exercise in pregnancy

Our group, have extendedly published researches in the last few years focused on benefits of exercise in pregnant women (26) (Appendix).

In a systematic review of nine trials, including 1,502 overweight or obese singleton gestations, Magro-Malosso et al. found that aerobic exercise for about 30 to 60 min, three to seven times per week, during pregnancy, is associated with a reduction in the incidence of preterm birth (Figure 5), and prevention of gestational diabetes mellitus (27). Benefits of exercise are significantly linked to physicians counselling, and maternal education (28).

In a secondary analysis of the Pessary Trial (29), we found that benefits of exercise remain also in high-risk pregnancies, such as singleton pregnancies with short cervical length, while in the same cohort, activity restriction increase the risk of adverse maternal and perinatal outcome, in a randomized trial conducted in our institution in the 2023 (30).

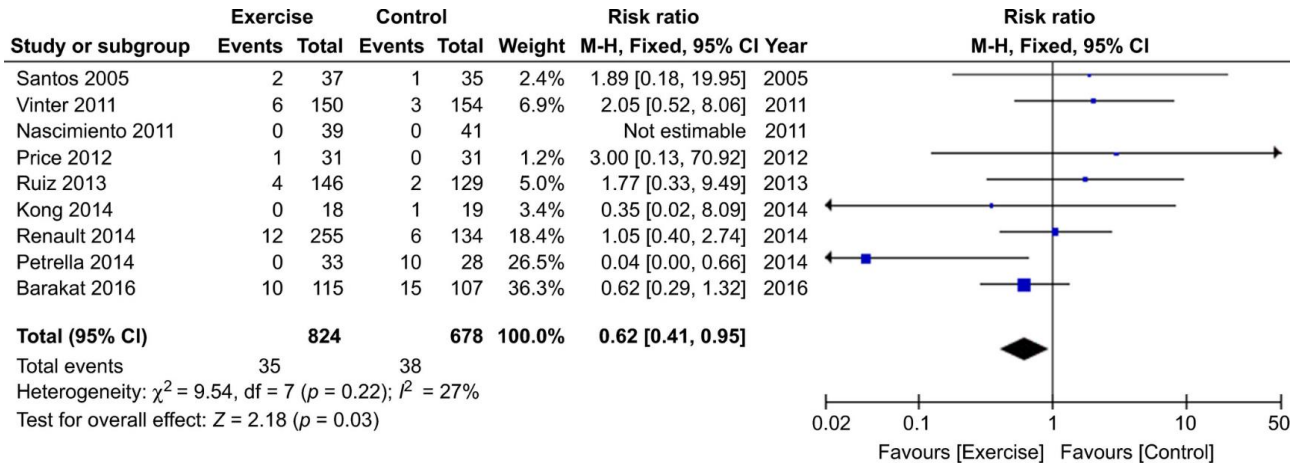

Figure 5. Risk of preterm birth in overweight or obese singleton gestations according to exercise habit in pregnancy. Adapted from Magro-Malosso ER, Saccone G, Di Mascio D, Di Tommaso M, Berghella V. Exercise during pregnancy and risk of preterm birth in overweight and obese women: a systematic review and meta-analysis of randomized controlled trials. Acta Obstet Gynecol Scand. 2017 Mar;96(3):263-273. (27)

Recently, compelling evidence also showed that physical activity and yoga are associated with benefits in depressed pregnant and postpartum women (31), while clinical data on exercise in prevention of postpartum depression are still limited (26,32).

In this context, randomized trials showed that moderate-intensity training effectively decreased stress and depression, during COVID-19 (32). Proposed mechanisms implicated in the pathophysiology of depression include neural alterations in the brain, associated with biochemical changes in growth factors such as brain-derived neurotrophic factor (BDNF) (33,34). Alterations in BDNF activity results in aberrant cortical function, neuronal dysfunction, and psychiatric disorders (35). There are also post-mortem studies that showed that serum BDNF levels are reduced in patient with depression (36). Acute form of aerobic exercise can increase BNF concentrations, when measured in plasma or serum (34, 37, 38) (Figure 6).

