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Omega-6 fatty acids and greater likelihood of suicide risk and major depression in early pregnancy

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Abstract

Objective—To estimate the prevalence of suicide risk (SR) and major depressive episode (MDE) in early pregnancy, and the relationship of fatty acids serum status to these outcomes.

Method—Cross-sectional analyses of 234 pregnant women enrolled in a prospective cohort study in Rio de Janeiro/Brazil were performed. SR and MDE were defined according to MINI International Neuropsychiatric Interview. Fatty acids compositions were determined in serum samples obtained between the 6th and 13th gestational week. Statistical analyses included univariate and multiple logistic regressions. Fatty acids data were expressed both as percent of total fatty acids and converted to Z scores then entered as continuous variable into regression models.

Results—The prevalence of SR was 19.6% and MDE was 17.0%. Higher likelihood of SR was observed among women with higher arachidonic acid [AA (20:4n-6): OR=1.45, 95% CI 1.02-2.07] and adrenic acid [AdA (22:4 n-6): OR=1.43, 95% CI 1.01-2.04], and for MDE: AA [OR=1.47, 95% CI 1.03-2.10], and AdA [OR=1.59, 95% CI 1.09-2.32], per standard deviation of fatty acid, in adjusted logistic regressions.

Conclusion—Higher serum status of AA and AdA, two omega-6 fatty acids, were associated with greater likelihood of SR and MDE among pregnant Brazilian women independently of confounding variables.

Keywords

Pregnancy; Suicide Risk; Major Depressive Disorder; Arachidonic Acid; Omega-6 Fatty Acids

INTRODUCTION

Pregnancy creates substantial hormonal and physiological changes, is often followed by stressful social and transitions and is a vulnerable time for onset of mental disorders (1). Although post partum depression has been extensively evaluated, less is known about occurrence and biological determinants of suicide risk (SR) and major depression episode (MDE) in early pregnancy. Deficiencies or excesses in neuroactive nutrients that are selectively concentrated in neural tissues, specifically highly unsaturated omega-3 (n-3 HUFA) and omega-6 (n-6 HUFA) fatty acids, may contribute to vulnerability towards these disorders (2). Both n-3 and n-6 fats cannot be made *de novo* but must be obtained from diet. Fish is a rich source of both n-3 and n-6 HUFAs and lower intakes have been associated to increased risk for depressive symptoms and suicidal thinking in cross-national and cohort based studies; while the majority of blood based studies indicate that n-3 HUFAs are protective, n-6 HUFAs are associated with increased risk [For review see (3, 4)]. Meta-analyses of randomized controlled trials have reported similar efficacy of n-3 HUFA supplementation as fish oils and pharmaceutical antidepressants in reducing significant depressive symptoms (5, 6).

The putative role of n-3 and n-6 HUFAs for depressive symptoms and suicidality is less clear. Selective transportation of HUFAs across the placenta biomagnifies concentrations to the fetus, but may also lead to maternal depletion when dietary intake is insufficient. In an epidemiological investigation, Golding et al. (7) found that mothers with low seafood intake during pregnancy would be at increased risk for depression. Randomized controlled intervention trials during perinatal period have shown promise, but have been difficult to adequately design and conduct (8). Suicidality during pregnancy has become a subject of increasing interest, however much less is known about its occurrence and the role of fatty acids. Lower levels of the n-3 HUFA docosahexaenoic acid (DHA; 22:6 n-3), was associated with increased suicide deaths among 1,600 active duty US Military personnel (9), and one intervention trial with n-3 HUFAs has reported a 45% reduction in suicidal ideation (10).

Thus, in the present study we sought to evaluate possible relationships between n-3 and n-6 HUFAs in maternal serum status and SR and MDE in early pregnancy. Our primary hypothesis was that lower n-3 HUFAs, in particular DHA, would represent greater risk for suicidality and major depression. To our knowledge this is the first epidemiological study on mood disorders among Brazilian pregnant women with investigation of fatty acids blood status. Evaluation of these issues in a Brazilian population, with biological samples, adds diversity to the body of data on HUFA status in pregnancy and to potential psychiatric risks.

METHODS

Study protocol

Design—The current investigation originated from a broader study with a prospective cohort design, performed in the city of Rio de Janeiro, Brazil. Enrollment of pregnant women in the cohort was open during 23 months (November 2009 - October 2011). Baseline assessment was performed between the 6th and the 13th weeks of gestation. At this time,

blood collection and a psychiatric interview were conducted followed by a general questionnaire (socioeconomic data, obstetric history, lifestyle, scales) and anthropometric assessment (body weight and height). All interviews were conducted in appointment days at a pre-natal care center of the Brazilian Unified Health System.

Eligibility criteria was defined as follow: (1) being between the 6th and 13th week of gestation; (2) being between 20 and 40 years of age; (3) being free from any chronic diseases such as hypertension and diabetes; (4) not presenting twin pregnancy, and (5) residing in the study catchment area. During recruitment phase, a continuous on-site researcher interviewed all women that access the pre-natal care at the first time. Women who attended the eligible criteria were invited to join the study. Ninety three percent of eligible women agreed to participate and an appointment for blood collection and clinical assessment were scheduled.

Psychiatric assessment—Psychiatric interviews were conducted using the Mini International Neuropsychiatric Interview (MINI; version 5.0.0) (11) an instrument with a standard model of a brief (15-30 minutes) structured interview for the evaluation of the existence of Axis I psychiatric disorders according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (12). This instrument is divided into modules (A-P), each one containing questions that represent different psychiatric disorders. The patients must answer yes or no to each of the questions. The interviews were performed by medical doctors and graduate students in mental health trained for this purpose.

