Psychiatry Research ■ (■■■■) ■■■–■■■

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Short-term supplementation of acute long-chain omega-3 polyunsaturated fatty acids may alter depression status and decrease symptomology among young adults with depression: A preliminary randomized and placebo controlled trial

Annie T. Ginty [a,*], Sarah M. Conklin [b]

[a] Department of Psychiatryy, University of Pittsburgh, Pittsburgh, PA, USA
[b] Psychology, Neuroscience, and Global Health Studies, Allegheny College, Meadville, PA, USA

ARTICLE INFO

Article history:
Received 28 October 2014
Received in revised form
1 April 2015
Accepted 23 May 2015

Keywords:
Omega-3 fatty acids
Depression
Undergraduates

ABSTRACT

The current study examined the psychological effects of acute and low-dose long-chain omega-3 polyunsaturated fatty acids (LCPUFAs) supplementation on young adults with depressive symptoms. Participants (N=23, M age (SD)=20.2 (1.25), 78% female), with a Beck Depression Inventory (BDI) score of greater than 10, were randomly assigned to a placebo (corn oil) or LCPUFAs group (1.4 g of eicosapentaenoic and docosahexaeonic acids) and were instructed to consume the assigned capsules daily for 21-days. BDI was completed prior to supplementation and at day 21. Group differences in depression status on day 21 were analyzed using chi-square tests. After 21-days of supplementation, there was a significant difference in depression status between groups. 67% of the LCPUFAs no longer met criteria for being depressed, while only 20% in the placebo group were no longer depressed. A mixed ANOVA revealed a significant group *x* time interaction for BDI scores. Post-hoc analyses revealed the LCPFUAs group had a significant reduction in BDI scores over time, while the placebo group's scores did not significantly change. These findings suggest that LCPUFAs may alter depression and depressive symptomology in young adults in a relatively short amount of time.

1. Introduction

Depression affects 350 million people worldwide, making it one of the most common mental disorders (World Health Organization, 2012). American College Health Association (2012) recently found that 30% of undergraduate students have felt so depressed that it hindered their ability to function and 6% seriously considered suicide in the 12 months prior to the survey. Despite the prevalence, over 33% of cases in developed countries and 66% of cases among undergraduate students do not receive proper treatment (Demyttenaere et al., 2004; Active Minds, 2014). Therefore, it is crucial to assess and develop appropriate treatment interventions that are accessible to the general public.

Long-chain omega-3 polyunsaturated fatty acids (LCPUFAs) have shown promise in reducing depressive symptoms among those with major depressive disorder (Grosso et al., 2014a, 2014b; Lin and Su, 2007). However, some suggest that the complexity of combining LCPUFAs with antidepressant therapies makes it difficult to interpret these results (Appleton et al., 2007). Research examining the influence of LCPUFAs on depressed individuals not currently taking antidepressants is limited to a middle-age population and has produced mixed results (Rogers et al., 2008; Lucas et al., 2009). LCPUFAs have shown some benefit in reducing depression (Fontani et al., 2005) and fatigue (Antypa et al., 2009) in healthy undergraduate students. However, there has been scant research examining how LCPUFAs influence depressive symptoms in undergraduate students who currently meet criteria for depression.

The aim of the current study was to examine the psychological effects of acute and low-dose, equivalent of adding two fatty fish meals per week to their diet, LCPUFAs supplementation on undergraduate students with BDI scores indicative of depression who were not receiving any other treatment.

2. Methods

2.1. Participants

Twenty-three undergraduate students (age range 18–21 years; 78% female) with a score of 10 or above on the Beck Depression

* Corresponding author.
E-mail address: atg25@pitt.edu (A.T. Ginty).

http://dx.doi.org/10.1016/j.psychres.2015.05.072
0165-1781/

Inventory (BDI) were included in the present study. Participants were recruited through flyers placed across the college campus and announcements in Introductory Psychology courses during the summer and beginning of fall and spring semesters. Advertisements, which were also used as recruitment for a larger study, asked for healthy young adult volunteers. Participants were screened for exclusion criteria prior to enrollment in the study and those who had a BDI score of 10 or above were included in this study. Exclusion criteria included: taking any type of antidepressant or antianxiety medication, a change in medication over the past month (e.g., inhalers), diets that exceeded 2 fatty fish meals per week, current use of omega-3 fatty acid supplementation, or smoking more than 1 pack of cigarettes per week. None of the participants in the study had a previous history of receiving medication for a clinical diagnosis. The study was approved by the college Institutional Review board and all participants gave informed consent and understood they could withdraw from the study at any time.