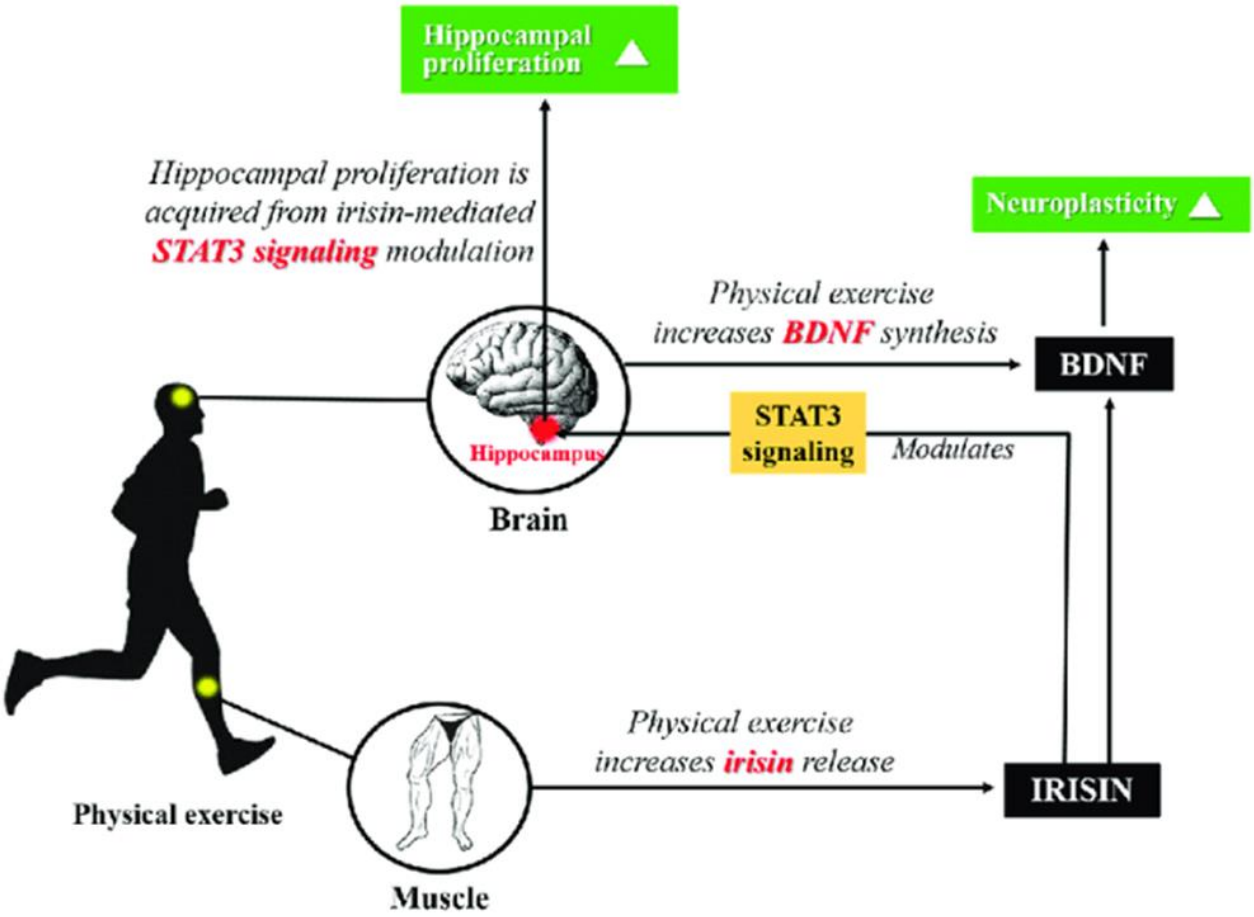

Figure 6. Exercise-irisin-BDNF axis. Physical exercise increases irisin levels and BDNF synthesis. In turn, irisin enhances BDNF synthesis and release, leading to augmented neuroplasticity achieved by the collaboration of irisin and BDNF. Additionally, irisin modulates STAT3 signaling leading to hippocampal proliferation. Adapted from Jin Y et al. (38)

OBJECTIVE

Thus, the aim of this study is to evaluate whether antenatal aerobic exercise decreases the incidence of postpartum depression in low-risk pregnant women.

