Omega-3 Supplementation and Emotional Blunting:

A Placebo-Controlled Investigation

By

Kathleen T. Rhyner

Submitted to the graduate degree program in Clinical Psychology and the Graduate Faculty of the University of Kansas in partial fulfillment of the requirements for the degree of Master of Arts.

Chairperson: Stephen Ilardi
Nancy Hamilton
 Sarah Kirk

Date Defended: May 23, 2013

Tl	ne Thes	is Com	nittee f	or Kath	leen T.	Rhyner	
certifies th	at this i	s the ap	proved	version	of the	following	g thesis:

Omega-3 Supplementation and Emotional Blunting:

A Placebo-Controlled Investigation

Chairperson: Stephen Ilardi

Date approved: May 23, 2013

Abstract

One side effect of SSRI medication is emotional blunting, characterized by a restricted range of emotions and decreased caring. Because omega-3 supplements also have established antidepressant properties, they might also induce emotional blunting.

Participants were randomized to receive omega-3 supplements or pill placebos for three weeks. Emotional blunting was evaluated via three assessment strategies: scores on an emotional blunting questionnaire, emotional reactions to a dysphoric mood induction, and daily mood ratings. As hypothesized, participants in the omega-3 group scored significantly higher on the emotional blunting questionnaire, with an effect size in the moderate range. They also scored significantly higher on 3 of the questionnaire's 4 subscales. However, omega-3 supplementation was not associated with a reduced emotional response to the mood-induction, nor with any reduction in the variability of daily mood ratings. These findings suggest that healthy individuals taking omega-3 supplements may experience moderate blunting in a subset of emotion-linked domains.

Table of Contents

Abstract	iii
Overview	1
Method	7
Results	11
Discussion	12
References	18

Omega-3 Supplementation and Emotional Blunting: A Placebo-Controlled Investigation

Four of the five most commonly prescribed antidepressant medications in the U.S. are selective serotonin reuptake inhibitors (SSRIs) (Drug Topics Staff, 2010a, 2010b). However, side effects of SSRIs – including nausea, headaches, sleep disturbances, and sexual dysfunction – are common, and they frequently result in discontinuation of the medication (Beasley, Koke, Nilsson & Gonzales, 2000). Another potential side effect of these medications, albeit one which has received relatively little research attention, is emotional blunting. For example, Daly et al. (2011) observed that 27 out of 265 individuals reported adverse effects of apathy from SSRI use. Apathy may be related to part of the construct of emotional blunting focused on decreased caring. Despite the fact that emotional blunting is commonly reported by patients and could have life-changing implications, many patients are never informed about the possibility of experiencing this particular side effect (Opbroek et al., 2002).

One complication of investigating the phenomenon of emotional blunting is the lack of a clearly defined construct across studies. Price, Cole, and Goodwin (2009), for example, define emotional blunting as experiencing "a restricted range of emotions that are a normal part of everyday life." Another name for this phenomenon is "Antidepressant Apathy Syndrome". Marin (1990) defined apathy as, "diminished motivation not attributable to diminished level of consciousness, cognitive impairment, or emotional distress," and differentiated apathy that is due to depression from apathy that is not due to depression. Marin hypothesized that apathy in depressed individuals is often illustrated by physical and social inactivity, decreased interest in activities, and internal emotional disturbance, whereas apathy that is not associated with depression is often

characterized by indifference, lack of motivation, poor attention, and disinhibition (Marin, 1990). In a somewhat related vein, another research group (Barnhart, Makela, & Latocha, 2004) has hypothesized that apathy in depression is associated with fatigue, whereas apathy associated with SSRIs is not. Finally, the construct of interest has also been referred to as "Amotivational Syndrome" which is defined by "apathy, lack of motivation, lack of appropriate concern, and in some cases disinhibition" (Garland & Baerg, 2001). Although these articles use different names and have some differences in definition, they all approach a similar construct, which will be referred to in this article as *emotional blunting*.

Emotional blunting is an important side effect of SSRIs, with a broad range of positive and negative implications. Many individuals with depression initially welcome SSRI-induced blunting of negative emotions and pain they have been experiencing. In fact, severely depressed individuals can sometimes experience an increase in their ability to function after the intensity of their negative emotions decreases (Price, Cole, & Goodwin, 2009). However, there are also many deleterious effects of emotional blunting. The first is the obvious inability to feel the full range of "normal" affect, particularly positive emotions. Some blunted individuals also report feeling detached from their emotions and "just not caring" about important aspects of their life, such as their job or relationships. Such reductions in positive emotions constitute a commonly reported reason why individuals discontinue the use of SSRIs to treat their depressive symptoms. (Price, Cole, & Goodwin, 2009).