2.2. Supplementation, design

Participants attended two laboratory visits (Visit 1 and Visit 2) during the summer or beginning of the academic semester. None of the visits took place during mid-term or final examinations. During Visit 1 participants completed questionnaires and were provided with either a 21-day supply of LCPUFAs or a matched placebo. Both the LCPUFAs and placebos were in identical foil blister packaging with different lot numbers printed on the foil. Participants were instructed to take the supplement every day until their follow-up visit (21 days later). Participants were randomly assigned using a number generator to one of two groups receiving either a 21-day supply of LCPUFAs (1000 mg EPA and 400 mg DHA) or a matched placebo (corn oil). The 1.4 g dose was selected on the basis that it could be obtained through minor diet changes in the future and the acute duration was selected based on the timing of therapeutic effects shown in a previous 8-week study of depressed adults (Su et al., 2003). LCPUFAs and placebos were provided by Nourish Life (Lake Forest, Illinois, USA) and were blinded with mint oil. The blind was broken by the manufacturer at the end of the study. The study was double-blinded neither participants nor experimenters knew which group participants were in until the last participant completed the study. After the last participant completed the study, sealed envelopes, were broken that revealed which groups the lot numbers were associated with.

2.3. Depression assessment

Participants completed the BDI at Visit 1 and during Visit 2, 21 days after supplementation. The BDI (Beck et al., 1996) is a 21-item self-report measure of depressive symptomatology (i.e., sadness, guilt, self-hate) during the past week. Participants respond to phrases that signal increasing symptom severity on a scale of 0–3. Scores can range from 0 to 63 with scores at or above 10 reflecting clinical significance (Deardorff and Funabiki, 1985). The BDI has acceptable internal consistency for both psychiatric (Cronbach's alpha $\alpha=0.86$) and non-psychiatric (chronbach's $\alpha=0.86$) individuals (Beck et al., 1988). The BDI demonstrates good test–retest reliability (0.96) among college students (Sprinkle et al., 2002). Recent research suggests it is important to examine the different components (e.g., cognitive, somatic) that contribute to depression (Stewart et al., 2012; Khambaty et al., 2014). With this in mind, the subscales (cognitive–affective and somatic–vegetative) were also calculated (Dozois et al., 1998). The cognitive–affective subscale consists of the following items: sadness, pessimism, past failures, guilty feelings, punishment feelings, self-dislike, self-criticalness, suicidal thoughts, indecisiveness, and worthlessness. The somatic–vegetative subscale consists of the following items: loss of pleasure, crying, agitation, loss of interest, loss of energy, changes in sleep, irritability, changes in appetite, concentration, tiredness–fatigue, and loss of interest in sex (Dozois et al., 1998).

2.4. Statistical analysis

Group differences in baseline BDI scores, age, and gender were explored using univariate ANOVAs and chi-square. Group differences in depression status at the final appointment were examined using chi-square test for independence. Analyses of group differences in depressive symptomatology across time were examined using a mixed-design ANOVA. Additional analyses using the last observation carried forward (LOCF) were used to accommodate missing follow-up BDI scores for two participants who did not complete Visit 2. A recent systematic review of analgesic clinical trials found LOCF to be the most common method used to impute missing data; 42% used this approach (Gewandter et al., 2014).

3. Results

Twenty-one of the 23 participants completed the study. Two participants did not return for the follow-up testing, one from the LCPUFA group and one from the placebo group. Therefore, the final analysis included 21 participants, LCPUFA ($n=12$, %female=62) and placebo ($n=9$, %female=100).

3.1. Demographics and baseline BDI

There were no differences between groups in baseline BDI scores ($p=0.54$) or age ($p=0.56$). There was a significance difference for gender, $\chi^2(21)=4.92$, $p=0.03$. Means and standard deviations are reported in Table 1.