MATERIAL AND METHODS

Study design and participants

This was a single-center prospective observational study performed at University of Naples Federico II. Outpatient pregnant women referred to our Division from January 1, 2021 to August 30, 2023 were included in the study. Data were collected in a dedicated database, anonymized.

Eligible women were those referred to our institution for first trimester prenatal visit, with low-risk pregnancies. Inclusion criteria were: 18-50 years of age, singleton pregnancy, low-risk gestation, gestational age at the time of fist prenatal visit <14 weeks. Exclusion criteria were: multiple pregnancies, rupture of membranes at the time of randomization, lethal fetal structural abnormality, vaginal bleeding at the time of randomization, history of prior postpartum depression, high-risk pregnancy (i.e. chronic hypertension, diabetes, prior spontaneous preterm birth, cerclage or pessary in a prior pregnancy, history of cervical insufficiency, maternal cardiac disease), miscarriage in the last 12 months.

Intervention and control groups

Women eligible for the study were approached at the time of the first prenatal visit, were informed about the study, and pamphlet, in Italian language, regarding the importance of aerobic exercise in pregnancy were provided, along with oral counselling (Figure 7).

Participants were asked about their exercise habit and were divided into three different groups, for the purpose of the study: women who use to perform aerobic exercise at least 3 times per week; women who use to perform aerobic exercise less than 3 times per week; women who do not perform any exercise. Women were also asked again about their exercise habit in the third trimester of pregnancy, and therefore were divided again into the three groups (9).