Among clinicians, SSRI-induced emotional blunting is becoming an increasingly well-recognized phenomenon. Case reports by Hoehn-Saric, Lipsey, and McLeod (1990)

describe emotional blunting in patients taking Fluvoxamine and Fluoxetine for depression and panic disorder, while other case reports describe similar symptoms in patients taking a variety of SSRIs for depression, anxiety, and OCD (Garland & Baerg, 2001; George, Trimble, & Robertson, 1993). One study by Opbroek et al. (2002) observed that 80% of participants in a study of SSRI-induced sexual dysfunction also reported the blunting of some emotions. This study investigated several domains of emotional blunting, and found that the most frequently altered emotions were related to sexual desire, the ability to cry, motivation, and creativity. Several other case studies have also documented that SSRIs may reduce one's ability to cry (Oleshansky & Labbate, 1996).

It is often difficult, however, to differentiate emotional blunting from the apathy present in depression. Nevertheless, many individuals taking SSRIs claim to be capable of differentiating the two phenomena (Price, Cole, & Goodwin, 2009). It has been found that the effect of emotional blunting can be reduced by titrating the dose of medication to a level that is still helpful for treating depression but that causes fewer emotional side effects (Hoehn-Saric, Lipsey, & McLeod, 1990). One relevant case study describes an SSRI-treated OCD patient who had changes in cerebral blood flow similar to those seen in frontal lobe syndrome, which is itself characterized by decreased motivation (Hoehn-Saric, Harris, Pearlson, & Cox, 1991). Another case study described a patient prescribed an SSRI for OCD and Tourette's syndrome who experienced severe apathy and indifference, but not depression (George, Trimble, & Robertson, 1993). Emotional blunting does not only affect adults: Garland and Baerg (2001) also documented similar effects in four adolescents and one child. Although emotional blunting does have some overlap in symptoms with depression, the aforementioned studies illustrate that emotional

blunting can exist as a phenomenon independent from depression – one that can be caused by SSRIs.

The neurological mechanisms that underlie emotional blunting are currently unknown. SSRIs are believed to treat depression by increasing the functional activity of serotonergic circuits in the brain, which may in turn induce beneficial changes such as a reduction in the brain's stress response (Nemeroff & Owens, 2004), increased social drive (Warwick et al., 2012), decreased intensity of emotional pain (Matsuzawa-Yanagida et al., 2008), and more restorative sleep (Nakamaru-Ogiso et al., 2012). But how might serotonergic drugs also induce emotional blunting? One hypothesis is that the serotonin-based circuits that connect the raphe nuclei to the frontal lobe are capable of inhibiting not only negative emotions, but positive emotions as well, inasmuch as the frontal lobe is crucial in the regulation of both motivation and emotional valence.

Emotional blunting could be caused in part by the downstream effects of serotonin on the dopamine system, as well, although this mechanism is not yet fully understood.

(Barnhart, Makela, & Latocha, 2004)

Several studies have also shown that SSRIs can cause changes in the processing of emotional material. For example, Harmer, Mackay, Reid, Cowen, and Goodwin (2006) found that negative facial expressions are processed differently after a week of antidepressant medication. Specifically there is a reduced recognition of fearful facial expressions. Another study also showed a decreased response to sad facial expressions after eight weeks of SSRIs (Fu et al., 2004). These findings are consistent with reported experiences of emotional blunting and could explain symptoms of emotional blunting such as reduced concern or caring for others if individuals on SSRIs are unable to

recognize expressions of sadness or fear in others. Another recent study found healthy participants given SSRIs showed diminished neural responses to aversive and rewarding stimuli (chocolate and rotten strawberries) on an fMRI (McCabe, Mishor, Cowen, & Harmer, 2010). This decrease in responsiveness to both positive and negative stimuli is consistent with reported experiences of emotional blunting.

There is a growing body of research on another treatment for depression that is associated with relatively few side effects: omega-3 fatty acids. Omega-3s, in fact, are becoming increasingly popular in the treatment of depression (Gören & Tewksbury, 2011). Several recent reviews and meta-analyses have provided support for the efficacy of omega-3 supplements in the treatment of depression (Parker et al., 2006; Ross, Seguin, & Sieswerda, 2007; Martins, 2009; Sublette, Ellis, Geant & Mann, 2011). The effects of omega-3s are commonly seen within four weeks of treatment. One study of omega-3 supplements for treatment of individuals with depression reported a statistically significant difference between the omega-3 condition and placebo condition after two weeks, and a "highly significant difference" between groups at weeks three and four (Nemets, Stahl & Belmaker, 2002).