3.2. Group changes in depression across time

Chi-square analyses indicated a significant difference in depression status between groups after supplementation, $p=0.04$, 67% of the LCPUFA group no longer had a BDI score equal to or greater than 10, but only 20% of the placebo group met such criteria. There was a significant group x time interaction for total BDI score, $F(1,19)=4.72$, $p=0.043$, ${}_{p}\eta^2=0.199$. Post-hoc analyses revealed the LCPUFAs group had a significant reduction in depressive symptomatology over time, while the placebo group's scores did not significantly change. There was a main effect for time, $F(1,19)=9.46$, $p=0.006$, ${}_{p}\eta^2=0.33$, but not for group ($p=0.34$). There was a significant group x time interaction for the cognitive–affective subscale of the BDI, $F(1,19)=7.02$, $p=0.016$, ${}_{p}\eta^2=0.270$. Post-hoc analyses revealed the LCPUFAs group had a significant reduction in cognitive–affective symptomatology over time, while the placebo group's scores did not significantly change. There was also a main effect for time, $F(1,19)=5.34$, $p=0.032$, ${}_{p}\eta^2=0.219$, but no main

Table 1
Demographic and baseline depression characteristics between groups. BDI and Age are reported as mean (standard deviation).

	LCPUFAs ($n=12$)	Placebo ($n=9$)
%female	62%	100%
Age (years)	20.33 (1.15)	20.00 (1.14)
BDI total	15.58 (5.21)	15.89 (5.46)
BDI cognitive–affective subscale	7.00 (4.52)	9.00 (4.30)
BDI somatic–vegetative subscale	8.17 (2.29)	6.89 (2.93)

Please cite this article as: Ginty, A.T., Conklin, S.M., Short-term supplementation of acute long-chain omega-3 polyunsaturated fatty acids may alter depression status and decrease.... Psychiatry Research (2015), http://dx.doi.org/10.1016/j.psychres.2015.05.072

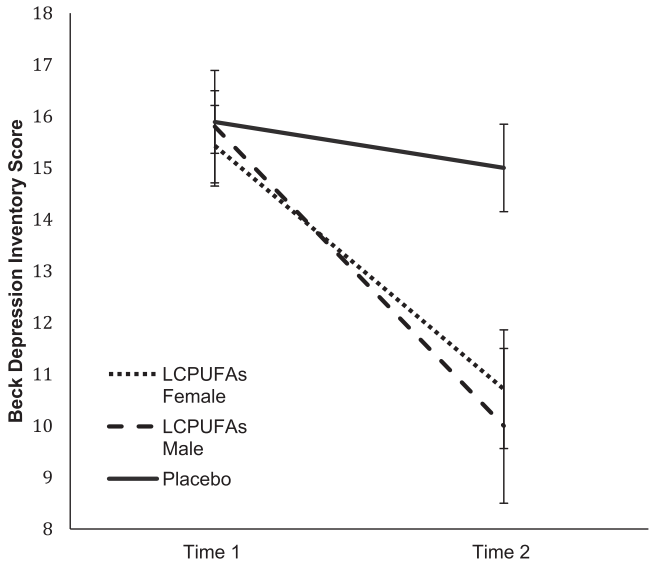

Fig. 1. Beck Depression Inventory (BDI) scores at Time 1 and Time 2 for the LCPUFAs Female, LCPUFAs Male, and Placebo groups. There was a significant reduction in depressive symptomology ($p < 0.05$) for the LCPUFAs group, but not for the placebo group. In the LCPUFA group, both males and females displayed a similar magnitude of decrease in depressive symptomology.

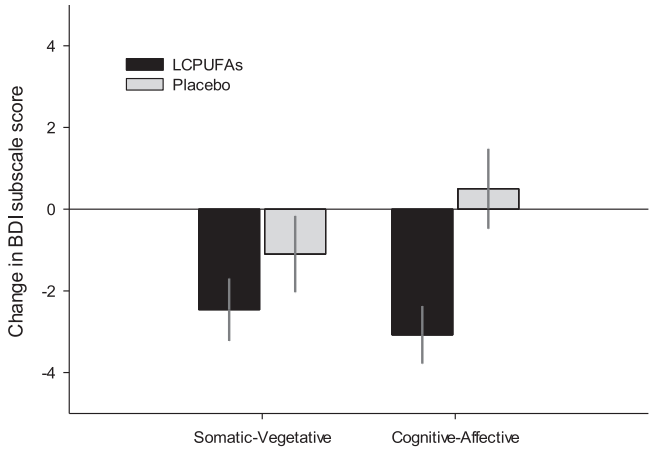

Fig. 2. Beck Depression Inventory (BDI) subscale score changes between Time 1 and Time 2 for LCPUFAs and Placebo groups. There were significant differences between groups for the cognitive–affective subscale, but not for the somatic–vegetative subscale.