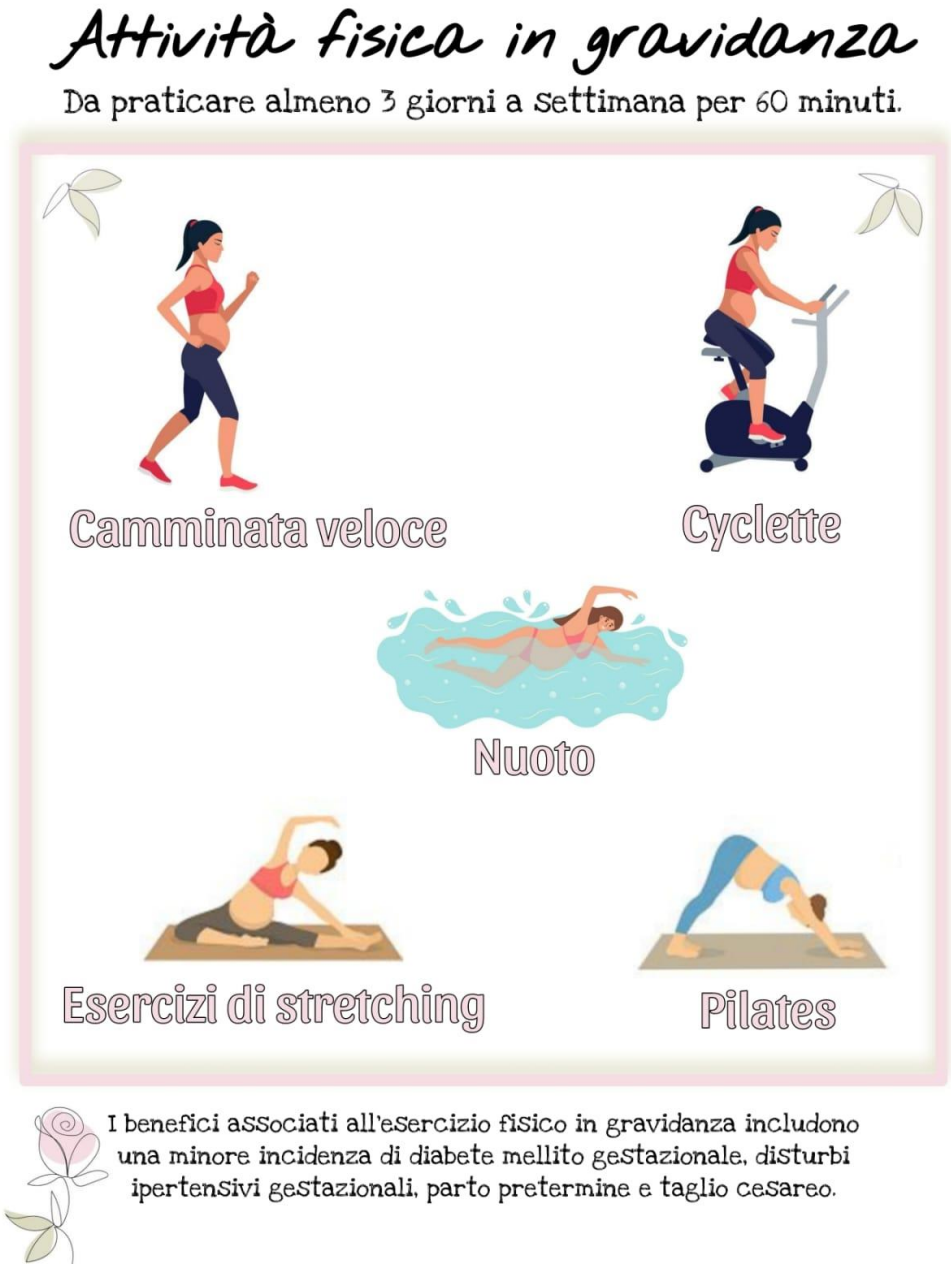

Figure 7. Graphic information provided to the pregnant women regarding exercise during pregnancy

Along with the graphic information provided to the patient, we also provided to all participants a recommended training program, divided into three training stages ensuring progressive overload. Stage one included 15 minutes of aerobic exercise and 15 minutes of strength and pelvic floor exercise. Stage two included 20 minutes of aerobic exercise and 20 minutes of strength and pelvic floor exercise. Stage three included 30 minutes of aerobic exercise and 30 minutes of strength and pelvic floor exercise. All session were preceded by a 5 minutes of active stretching exercise.

For the purpose of the study, we aimed to compared women who performed aerobic exercise at least 3 times per week during pregnancy (at least until 30 weeks) (intervention group), with those who did not perform any exercise during pregnancy (control group).

Participants in both groups received general nutritional counselling from the health-care providers, as per standard of care.

Primary and secondary outcomes

The primary outcome of the study was the incidence of postpartum depression, defined as EPDS score ≥12, 3 months after delivery. The EPDS (Edinburgh Postnatal Depression Scale) is a postpartum depression screening that consists of 10 items scored on a 4-point Likert scale (0-3) addressing common depressive symptoms experienced in the preceding week. A composite scale is calculated by taking the sum of all items, ranging from 0 (absence of depressive symptoms) to 30 (highest score) (39).

The secondary outcomes were: pregnancy-induced hypertension, preterm birth, mode of delivery, and perinatal outcomes. Data on pregnancy outcomes were obtained from hospital maternity records. In case of preterm birth, records were examined to determine whether the delivery was medically indicated (iatrogenic preterm birth) or spontaneous.

We also assessed women positive for the EPDS screening, with the structured clinical interview for DSM-5 (SCID-5) at 3 months follow-up. The SCID-5 was used to assess depressive symptoms including depressed mood, diminished pleasure in normal everyday activities, weight loss/decreased appetite, sleep problems, psychomotor disturbances, low energy level, feelings of guilt or worthlessness, impaired cognitive function, and suicidal thoughts. The interview resulted in a dichotomous yes/no for depression (40).

Statistical analysis

Data are shown as means, or as number (percentage). Univariate comparisons of dichotomous data were performed with the use of the chi-square test with continuity correction. Comparisons between groups were performed with the use of the T-test to test group means by assuming equal within-group variances.

The effect of exercise in pregnancy on the cumulative incidence of each outcome was quantified as the unadjusted relative risk (RR) and its 95% confidence interval (CI). 95% CIs were assessed by using the bootstrap method. No adjustment for multiple comparisons was made, so the findings of the secondary outcomes should be considered exploratory.

A 2-sided P value less than .05 was considered significant. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) v. 19.0 (IBM Inc).