SR was performed by means of ‘suicidality’ level obtained by the MINI interview. In this module, six questions are applied and positive answers received a unique score as follows: “In the past month did you: (1) think that would be better off dead or wish you were dead? (Score = 1); (2) want to harm yourself or to hurt or to injure yourself? (Score = 2); (3) think about suicide? (Score = 6); (4) have you a suicide plan? (Score = 10); (5) attempt suicide? (Score = 10); (6) in your past lifetime, did you ever make a suicide attempt? (Score = 4). In this instrument, a positive answer of at least one of these features is considered as SR. This variable was entered as binary (SR = yes/no) into logistic regression. The module for MDE provides the current status of this episode (yes or no) and was entered as binary (MDE = yes/no) into logistic regression. For the present investigation, both SR and MDE were considered as dependent variable and a theoretical model was built for each outcome.

Independent variables—To build the theoretical model for SR and MDE, the following independent variables were included in the analyses: socio-economic: monthly per capita family income (in tertiles of American dollars); socio-demographic: age (20-29; 30-40 years), marital status (married or stable relationship, single), self-reported skin color (white, non-white), education (< 8, ≥ 9 years), work status (yes, no); lifestyle: smoking habit (yes, no), current alcohol consumption (yes, no), sleeping hours at night (<8, ≥ 8 years); obstetric: parity (0, 1, ≥ 2), previous history of abortion (no, yes), desire to be pregnant (yes, no); home crowding, defined as number of people per dorms (<2, ≥ 2); reported family history of depression (first-degree relative) (yes, no), reported family history of suicide (first-degree relative) (yes, no). Additionally, some confounding factors were also considered: number of close friends (0-1, ≥ 2), number of close relatives (0-1, ≥ 2).

Nutritional status was included in the theoretical model defined by pre-pregnancy body index mass (BMI [weight (kg)/stature (m²)] obtained at the baseline (between the 6th and 13th weeks). The cut-off points proposed by the World Health Organization (13) and recently endorsed by the Institute of Medicine were considered for the classification of the women's initial nutritional status (14). The women were weighted with a digital scale (Filizzola Ltd., Sao Paulo, Brazil). Stature was measured in duplicate with a Seca Portable Stadiometer (Seca Ltd., Hamburg, Germany). All anthropometric measurements were standardized and taken by trained interviewers (15).

Ethics Approval—The study protocol was approved by the research ethics committee of the Institute of Psychiatry of the Rio de Janeiro Federal University (CAAE: 0012.0.249.000-09) and Municipal Secretary of Health of the city of Rio de Janeiro (CAAE: 0139.0.314.000-09). All participants signed two-way term of consent, which was obtained freely and spontaneously, after all necessary clarifications had been provided.

Sample analysis—Blood samples (5 ml) were collected into vacutainer tubes with separator gel from each woman by a health clinic professional in the 1st clinical visit, when women had 13 weeks of pregnancy. Women were advised to fast for 12 h. Serum and plasma were separated after centrifugation at 1500g and 4°C for 15 minutes, and stored at -80°C for later measurements. To perform the fatty acid blood composition, serum samples were shipped in dry ice to the Section of Nutritional Neurosciences, Laboratory of Membrane Biochemistry and Biophysics, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, and analyzed on the premises by an appropriately trained technician. Sample were received in January 2012, and assayed for total fatty acid composition employing a high-throughput robotic direct methylation coupled with fast gas-liquid chromatography developed and validated by the referred institution, with inter-assay variance of <0.5% (16, 17).

Statistical analysis—The database was constructed by way of duplicate typing followed by an analysis of the data consistency. Both procedures were conducted using the software Census and Survey Processing System (CSPPro) version 4.1.002.

We first analysed the prevalence distribution of the two outcomes (SR or MDE) according to key confounding variables that were previously determined in a theoretical model. In the first stage, the distribution of each co-variable of the sample was investigated according to each outcome with the objective of defining the categories with higher prevalence. The prevalences were compared by means of the chi-squared test for proportions. In the second stage, all variables with a p-value < 0.20 were taken to the multivariate model to compose the final model of each outcome. Two independent multivariate models were built only with the co-variables that presented a p-value < 0.05 for each outcome.

The third stage considered the independent effect of each individual fatty acid on the two outcomes, adjusting for the variables included on the final multivariate model. Fatty acid data were converted to Z scores and entered as continuous variables into logistic regression analyses models. Each individual fatty acid was assessed (eg, increase in Z score) for SR and MDE. An independent multivariate model for each fatty acid was adjusted by key

confounders previously identified for the corresponding outcome. However, considering the possible fatty acid mobilization in early pregnancy, gestational week was entered into the model as a continuous variable to adjust the fatty acid levels. The strength of the association was measured using Odds Ratio and 95% confidence intervals. All statistical analyses were conducted with the Statistical Package for Social Science version 19.0.

RESULTS

Two hundred and thirty four women were enrolled in the study. The prevalence of SR observed in the sample was 19.6% (n=46). The greater prevalence of SR was observed in women with 2 children (38.2%), single (36.0%), with current alcohol consumption (31.9%), with the lowest monthly percapita income family (29.5%), and in those with home crowding > 2 persons per dorms (28.2%) (Table 1). The prevalence of MDE observed in the sample was 17.0% (n=40), and greater prevalence was observed among smokers (44.4%), single (36%), with 2 children (24.4%), with women with 1 close relatives (24.0%), women with the lowest monthly percapita income family (23.6%), and with those at youngest age (19.8%) (Table 1).

In the final model for SR, the variables that remained associated with this outcome were marital status and parity, increasing the chances for occurrence of SR in 2.98 times (95% CI: 1.16-2.72) and 5.82 (95% CI: 2.15-12.34), respectively (Data not shown). In the final model for MDE, the variables that remained associated with MDE were marital status (OR = 3.07; 95% CI: 1.19-7.92), current smoking habit (OR = 5.42; 95% CI: 1.89-15.50), and number of close relatives (OR = 2.32; 95% CI: 1.11-4.85) (Data not shown).