effect of group ($p=0.72$). There was a significant main effect for time, $F(1,19)=9.27$, $p=0.007$, ${}_{p}\eta^2=0.328$, but no interaction ($p=.21$) or main effect for group ($p=.22$) on the somatic–vegetative subscale. Post-hoc analyses demonstrated that both groups decreased over time. Fig. 1 depicts average BDI scores at Time 1 and Time 2; the LCPUFAs group is split further into a female and male group to examine if the gender imbalance between groups was driving the results. Fig. 2 displays the change in the cognitive–affective and somatic–vegetative symptoms from Visit 1 to Visit 2 by group.

3.3. Sensitivity analyses

Additional analyses using the LOCF method to compute missing data for the two participants who dropped out before Visit 2 did not change overall results.

4. Discussion

The present double-blind, placebo controlled study examined the psychological effects of a short-term and low dose LCPUFAs supplementation (1.4 g, 1000 mg EPA and 400 mg DHA) on unmedicated and untreated undergraduate students with symptoms of depression. The results demonstrated that LCPUFAs, but not placebo, were successful in reducing depressive symptomology and depression below clinically indicated levels. The reduction in overall depressive symptoms was driven by a decrease in the cognitive–affective subscale of depression on the BDI-II.

Our results support two meta-analyses examining the effectiveness of LCPUFAs in reducing depression (Grosso et al., 2014a; Lin and Su, 2007). Previous research examining the influence of LCPUFAs on depressive levels in an unmedicated middle-aged sample with psychological distress (Lucas et al., 2009) and healthy undergraduate students (Fontani et al., 2005) also found similar results. However, our findings are at odds with a similar study examining the influence of LCPUFAs on an unmedicated, middle-aged population with depression (Rogers et al., 2008). This could be due to the difference in EPA (1000 mg in the current study, 630 mg in the other study); EPA has been shown to be more effective in reducing depressive symptomology than DHA (Lin and Su, 2007).

To our knowledge, this is the first study to demonstrate the effectiveness of a short-term, low-dose of LCPUFAs in reducing depressive symptomology in undergraduate students meeting clinical criteria for depression not currently receiving any other treatment. According to the American College Health Association's National College Health Assessment (2011) over two-thirds of college students report feeling “very sad” and one-third feel so sad it inhibits their ability to function. However, a recent study found that only 36% of undergraduates who had clinically significant depression levels were actually receiving some form of treatment (Eisenberg et al., 2007). Each year, over 1000 undergraduate students commit suicide in the United States and most of these students were not seen by their college's counseling center (Active Minds, 2014; Gallagher, 2006). Therefore, it is important to continue to conduct studies in this particular population to examine ways to reduce depressive symptomology. Results from studies such as this suggest that dietary changes may be a relatively easy and inexpensive option for students who are currently struggling with depression.

A decrease in HPA axis activity and inflammation levels or a change in neurotransmitter system activity could explain the reduction in depression symptoms in the LCPUFAs group. A deficiency of LCPUFA has been associated with hyperactivity of the hypothalamic–pituitary–adrenal (HPA) axis (Nieminen et al., 2006) and a recent animal study demonstrated that HPA hyperactivity caused by LCPUFA deficiency led to atrophy in the prefrontal cortex and negative mood (Larrieu et al., in press). Atrophy of the prefrontal cortex has been associated with depression (e.g., Drevets et al., 1997). A recent study, demonstrated that a 3-week supplementation of LCPUFAs resulted in decreased basal HPA axis activity and decreases in stress/anxiety ratings before and after a psychological challenge (Barbadoro et al., 2013). A positive relationship between dietary LCPUFAs intake and the volume of multiple prominent nodes of corticolimbic circuitry has been established (Conklin et al., 2007a). Therefore, it is plausible that the increase in LCPUFAs in this sample led to a decrease in HPA axis activity and/or structural change in brain areas associated with affective experience. However, it seems unlikely that 21-days of supplementation could alter gray matter volume. This is something that needs to be explored in future studies.