With low omega-3 intake there may be a loss of function in both serotonin and dopamine systems due to the absence of the essential fatty acids needed to support these systems. Omega-3s also have anti-inflammatory properties, and they can decrease inflammation in the brain caused by the activation of the brain's stress response in depression. (Ilardi, 2009) It is not currently known whether or not the primary benefit of omega-3 supplements is a result of their effect on the serotonin system or their anti-inflammatory properties. The potential similarities in mechanisms between omega-3

supplements and SSRIs suggest that it is possible for emotional blunting side effects to also be caused by omega-3 supplements.

The potential of emotional blunting as a side effect of omega-3 supplementation has not previously been investigated. In addition to the hypothesized similarity in mechanisms between SSRIs and omega-3s, anecdotal reports also support this as a possibility. Antypa, Van der Does, Smelt, and Rogers (2009) observed that healthy individuals who took omega-3 supplements for four weeks made more risky decisions than did a placebo group on a risky decision-making task, a finding that may suggest an increase in disinhibition with omega-3 supplementation. The same study also found decreased scores on a control/perfectionism scale, possibly supporting the decreased level of caring associated with emotional blunting. If emotional blunting is a potential side effect of omega-3 supplements, it is important for individuals to be made aware of this when considering their use for treatment of depression or other conditions.

The primary aim of the present study, therefore, is to examine the effect of omega-3 supplements on emotional blunting, and specifically to test the hypothesis that omega-3 supplements may increase emotional blunting, as compared to the effects of a pill placebo. Given the inherent difficulty of investigating a relatively new construct, I used three different methods to test this hypothesis:

1. I compared the differences in emotional blunting after 3 weeks of taking an omega-3 supplement or pill placebo on the OQuESA, a new self-report measure specifically designed for the purpose of assessing emotional blunting in the context of treatment. I expected to find that OQuESA scores for the omega-3

- group would be significantly higher than OQuESA scores for the placebo group at the end of three weeks.
- 2. I compared differences in reactivity to a mood induction after the 3 weeks of pills using the MAACL-R. I expected to find that MAACL-R scores for the omega-3 group would be significantly lower than the MAACL-R scores for the placebo group, thereby illustrating decreased emotional reactivity.
- 3. I used daily mood ratings of positive and negative mood to compare the variability in mood over the course of three weeks for members of each group. I expected to find a significant decrease in mood variability over time for the omega-3 group compared to the control group.

Method

Participants

Participants were 117 undergraduate students (33 men, 84 women) who ranged in age from 17 to 23 (M = 18.66, SD = 1.01). The majority of participants described their racial identification as Caucasian (83%). Participants were enrolled in an introductory psychology course and participated in this study in exchange for course credit. Exclusion criteria for this study included: (a) the presence of a current depressive episode, as indicated by a BDI-II score of >13; (b) being pregnant or nursing; (c) a self-reported diagnosis of diabetes or a bleeding disorder; (d) a self-reported current diagnosis of major depressive disorder or bipolar disorder; (e) known or suspected allergies to omega-3 supplements or pill placebo ingredients (gelatin and mineral oil); (f) current use of omega-3 supplements; or (g) current use of any psychoactive medications, including antipsychotics, antidepressants, anxiolytics, or stimulants.

Measures

Beck Depression Inventory-II (BDI-II). The BDI-II (Beck, Steer, & Brown, 1996) is a 21-item questionnaire designed to assess the current presence and severity of depressive symptoms. Individuals are asked to rate the items based on how they have been feeling within the past two weeks on a scale from 0 to 3, with 3 being the most severe. The cutoffs for scores include: 0-13 for minimal depression, 14-19 for mild depression, 20-28 for moderate depression, and 28-63 for severe depression. The BDI-II has a high internal consistency with a reported alpha of 0.91 (Beck, Steer, Ball & Ranieri, 1996) and a high test-retest reliability, r = 0.93 (Beck, Steer, & Brown, 1996).

Oxford Questionnaire of the Emotional Side-effects of Antidepressants (OQuESA). The OQuESA (Price, Cole, Doll & Godwin, 2012) is a 26-item questionnaire designed to assess blunting of emotional experiences. The OQuESA is divided into three sections. Section 1 consists of 12 items that ask the respondents to rate their emotional experiences during the past week on a five-point Likert scale. Section 2 consists of 8 items that ask respondents to compare their emotional experiences during the past week with their experiences before beginning antidepressant medication on a five-point Likert scale. Section 3 consists of 6 items that ask respondents to rate their beliefs about the emotional side effects of their antidepressant medication on a five-point Likert scale. Four dimensions can be scored, including general reduction in emotions, reduction in positive emotions, emotional detachment from others, and not caring. A total score can be computed by adding the scores from all four dimensions. The OQuESA has a high internal consistency, with a total score alpha of 0.93 and a high total score test-retest reliability, r = 0.90 (Price, Cole, Doll & Goodwin, 2012). For the purposes of the

current study, all references to "antidepressants" or "current illness/problem" in the questionnaire were replaced with "capsules" to refer to the Omega-3 supplement or pill placebo.