Sample size calculation

Calculation of the sample size was based on the following considerations: a prevalence of activity restriction in pregnancy of about 10% or less; incidence of aerobic exercise at least two times per week of about 20% or less. We also estimated an incidence of peripartum depression of about 5 to 15% in our cohort. We determined that a sample size of about 450-500 patients would provide a power of 80% to detect a 10% relative reduction in the primary outcome from a baseline risk of 15%, with a 2-sided type 1 error of 5%.

RESULTS

During the study period, 485 pregnant women, who met the inclusion criteria, were classified, regarding their exercise habit. In our cohort, 116 (23.9%) performed aerobic exercise at least 3 times per week during pregnancy; 246 (50.7%) performed aerobic exercise less than 3 times per week during pregnancy; and 123 (25.4%) performed no exercise during pregnancy (Figure 6).

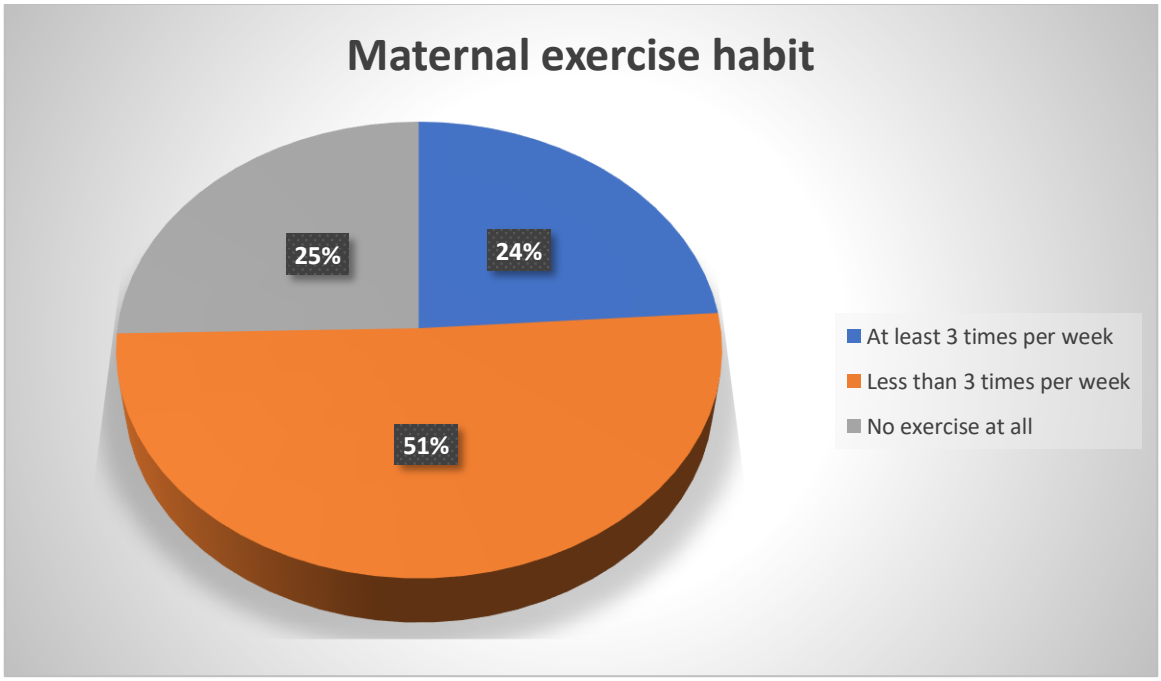

Figure 8. Distribution of the cohort according to women exercise habit

Table 6 shows the baseline demographic and clinical characteristics for intervention and control group. No statistically significant differences were found in maternal demographics.

	Intervention group **N = 116**	**Control group** **N = 123**	**p-value**
Age	27.4±4.8	28.2±5.1	NS
Smoking	37/116	41/123	NS
BMI	24.8±6.3	25.3±4.9	NS
Nulliparous	83/116	91/123	NS
Prior preterm birth	74/116	81/123	NS
Prior uterine surgery	4/116	6/123	NS

Table 6. Maternal characteristics of the participants. Data are shown as mean with standard deviation or as number. NS, non-significant; BMI, body mass index

We found that women who performed aerobic exercise, at least 3 times per week, during pregnancy, had significantly lower risk of gestational diabetes mellitus (11/116 vs 33/123; RR 0.35, 95% CI 0.19 to 0.67; p=0.001); and lower rate of EPDS score ≥12 (17/116 vs 32/123; RR 0.56, 95% CI 0.33 to 0.93; p=0.03) (Figure 9). Moreover, those who received EPDS score ≥12, had a lower risk of postpartum depression diagnosis at SCID-5, in case of exercise during pregnancy (5/17 vs 22/32; RR 0.43, 95% CI 0.20 to 0.93; p=0.03) (Figure 10) (Table 7).