In multivariate models of SR, each standard deviation of higher arachidonic acid (AA; 20:4n-6) and adrenic acid (AdA; 22:4n-6) were associated, respectively, with 45% (OR = 1.45; 95% CI: 1.02-2.07) and 43% (OR = 1.43; 95% CI: 1.01-2.04) greater chances of SR after controlling for marital status, parity, and gestational week (Table 2). In the multivariate models of MDE, each standard deviation of higher AA and AdA were associated, respectively, with 47% (OR = 1.47; 95% CI: 1.03-2.10) and 59% (OR = 1.59; 95% CI: 1.09-2.32) greater chances of MDE, after controlling for marital status, smoking habit, number of close relatives, and gestational week (Table 3).

DISCUSSION

The present investigation revealed that higher blood status of AA and AdA, two omega-6 fatty acids, were associated with higher likelihood of SR and MDE among low-income Brazilian pregnant women studied in early pregnancy. These results remained significant after adjustment for confounders identified after multiple regression model with social, demographic and behaviour variables. Gestational week was added into the model to control residual effect of fatty acid mobilization that possible occur in the first weeks of pregnancy. These results are consistent with findings of higher levels of AA associated with depressive symptoms among elderly subjects with mild cognitive impairment (18) and fatty acids associated with increased risk of US military suicide deaths (9) and seasonal variations in serum AA and suicide (19). To our knowledge, this is the first study that examines essential

fatty acid status and SR in pregnancy, and the first to provide evidences that excess of long chain n-6 PUFA serum levels may be associated with greater likelihood of SR and MDE.

The strengths of the present study are the prevalence on mood disorders based on a specific diagnostic instrument for mental disorders (11); the suicidality module consists of six questions regarding to suicidal behavior to derive the variable of SR. Another important strength of the present investigation is the use of serum concentrations of fatty acids which are known as biological markers of dietary intake in epidemiological investigations (20). For this reason, we judged that inclusion of dietary data would be less accurate for establishing omega-3 and omega-6 status considering difficulties in determining energy intake usually associated with dietary questionnaires (21), especially during pregnancy (22). The main limitation of this investigation is the socioeconomic background of the study sample. A study review of long chain essential fatty acids status in Brazilian pregnant women showed inadequacy of dietary DHA intake and low maternal DHA blood status compared to the international literature (23). That is probably the critical reason why we have not found a positive association of lower omega-3 blood status with SR or MDE. Thus, there are limits on the external validity of this study, as our results derive from women of low socioeconomic background attending a public health center in the city of Rio de Janeiro and may not be generalizable to women of higher education or socioeconomic level.

AA and AdA are nutritionally fatty acids, primally obtained from animal products contained in the diet, or converted from the nutritionally essential linoleic acid (18:2 n-6), mostly in the liver (24, 25). AA and DHA (22:6 n-3) are the main lipid component of central neuro system (CNS) and indispensable to its normal development and biochemistry (26). In the last century, populations exposed to a western dietary pattern have experienced a shift in their fat consumption, with higher intake from processed food, mostly manufactured with vegetable oils rich in omega-6 fatty acids such as soybean, corn and sunflower and significant lower intake of dietary sources of omega-3 fatty acids (e.g. oily fish, green vegetables and nuts) (27). Suicidality and major depression are both linked to the neurobiology of inflammatory response in the brain (28-30). AA is a substrate for the synthesis of inflammatory cytokines (31), and long chain omega-3 fatty acids DHA and eicosapentaenoic acid (EPA; 20:5 n3) have anti-inflammatory and inflammation resolving properties (32, 33). Although the present investigation does not provide evidence to support the hypothesis of omega-3 insufficiency as a possible risk for mood disorders, our findings suggest that higher AA and AdA status may be considered as a risk factor for SR and MDE in early pregnancy.

Several biological mechanisms are consistent with the association between higher AA and AdA and SR and MDE. Excessive serum levels AA and its cascade were first implicated in the pathogenesis of affective disorders in 1989 (34) and the net overlapping effects of at least three mood stabilizers are decreased turnover of AA, as well as decreased brain cyclo-oxygenase-2 and prostaglandin E(2) (35). Two randomized clinical trials have reported that inhibition cyclo-oxygenase-2 with Celebrex significantly reduced depressive symptoms (36). A critical role for excess prostaglandin E(2) has been further evaluate in animal models of depression (37) and social defeat stress (38). An evaluation of fatty acid compositions in adolescent brains from autopsy found that suicide victims indicated a possible selective

abnormality in AA metabolism; victims do not exhibit the normal age-related decrease in AdA composition and the ratio AA/DHA (39). Another putative link between diet, serum levels of n-6 long chain PUFA and mood disorders is the endocannabinoid system of the CNS, which is involved in regulating physiological and pathophysiological aspects of mood in addition to other functions (40). The two principal endocannabinoids - anandamide (AEA) and 2-arachidonoylglycerol (2-AG) - are structurally derived from essential n-6 fatty acids, mainly AA, and act as cellular signaling functions in relation to modulation of neurotransmitter release implicated in the pathophysiology of suicide and depression (41). Selective dietary elevation of LA in animals since pregnancy resulted in higher content of n-6 PUFA in brain composition, including AA and ADA, and brain 2-AG (42).

In the past years, some fish oil supplementation trials in pregnancy have been conducted focused on treatment or prevention of maternal depression (43-46). Despite of plausible neurotrophic effect of n-3 PUFA on mental health only one study in pregnancy reported a positive effect of DHA and EPA over placebo (44). However, intervention trials for depressive disorders are difficult to conduct for many reasons; subjects with sufficient depressive symptomatology must ethically be treated, prevention trials must be large for adequate statistical power and placebo responses are substantial.