Multiple Affect Adjective Check List—Revised (MAACL-R).). The MAACL-R (Lubin & Zuckerman, 1999) is a self-report instrument designed to measure an individual's current affect. The measure consists of 132 items, all of which are adjectives measuring positive or negative affect. Participants are asked to check the items that describe how they feel in the moment. The dysphoria composite score is obtained by adding scores from the Anxiety, Depression, and Hostility scales. Because the checklist is designed to assess current mood state, it has low test-retest reliability by nature, but acceptable internal consistency (α = .75-.90) (Maloni, Chance, Zhang & Cohen 1993). *Procedure*

Participants were recruited through the mass testing procedure of introductory psychology students at a large university in the Midwestern United States. After the initial screening process, individuals who met the initial study criteria were invited to the lab to participate in the study. Upon arrival, participants were informed that they would be participating in an experiment to investigate the effects of omega-3 supplements on emotional experiences. After giving informed consent, each participant was tested individually. All participants first completed the OQuESA, BDI-II, and demographics form. After completing the questionnaires, participants who qualified for the study were given a negative mood induction similar in procedure to that used by Ingram, Bernet, and McLaughlin (1994). Specifically, participants were asked to reflect on a sad event in

their lives while listening to sad music for a period of eight minutes. Immediately following the mood induction, participants completed the MAACL-R questionnaire.

After completing the mood induction and the MAACL-R, participants were randomly assigned via a random number generator to the omega-3 group or the placebo group. The participants assigned to the omega-3 group were given 3 weeks' worth of omega-3 fish oil supplements. The assigned daily dose of omega-3 fatty acids was 2,126 mg (800 mg EPA and 400 mg DHA). Participants were informed that they could be assigned omega-3 supplements or a pill placebo. Participants were instructed to take two pills per day. Participants in the placebo group were given 3 weeks' worth of mineral oil placebo pills that closely mimic the appearance of omega-3 supplements. Instructions for the placebo group were identical to those for the omega-3 group. Participants were also given notecards with the dates for the next three weeks written on them. Participants were instructed to text or email a picture of themselves taking the pills with the correct date card to a secure email address each day to be used as a means of documenting protocol adherence. They were also instructed to include a rating each day on a scale from 1 to 10 of the "most positive" their mood was that day, and a separate rating on a scale from -1 to -10 on the "most negative" their mood was that day.

After three weeks, participants returned to the lab. Participants first completed the OQuESA and BDI-II. After completing the questionnaires, all participants were given a negative mood induction. Participants were asked to reflect on a sad event in their lives while listening to sad music for a period of eight minutes. Immediately following the mood induction, participants completed the MAACL-R questionnaire. Before leaving the lab, all participants were verbally debriefed about the purpose of the

study. Questionnaires from the second experimental session were analyzed for differences in emotional blunting between groups.

Results

Only individuals who returned for the second experimental session and completed 16 or more days of the adherence check were included in the analyses. Out of 181 participants who completed the first experimental session, 43 participants did not return for the second experimental session and 21 participants did not complete 16 or more days of the adherence check. In total, 117 participants, 58 participants in the placebo group and 59 participants in the omega-3 group, were included. Both groups had an adherence rate of approximately 95% with respect to the daily ingestion of omega-3 and placebo capsules, respectively.

Contrary to the study hypothesis, a one-way analysis of variance (ANOVA) revealed that scores did not differ significantly between the omega-3 group (M = 4.97, SD = 4.23) and the placebo group (M = 4.84, SD = 5.02) on the MAACL-R dysphoria scale following the study's negative mood induction procedure [F(1,115) = 0.02; p = 0.888].

In order to evaluate hypothesized differences between the omega-3 group and placebo group in emotional intensity and variability over the course of the 3-week study, I employed a multilevel (latent growth curve) analysis, a strategy particularly well suited to evaluating between-group differences in the trajectory of construct variability. The model intercepts of the two groups were not significantly different on Day 1, indicating the absence of any preexisting differences between groups on emotional variability (z = -0.26, p = 0.945). Further, there was no significant difference between the model's slope estimates of the two groups over the 3-week assessment, which suggests that variability

in emotional intensity did not significantly differ between the two groups over the course of the study (z = 1.19, p = 0.361).

