Associations between omega fatty acid consumption and depressive symptoms among individuals seeking behavioural weight loss treatment

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Summary

Objective

The typical Western diet is deficient in omega-3 and high in omega-6 fatty acids (FAs). These FAs may play a role in depressive symptoms via inflammatory processes, especially in the context of obesity, a pro-inflammatory state. This study investigated associations between omega-3 and omega-6 FA intake and depressive symptoms in adults seeking behavioural weight loss treatment (BWLT).

Methods

One hundred eighty-eight persons with overweight or obesity (83.50% women, 93.10% White, 55.01 ± 10.09 years old, body mass index 36.02 ± 15.79 kg/m) seeking BWLT completed the Block Food Frequency Questionnaire, which provides estimates of dietary FA intake, daily total energy intake (TEI) and macronutrient composition of the diet. Depressive symptoms were measured via the Center for Epidemiological Studies Depression Scale. Correlation and linear regression estimated associations between depressive symptoms and FAs.

Results

On average, participants reported consuming 1866.2 ± 665.1 kcals/d, with 38% of TEI from fat and an omega-6:3 ratio of 9.2 (13.9 g omega-6 to 1.5 g omega-3). In univariate models, omega-6 intake was associated with depressive symptoms \( r = .182, p = .012 \); however, this association was no longer statistically significant after controlling for TEI. Omega-3 intake was not associated with depressive symptoms.

Conclusion

The expected association between omega-3 and omega-6 FAs and depressive symptoms was largely unsupported. A robust association between FA intake and depressive symptoms may have been masked by a high level of chronic inflammation in this sample caused by excess weight and overall poor diet. Additional research is needed to determine whether BWLT improves FA intake, and whether associations between FA intake and depressive symptoms are strengthened after successful weight loss and improved diet.

Keywords: Diet, mood, omega fatty acids.

Introduction

Overweight and obesity increase the risk of diminished psychological well-being and health-related quality of life (i.e., physical, mental, emotional and social functioning) (1,2). Obesity and its comorbidities, including cardiovascular disease and depression, have become increasingly prevalent in the USA (3). Commonly cited pathways for
the effect of body weight on psychological well-being include impaired physical functioning (e.g., limited mobility and sleep apnea) (4), increased rates of chronic disease (e.g., type 2 diabetes and hypertension) (5) and social stigma (e.g., being perceived as lazy) (6). A less recognized potential pathway between body weight and psychological well-being is suboptimal intake of polyunsaturated or ‘essential’ fatty acids (7). A few epidemiological studies and small clinical trials support an inverse association between essential fatty acid intake and depression, anxiety and hostility; however, because mental health is such a relevant contributor to the global burden of disease, more research is needed to understand its interplay with diet (8–12).

Omega-3 fatty acids (n-3 FAs) are known to reduce the risk of heart disease by lowering blood pressure and reducing inflammation (3). Further, n-3 FAs play an important role in essential body functions, including improving cellular communication in the brain and reducing blood clot formation (13). The most commonly consumed n-3 FA is α-linoleic acid (ALA), which is found in the highest concentrations in soybean and canola oils in the Western diet (14,15). However, the two essential n-3 FAs with the highest concentration in the brain that are primarily responsible for its anti-inflammatory effects – eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) – are only abundant in fatty fish and some shellfish (3). Marine sources are thus considered the best sources of dietary EPA and DHA (16).

As aforementioned, low levels of essential n-3 FAs may be a modifiable risk factor for mental illnesses, with suboptimal intakes associated with clinical depressive disorders, pessimism and impulsivity (17–19). While not all studies find an association between n-3 FAs and psychological well-being (20,21), a number of epidemiological studies have found a significant inverse relation between intake of n-3 FAs from marine sources and the prevalence of depressive symptoms (22). Further, several studies show lower levels of circulating n-3 FAs in the blood of depressed patients as compared with healthy control subjects (23–28). While total n-3 FA intake may be high due to consumption of processed foods containing canola and soybean oil, mean intake of EPA and DHA from marine sources is low in the Western diet, with the average American adult consuming less than half of the recommended 250 mg/d (29).