Another possible mechanism linking supplemental LCPUFA with mood improvement could be a reduction in inflammation as

Please cite this article as: Ginty, A.T., Conklin, S.M., Short-term supplementation of acute long-chain omega-3 polyunsaturated fatty acids may alter depression status and decrease.... Psychiatry Research (2015), http://dx.doi.org/10.1016/j.psychres.2015.05.072

a result of the increase in LCPUFAs. High levels of omega-6 PUFAs compared to omega-3 PUFAs are related to higher levels of depression and inflammation (Conklin et al., 2007b; Kiecolt-Glaser et al., 2007). Two randomized controlled trials have shown the LCPUFAs can reduce inflammation levels in healthy medical students (Kiecolt-Glaser et al., 2011) and healthy middle-aged adults (Kiecolt-Glaser et al., 2012). Both higher cognitive–affective symptoms (Kupper et al., 2012; Shaffet et al., 2011) and somatic–vegetative symptoms have been associated with increased levels of inflammation (Dannehl et al., 2014). In this study we only saw a significant decrease in cognitive–affective symptoms. Recent reviews have discussed the importance of reducing inflammation as a method of treatment for depression (Raison and Miller, 2013; Leonard, 2014).

An additional mechanism that could explain the findings is changes in serotoninergic and dopaminergic transmission (Grosso et al., 2014b). The unsaturated structure of LCPUFAs facilitates alteration of membrane fluidity (Calder et al., 1994) and thereby the function and regulation of monoaminergic systems, specifically serotonergic and dopaminergic diffuse modulatory systems (Grosso et al., 2014b). Deficient levels of PUFAs are associated with deficits of serotonin and dopamine in the prefrontal cortex (McNamara et al., 2009, 2010). Cognitive–affective components of depression are associated with impaired prefrontal cortex activity (Heinzel et al., 2009; Mayberg, 1997, 2003; Mayberg et al., 1999). A recent study found that providing rats with LCPUFAs increased dopamine levels in the frontal cortex by 40% (Chalon et al., 1998). It could be possible that the decrease in depression, specifically the decrease in cognitive–affective symptoms, could be driven by alternations in neuromodulation, specifically serotoninergic and dopaminergic transmission.

The study is not without limitations. First, the sample size is small. However it is similar to other studies examining the association between LCPUFAs supplementation and mood (e.g., Su et al., 2003; Zanarini and Frankenburg, 2003; Nemets et al., 2002). Second, the gender composition was different between groups. The placebo group consisted only of females and future studies should use stratified randomization. However, Fig. 1 demonstrates that the reduction in depressive symptomology across time was similar for both males and females in the LCPUFAs group. Third, blood samples were not obtained to verify compliance. Although blood sampling would have been useful, practical considerations prevented this from occurring. Fourth, participants were not asked if they knew what group they were in. However, a recent study using the same concentration and same mint blind in a similar age group, but completely independent sample, found that participants were unable to correctly guess if they were in the LCPUFAs or placebo group (Ginty and Conklin, 2012). Finally, the study could have benefited from additional measurements of depression or a confirmed clinical diagnosis of depression. One of the aims was to examine the effects of LCPUFAs on depressive symptoms in participants not currently receiving any treatment for depression. Having participants with a confirmed clinical diagnosis by a clinician would have made it difficult to enroll participants not receiving treatment. Additionally, the BDI is a widely used, and well respected measure and is recommended by the National Institute of Health and Clinical Excellence for use in the primary care setting to identify depression and responsiveness to treatment (Smarr and Keefer, 2011).

In conclusion, this study is the first to demonstrate the positive psychological effects of short-term low doses of LCPUFA supplementation on undergraduate students with depression. The nature of the dose, equivalent to two fatty fish meals per week, is something that could easily be modified in the diet of undergraduate students. A larger study is needed to examine these effects and other potential dietary strategies.

Acknowledgment

The authors would like to thank Siera Goodnight, Josh Sesek, and Mia Symoniak for their assistance with participant recruitment and data collection and Gretchen Vannice for her assistance with coordinating manufacture and delivery of supplements and placebos. The authors gratefully acknowledge the Grant support from T32HL07560.

References

Active Minds, 2014. The Issue: Student Mental Health. (accessed: 10.20.14), ⟨http://activeminds.org/issues-a-resources/the-issue⟩.

American College Health Association, 2012. American College Health Association-National College Health Assessment II: Reference Group Executive Summary Fall 2011. American College Health Association, Hanover, MD.

Antypa, N., Van der Does, A.J., Smelt, A.H., Rogers, R.D., 2009. Omega-3 fatty acids (fish-oil) and depression-related cognition in healthy volunteers. J. Psychopharmacol. 23, 831–840.