Because OQuESA total scores were positively skewed in the study sample, they did not meet the requisite assumptions for use in ANOVA modeling. Accordingly, negative binomial regression was selected as a more appropriate strategy to evaluate potential differences in OQuESA scores between the omega-3 and placebo groups. The omega-3 group (M = 37.88, SD = 13.65) reported significantly more emotional blunting than did the placebo group (M = 33.02, SD = 9.93) on the OQuESA ($\beta = 1.15$, p < 0.05). The Cohen's effect size estimate for this difference (d = 0.41) is considered a moderate effect.

Three of the four subscales of the OQuESA were also found to differ significantly between the two groups: *general reduction of emotions* was greater in the omega-3 group (M = 9.07, SD = 3.58) than the placebo group (M = 7.31, SD = 2.78) (F = 5.72, p = 0.018), *reduction in positive emotions* was greater in the omega-3 group (M = 7.22, SD = 3.33) than the placebo group (M = 6.16, SD = 2.12) (F = 4.241, p = 0.042), and *not caring* was greater in the omega-3 group (M = 6.85, SD = 2.56) than the placebo group (M = 5.97, SD = 2.04) (F = 4.236, p = 0.042). There was no significant difference on emotional detachment from others between the omega-3 group (M = 7.27, SD = 3.62) and the placebo group (M = 6.95, SD = 3.14) (F = .265, p = .608).

Discussion

The main aim of the present research was to investigate the degree to which omega-3 supplementation – an evidence-based treatment for major depressive disorder (Parker et al., 2006; Ross, Seguin, & Sieswerda, 2007; Martins, 2009; Sublette, Ellis,

Geant & Mann, 2011) – has the potential to induce emotional blunting. Such blunting has been commonly observed in SSRI therapy (Opbroek et al., 2002), and in light of the potential similarities between SSRIs and omega-3 supplements in their facilitation of increased cerebral serotonergic signaling, it was hypothesized that omega-3 supplements may have similar effects on the intensity of emotional experience. Notably, there has been no published research to date directly germane to this question.

As hypothesized, study participants in the omega-3 condition reported significantly more emotional blunting than did those in the placebo condition following 3 weeks of supplementation. Specifically, participants who took omega-3s scored approximately 0.41 standard deviations higher (Cohen's *d*) than those in the placebo group on the study's principal measure of emotional blunting, the Oxford Questionnaire of the Emotional Side-effects of Antidepressants (OQuESA). This moderate-sized between-group difference was roughly the equivalent of responding *I agree* rather than *I agree a little* on any 5 of the OQuESA's 31 items (e.g., "I don't look forward to things with eager anticipation"; "My emotions lack intensity"; "I don't have much sympathy for other people"). Importantly, the observed emotional blunting effect of omega-3s is modest in comparison with the very large effect that has been reported among depressed individuals receiving SSRI pharmacotherapy (Opbroek et al., 2002).

Participants in the omega-3 condition also scored significantly higher on three of the OQuESA's four subscales: *general reduction of emotions*, *reduction in positive emotions*, and *not caring*. There was, however, no significant difference between groups on *emotional detachment from others*. It is possible, therefore, that omega-3 supplements

have a more noticeable effect on the subjective experience of emotional *intensity* than on the specific quality of one's emotional connection to others.

Interestingly, no evidence of emotional blunting in association with omega-3s was observed in the study's experimental induction of dysphoric mood. While it is possible that omega-3s simply exert no pronounced effect in blunting transient dysphoria, this particular null result may also be a mere artifact of the mood rating scale (the MAACL-R) employed in the study's mood-induction procedure. The MAACL-R, although a widely used measure in the experimental literature (Lubin, Swearngin & Zuckerman, 1997), only provides a checklist of various possible emotional states, without assessing the *intensity* of each such emotion.

The study's multilevel latent growth curve analysis of daily emotional intensity during the 3 weeks of supplementation also revealed no significant between-group differences. In other words, participants in both groups exhibited equal variability in the average intensity of both positive and negative emotions over the course of the study. However, it should be noted that the sample size was not sufficient to reliably detect small-to-moderate effects within a multilevel model, so this null result should be interpreted with some caution.

Taken together, the study's three principal tests of emotional blunting in the context of omega-3 supplementation suggest that healthy individuals taking omega-3 supplements may experience moderate blunting in a limited subset of emotion-linked domains. Specifically, participant responses to the primary self-report questionnaire measure (OQuESA) indicate a significant reduction in the perceived intensity of both positive and negative moods, along with a reduced intensity of caring, following 3 weeks

of omega-3 supplementation. But this blunting effect was modest, and it was not, in fact, observed during the study's experimental manipulation of dysphoric mood.