By contrast, the intake of omega-6 (n-6) FAs has more than tripled within the past 55 years with the increased use of cooking oils, shortenings and margarines in processed and fast foods (30). N-6 FAs are most prevalent in the form of linoleic acid (LA), found in vegetable oils (such as corn, canola and soy) used in processed foods and animal products (31). The downstream metabolites of LA are pro-inflammatory, with the increased risk of inflammation associated with a variety of both physical and mental illness (32,33). Although moderate n-6 FA intake is essential to support brain and body functioning, several studies have found a relation between high n-6 FAs and depressive symptoms, with the risk of developing depressive symptoms increasing with the amount of processed food consumed (34,35). Whereas the Institute of Medicine has indicated that n-6 FA adequate intake ranges from 11 to 12 g/d for women and 14 to 17 g/d for men (36), recommended intakes for n-6 FAs are contentious. Further, because n-6 and n-3 FAs compete for the same conversion enzymes in vivo, recommendations are more interpretable as a ratio of n-6 : n-3, which is ideal at 2:1 (37), and it is suggested that LA intake is limited to 2.0% of total energy intake (37) to allow for optimal conversion of ALA to EPA and DHA (3). Research supports that diets with a high n-6 : n-3 ratio are significantly associated with depressive symptoms (38–42).

Persons with overweight and obesity are known to consume a diet with a high n-6 : n-3 ratio, with excessive intake of FAs from animal-derived fats and refined grains (43) and insufficient consumption of n-3 FAs (especially EPA and DHA). However, it is unknown whether essential FA intake is associated with depressive symptoms among a sample composed exclusively of persons with overweight/obesity who are already at risk for both inflammation and impairments in mood due to excess weight. This question has particular relevance for individuals seeking behavioural treatment for weight loss and for weight loss in general, which typically produces improvements in mood as a secondary benefit (44). If suboptimal essential FA intake at baseline is associated with higher levels of depressive symptoms, there may be reason to believe that targeting n-3 and n-6 FA consumption among individuals could help to maximize the beneficial effects of behavioural weight loss treatment on psychological well-being. Therefore, this study aimed to examine associations between n-3 and n-6 FA consumption and depressive symptoms among persons with overweight/obesity seeking behavioural weight loss treatment.

Research design and methods

Study design and participants

This study involved secondary analysis of baseline data from an 18-month randomized controlled trial of behavioural weight loss treatment. The sample consisted of participants between the ages of 18 and 70 years, with a body mass index (BMI) of 25–45 kg m². Study exclusion criteria included: current participation in another weight loss programme; weight loss of ≥5% body weight during the prior 6 months; current use of weight loss medication;
report of chest pain during physical activity or a heart condition; medical conditions that might render unsupervised unsafe physical activity; less than 6 months post-partum or planning to become pregnant within the approaching 18 months; plans to relocate outside of the geographic region; history of a diagnosed eating disorder excluding binge eating disorder, substance abuse or other serious untreated psychiatric problem (e.g. bipolar disorder) that would preclude them from following study protocol. Participants were recruited via advertising in local print media and flyers mailed to the home. Screening for eligibility was conducted by phone. Participants then attended a baseline orientation and an assessment session, where they completed informed consent procedures, had their height and weight measured and completed questionnaires described later. Study procedures were approved by the Institutional Review Board of The Miriam Hospital of Providence, RI, USA.

Measures

Body weight was measured to the nearest .1 kg, in light clothing and without shoes, on a digital scale. Height was measured to the nearest millimetre using a wall-mounted stadiometer. BMI was calculated as kg/m². Participants completed a demographic questionnaire reporting their age, sex, race, ethnicity and level of education.

Characteristics of participants’ diets, including daily total energy intake (kcal); percent of daily energy from carbohydrate, fat and protein; and daily consumption of n-3 (both total and ALA, EPA and DHA individually) and n-6 FAs and their ratio (n-6 : n-3) were estimated using the Block Food Frequency Questionnaire (FFQ) (45). This validated self-report measure assesses the frequency, portion and preparation of 110 food and drink items consumed over the past year. Research supports that reported essential FA intake from an FFQ reliably correlates with serum levels (46).

Depressive symptoms were measured by the Center for Epidemiological Studies Depression Scale (CES-D 10), a validated measure shown to have high internal consistency and sensitivity in identifying depressive symptoms among adult populations (47,48). The 10-question scale measures depressive symptoms such as: feelings of loneliness, helplessness, sleep disturbance and psychomotor retardation (‘I could not get going’). Participants recorded the frequency of depressive symptoms during the previous week on a four-point scale, ranging from 0 (‘less than one day’) to 3 (‘most or all of the time’).