Our investigation reveals that SR (19.6%) and MDE (17.0%) are high among low-income Brazilian women in early pregnancy (13 weeks gestation), using an individual structured psychiatric interview. Regarding maternal depression, reported prevalence's from developing countries are higher compared to developed ones. A recent systematic review conducted by Fisher et al. (2012) covering 17 low- to middle-income countries summarized mean prevalence of antenatal depression of 15.6% (95% CI 15.4 – 15.9) (47). Regarding suicidality, our findings are in line with a cross-sectional study carried out by Pinheiro et al. (2012) focused on pregnant teenagers attending the public pre-natal care centers in a southern city of Brazil (48). In this study, SR was accounted as 13.3% and MDE as 17.8%. Other studies on suicidality in pregnancy were focused unique on suicide ideation, and reported prevalences ranged from 2.9% (49) to 14.6% (50). The main reason for this difference is that the MINI defines SR as a sum of several components (thoughts of death, self-harm and suicidal ideation, and suicide attempt [past and recent]) related to suicidality, thus the result is not restricted to thoughts of suicidal ideation as by self-reported scales.

Our study provide evidences that SR and MDE are common public health and clinic problems among low-income Brazilian women in early pregnancy. Moreover, this is the first epidemiological study on mood disorders among Brazilian pregnant women with investigation of fatty acids blood levels, and the first to provide evidences that excess of long chain n-6 PUFA serum status might be associated with greater likelihood of SR and MDE.

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References

1. Christian LM. Physiological reactivity to psychological stress in human pregnancy: current knowledge and future directions. *Prog Neurobiol.* 2012; 99:106–116. [PubMed: 22800930]
2. Hibbeln JR, Davis JM. Considerations regarding neuropsychiatric nutritional requirements for intakes of omega-3 highly unsaturated fatty acids. *Prostaglandins Leukot Essent Fatty Acids.* 2009; 81:179–186. [PubMed: 19619995]
3. Hibbeln JR. Depression, suicide and deficiencies of omega-3 essential fatty acids in modern diets. *World Rev Nutr Diet.* 2009; 99:17–30. [PubMed: 19136836]
4. Milte CM, Sinn N, Howe PR. Polyunsaturated fatty acid status in attention deficit hyperactivity disorder, depression, and Alzheimer's disease: towards an omega-3 index for mental health? *Nutr Rev.* 2009; 67:573–590. [PubMed: 19785689]
5. Sublette ME, Ellis SP, Geant AL, Mann JJ. Meta-analysis of the effects of eicosapentaenoic acid (EPA) in clinical trials in depression. *J Clin Psychiatry.* 2011; 72:1577–1584. [PubMed: 21939614]
6. Lin PY, Huang SY, Su KP. A meta-analytic review of polyunsaturated fatty acid compositions in patients with depression. *Biol Psychiatry.* 2010; 68:140–147. [PubMed: 20452573]
7. Golding J, Steer C, Emmett P, Davis JM, Hibbeln JR. High levels of depressive symptoms in pregnancy with low omega-3 fatty acid intake from fish. *Epidemiology.* 2009; 20:598–603. [PubMed: 19289957]
8. Jans LA, Giltay EJ, Van der Does AJ. The efficacy of n-3 fatty acids DHA and EPA (fish oil) for perinatal depression. *Br J Nutr.* 2010; 104:1577–1585. [PubMed: 21078211]
9. Lewis MD, Hibbeln JR, Johnson JE, Lin YH, Hyun DY, Loewke JD. Suicide deaths of active-duty US military and omega-3 fatty-acid status: a case-control comparison. *J Clin Psychiatry.* 2011; 72:1585–1590. [PubMed: 21903029]
10. Hallahan B, Hibbeln JR, Davis JM, Garland MR. Omega-3 fatty acid supplementation in patients with recurrent self-harm. Single-centre double-blind randomised controlled trial. *Br J Psychiatry.* 2007; 190:118–122. [PubMed: 17267927]
11. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry.* 1998; 59:22–33. [PubMed: 9881538]
12. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders DSM-IV-TR (Text Revision). Fourth Edition. American Psychiatric Publishing; USA: 2000.
13. Physical status: the use and interpretation of anthropometry. World Health Organization; Geneva: 1995.
14. Weight gain during pregnancy: reexamining the guidelines nutrition during pregnancy. National Academic Press; USA: 2009.
15. Lohman, GT.; Roche, AF.; Martorell, R. Anthropometric standardization reference manual. Human Kinetics Books; USA: 1998.
16. Masood MA, Salem N. High-throughput analysis of plasma fatty acid methyl esters employing robotic transesterification and fast gas chromatography. *Lipids.* 2008; 43:171–180. [PubMed: 18084789]
17. Lin YH, Salem N, Wells EM, et al. Automated high-throughput fatty acid analysis of umbilical cord serum and application to an epidemiological study. *Lipids.* 2012; 47:527–539. [PubMed: 22430941]
18. Milte CM, Sinn N, Street SJ, Buckley JD, Coates AM, Howe PR. Erythrocyte polyunsaturated fatty acid status, memory, cognition and mood in older adults with mild cognitive impairment and healthy controls. *Prostaglandins Leukot Essent Fatty Acids.* 2011; 84:153–161. [PubMed: 21392955]