So, how might we best evaluate the clinical significance – if any – of such a moderate level of omega-3-induced emotional blunting? Certainly, some blunting of negative mood could be desirable for individuals suffering from major depression or other painful mood disorders. On the other hand, the blunting of positive emotions and reduced caring are potentially harmful side effects that would be regarded as undesirable, regardless of the magnitude of the blunting effect. Moreover, many of those who supplement with omega-3s may have limited awareness of their own emotional blunting, inasmuch as no one is presently on the lookout for this potential side effect. Unlike antidepressant medication, omega-3 supplements do not require a prescription, and they can be taken without any monitoring by a healthcare provider. Many individuals take omega-3 supplements for treatment or prevention of depressive symptoms, as well as myriad reasons unrelated to psychiatric concerns, e.g., to protect heart health, to combat inflammatory conditions, to increase eye moisture, etc. Accordingly, those taking omega-3 supplements should be informed about their potential emotional blunting effect in order to increase awareness, and to allow for informed decisions regarding omega-3 use.

There are several notable limitations of the current study. First, the use of self-report questionnaires is vulnerable to response bias. Although most of the participants were not familiar with the concept of emotional blunting, a variety of potential biases in responses could have occurred due to the use of self-report questionnaires. For example, participants may conceivably report more emotional blunting when they believe they are

in the omega-3 condition and less emotional blunting when they believe they are in the placebo condition. We did not assess participants' beliefs about their group assignment.

Additionally, as noted previously, the use of a healthy, predominantly female undergraduate sample may limit the generalizability of study results to other populations. In order to help ensure a high level of adherence, this study also used a dose of omega-3 supplementation that was slightly lower than the commonly recommended dose for treating depression. It is possible that a higher dose of omega-3s would have yielded larger mood-related effects of supplementation, and may thereby have influenced the outcome of some study analyses.

It should also be noted that the study was only three weeks in duration, which is shorter than most published trials of omega-3 supplementation for depression, as well as virtually all trials of antidepressant medication. A study of longer duration could conceivably detect additional mood-related effects that take a longer period of time to develop. Finally, the adherence check for the study required participants to send pictures of themselves taking the capsules each day. Although this methodology is superior to the use of a mere self-report questionnaire to assess protocol adherence, the use of biological measures – e.g., blood assays of omega-3 composition – would doubtless provide a more accurate assessment of adherence.

Because this is the first study investigating the effects of omega-3 supplements on emotional blunting, additional studies should be conducted to attempt replication of these results. Additional studies could also be conducted to determine dose-specific effects of omega-3 supplements on emotional blunting. The current study used an 800 mg daily dose of EPA – the antidepressant molecular form of omega-3 – which is slightly below

the commonly accepted antidepressant dosing range of 1000 mg per day. Due to the continued lack of agreement in the literature about the biochemical mechanisms of omega-3 supplements responsible for their antidepressant effects, it follows that similar studies attempting to parcel out these effects should be conducted assessing emotional blunting. These studies may also help to illuminate the connection between antidepressant effects and emotional blunting, and the potential similarities between the effects of SSRIs and omega-3 supplements on the brain's emotion-regulation systems.

Future studies could also use questionnaires assessing a broader range of emotional experiences over time to assess daily variability in emotional reactivity, and could investigate emotional reaction to mood inductions with a questionnaire that would allow participants to report intensity of emotions such as the Profile of Mood States (POMS). Future studies should also investigate additional experimental methods in addition to self-report questionnaires to assess the development of emotional blunting. Finally, future studies should also investigate this phenomenon in populations other than healthy college students, including those with depression, anxiety, or other psychological disorders.

References

- Antypa, N., Van, d. D., Smelt, A. H. M., & Rogers, R. D. (2009). Omega-3 fatty acids (fish-oil) and depression-related cognition in healthy volunteers. *Journal of Psychopharmacology*, 23(7), 831-840. doi: http://dx.doi.org/10.1177/0269881108092120.
- Barnhart, W. J., Makela, E. H., & Latocha, M. J. (2004). SSRI-induced apathy syndrome: A clinical review. *Journal of Psychiatric Practice*, *10*(3), 196-199. doi: http://dx.doi.org/10.1097/00131746-200405000-00010.
- Beasley, C. M., Koke, S. C., Nilsson, M. E., & Gonzales, J. S. (2000). Adverse events and treatment discontinuations in clinical trials of fluoxetine in major depressive disorder: An updated meta-analysis. *Clinical Therapeutics: The International Peer-Reviewed Journal of Drug Therapy, 22*(11), 1319-1330. doi: http://dx.doi.org/10.1016/S0149-2918(00)83028-3.
- Beck, A. T., Steer, R. A., Ball, R., & Ranieri, W. F. (1996). Comparison of beck depression Inventories–IA and –II in psychiatric outpatients. *Journal of Personality Assessment,* 67(3), 588-597. Retrieved from http://search.proquest.com/docview/618795246?accountid=14556.
- Beck A. T., Steer R. A., & Brown, G. K. (1996) *Manual for the Beck Depression Inventory-II*.