Statistical analyses

All analyses were completed using IBM SPSS Statistics for Windows, Version 20.0 (Released 2011, IBM Corp., Armonk, NY, USA). Descriptive statistics including means with standard deviations and counts with percentages were used to characterize participants’ demographic and anthropomorphic characteristics, dietary intake and depressive symptoms. Bivariate correlation was used to test for associations between BMI (kg/m²), depressive symptoms and dietary characteristics. Separate linear regression models were used to predict depressive symptoms from daily intake of n-3 (both total and ALA, EPA and DHA individually) and n-6 FAs and their ratio (n-6 : n-3), controlling for BMI (kg/m²), gender and daily total energy intake (kcal).

Results

Four participants were excluded from analysis as they were clear outliers (≥10 standard deviations beyond the mean) on FFQ measures. The remaining n = 188 participants included in the analysis were largely female, middle-aged, non-Hispanic White with at least a college education (Table 1). The majority (n = 156, 83%) were obese (BMI > 30 kg/m²), and depression scores were low to moderate on average, ranging from 0 to 24 out of a maximum of 30.

Table 1 shows that participants reported a diet high in fat (38% of total energy intake) and high in n-6 FAs (14 g/d). Total n-3 FA intake was also high (1.5 g/d) but consisted mostly of ALA (1.36 g/d) with very low levels of EPA (0.04 g/d) and DHA (0.07 g/d). Table 2 shows the recommended daily intakes for n-3 and n-6 FAs in comparison with levels reported by participants. On average, this sample reported consuming less than recommended levels of EPA and DHA and more than the recommendations for n-6 FAs. The n-6 : n-3 ratio shows that participants consumed 9.38 g of n-6 for every 1 g of n-3 FAs.

Results of the bivariate correlations are presented in Table 3. Higher levels of depressive symptoms were significantly associated with higher total energy intake and consuming higher levels of n-6 FAs. Consuming an additional 35 kcal or 0.3 g of n-6 FAs per day was associated with a one-unit increase in depressive symptoms. Notably, depressive symptoms were not associated with BMI (kg/m²), n-3 FAs or n-6 : n-3 ratio. Linear regression analyses controlling for BMI (kg/m²), gender and daily total energy intake failed to find an association between depressive symptoms and total n-3 FA intake (b = -.63, SE = .77, t = .812, p = .418), n-6 (b = .02, SE = .79, t = .238, p = .812) or the ratio of n-6 to n-3 (b = .16, SE = .18, t = .902, p = .368). The same pattern held when testing ALA, EPA and DHA in the model instead of total n-3 FA intake.
Education (%)

Body mass index, mean (SD), kg/m²

Weight, mean (SD), kg

95.83 (17.33)

Some college

37 (19.7)

Ethnicity, n (%)

Race, Age, mean (SD), years

55.01 (10.09)

Sex, n (%)

Education (%)

High school or less

17 (9)

Vocational training

9 (4.8)

Some college

37 (19.7)

College/University degree

58 (30.9)

Graduate degree

67 (35.6)

Weight, mean (SD), kg

95.83 (17.33)

Body mass index, mean (SD), kg/m²

36.20 (15.79)

Energy intake, mean (SD), kcal

1866.22 (665.11)

Fat, % energy intake

38.03 (5.55)

Protein, % energy intake

16.35 (3.04)

Carb, % energy intake

44.37 (6.60)

Total omega-3 intake, mean (SD), g

1.49 (0.61)

Alpha-linolenic acid, mean (SD), g

1.36 (0.56)

Eicosapentaenoic acid, mean (SD), g

0.04 (0.05)

Docosahexaenoic acid, mean (SD), g

0.07 (0.05)

Total omega-6 intake, mean (SD), g

13.95 (6.01)

Linoleic acid

13.84 (5.98)

Omega-6 : omega-3 ratio, (SD), g

9.38 (1.56)

CES-D score, mean (SD)

9.57 (3.77)