Appleton, K.M., Peters, T.J., Hayward, R.C., Heatherley, S.V., McNaughton, S.A., Rogers, P.J., Gunnell, D., Ness, A.R., Kessler, D., 2007. Depressed mood and *n*-3 polyunsaturated fatty acid intake from fish: non-linear or confounded association? Soc. Psychiatry. Epidemiol. 42, 100–104.

Barbadoro, P., Annino, I., Ponzio, E., Romanelli, R.M., D'Errico, M.M., Prospero, E., Minelli, A., 2013. Fish oil supplementation reduces cortisol basal levels and perceived stress: a randomized, placebo-controlled trial in abstinent alcoholics. Mol. Nutr. Food Res. 57, 1110–1114.

Beck, A.T., Steer, R.A., Brown, G.K., 1996. Manual for the Beck Depression Inventory-II. Psychological Corporation, San Antonio, TX.

Beck, A.T., Steer, R.A., Carbin, M.G., 1988. Psychometric properties of the beck depression inventory: twenty-five years of evaluation. Clin. Psychol. Rev. 8, 77–100.

Calder, P.C., Yaqoob, P., Harvey, D.J., Watts, A., Newsholme, E.A., 1994. Incorporation of fatty acids by concanavalin A-stimulated lymphocytes and the effect on fatty acid composition and membrane fluidity. Biochem. J. 300, 509–518.

Chalon, S., Delion-Vancassel, S., Belzung, C., et al., 1998. Dietary fish oil affects monoaminergic neurotransmission and behavior in rats. J. Nutr. 128, 2512–2519.

Conklin, S.M., Gianaros, P.J., Brown, S.M., Yao, J.K., Hariri, A.R., Manuck, S.B., Muldoon, M.F., 2007. Long-chain omega-3 fatty acid intake is associated positively with corticolimbic gray matter volume in healthy adults. Neurosci. Lett. 421, 209–212.

Conklin, S.M., Manuck, S.B., Yao, J.K., Flory, J.D., Hibbeln, J.R., Muldoon, M.F., 2007b. High omega-6 and low omega-4 fatty acids are associated with depressive symptoms and neuroticism. Psychosom. Med. 69, 932–934.

Dannehl, K., Rief, W., Schwarz, M.J., Hennings, A., Riemer, S., Selberdinger, V., Stapf, T., Euteneuer, F., 2014. The predictive value of somatic and cognitive depressive symptoms for cytokine changes in patients with major depression. Neuropsychiatr. Dis. Treat. 10, 1191–1197.

Deardorff, W.W., Funabiki, D., 1985. A diagnostic caution in screening depressed college students. Cognit. Ther. Res. 9, 227–284.

Demyttenaere, K., Bruffaerts, R., Posada-Villa, J., Gasquet, I., Kovess, V., Lepine, J.P., Angermeyer, M.C., Bernert, S., de Girolamo, G., Morosini, P., Polidori, G., et al., 2004. Prevalence, severity, and unmet need for treatment of mental disorders in the World Health Organiation world mental healthy surveys. JAMA 291, 2581–2590.

Dozois, D.J.A., Dobson, K.S., Ahnberg, J.L., 1998. A psychometric evaluation of the Beck Depression Inventory-II. Psychol. Assess. 10, 83.

Drevets, W.C., Price, J.L., Simpson, Jr, Todd, R.D., Reich, T., Vannier, M., Raichle, M.E., 1997. Subgenual prefrontal cortex abnormalities in mood disorders. Nature 386, 824–827.

Eisenberg, D., Gollust, S.E., Golberstein, E., Hefner, J.L., 2007. Prevalence and correlates of depression, anxiety, and suicidality among university students. Am. J. Orthopsychiatr. 77, 534–542.

Fontani, G., Corradeschi, F., Felici, A., Alfatti, F., Migliorini, S., Lodi, L., 2005. Cognitive and physiological effects of Omega-3 polyunsaturated fatty acid supplementation in healthy subjects. Eur. J. Clin. Investig. 35, 691–699.

Gallagher, R.P., 2006. National survey counseling center directors 2006. Washington, D.C. International Association of Counseling Services.

Gewandter, J.S., McDermott, M.P., McKeown, A., Smith, S.M., Williams, M.R., Hunsinger, M., Farrar, J., Turk, D.C., Dworkin, R.H., 2014. Reporting of missing data and methods used to accommodate them in recent analgesic clinical trials: ACTTION systematic review and recommendations. Pain 155, 1871–1877.