 San Antonio, TX: Psychological Corporation.
- Daly, E. J., Trivedi, M. H., Fava, M., Shelton, R., Wisniewski, S. R., Morris, D. W., Stegman,
 D., Preskorn, S. H. & Rush, A. J. (2011). The relationship between adverse events during selective serotonin reuptake inhibitor treatment for major depressive disorder and nonremission in the suicide assessment methodology study. *Journal of Clinical Psychopharmacology*, 31(1), 31-8. doi:10.1097/JCP.0b013e318205e17b.

- Drug Topics staff (2010a). 2009 Top 200 generic drugs by total prescriptions. Available at: http://drugtopics.modernmedicine.-com/drugtopics/data/articlestandard/drugtopics/252010/674982/ article.pdf.
- Drug Topics staff (2010b). 2009 Top 200 branded drugs by total prescriptions. Available at: http://drugtopics.modernmedicine. com/drugtopics/data/articlestandard//drugtopics/252010/674969/ article.pdf.
- Fu, C. H. Y., Williams, S. C. R., Cleare, A. J., Brammer, M. J., Walsh, N. D., Kim, J., . . . Bullmore, E. T. (2004). Attenuation of the neural response to sad faces in major depression by antidepressant treatment: A prospective, event-related functional magnetic resonance imaging study. *Archives of General Psychiatry*, 61(9), 877-889. doi: http://dx.doi.org/10.1001/archpsyc.61.9.877.
- Garland, E. J., & Baerg, E. A. (2001). Amotivational syndrome associated with selective serotonin reuptake inhibitors in children and adolescents. *Journal of Child and Adolescent Psychopharmacology*, *11*(2), 181-186. doi: http://dx.doi.org/10.1089/104454601750284090.
- George, M. S., Trimble, M. R., & Robertson, M. M. (1993). Fluvoxamine and sulpiride in comorbid obsessive-compulsive disorder and gilles de la tourette syndrome. *Human Psychopharmacology: Clinical and Experimental, 8*(5), 327-334. Retrieved from http://search.proquest.com/docview/618486824?accountid=14556.
- Gören, J. L., & Tewksbury, A. T. (2011). The use of omega-3 fatty acids in mental illness.

 *Journal of Pharmacy Practice, 24(5), 452-471.

 doi:http://dx.doi.org/10.1177/0897190011422876.

- Harmer, C. J., Mackay, C. E., Reid, C. B., Cowen, P. J., & Goodwin, G. M. (2006).

 Antidepressant drug treatment modifies the neural processing of nonconscious threat cues. *Biological Psychiatry*, *59*(9), 816-20. doi:10.1016/j.biopsych.2005.10.01.
- Hoehn-Saric, R., Harris, G. J., Pearlson, G. D., & Cox, C. S. (1991). A fluoxetine-induced frontal lobe syndrome in an obsessive compulsive patient. *Journal of Clinical Psychiatry*, *52*(3), 131-133. Retrieved from http://search.proquest.com/docview/617955811?accountid=14556.
- Hoehn-Saric, R., Lipsey, J. R., & McLeod, D. R. (1990). Apathy and indifference in patients on fluvoxamine and fluoxetine. *Journal of Clinical Psychopharmacology*, *10*(5), 343-345.

 Retrieved from http://search.proquest.com/docview/617919728?accountid=14556.
- Ingram, R. E., Bernet, C. Z., & McLaughlin, S. C. (1994). Attentional allocation processes in individuals at risk for depression. *Cognitive Therapy and Research*, 18(4), 317-332.Retrieved from http://search.proquest.com/docview/618526485?accountid=14556.
- Ilardi, S. (2009). *The Depression Cure: The Six-Step Program to Beat Depression Without Drugs*. London, England: Vermilion.
- Lubin, B., Swearngin, S. E. & Zuckerman, M. (1997). Research with the Multiple Affect Adjective Check List (MAACL and MAACL-R): 1960-1996. San Diego, CA: Educational and Industrial Testing Service.
- Lubin, B. & Zuckerman, M. (1999). *Manual for the Mulitiple Affect Adjective Check List— Revised.* San Diego, CA: Educational and Industrial Testing Service.
- McCabe, C., Mishor, Z., Cowen, P. J., & Harmer, C. J. (2010). Diminished neural processing of aversive and rewarding stimuli during selective serotonin reuptake inhibitor treatment.