Table 1 Characteristics of participants

Full sample (N = 188)

| Characteristic | Value |
|---------------|-------|
| Sex, n (%)    |       |
| Men           | 31 (16.5) |
| Women         | 157 (83.5) |
| Age, mean (SD), years | 55.01 (10.09) |
| Race, n (%)   |       |
| Asian         | 2 (1.1) |
| African-American | 6 (3.2) |
| White         | 175 (93.1) |
| Other         | 5 (2.7) |
| Ethnicity, n (%) |   |
| Hispanic      | 4 (2.1) |
| Non-hispanic  | 184 (97.9) |
| Education (%) |       |
| High school or less | 17 (9) |
| Vocational training | 9 (4.8) |
| Some college  | 37 (19.7) |
| College/University degree | 58 (30.9) |
| Graduate degree | 67 (35.6) |
| Weight, mean (SD), kg | 95.83 (17.33) |
| Body mass index, mean (SD), kg/m² | 36.20 (15.79) |
| Energy intake, mean (SD), kcal | 1866.22 (665.11) |
| Fat, % energy intake | 38.03 (5.55) |
| Protein, % energy intake | 16.35 (3.04) |
| Carb, % energy intake | 44.37 (6.60) |
| Total omega-3 intake, mean (SD), g | 1.49 (0.61) |
| Alpha-linolenic acid, mean (SD), g | 1.36 (0.56) |
| Eicosapentaenoic acid, mean (SD), g | 0.04 (0.05) |
| Docosahexaenoic acid, mean (SD), g | 0.07 (0.05) |
| Total omega-6 intake, mean (SD), g | 13.95 (6.01) |
| Linoleic acid | 13.84 (5.98) |
| Omega-6 : omega-3 ratio, (SD), g | 9.38 (1.56) |
| CES-D score, mean (SD) | 9.57 (3.77) |

Discussion

In this study of persons with overweight or obesity presenting for behavioural weight loss treatment, n-3 FAs (both total and ALA, EPA, and DHA individually) were not related to depressive symptoms, and n-6 FAs were only related to depressive symptoms before controlling for total energy intake. This stands in contrast to epidemiological studies linking higher n-3 FA intake and lower levels of depressive symptoms in national populations (42,49), several of which found an association with a higher ratio of n-6 :n-3 and increased depressive symptoms (39,50,51). In this sample, the link between omega FAs and depressive symptoms was likely masked by the limited range in EPA and DHA intake, and a pre-existing inflammatory state stemming from overall poor diet and excess weight (52,53).

Obesity is associated with both chronic inflammation and depression (54–56). Therefore, we hypothesized that omega FAs, which are thought to affect mood via regulation of inflammatory pathways, might be related to depressive symptoms in a sample of persons with overweight or obesity (57–59). However, chronic inflammation, which is a hallmark of overweight/obesity, could overwhelm any positive effect of n-3 FA intake on inflammation, thus explaining our null findings. Furthermore, animal models show that a high-fat diet can increase depressive symptoms via brain inflammation, even in the absence of obesity (60). Additional research incorporating biomarkers to measure omega FA levels and inflammatory states is needed to test for this possibility. The strength of the association between FAs and depressive symptoms for normal weight versus persons with overweight/obesity should also be compared in national samples.

The observed pattern of omega FA intake also limited our opportunity to detect effects on depressive symptoms. The majority of n-3 FA intake was via ALA, which is only likely to have anti-inflammatory effects when converted by the body to EPA and DHA. However, very little of ALA is converted to EPA and DHA in the presence of high levels of n-6 FAs because of competition for enzymes (61). In this sample, n-3 FAs were unlikely to have an anti-inflammatory effect and subsequent positive effects on depressive symptoms, both because (i) Overall consumption of EPA and DHA from fatty fish and shellfish was well below recommended levels and (ii) Because of little opportunity to convert ALA to EPA and DHA given an unfavourable n-6 to n-3 ratio (29).

While persons with overweight/obesity might be expected to report consuming poor-quality diets, the low level of EPA and DHA gleaned from rich dietary sources is an important finding of this study. EPA and DHA deficiency could have important health implications beyond depressive symptoms (14). For example, low EPA and DHA are not only associated with obesity (62) but also with cardiovascular disease, attention deficit hyperactivity disorder and dementia (63–65).