Ginty, A.T., Conklin, S.M., 2012. Preliminary evidence that acute long-chain omega-3 supplementation reduces cardiovascular reactivity to mental stress: a randomized and placebo controlled trial. Biol. Psychol. 89, 269–272.

Grosso, G., Pajak, A., Marventano, S., Castellano, S., Galvano, F., Bucolo, C., Drago, F., Carci, F., 2014a. Role of omega-3 fatty acids in the treatment of depressive disorders: a comprehensive meta-analysis of randomized clinical trials. PLOS one 9, 1–18.

Grosso, G., Galvano, F., Marventano, S., Malaguarnera, M., Bucolo, C., Drago, F.,

Caraci, F.R., 2014. Omega-3 fatty acids and depression: scientific evidence and biological mechanisms. Oxid. Med. Cell. Longev., 313570.
Heinzel, A., Grimm, S., Beck, J., Schuepbach, D., Hell, D., Boesiger, B., Boeker, H., Northoff, G., 2009. Segregated neural representation of psychological and somatic–vegetative symptoms in severe major depression. Neurosci. Lett. 456, 49–53.
Khambaty, T., Stewart, J.C., Muldoon, M.F., Kamarck, T.W., 2014. Depressive symptom clusters as predictors of 6-year increases in insulin resistance: Data from the Pittsburgh healthy heart project. Psychosom. Med. 76, 363–369.
Kiecolt-Glaser, J.K., Belury, M.A., Andridge, R., Malarkey, W.B., Glaser, R., 2011. Omega-3 supplementation lowers inflammation and anxiety in medical students: a randomized controlled trial. Brain Behav. Immun. 25, 1725–1734.
Kiecolt-Glaser, J.K., Belury, M.A., Andridge, R., Malarkey, W.B., Hwang, B.S., Glaser, R., 2012. Omega-3 supplementation lowers inflammation in healthy middle-aged and older adults: a randomized controlled trial. Brain Behav. Immun. 26, 988–995.
Kiecolt-Glaser, J.K., Belury, M.A., Porter, K., Beversdorf, D.Q., Lemeshow, S., Glaser, R., 2007. Depressive symptoms, omega-6: omega-3 fatty acids, and inflammation in older adults. Psychosom. Med. 69, 217–224.
Kupper, N., Widdershoven, J.W., Pedersen, S.S., 2012. Cognitive/affective and somatic/affective symptom dimensions of depression are associated with current and future inflammation in heart failure patients. J. Affect. Disord. 136, 567–576.
Lin, P.Y., Su, K.P., 2007. A meta-analytic review of double-blind, placebo-controlled trials of antidepressant efficacy of omega-3 fatty acids. J. Clin. Psychiatry. 68, 1056–1061.
Larrieu, T., Hilal, L.M., Fourrier, C., De Smedt-Peyrusse, V., Sans, N., Capuron, L., Laye, S., 2015. Nutritional omega-3 modulates neuronal morphology in the prefrontal cortex along with depression-related behavior through corticosterone secretion. Transl. Psychiatry. 4, e437, in press, http://dx.doi.org/10.1038/tp.2014.77 issue 4:e437.
Leonard, B.E., 2014. Impact of inflammation on neurotransmitter changes in major depression: an insight into the action of antidepressants. Prog. NeuroPsychopharmacol. Biol. Psychiatry. 48, 261–267.
Lucas, M., Asselin, G., Merette, C., Poulin, M.J., Dodin, S., 2009. Ethyl-eicosapentaenoic acid for the treatment of psychological distress and depressive symptoms in middle-aged women: a double-blind, placebo-controlled, randomized clinical trial. Am. J. Clin. Nutr. 89, 641–651.
Mayberg, H.S., 1997. Limbic-cortical dysregulation: a proposed model of depression. J. Neuropsychiatr. Clin. Neurosci. 9, 471–481.
Mayberg, H.S., 2003. Modulating dysfunctional limbic-cortical circuits in depression: towards development of brain-based algorithms for diagnosis and optimsied treatment. Br. Med. Bull. 65, 192–207.
Mayberg, H.S., Liotti, M., Brannan, S.K., McGinnis, S., Mahurin, R.K., Jerabek, P.A., Silva, J.A., Tekell, J.L., Martin, C.C., Lancaster, J.L., Fox, P.T., 1999. Reciprocal limbic-cortical function and negative mood: converging PET findings in depression and normal sadness. Am. J. Psychiatry. 156, 675–682.