19. De Vriese SR, Christophe AB, Maes M. In humans, the seasonal variation in poly-unsaturated fatty acids is related to the seasonal variation in violent suicide and serotonergic markers of violent suicide. *Prostaglandins Leukot Essent Fatty Acids*. 2004; 71:13–18. [PubMed: 15172679]
20. Arab L, Akbar J. Biomarkers and the measurement of fatty acids. *Public Health Nutr*. 2002; 5:865–871. [PubMed: 12638594]
21. Bingham SA. Biomarkers in nutritional epidemiology. *Public Health Nutr*. 2002; 5:821–827. [PubMed: 12638591]
22. Neuhouwer ML, Tinker L, Shaw PA, et al. Use of recovery biomarkers to calibrate nutrient consumption self-reports in the Women's Health Initiative. *Am J Epidemiol*. 2008; 167:1247–1259. [PubMed: 18344516]
23. Torres AG, Trugo NM. Evidence of inadequate docosahexaenoic acid status in Brazilian pregnant and lactating women. *Rev Saude Publica*. 2009; 43:359–368. [PubMed: 19287877]
24. Salem N, Pawlosky R, Wegher B, Hibbeln J. In vivo conversion of linoleic acid to arachidonic acid in human adults. *Prostaglandins Leukot Essent Fatty Acids*. 1999; 60:407–410. [PubMed: 10471130]
25. Rapoport SI, Rao JS, Igarashi M. Brain metabolism of nutritionally essential polyunsaturated fatty acids depends on both the diet and the liver. *Prostaglandins Leukot Essent Fatty Acids*. 2007; 77:251–261. [PubMed: 18060754]
26. Chen CT, Green JT, Orr SK, Bazinet RP. Regulation of brain polyunsaturated fatty acid uptake and turnover. *Prostaglandins Leukot Essent Fatty Acids*. 2008; 79:85–91. [PubMed: 18938067]
27. Blasbalg TL, Hibbeln JR, Ramsden CE, et al. Changes in consumption of omega-3 and omega-6 fatty acids in the United States during the 20th century. *AJCN*. 2011; 93:950–962.
28. Erhardt S, L C, Linderholm KR, Janelidze S, et al. Connecting inflammation with glutamate agonism in suicidality. *Neuropsychopharmacology*. 2012; 3 Epub ahead of print.
29. Maes M, Song C, Yirmiya R. Targeting IL-1 in depression. *Expert Opin Ther Targets*. 2012; 16:1097–1112. [PubMed: 22925041]
30. Maes M. Evidence for an immune-response in major depression - a review and hypothesis. *Prog Neuropsychopharmacol Biol Psychiatry*. 1995; 19:11–38. [PubMed: 7708925]
31. Lotrich FE, Sears B, McNamara RK. Elevated ratio of arachidonic acid to long-chain omega-3 fatty acids predicts depression development following interferon-alpha treatment: relationship with interleukin-6. *Brain Behav Immun*. 2012; 19 Epub ahead of print.
32. McNamara RK, Jandacek R, Rider T, Tso P, Cole-Strauss A, Lipton JW. Omega-3 fatty acid deficiency increases constitutive pro-inflammatory cytokine production in rats: relationship with central serotonin turnover. *Prostaglandins Leukot Essent Fatty Acids*. 2010; 83:185–191. [PubMed: 20817496]
33. Calder PC. The relationship between the fatty acid composition of immune cells and their function. *Prostaglandins Leukot Essent Fatty Acids*. 2008; 79:101–108. [PubMed: 18951005]
34. Hibbeln JR, Palmer JW, Davis JM. Are disturbances in lipid-protein interactions by phospholipase-A2 a predisposing factor in affective illness? *Biol Psychiatry*. 1989; 25:945–961. [PubMed: 2566335]
35. Bazinet RP. Is the brain arachidonic acid cascade a common target of drugs used to manage bipolar disorder? *Biochem Soc Trans*. 2009; 37:1104–1109. [PubMed: 19754461]
36. Akhondzadeh S, Jafari S, Raisi F, et al. Clinical trial of adjunctive celecoxib treatment in patients with major depression: a double blind and placebo controlled trial. *Depress Anxiety*. 2009; 26:607–611. [PubMed: 19496103]
37. Song C, Zhang XY, Manku M. Increased phospholipase A2 activity and inflammatory response but decreased nerve growth factor expression in the olfactory bulbectomized rat model of depression: effects of chronic ethyl-eicosapentaenoate treatment. *J Neurosci*. 2009; 29:14–22. [PubMed: 19129380]
38. Tanaka K, Furuyashiki T, Kitaoka S, et al. Prostaglandin E2-mediated attenuation of mesocortical dopaminergic pathway is critical for susceptibility to repeated social defeat stress in mice. *J Neurosci*. 2012; 32:4319–4329. [PubMed: 22442093]