In contrast to n-3 FAs, the pro-inflammatory n-6 FAs (56) were consumed at much higher levels. While n-6 FAs might be expected to have an effect on depressive symptoms, they would likely do so by exacerbating an already elevated level of chronic inflammation (56). Some evidence of this association was detected in the correlation between n-6 FA intake and depressive symptoms; however, the association was accounted for by total energy intake. This likely indicates that n-6 FAs served primarily as a proxy of overall dietary quality, as n-6 FA consumption is known to relate to both overall total energy intake and dietary quality (53,66). Furthermore, poor
dietary quality is a known contributor to inflammation (41,67). Thus, the observed pattern of FA intake reinforces the hypothesis that chronic inflammation is an important influence in persons with overweight/obesity and that FA intake may not affect depressive symptoms.

Despite not finding a robust effect of FAs on depressive symptoms, the influence of FAs on mood may become more powerful as the behavioural weight loss seekers lose weight, improve the quality of their diet and become physically active, all of which might improve a chronic state of inflammation (48,66). Additionally, the omega FA profile would be expected to change in favour of increased n-3 FA intake via rich dietary sources and reduced n-6 FA intake. In this scenario,
FAs could be expected to have a greater impact on depressive symptoms. Additional research is needed to determine whether individuals who are seeking to maximize improvements in mood, which are often seen as a secondary benefit of behavioral weight loss treatment (44), may benefit from coaching regarding the beneficial effects of a healthy FA profile.

This study is important because it is one of few to explore associations between omega FA consumption and mood specifically in persons with overweight/obesity. This paper is also among the first to identify FAs as potentially important for maximizing improvements in psychological well-being that are typically achieved as a secondary benefit of behavioral weight loss treatment. The large sample size and use of a gold-standard dietary assessment tool are also methodological strengths. This study also has several limitations. First, the analysis was based on cross-sectional baseline data, so any causal or temporal relationship between dietary intake, mood, and weight cannot be determined. Second, FFQs are known to be imperfect, as they provide an estimate of relative intake for total energy and FA intake. However, it is likely that, as a measure of inter-individual variability in total caloric intake and FA consumption, the measure was acceptable for the purposes of this study. Lastly, while the CES-D is an oft-used and validated measure, depressive symptomology was self-reported and could not be used to establish a clinical diagnosis of depression. Future direction might incorporate the use of a more sensitive instrument for differences in minor depressive symptomology.

This research contributes to a growing body of literature on the relation between FAs and mood. Additional research is needed to determine for whom and under what circumstances FAs are related to mood, and whether the effect of FAs can be hampered to improve mood, particularly among populations such as the persons with overweight/obesity who are routinely observed to experience impairments in mood.

Conflict of Interest Statement

No conflict of interest was declared.

