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# γ-Linolenate Reduces Weight Regain in Formerly Obese Humans[1,2]

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## Abstract

The purpose of this study was to determine whether γ-linolenate (GLA) supplementation would suppress weight regain following major weight loss. Fifty formerly obese humans were randomized into a double-blind study and given either 890 mg/d of GLA (5 g/d borage oil) or 5 g/d olive oil (controls) for 1 y. Body weight and composition and adipose fatty acids of fasting subjects were assessed at 0, 3, 12, and 33 mo. After 12 subjects in each group had completed 1 y of supplementation, weight regain differed between the GLA (2.17 ± 1.78 kg) and control (8.78 ± 2.78 kg) groups ($P < 0.03$). The initial study was terminated, and all remaining subjects were assessed over a 6-wk period. Unblinding revealed weight regains of 1.8 ± 1.6 kg in the GLA group and 7.6 ± 2.1 kg in controls for the 13 and 17 subjects, respectively, who completed a minimum of 50 wk in the study. Weight regain did not differ in the remaining 10 GLA and 5 control subjects who completed <50 wk in the study. In a follow-up study, a subgroup from both the original GLA (GLA-GLA, $n = 9$) and the original control (Control-GLA, $n = 14$) populations either continued or crossed over to GLA supplementation for an additional 21 mo. Interim weight regains between 15 and 33 mo were 6.48 ± 1.79 kg and 6.04 ± 2.52 kg for the GLA-GLA and Control-GLA groups, respectively. Adipose triglyceride GLA levels increased 152% ($P < 0.0001$) in the GLA group at 12 mo, but did not increase further after 33 mo of GLA administration. In conclusion, GLA reduced weight regain in humans following major weight loss, suggesting a role for essential fatty acids in fuel partitioning in humans prone to obesity. J. Nutr. 137: 1430–1435, 2007.

## Introduction

Essential fatty acids (EFA)[4] impart important physical characteristics to membranes, and they provide substrate for the synthesis of eicosanoids and oxy-lipids. Varying EFA availability influences lipogenesis (1,2), insulin sensitivity (3), and adipocyte differentiation (4). These processes, in turn, provide credible links between EFA status and the storage of dietary energy as fat.

We previously reported a distortion in EFA distribution in obese humans that does not resolve despite major weight loss (5). There are many reports of similar distortions in EFA metabolism in single gene (6,7) and multiple gene (8) animal models of obesity. The consistent manifestation of this distorted EFA distribution in obese animals is a reduction in the proportion of arachidonate (ARA) in serum or membrane phospholipids (PL) and an increase in its proportion in serum or liver cholesteryl esters. When a reduction in PL ARA in obese Zucker rats is corrected by administering dietary γ-linolenate (GLA) to increase liver ARA production, the obese genotype reduces food intake and weight gain. When the lean genotype of the Zucker rat is given the same dose of GLA, however, there is no effect on food intake or body weight (7,9).

In a study of the fatty acid composition of serum lipid fractions in adult identical twins living apart, Kunesova et al. (10) reported remarkable concordance for serum PL EFA within twin pairs. These twin resemblances were not seen in other serum or adipose lipid fractions and could not be explained by dietary similarity. To our knowledge, this study provides the first evidence that genotype is a strong determinant of PL fatty acid (FA) composition in humans independent of diet. Furthermore, it is consistent with our hypothesis that some of the interindividual variance in the propensity for obesity in humans can be due to variations in the genetically mediated FA composition of membranes.

The predominant EFA in mammalian somatic membranes is ARA, which is either consumed directly in the diet or produced via Δ6 and Δ5 desaturases from its linoleate precursor. Variations in ARA synthesis in humans has recently been reported to result from polymorphisms in the promoter region of Δ6 desaturase (11,12), and impaired promoter function for this gene has been linked to hypertriglyceridemia (13). Thus, there is a direct physiological link between variations in ARA production, membrane ARA, and lipid metabolism in humans.

As a result of our prior observations of distorted EFA distribution in obese humans that persisted after major weight loss (5), as well as the selective effect of GLA on food intake and

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[4] Abbreviations used: ARA, arachidonic acid; CRP, C-reactive protein; DGLA, dihomo-γ-linolenic acid; EFA, essential fatty acid; FA, fatty acid; GLA, γ-linolenic acid; PL, phospholipid; WBC, white blood cell; VLED, very low energy diet.
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weight gain in the obese Zucker rat (7,9), we performed a study to assess the effect of GLA as an adjunct to the treatment of human obesity. We chose formerly obese adults as our subjects to limit the potential for dilution of GLA into body fat stores and also because this group has a strong propensity for weight regain.

## Subjects and Methods

*Subjects and study design.* The study protocol was approved by the Human Subjects Review Committee at the University of California at Davis. All subjects gave written informed consent prior to participation. Subject selection criteria for this study included a recent minimum weight loss of 12 kg by a very low energy diet (VLED), subsequent participation in a behavioral weight maintenance program for a minimum of 6 mo, a current BMI of <34, and absence of hypertension, heart disease, and diabetes. The behavioral weight maintenance program involved weekly group meetings with a behaviorist who encouraged subjects to consume a low fat, high carbohydrate diet, and to exercise regularly.