39. McNamara RK, Jandacek R, Rider T, et al. Fatty acid composition of the postmortem prefrontal cortex of adolescent male and female suicide victims. *Prostaglandins Leukot Essent Fatty Acids*. 2009; 80:19–26. [PubMed: 19064316]
40. DiLeone RJ. Neuroscience gets nutrition. *Nat Neurosci*. 2011; 14:271–272. [PubMed: 21346742]
41. Vinod KY, Hungund BL. Role of the endocannabinoid system in depression and suicide. *Trends Pharmacol Sci*. 2006; 27:539–545. [PubMed: 16919786]
42. Alvheim AR, Malde MK, Osei-Hyiaman D, et al. Dietary linoleic acid elevates endogenous 2-AG and anandamide and induces obesity. *Obesity (Silver Spring)*. 2012; 20:1984–1994. [PubMed: 22334255]
43. Freeman MP, Davis M, Sinha P, Wisner KL, Hibbeln JR, Gelenberg AJ. Omega-3 fatty acids and supportive psychotherapy for perinatal depression: a randomized placebo-controlled study. *J Affect Disord*. 2008; 110:142–148. [PubMed: 18206247]
44. Su KP, Huang SY, Chiu TH, et al. Omega-3 fatty acids for major depressive disorder during pregnancy: results from a randomized, double-blind, placebo-controlled trial. *J Clin Psychiatry*. 2008; 69:644–651. [PubMed: 18370571]
45. Rees AM, Austin MP, Parker GB. Omega-3 fatty acids as a treatment for perinatal depression: randomized double-blind placebo-controlled trial. *Aust N Z J Psychiatry*. 2008; 42:199–205. [PubMed: 18247194]
46. Makrides M, Gibson RA, McPhee AJ, et al. Effect of DHA supplementation during pregnancy on maternal depression and neurodevelopment of young children: a randomized controlled trial. *JAMA*. 2010; 304:1675–1683. [PubMed: 20959577]
47. Fisher J, Cabral de Mello M, Patel V, et al. Prevalence and determinants of common perinatal mental disorders in women in low- and lower-middle-income countries: a systematic review. *Bull World Health Organ*. 2012; 90:139G–149G.
48. Pinheiro RT, da Cunha Coelho FM, da Silva RA, et al. Suicidal behavior in pregnant teenagers in southern Brazil: social, obstetric and psychiatric correlates. *J Affect Disord*. 2012; 136:520–525. [PubMed: 22119083]
49. Gavin AR, Tabb KM, Melville JL, Guo YQ, Katon W. Prevalence and correlates of suicidal ideation during pregnancy. *Arch Women Ment Health*. 2011; 14:239–246.
50. Lindahl V, Pearson JL, Colpe L. Prevalence of suicidality during pregnancy and the postpartum. *Arch Women Ment Health*. 2005; 8:77–87.

Significant outcomes

- Our study determined fatty acid serum composition early in pregnancy, and identified suicide risk (SR) and major depressive episode (MDE) based on a diagnostic psychiatric interview.
- In adjusted multivariate regression models, each standard deviation of higher arachidonic acid (AA) and adrenic acid (AdA) serum status – two omega-6 fatty acids – were associated with greater likelihood of SR and MDE in early pregnancy independently of confounding variables.
- Our findings suggest that higher AA and AdA serum status may be consequence of a western dietary pattern, characterized by higher consumption of omega-6 and lower omega-3 fatty acids.

Limitations

- The cross-sectional analysis applied in the present investigation limit to establish whether likelihood between exposure and outcome is a true cause-effect relationship.
- Our results derive from Brazilian pregnant women of low socioeconomic background. Further studies needs to confirm our findings in other populational groups.

Table 1

Number of cases and prevalence of current suicide risk or major depressive episode at 1st trimester of pregnancy, Rio de Janeiro, (2009-2011) (n=234)

Variable	Current Suicide Risk ^a				Major Depressive Episode ^a			
	N	%	n	Prevalence (%)	P value [*]	n	Prevalence (%)	P value [*]
Monthly per capita family income (American Dollar \$) [§]								
3 rd tertile (357.65)	78	33.6	9	11.8	0.020	4	5.3	0.004
2 nd tertile (197.25-357.64)	78	33.6	14	17.9		16	20.5	
1 st tertile (197.24)	76	32.8	23	29.5		19	24.4	
Age (years)								
20 – 29	162	69.2	31	19.1		32	19.8	0.040
30 – 40	72	30.8	15	20.8	0.446	7	9.7	
Marital status								
Married or stable partnership	209	89.3	37	17.7		30	14.4	0.011
Single	25	10.7	9	36.0	0.034	9	36.0	
Self-reported skin color								
White	59	25.2	9	15.3		7	11.9	0.174
Non-white	175	74.8	37	21.1	0.216	32	18.3	
Education (years)								
9	134	57.3	25	18.7		21	15.7	0.382
8	100	42.7	21	21.0	0.388	18	18.0	
Smoking habit (current)								
No	216	92.3	41	19.0		31	14.4	0.004
Yes	18	7.7	5	27.8	0.265	8	44.4	
Alcohol consumption (current)								
No	187	79.9	31	16.6		31	16.6	0.546
Yes	47	20.1	15	31.9	0.018	8	17.0	
Sleeping hours at night								
8	152	65.0	30	19.7		27	17.8	0.338
< 8	82	35.0	16	19.5	0.556	12	14.6	
Parity								

Variable	Current Suicide Risk ^a			Major Depressive Episode ^a		
	N	%	n	Prevalence (%)	P value [*]	P value [*]
0	88	37.6	9	10.2		10.2
1	91	38.9	16	17.6	<0.001	18.7
2	55	23.5	21	38.2		23.6
Previous history of abortion						
No	177	75.6	30	16.9		15.8
Yes	57	24.4	16	28.1	0.053	19.3
Desire to be pregnant						
Yes	99	42.3	15	15.2		16.2
No	135	57.7	31	23.0	0.093	17.0
Work status						
Yes	159	67.9	29	18.2		13.8
No	75	32.1	17	22.7	0.265	22.7
Home crowding (persons/dorms)						
2	156	66.7	24	15.4		14.1
>2	78	33.3	22	28.2	0.017	21.8
Pre-pregnancy BMI (kg/m²)[‡]						
24.9	132	56.4	21	15.9		13.6
25.0	102	43.6	25	24.5	0.070	20.6
Number of close relatives[‡]						
2	137	58.8	24	17.5		11.7
0-1	96	41.2	21	21.9	0.253	24.0
Number of close friends[‡]						
2	113	48.5	18	15.9		16.8
0-1	120	51.5	27	22.5	0.135	16.7
Reported family history of depression (first-degree relative)^{††}						
No	173	74.9	34	19.7		17.9
Yes	58	25.1	11	19.0	0.538	12.1
Reported family history of suicide (first-degree relative)^{††}						

Variable	Current Suicide Risk ^a				Major Depressive Episode ^a			
	N	%	n	Prevalence (%)	P value [*]	n	Prevalence (%)	P value [*]
No	219	94.4	43	19.6	0.295	35	16.0	0.313
Yes	12	5.2	1	8.3		3	25.0	

^a M.I.N.I. International Neuropsychiatric Interview (DSM-IV; version 5.0.0.);

^{*} Fisher exact test *P*-value refers to chi-square for proportions for all dichotomous variables. For non-dichotomous variables, Yates correction was applied;

^s Two missing values for monthly per capita family income;

[†] Body mass index (BMI) classification according to the World Health Organization (1995);

[‡] One missing values for both close friends and close relatives variables;

^{††} Three answers as 'I don't know' of both 'reported family history of depression' and 'reported family history of suicide'.