- Biological Psychiatry, 67(5), 439-445. doi: http://dx.doi.org/10.1016/j.biopsych.2009.11.001.
- Maloni, J. A., Chance, B., Zhang, C., & Cohen, A. W. (1993). Physical and psychosocial side effects of antepartum hospital bed rest. *Nursing Research*, *42*(4), 197-203. Retrieved from http://search.proquest.com/docview/618421093?accountid=14556.
- Marin, R. S. (1990). Differential diagnosis and classification of apathy. *The American Journal of Psychiatry*, *147*(1), 22-30. Retrieved from http://search.proquest.com/docview/617735777?accountid=14556.
- Martins, J. G. (2009). EPA but Not DHA Appears To Be Responsible for the Efficacy of Omega-3 Long Chain Polyunsaturated Fatty Acid Supplementation in Depression: Evidence from a Meta-Analysis of Randomized Controlled Trials. *Journal of the American College of Nutrition*, 28(5), 525-542.
- Matsuzawa-Yanagida, K., Narita, M., Nakajima, M., Kuzumaki, N., Niikura, K., Nozaki, H., . . . Suzuki, T. (2008). Usefulness of antidepressants for improving the neuropathic pain-like state and pain-induced anxiety through actions at different brain sites.

 *Neuropsychopharmacology, 33(8), 1952-1965.

 doi:http://dx.doi.org/10.1038/sj.npp.1301590.
- Nakamaru-Ogiso, E., Miyamoto, H., Hamada, K., Tsukada, K., & Takai, K. (2012). Novel biochemical manipulation of brain serotonin reveals a role of serotonin in the circadian rhythm of sleep–wake cycles. *European Journal of Neuroscience*, *35*(11), 1762-1770. doi:http://dx.doi.org/10.1111/j.1460-9568.2012.08077.x.

- Nemeroff, C. B., & Owens, M. J. (2004). Pharmacologic differences among the SSRIs: Focus on monoamine transporters and the HPA axis. *CNS Spectrums*, *9*(6), 23-31. Retrieved from http://search.proquest.com/docview/620450405?accountid=14556.
- Nemets, B., Stahl, Z., & Belmaker, R. H. (2002). Addition of omega-3 fatty acid to maintenance medication treatment for recurrent unipolar depressive disorder. *The American Journal of Psychiatry*, *159*(3), 477-479. doi: http://dx.doi.org/10.1176/appi.ajp.159.3.477.
- Oleshansky, M. A., & Labbate, L. A. (1996). Inability to cry during SRI treatment. *Journal of Clinical Psychiatry*, *57*(12), 593-593. Retrieved from http://search.proquest.com/docview/619038462?accountid=14556.
- Opbroek, A., Delgado, P. L., Laukes, C., McGahuey, C., Katsanis, J., Moreno, F. A., & Manber, R. (2002). Emotional blunting associated with SSRI-induced sexual dysfunction. Do SSRIs inhibit emotional responses? *International Journal of Neuropsychopharmacology*, *5(2)*, 147-151. doi:10.1017\S1461145702002870.
- Parker, G., Gibson, N., Brotchie, H., Heruc, G., Rees, A., & Hadzi-Pavlovic, D., (2006).

 Omega-3 Fatty Acids and Mood Disorders. *American Journal of Psychiatry*, 163, 969-978.
- Price, J., Cole, V., Doll, H., & Goodwin, G. M. (2012). The Oxford Questionnaire on the Emotional Side-effects of Antidepressants (OQuESA): Development, validity, reliability and sensitivity to change. *Journal of Affective Disorders*, *140*(1), 66-74. doi: http://dx.doi.org/10.1016/j.jad.2012.01.030.

- Price, J., Cole, V., & Goodwin, G. M. (2009). Emotional side-effects of selective serotonin reuptake inhibitors: Qualitative study. *The British Journal of Psychiatry*, 195(3), 211-217. doi: http://dx.doi.org/10.1192/bjp.bp.108.051110.
- Ross, B., Seguin, J., & Sieswerda, L. E., (2007). Omega-3 fatty acides as treatments for mental illness: which disorder and which fatty acid? *Lipids in Health and Disease*, 6(21).
- Sublette, M. E., Ellis, S. P., Geant, A. L. & Mann, J. J. Meta-analysis of the effects of eicosapentaenoic acid (EPA) in clinical trials in depression. *Journal of Clinical Psychiatry*, 72(12), 1577-84. doi: 10.4088/JCP.10m06634.
- Warwick, J. M., Carey, P. D., Cassimjee, N., Lochner, C., Hemmings, S., Moolman-Smook, H., . . . Stein, D. J. (2012). Dopamine transporter binding in social anxiety disorder: The effect of treatment with escitalopram. *Metabolic Brain Disease*, 27(2), 151-158. doi:http://dx.doi.org/10.1007/s11011-012-9280-3.