	Intervention group N = 116	**Control group N = 123**	**RR (95% CI)**	**p-value**
Preterm birth <37 weeks	16/116	21/123	NS	NS
GDM	11/116	33/123	**0.35 (0.19 to 0.67)**	**0.001**
PIH	29/116	34/123	NS	NS
Cesarean delivery	37/116	44/123	NS	NS
Perinatal death	0/116	0/123	-	NS
Admission to NICU	6/116	4/123	NS	NS
EPDS score ≥12	17/116	32/123	**0.56 (0.33 to 0.96)**	**0.03**
Postpartum depression at SCID-5	5/17	22/32	**0.43 (0.20 to 0.93)**	**0.03**

Table 6. Primary and secondary outcomes. Data are shown as mean with standard deviation or as number. RR, relative risk; CI, confidence interval; GDM, gestational diabetes mellitus; PIH, pregnancy induced hypertension; NICU, neonatal intensive care unit; EPDS, Edinburgh Postnatal Depression Scale; SCID, Structured Clinical Interview for DSM-5; NS, non-significant. Boldface data, statistically significant

Figure 9. Incidence of EPDS score ≥12 according to women exercise habit (17/116 vs 32/123; RR 0.56, 95% CI 0.33 to 0.93; p=0.03)

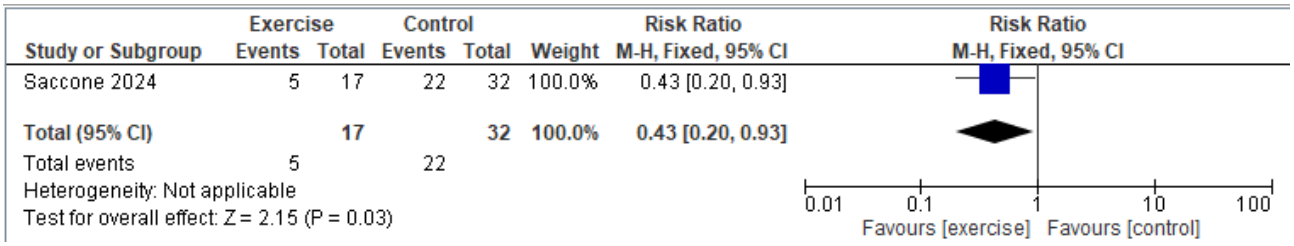

Figure 10. Diagnosis of postpartum depression at SCID-5 according to women exercise habit (5/17 vs 22/32; RR 0.43, 95% CI 0.20 to 0.93; p=0.03)

CONCLUSIONS

This study, of low-risk singleton gestations, showed that aerobic exercise during pregnancy reduces the risk of postpartum depression. This study did support earlier findings of a meta-analysis that showed that, compared with traditional control approaches (psychosocial and psychological interventions), exercise seems have a superior effect on postpartum depression symptoms (41-43). Moreover, no detrimental effects, were found, associated with exercise in our cohort.

Postpartum depression is usually defined as the occurrence of a minor or major depression in pregnancy or after delivery (1). Postpartum depression negatively affects women and their family. It is also an important risk factor for future major depressive episodes (3). The primary prevention of postpartum depression may therefore help to avoid a long, costly, and hard-to-access process of recovery (3).

Physical activity, mostly aerobic exercise, have been proposed for treatment and prevention of postpartum depression (44-51). Physical activity, indeed, may reduce depressive symptoms through biological mechanisms, for example by increasing beta-endorphins levels, which are associated with improved mood, euphoria and enthusiasm but also pain reduction (52) and increasing levels of brain neurotransmitters (including dopamine, serotonin and noradrenaline) associated with feelings of satisfaction and euphoria (48).