Table 2

Serum fatty acid status and adjusted odds ratios of current suicide risk at 1st trimester of pregnancy, Rio de Janeiro, 2009-2011 (n=234)

Fatty acids ^a	Current Suicide Risk			Unadjusted		Adjusted *	
	No (n=188) Mean (SD)	Yes (n=46) Mean (SD)		Odds Ratio (95% CI) ^b		Odds Ratio (95% CI) ^b	
Omega-6 polyunsaturated fatty acids (%)							
LA	18:2 n-6 31.00 (3.43)	30.44 (3.68)		0.85 (0.62-1.17)		0.78 (0.56-1.08)	
	18:3 n-6 0.33 (0.13)	0.37 (0.14)		1.30 (0.95-1.77)		1.26 (0.91-1.74)	
	20:2 n-6 0.32 (0.07)	0.31 (0.06)		0.87 (0.60-1.25)		0.80 (0.53-1.21)	
	20:3 n-6 1.88 (0.46)	1.94 (0.44)		1.12 (0.82-1.53)		1.21 (0.86-1.69)	
AA	20:4 n-6 9.17 (1.56)	9.62 (1.89)		1.34 (0.96-1.87)		1.45 (1.02-2.07)	
AdA	22:4 n-6 0.39 (0.09)	0.41 (0.10)		1.29 (0.93-1.79)		1.43 (1.01-2.04)	
	22:5 n-6 0.39 (0.09)	0.41 (0.10)		1.10 (0.80-1.51)		1.29 (0.91-1.83)	
n-6 HUFA	78.07 (3.89)	78.76 (3.85)		1.22 (0.85-1.77)		1.17 (0.81-1.69)	
Omega-3 polyunsaturated fatty acids (%)							
	18:3 n-3 0.63 (0.14)	0.62 (0.15)		0.96 (0.70-1.32)		0.80 (0.56-1.14)	
EPA	20:5 n-3 0.42 (0.22)	0.44 (0.20)		1.09 (0.80-1.49)		1.10 (0.78-1.56)	
DPA	22:5 n-3 0.53 (0.11)	0.55 (0.14)		1.20 (0.86-1.66)		1.23 (0.87-1.73)	
DHA	22:6 n-3 2.46 (0.56)	2.42 (0.58)		0.94 (0.66-1.32)		1.07 (0.75-1.52)	
n-3 HUFA	21.93 (3.89)	21.24 (3.85)		0.82 (0.57-1.80)		0.85 (0.59-1.23)	
Monounsaturated fatty acids (%)							
	16:1 n-7 1.63 (0.60)	1.67 (0.57)		1.07 (0.79-1.45)		1.08 (0.79-1.48)	
	18:1 n-9 15.98 (1.81)	15.91 (1.75)		0.96 (0.70-1.34)		1.06 (0.75-1.50)	
	18:1 n-7 1.69 (0.21)	1.70 (0.25)		1.04 (0.75-1.44)		1.24 (0.87-1.76)	
	20:1 n-9 0.15 (0.03)	0.15 (0.03)		0.90 (0.63-1.29)		0.99 (0.66-1.47)	
	24:1 n-9 1.12 (0.19)	1.12 (0.20)		0.99 (0.72-1.36)		1.16 (0.81-1.64)	
Total	20.58 (2.32)	20.56 (2.11)		0.99 (0.72-1.37)		1.11 (0.79-1.57)	
Saturated fatty acids (%)							
	14:0 0.68 (0.26)	0.66 (0.26)		0.95 (0.69-1.29)		0.89 (0.63-1.25)	
	16:0 21.90 (1.75)	21.93 (1.72)		1.01 (0.74-1.39)		0.96 (0.68-1.35)	
	18:0 7.47 (0.68)	7.43 (0.62)		0.93 (0.66-1.31)		0.92 (0.62-1.35)	

Fatty acids ^a	Current Suicide Risk		Unadjusted		Adjusted [*]	
	No (n=188) Mean (SD)	Yes (n=46) Mean (SD)	Odds Ratio (95% CI) ^b	Odds Ratio (95% CI) ^b	Odds Ratio (95% CI) ^b	Odds Ratio (95% CI) ^b
20:0	0.31 (0.05)	0.32 (0.05)	1.12 (0.82-1.54)	1.12 (0.82-1.54)	1.34 (0.93-1.91)	1.34 (0.93-1.91)
22:0	0.85 (0.13)	0.87 (0.20)	1.19 (0.87-1.61)	1.19 (0.87-1.61)	1.17 (0.85-1.62)	1.17 (0.85-1.62)
24:0	0.73 (0.12)	0.74 (0.16)	1.12 (0.81-1.55)	1.12 (0.81-1.55)	1.08 (0.77-1.50)	1.08 (0.77-1.50)
Total	31.94 (1.68)	31.95 (1.49)	1.01 (0.73-1.39)	1.01 (0.73-1.39)	0.94 (0.67-1.32)	0.94 (0.67-1.32)

^a Fatty acids are expressed as percentage of total serum fatty acids;

