

Omega-3 Fatty Acid Decreases Irritable Mood in Bipolar Mood Disorder

Omega-3 fatty acids (O-3FA) may have a beneficial effect on irritable mood. Omega-3 fatty acid administration in patients with bipolar disorder is theorized to result in greater membrane fluidity, as detected by reductions in Tesla-2 (T2) values in MRI scans.¹

Effectiveness of O-3FA in depression, bipolar disorder and aggression has been shown.² Placebo-controlled studies in medicated patients suggest that add-on treatment with omega-3 fatty acids, particularly eicosapentaenoic acid (EPA), may ameliorate symptoms of major depressive disorder.³ One placebo-controlled study of 20 patients revealed that eicosapentaenoic acid (EPA) was effective in stabilizing the moods of depressed patients.⁴ One study suggests that O-3FA may help decrease aggressive tendencies.⁵ A recent, open ended, O-3FA add-on study has shown beneficial effect of O-3FA on irritability in 19 patients with mood disorders.⁶

This is a report on a 37-patient continuation study of the open ended, O-3FA add-on study. Subjects consisted of the original 19 patients⁶, along with 18 new patients recruited and followed in the same fashion as the first nineteen.⁶ Subjects carried a DSM-IV-TR⁷ diagnosis of Bipolar Disorder and were visiting a Mood Disorder Clinic regularly through the length of the study. At each visit, patients' clinical status was monitored using the Clinical Monitoring Form⁸. Subjects reported on the frequency and severity of irritability experienced during the preceding ten days; frequency was measured by way of percentage of days in which subjects experienced irritability, while severity of that irritability was rated on a Likert scale of 1 - 4 (if present). The irritability component of Young Mania Rating Scale⁹ (YMRS) was also recorded quarterly on 13 of the 39 patients

consistently.

Dosage: Starting dose and last maintenance dose were available for 37 subjects.

Subjects self-medicated, and the last maintenance dose was therefore chosen by each subject. The mean starting dose was 1824.32 mg (SD 1075.07), and the mean for the last maintenance dose was considerably higher at 2878.38 mg (SD 2011.79). The increase was statistically significant using a paired sample t-test ($t = -3.44$, 36df, $p = .001$). Table 1 summarizes dosage under three conditions. Figures for the Initial Dose include two subjects ($n = 39$) for whom no corresponding follow-up data were available.

	Initial	Last Recorded	Final ^{T1}
n	39	37	13
Mean	1833.33	2878.38	2615.38
Mode	1000 ^{T2, T3}	1000	2000
Median	2000	2000	2000
SD	1071.91	2011.79	1894.66

T1= Final group results ($n = 13$) are discussed below.
T2= Multiple modes exist. The smallest value is shown.
T3= One gram (1,000 milligram) of fish oil; of which about 180 milligrams is (eicosapentaenoic acid) EPA and 120 milligrams is DHA (docosahexaenoic acid), (for a total of 300 milligrams of omega 3's) in each clear capsule.

Percentage of Irritable (Days). The initial mean was 63.51 (SD 34.17), indicating that on average, subjects were irritable for about six of the previous ten days. The mean for the last recorded percentage was less than half of the initial score: 30.27 (SD 34.03). The decrease was found to be statistically significant using a paired sample t-test ($t = 4.36$, 36 df, $p < .001$). The difference between the distributions was examined using the non-parametric sign test. The number of negative differences (25) significantly exceeded positive differences (7); there were five ties, and the pre/post distributions were significantly different ($p < .003$).

YMRS Irritability Sub-score. Thirty four subjects had initial and last recorded YMRS irritability sub-scores. As with the above means there was a sizable decrease. The initial mean score was 3.18 (SD 1.09). The mean for the last recorded percentage was 1.68 (SD 1.89). The decrease was found to be statistically significant using a paired sample t-test ($t=4.21$, 33 df, $p<.001$).

YMRS Total Score. Starting and last recorded YMRS scores were available for 34 subjects. The mean starting score 10.71 (SD 6.77), and the mean for the last recorded score was 4.85 (SD 5.63). The decrease found to be statistically significant using a paired sample t-test ($t=4.14$, 33 df, $p<.001$).