In our observational study, we found a potential moderate preventive effect of prenatal aerobic exercise on perinatal depressive symptoms, with no detrimental effects on fetal outcomes, or risk of preterm birth. We also found a reduced risk of gestational diabetes mellitus, that is a complication associated with obesity and sedentary lifestyle (24,26)

Different theories can be discussed to explain our findings.

Exercise induces beneficial responses in the brain, which is accompanied by an increase in BDNF, a trophic factor associated with cognitive improvement and the alleviation of depression and anxiety (53). Also, aerobic exercise, such as running, increases the number of dendritic spines in medial prefrontal cortex and expression of synaptic markers in several regions supporting cognitive function (54) (Figure 11). Depression is closely associated with alterations in dendritic spine morphology and spine density (55). Generally, chronic stress causes dendritic atrophy and spine loss in the neurons of the hippocampus and prefrontal cortex. Meanwhile, neurons of the amygdala and nucleus accumbens exhibit an increase in spine density. These alterations induced by chronic stress are often accompanied by depression-like behaviors (56,57). Notably, in recent studies, non-pharmaceutical interventions, such as physical exercise and training, have been employed to improve the memory function of people with dementia, via slowing down the amyloid pathology and preventing the loss of synaptic contacts (54,56).

Finally, regarding the decreased risk of diabetes mellitus, noticed in our cohort, weight loss resulting from healthy eating and increased physical activity enables muscle cells to use insulin and glucose more efficiently, thus lowering diabetes risk (58)

In summary, based on our findings, aerobic exercise during pregnancy, with at least 3 session per week of 60-min, is a safe and effective approach to reduce the risk of post-partum depression. Future, large, well-designed, multicenter, randomized trial, are required to confirm our results.

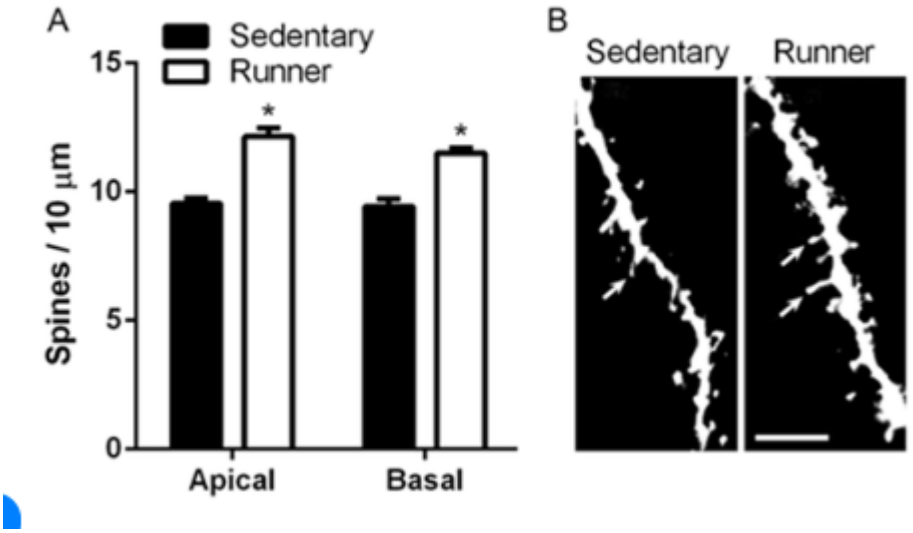

Figure 11. Running increases the number of dendritic spines in medial prefrontal cortex and expression of synaptic markers in several regions supporting cognitive function. A. Running increases dendritic spine density on both apical and basal dendrites in the medial prefrontal cortex. B. Representative images of DiI labeled layer 2/3 pyramidal neuron apical dendrites in the medial prefrontal cortex and in sedentary and running animals. Scale Bar = 5 µm.

Adapted from Xu B et al. (52)

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APPENDIX

Published papers authored by Gabriele Saccone, on exercise in pregnancy

1. Magro Malosso ER, Saccone G, Di Mascio D, Berghella V. Maternal education predicts compliance to exercise during pregnancy. Acta Obstet Gynecol Scand. 2019 Jun;98(6):809. doi: 10.1111/aogs.13550. Epub 2019 Feb 18. PMID: 30698274.
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