McNamara, R.K., Albe, J., Liu, Y., et al., 2009. Omega-3 fatty acid deficiency during perinatal development increases serotonin turnover in the prefrontal cortex and decreases midbran tryptophan hydroxylase-2 expression in adult female rats: dissociation from estrogenic effects. J. Psychiatry. Res. 43, 656–663.
McNamara, R.K., Jandacek, R., Rider, T., Tso, P., Cole-Strauss, A., Lipton, J.W., 2010. Omega-3 fatty acid deficiency increases constitutive pro-inflammatory cytokine production in rats: relationship with central serotonin turnover. Prostaglandins Leukot. Essent. Fat. Acid. 83, 185–191.
Nieminen, L.R., Makino, K.K., Mehta, N., Vikkunen, M., Kim, H.Y., Hibbeln, J.R., 2006. Relationship between omega-3 fatty acids and plasma neuroactive steroids in alcoholism, depression and controls. Prostaglandins Leukot. Essent. Fat. Acid. 75, 309–314.
Nemets, B., Stahl, Z., Belmaker, R.H., 2002. Addition of omega-3 fatty acid to maintenance medication treatment for recurrent unipolar depressive disorder. Am. J. Psychiatry. 159, 477–479.
Raison, C.L., Miller, A.H., 2013. Role of inflammation in depression: implications for phenomenology, pathophysiology and treatment. Mod. Trends Pharmacopsychiatr. 28, 33–48.
Rogers, P.J., Appleton, K.M., Kesller, D., Peters, T.J., Gunnell, D., Hayward, R.C., Heatherley, S.V., Christian, L.M., McNaughton, S.A., Ness, A.R., 2008. No effect of *n*-3 long-chain polyunsaturated fatty acid (EPA and DHA) supplementation on depressed mood and cognitive function: a randomised controlled trial. Br. J. Nutr. 99, 421–431.
Shaffer, J.A., Edmondson, D., Chaplin, W.F., Schwartz, J.E., Shimbo, D., Burg, M.M., Rieckmann, N., Davidson, K.W., 2011. Directionality of the relationship between depressive symptom dimensions and C-reactive protein in patients with acute coronary syndromes. Psychosom. Med. 73, 370–377.
Smarr, K.L., Keefer, A.L., 2011. Measures of depression and depressive symptoms: Beck Depression Inventory-II, Center for Epidemiologic Studies Depression Scale (CES-D), Geriatric Depression Scale (GDS), Hospital Anxiety Depression Scale (HADS), Patient Health Questionnaire-9 (PHQ-9). Arthr. Care Res. S11, S454–S466.
Sprinkle, S.D., Lurie, D., Insko, S.L., Atkinson, G., Jones, G.L., Logan, A.R., Bissada, N.N., 2002. Criterion validity, severity cut scores, and test-retest reliability of the Beck Depression Invenstory-II in a university counseling center sample. J. Couns. Psychol. 49, 381–385.
Stewart, J.C., Zielke, D.J., Hawkins, M.A., Williams, D.R., Carnethon, M.R., Knox, S.S., Matthews, K.A., 2012. Depressive symptom clusters and 5-year incidence of coronary artery calcification: clinical perspective. The coronary artery risk development in young adults study. Circulation 74, 33–38.
Su, K.P., Huang, S.Y., Chiu, C.C., Shen, W.W., 2003. Omega-3 fatty acids in major depressive disorder. A preliminary double-blind, placebo-controlled trial. Eur. Neuropsychopharmacol. 13, 267–271.
World Health Organization, 2012. World Mental Health Day. (accessed: 10.21.14). ⟨http://www.who.int/mental_health/management/depression/wfmh_paper_depression_wmhd_2012.pdf⟩.
Zanarini, M.C., Frankenburg, F.R., 2003. Omega-3 fatty acid treatment of women with borderline personality disorder: a double-blind, placebo-controlled pilot study. Am. J. Psychiatry. 160, 167–169.

Please cite this article as: Ginty, A.T., Conklin, S.M., Short-term supplementation of acute long-chain omega-3 polyunsaturated fatty acids may alter depression status and decrease.... Psychiatry Research (2015), http://dx.doi.org/10.1016/j.psychres.2015.05.072