References

1. Taylor VH, Forhan M, Vigod SN, McIntyre RS, Morrison KM. The impact of obesity on quality of life. Best Pract Res Clin Endocrinol Metab 2013; 27: 139–146.
2. Miller AA, Spencer SJ. Obesity and neuroinflammation: a pathway to cognitive impairment. Brain Behav Immun 2014; 42: 10–21.
3. Grosso G, Galvano F, Marventano S, et al. Omega-3 fatty acids and depression: scientific evidence and biological mechanisms. Oxid Med Cell Longev 2014; 2014: 313570.
4. Drager LF, Togheiro SM, Paltosky YV, Lorenzi-Filho G. Obstructive sleep apnea: a cardiometabolic risk in obesity and the metabolic syndrome. J Am Coll Cardiol 2013; 62: 569–576.
5. Lumeng CN, Saltiel AR. Inflammatory links between obesity and metabolic disease. J Clin Invest 2011; 121: 2111–2117.
6. Puhl RM, Heuer CA. Obesity stigma: important considerations for public health. Am J Public Health 2010; 100: 1019–1028.
7. Lin PY, Huang SY, Su KP. A meta-analytic review of polyunsaturated fatty acid compositions in patients with depression. Biol Psychiatry 2010; 68: 140–710.
8. Nemets B, Stahl Z, Belmaker RH. Addition of omega-3 fatty acid to maintenance medication treatment for recurrent unipolar depressive disorder. Am J Psychiatry 2002; 159: 477–479.
9. Peet M, Horrobin DF. A dose-ranging study of the effects of ethyl-eicosapentaenoate in patients with ongoing depression despite apparently adequate treatment with standard drugs. Arch Gen Psychiatry 2002; 59: 913–919.
10. Freeman MP, Hibbeln JR, Wisner KL, Brumbach BH, Watchman M, Gelenberg AJ. Supplementation with omega-3 fatty acids may help reduce postpartum depression. Acta Psychiatr Scand 2006; 113: 31–35.
11. Green P, Hersh H, Monselise A, Marom S, Presburger GI, Weizman A. Red cell membrane omega-3 fatty acids are decreased in nondepressed patients with social anxiety disorder. Eur Neuropsychopharmacol 2006; 16: 107–113.
12. Iribarren C, Markovitz JH, Jacobs DR Jr, Schreiner PJ, Daviglus M, Hibbeln JR. Dietary intake of n-3, n-6 fatty acids and fish: relation with hostility in young adults – the CARDIA study. Eur J Clin Nutr 2004; 58: 24–31.
13. Leaf A. Prevention of sudden cardiac death by n-3 polyunsaturated fatty acids. J Cardiovasc Med 2007; 8: S27–S29.
14. Koralek DO, Peters U, Andriele G, et al. A prospective study of dietary alpha-linolenic acid and the risk of prostate cancer (United States). Cancer Causes Control 2006; 17: 783–791.
15. Kris-Etherton PM, Harris WS, Appel LJ. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. Arterioscler Thromb Vasc Biol 2003; 23: e20–e30.
16. Sinn N, Milte C, Howe PRC. Oiling the brain: a review of randomized controlled trials of omega-3 fatty acids in psychopathology across the lifespan. Nutrients 2010; 2: 128–170. doi:10.3390/nu2020128.
17. Conklin SM, Manuck SB, Yao JK, Floy JD, Hibbeln JR, Muldoon MF. High ω-6 and low ω-3 fatty acids are associated with depressive symptoms and neuroticism. Psychosom Med 2007; 69: 932–934.
18. Liu JJ, Galfalvy HC, Cooper TB, et al. Omega-3 polyunsaturated fatty acid status in major depression with comorbid anxiety disorders. J Clin Psychiatry 2013; 74: 732–738.
19. Liu JJ, Green P, Mann JJ, Rapoport SI, Sublette ME. Pathways of polyunsaturated fatty acid utilization: implications for brain function in neuropsychiatric health and disease. Brain Res 2015; 1597: 220–246.
20. Appleton KM, Rogers PJ, Ness AR. Updated systematic review and meta-analysis of the effects of n-3 long-chain polyunsaturated fatty acids on depressed mood. Am J Clin Nutr 2010; 91: 757–770.
21. Hoffmire CA, Block RC, Thevenet-Morrison K, van Wijngaarden E. Associations between omega-3 poly-unsaturated fatty acids from fish consumption and severity of depressive symptoms: an analysis of the 2005–2008 National Health and Nutrition Examination Survey. Prostaglandins Leukot Essent Fatty Acids 2012; 86: 155–160.
22 Li F, Liu X, Zhang D. Fish consumption and risk of depression: a meta-analysis. J Epidemiol Community Health 2015; jech-2015.

23 Hibbeln JR, Umhau JC, George DT, Salem N. Do plasma polyunsaturates predict hostility and violence? World Rev Nutr Diet 1996; 82: 175–186.

24 Bountziouka V, Polychronopoulos E, Zeimpekis A, et al. Long-term fish intake is associated with less severe depressive symptoms among elderly men and women: the MEDIS (MEDiterranean ISlands Elderly) epidemiological study. J Aging Health 2009; 21: 864–880.

25 Suominen-Taipale AL, Partonen T, Turunen AW, Männistö S, Jula A. Omega-3 fatty acids consumption and depressive symptoms in major depression: decreased omega 3 fatty acid levels in patients with recent depressive episodes: a cross-sectional analysis. PLoS One 2010; 5: e10530.

26 Edwards R, Peet M, Shay J, Horrobin D. Omega-3 polyunsaturated fatty acids level in the diet and in red blood cell membranes of depressed patients. J Affect Disord 1998; 48: 149–155.

27 Maes M, Smith R, Christophe A, Cosyns P, Desrnyer R, Meltzer H. Fatty acid composition in major depression: decreased omega 3 fractions in cholesteryl esters and increased C20:4 omega 6/C20:5 omega 3 ratio in cholesteryl esters and phospholipids. J Affect Disord 1996; 38: 35–46.