^b Odds ratios of current suicide risk per standard deviation for each fatty acids,

^{*} adjusted by parity, marital status and gestational week, using binary logistic regression;

Abbreviations: SD = standard deviation; CI = confidence interval; LA = linolenic acid; AA = arachidonic acid; AdA = adrenic acid; HUFA = highly unsaturated fatty acid; EPA = eicosapentaenoic acid; DPA = docosapentaenoic acid; DHA = docosahexaenoic acid

Table 3

Serum fatty acid status and adjusted odds ratios of major depressive episode at 1st trimester of pregnancy, Rio de Janeiro, 2009-2011 (n=234)

Fatty acids ^a	Major Depressive Episode			Unadjusted		Adjusted [*]	
	No (n=194) Mean (SD)	Yes (n=40) Mean (SD)		Odds Ratio (95% CI) ^b		Odds Ratio (95% CI) ^b	
Omega-6 polyunsaturated fatty acids (%)							
LA	18:2 n-6 30.99 (3.41)	30.39 (3.81)		0.84 (0.60-1.18)		0.74 (0.52-1.06)	
	18:3 n-6 0.34 (0.14)	0.36 (0.14)		1.15 (0.82-1.60)		1.13 (0.78-1.62)	
	20:2 n-6 0.32 (0.07)	0.31 (0.06)		0.75 (0.50-1.12)		0.67 (0.42-1.05)	
	20:3 n-6 1.91 (0.48)	1.81 (0.35)		0.81 (0.57-1.15)		0.78 (0.53-1.15)	
AA	20:4 n-6 9.16 (1.57)	9.73 (1.87)		1.44 (1.01-2.06)		1.47 (1.03-2.10)	
AdA	22:4 n-6 0.38 (0.09)	0.41 (0.09)		1.39 (0.99-1.94)		1.59 (1.09-2.32)	
	22:5 n-6 0.36 (0.13)	0.36 (0.12)		1.02 (0.73-1.43)		1.12 (0.78-1.63)	
n-6 HUFA	78.01 (3.88)	79.15 (3.80)		1.43 (0.94-2.18)		1.25 (0.82-1.90)	
Omega-3 polyunsaturated fatty acids (%)							
	18:3 n-3 0.63 (0.14)	0.61 (0.13)		0.87 (0.61-1.23)		0.80 (0.56-1.14)	
EPA	20:5 n-3 0.43 (0.22)	0.41 (0.21)		0.93 (0.64-1.35)		1.02 (0.69-1.49)	
DPA	22:5 n-3 0.53 (0.11)	0.53 (0.11)		0.95 (0.66-1.37)		1.01 (0.70-1.47)	
DHA	22:6 n-3 2.46 (0.54)	2.40 (0.65)		0.89 (0.61-1.28)		1.06 (0.72-1.55)	
n-3 HUFA	21.99 (3.88)	20.85 (3.80)		0.70 (0.46-1.06)		0.80 (0.52-1.21)	
Monounsaturated fatty acids (%)							
	16:1 n-7 1.62 (0.59)	1.70 (0.62)		1.13 (0.83-1.55)		1.18 (0.84-1.65)	
	18:1 n-9 15.96 (1.79)	15.98 (1.84)		1.01 (0.72-1.43)		1.05 (0.72-1.52)	
	18:1 n-7 1.69 (0.21)	1.72 (0.24)		1.18 (0.84-1.66)		1.22 (0.84-1.78)	
	20:1 n-9 0.15 (0.03)	0.15 (0.03)		0.84 (0.57-1.24)		0.85 (0.56-1.29)	
	24:1 n-9 1.12 (0.19)	1.16 (0.20)		1.28 (0.91-1.80)		1.38 (0.94-2.01)	
Total	20.54 (2.25)	20.72 (2.42)		1.08 (0.77-1.52)		1.14 (0.79-1.64)	
Saturated fatty acids (%)							
	14:0 0.68 (0.27)	0.64 (0.24)		0.85 (0.60-1.21)		0.87 (0.60-1.28)	
	16:0 21.88 (1.73)	22.05 (1.80)		1.09 (0.79-1.52)		1.22 (0.85-1.75)	
	18:0 7.48 (0.68)	7.37 (0.62)		0.84 (0.58-1.20)		0.76 (0.51-1.13)	

Fatty acids ^a	Major Depressive Episode		Unadjusted		Adjusted [*]	
	No (n=194) Mean (SD)	Yes (n=40) Mean (SD)	Odds Ratio (95% CI) ^b	Odds Ratio (95% CI) ^b	Odds Ratio (95% CI) ^b	Odds Ratio (95% CI) ^b
20:0	0.32 (0.05)	0.32 (0.05)	1.06 (0.76-1.49)	1.19 (0.82-1.72)		
22:0	0.85 (0.14)	0.85 (0.17)	1.03 (0.74-1.44)	1.07 (0.75-1.52)		
24:0	0.73 (0.12)	0.72 (0.17)	0.94 (0.66-1.34)	0.94 (0.65-1.36)		
Total	31.94 (1.67)	31.95 (1.54)	1.01 (0.72-1.41)	1.10 (0.76-1.58)		

^a Fatty acids are expressed as percentage of total serum fatty acids; Bold typeface indicate significant items;

^b Odds ratios of major depressive episode per standard deviation for each fatty acids,

^{*} adjusted by marital status, current smoking habit, close relatives and gestational week, using binary logistic regression;

Abbreviations: SD = standard deviation; CI = confidence interval; LA = linolenic acid; AA = arachidonic acid; AdA = adrenic acid; HUFA = highly unsaturated fatty acid; EPA = eicosapentaenoic acid; DPA = docosapentaenoic acid; DHA = docosahexaenoic acid.