Severity. Thirty six subjects had initial and last recorded severity scores on the ADE. Again, a decrease was found. The initial mean score was 2.14 (SD 1.22). The mean for the last recorded score was 0.94 (SD 0.92). This decrease was found to be statistically significant using a paired sample t-test ($t=5.23$, 35 df, $p<.001$).

Composite: Severity and Irritability. As an exploratory measure, a composite score was created by multiplying the ADE severity score, which has a maximum of 4 points, by the percentage of the ten days prior to measurement which the patient was rated as irritable. The initial mean on this composite was 159.72. As with other measures, there was wide variation: SD= 122.92. The mean for this measure on the last recorded scores was percentage was about one-fourth of the initial score: 43.89 (SD 64.38). The decrease was found to be statistically significant using a paired sample t-test ($t=5.00$, 35 df, $p<.001$).

Last Recorded Maintenance Dose and Percentage of Irritability After. Because of apparent wide variation on these two measures and a concern that outliers may have affected some results, the last recorded irritability scores were plotted against the

maintenance dose. This revealed a rather bimodal pattern, in which relatively lower irritability measures ($\leq 50\%$) clustered in the quadrant with lower dosage levels ($\leq 4,000$ mg).

Duration and YMRS Total. In response to a similar observation regarding wide variation in the last recorded values (84 days to 5.5 years) the values were also plotted. A clearly bimodal pattern appeared in which 11 subjects (about one-third of study participants) clustered in the quadrant representing short duration (<500 days) and higher YMRS totals (>7). The remaining two-thirds of subjects clustered in the quadrant representing short duration and lower YMRS totals (<6).

Subject Weight. The mean start weight was 176.97 lbs (SD 43.13), and the mean for the last weight recorded was slightly higher at 178.59 lbs (SD 43.24). The increase was not statistically significant.

Follow-up Subjects. Follow-up information, recorded after the collection of the “last” scores for most of the above variables, was available for 13 of the 37 subjects. Final YMRS total or scale scores were not available for this sub-group.

Omega 3 Duration. The final date recorded for the duration of O3 was derived based from an O3 start date and a “final” date recorded for O3. The time period ranged 84 days to 1995 days (5.46 years). The mean duration of O3 for this group was 439.62 days (SD = 487.46).

Dosage. For these subjects, the mean starting dose was 1807.69 mg (SD 990.34), and the mean for the last maintenance dose was higher at 2615.38 mg (SD 1894.66). The increase was not significant.

Percentage Irritable (Days). The initial mean was 82.31 (SD 20.88). The mean for the last recorded percentage was dramatically lower: 25.38 (SD 32.04). The decrease was found to be statistically significant using a paired sample t-test ($t=6.52$ 12 df, $p<.001$). The difference between the distributions was examined using a sign test. The number of negative differences (12) significantly exceeded positive differences (0); there was one tie, and the pre/post distributions were significantly different ($p <.001$).

Severity The initial mean score for the 13 subjects with final scores was 2.69 (SD 0.95). The mean for the final score was 0.77 (SD 0.83). This decrease was found to be statistically significant using a paired sample t-test ($t=6.22$, 12 df, $p<.001$).

Composite: Severity and Irritability. An exploratory composite score, described above, was also created for the subjects with final scores. For these subjects, the initial mean was higher than that of the total group, 223.08. Again, there was wide variation: SD= 104.19. The mean for this measure on the last recorded scores was percentage was much lower than the initial score: 33.08 (SD 39.87). The decrease was found to be statistically significant using a paired sample t-test ($t=6.70$, 12 df, $p<.001$).

Weight. For these 13 subjects, the mean start weight was 166.23 lbs (SD 35.68), and the mean for the final weight recorded was also slightly higher at 168.23 lbs (33.62). As with the previous finding regarding weight, the increase was not statistically significant.

Omega-3 Fatty Acid intake helped with the irritability component of patients suffering from bipolar disorder with a significant presenting sign of irritability. O-3FA may also help with the irritability component of different clinical conditions, such as schizophrenia, borderline personality disorder and other psychiatric conditions with a common presenting sign of irritability.

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