28 Mamalakis G, Tornaritis M, Kafatos A. Depression and adipose essential polyunsaturated fatty acids. Prostaglandins Leukot Essent Fatty Acids 2002; 67: 311–318.

29 Papainikolaou Y, Brooks J, Reider C, Fulgoni VL. U.S. adults are not meeting recommended levels for fish and omega-3 fatty acid intake: results of an analysis using observational data from NHANES 2003–2008. Nutr J 2014; 13: 31.

30 Chilton FH, Murphy RC, Wilson BA, et al. Diet-gene interactions and PUFA metabolism: a potential contributor to health disparities and human diseases. Nutrients 2014; 6: 1993–2022.

31 Orsavova J, Misurova L, Ambrozova JV, Vicha R, Micek J. Fatty acids composition of vegetable oils and its contribution to dietary energy intake and dependence of cardiovascular mortality on dietary intake of fatty acids. Int J Mol Sci 2015; 16: 12871–12890.

32 Lazic M, Inzaugarat ME, Povero D, et al. Reduced dietary omega-6 to omega-3 fatty acid ratio and 12/15-lipoxygenase deficiency are protective against chronic high-fat diet-induced steatohepatitis. PLoS One 2014; 9: e107658.

33 Garland MR, Hallahan B, McNamara M, et al. Lipids and essential fatty acids in patients presenting with self-harm. Br J Psychiatry 2007; 190: 112–117.

34 Lucas M, Choccano-Bedoya P, Shulze MB, et al. Inflammatory dietary pattern and risk of depression among women. Brain Behav Immun 2013; 36: 46–53.

35 Lopez-Garcia E, Shulze MB, Fung TT, et al. Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction. Am J Clin Nutr 2004; 80: 1029–1035.

36 Trumbo P, Schlicker S, Yates AA, Poos M. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids. Journal of the American Dietetic Association 2002; 102: 1621–30.

37 Simopoulos AP. The importance of the ratio of omega-6/omega-3 essential fatty acids. Biomed Pharmacother 2002; 56: 365–379.

38 Frasure-Smith N, Lesperance F, Julien P. Major depression is associated with lower omega-3 fatty acid levels in patients with recent acute coronary syndromes. Biol Psychiatry 2004; 55: 891–896.

39 Kiecolt-Glaser JK, Belury MA, Porter K, Beversdorf DQ, Lemeshow S, Glaser R. Depressive symptoms, omega-6/omega-3 fatty acids, and inflammation in older adults. Psychosom Med 2007; 69: 217–224.

40 Tielemier H, van Tuijl HR, Hofman A, Kiliaan AJ, Breteler MM. Plasma fatty acid composition and depression are associated in the elderly; the Rotterdam Study. Am J Clin Nutr 2003; 78: 40–46.

41 da Rocha CM, Kac G. High dietary ratio of omega-6 to omega-3 polyunsaturated acids during pregnancy and prevalence of postpartum depression. Matern Child Nutr 2012; 8: 36–48.

42 Beydoun MA, Kuczmarski MTF, Beydoun HA, Hibbeln JR, Evans MK, Zonderman AB. ω-3 Fatty acid intakes are inversely related to elevated depressive symptoms among United States women. J Nutr 2013; 143: 1743–1752.

43 Manzel A, Muller DN, Hafler DA, Erdman SE, Linker RA, Kleinenwiesfeld M. Role of “Western diet” in inflammatory autoimmune diseases. Curr Allergy Asthma Rep 2014; 14: 404.

44 Faulconbridge LF, Wadden TA, Rubin RR, et al. One-year changes in symptoms of depression and weight in overweight/obese individuals with type 2 diabetes in the look AHEAD study. Obesity (Silver Spring) 2012; 20: 783–793.

45 Subar AF, Thompson FE, Kipnis V, et al. Comparative validation of the block, Willett, and National Cancer Institute food frequency questionnaires: the eating at America’s table study. Am J Epidemiol 2001; 154: 1089–1099.

46 Sublette ME, Elizabeth, CJ Segal-Isaacson, et al. Validation of a food frequency questionnaire to assess intake of n-3 polyunsaturated fatty acids in subjects with and without Major Depressive Disorder. J Am Diet Assoc 2011; 111: 117–123.

47 Weissman MM, Sholomskas D, Pottinger M, Prusoff BA, Locke BZ. Assessing depressive symptoms in five psychiatric populations: a validation study. Am J Epidemiol 1977; 106: 203–214.

48 Radloff, LS. The CES-D scale: self-report depression scale for research in the general population. Appl Psychol Meas 1977; 1: 385–401.

49 Logan AC. Omega-3 fatty acids and major depression: a primer for the mental health professional. Lipids Health Dis 2004; 3: 25.

50 Adams PB, Lawson S, Sanigorski A, Sinclair AJ. Arachidonic acid to eicosapentaenoic acid ratio in blood correlates positively with clinical symptoms of depression. Lipids 1996; 31(Suppl): S157–S161.

51 Simopoulos AP. Evolutionary aspects of diet: the omega-6/omega-3 ratio and the brain. Mol Neurobiol 2011; 44: 203–215.

52 Teng KT, Chang CY, Chang LF, Nesaretnam K. Modulation of obesity-induced inflammation by dietary fats: mechanisms and clinical evidence. Nutr J 2014; 13: 12.

53 Reaven GM. The insulin resistance syndrome: definition and dietary approaches to treatment. Annu Rev Nutr 2005; 25: 391–406.

54 Khan SA, Ali A, Khan SA, et al. Unraveling the complex relationship triad between lipids, obesity, and inflammation. Mediators Inflamm 2014; 2014: 502749.

55 Dong C, Sanchez LE, Price RA. Relationship of obesity to depression: a family-based study. Int J Obes Relat Metab Disord 2004; 28: 790–795.

56 Sanchez-Villegas A, Henriquez P, Figuerais A, Ortuno F, Lahortiga F, Martinez-González MA. Long chain omega-3 fatty acids intake, fish consumption and mental disorders in the SUN cohort study. Eur J Nutr 2007; 46: 337–346.

57 Haast RA, Kiliaan AJ. Impact of fatty acids on brain circulation, structure and function. Prostaglandins Leukot Essent Fatty Acids 2015; 92: 3–14.

58 Innis SM. Dietary lipids in early development: relevance to obesity, immune and inflammatory disorders. Curr Opin Endocrinol Diabetes Obes 2007; 14: 359–364.

59 Leonard BE. Inflammation, depression and dementia: are they connected? Neurochem Res 2007; 32: 1749–1756.
60 Bruce-Keller AJ, Salbaum JM, Luo M, Blanchard E IV, Taylor CM, Welsh DA, Berthoud HR. Obese-type gut microbiota induce neuro-behavioral changes in the absence of obesity. *Biol Psychiatry* 2015; 77: 607–615.

61 Byelashov OA, Sinclair AJ, Kaur G. Dietary sources, current intakes, and nutritional role of omega-3 docosapentaenoic acid. *Lipid Tech* 2015; 27: 79–82.

62 Micallef M, Munro I, Phang M, Garg M. Plasma n-3 polyunsaturated fatty acids are negatively associated with obesity. *Br J Nutr* 2009; 102: 1370.

63 Ali S, Garg SK, Cohen BE, Bhave P, Harris WS, Whooley MA. Association between omega-3 fatty acids and depressive symptoms among patients with established coronary artery disease: data from the Heart and Soul Study. *Psychosom Med* 2009; 78: 125–127.

64 Gillies D, Sinn JK, Lad SS, Leach MJ, Ross MJ. Polyunsaturated fatty acids (PUFA) for attention deficit hyperactivity disorder (ADHD) in children and adolescents. *Cochrane Database Syst Rev* 2012; 7: CD007986.

65 Janssen CI, Kiliaan AJ. Long-chain polyunsaturated fatty acids (LCPUFA) from genesis to senescence: the influence of LCPUFA on neural development, aging, and neurodegeneration. *Prog Lipid Res* 2014; 53: 1–17.

66 Lopez EF, Kabarowski JH, Ingle KA, et al. Obesity superimposed on aging magnifies inflammation and delays the resolving response after myocardial infarction. *Am J Physiol Heart Circ Physiol* 2015; 308: H269–H280.

67 Murphy AM, Lyons CL, Finucane OM, Roche HM. Interactions between differential fatty acids and inflammatory stressors – impact on metabolic health. *Prostaglandins Leukot Essent Fatty Acids* 2015; 92: 49–55.