Fifty formerly obese women and men were randomized into this double-blind study. At baseline, the subjects were randomly assigned to treatment with 890 mg/d of GLA in the form of borage oil (5 g/d) or to a control group given olive oil (5 g/d). Both oil supplements were administered in a double-blind protocol as identical 500 mg capsules. To maintain consistency of vitamin and trace mineral intakes, subjects were required to take a balanced multivitamin-mineral supplement daily, which included 80 mg of d-$\alpha$-tocopherol. The participants were encouraged to maintain daily records of food intake and exercise. Anorexigenic medications were allowed if prescribed by the subject's physician, and their use was monitored.

Enrollment into the study occurred over a 7-mo period. After 12 subjects in each group had completed 1 y of lipid supplementation, the monitoring of their weights (simple ANOVA of group means while investigators and subjects remained unaware of treatment) revealed a difference in weight regain between the GLA (2.17 ± 1.78 kg) and control (8.78 ± 2.78 kg) groups ($P < 0.03$). Because this was the primary outcome variable of the study, and in recognition that weight regain is not benign, the initial study was terminated, and all remaining subjects came to the clinic for a final analysis over a 6-wk period. A subgroup of the original GLA group ($n = 9$) desired to continue supplementation (GLA-GLA), and some of the original control group ($n = 16$) also began GLA supplementation (Control-GLA) within 3 mo, initiating the nonrandomized borage continuation portion of the study. Repeated measures ANOVA indicated that for the first 9 mo of the randomized placebo controlled trial, there was no difference in weight regain between the 2 groups. After 12 mo of lipid supplementation, however, GLA affected weight regain (time × oil interaction, $P < 0.04$). Because this analysis indicated that GLA had to be administered for 1 y to have a measurable effect on weight regain, the results reported for the first year are only for those subjects completing a minimum of 50 wk in the study (completers).

*Sample collection.* During the first year, weights and blood pressure were measured monthly for the first 3 mo, and quarterly thereafter. Blood was collected from fasting subjects and serum obtained at baseline, 3, 12, and 33 mo by venipuncture with minimal hemostasis for standard clinical chemistry and hematological analyses, including total white blood cell (WBC) and differential counts (Physicians Clinical Laboratory). Bleeding time was also determined at these 3 time points using the Simplate device (Oragon Teknika). Body composition was determined by bioelectrical impedance (BodyStat 1500). Subcutaneous adipose tissue was obtained by aspiration biopsy of the gluteal region, using a 14-gauge needle following local anesthesia, and stored at −80°C.

*Laboratory methods.* Total lipids from adipose tissue were extracted according to the method of Folch et al. (14). The PL and triglyceride fractions were separated by TLC, and esterified with 5% HCl in methanol. The FA composition was determined by capillary GC (15). Serum glucose was measured using the glucose oxidase method (Yellow Springs Instruments).

*Statistical analysis.* Repeated measures ANOVA (PC-SAS software) (16) was used to detect differences due to treatment group and time as well as any group × time interaction. The threshold for significance was $P < 0.05$, using a one-tailed test for body weight change, and a two-tailed test for all other measured variables.

A step-wise regression procedure (PC-SAS) (16) was used to assess the possible influence of GLA and other independent variables on weight change during the study period. Variables were entered into the step-wise regression analysis if $P < 0.15$ (two-tailed) in the partial F tests. Unpaired *t* tests, assuming unequal variance, were used to assess differences in subject characteristics at baseline. Data are reported as means ± SEM.

## Results

*Enrollment and follow-up.* Fifty subjects were recruited, of whom 49 actually enrolled in the study at baseline. One subject chose not to participate after screening and randomization. At the termination of the randomized placebo-controlled trial, 45 subjects remained in the study. Subject characteristics did not differ between the 2 groups at baseline (**Table 1**). However, the GLA completers were younger than the control completers ($P < 0.01$). There were no reported side effects attributable to the administration of either oil supplement.

*Weight regain.* After the first year, the GLA group's body weight did not change, whereas the control group gained weight ($P < 0.001$, time × oil interaction, $P < 0.04$) (**Fig. 1**). Between 15 and 33 mo, when all subjects were receiving GLA, the weight regains did not differ between the GLA-GLA (6.48 ± 1.79 kg) and Control-GLA (6.04 ± 2.52 kg) groups (**Fig. 2**).

*Fat regain.* During the first year, fat weight did not change in the GLA group, whereas fat weight increased ($P < 0.01$) in the control group (**Table 2**; time × oil interaction, $P < 0.05$). Fat regain between 15 and 33 mo was similar in the GLA-GLA (6.40 ± 1.17 kg) and Control-GLA (5.69 ± 1.97 kg) groups.

*Adipose fatty acid composition.* Adipose GLA concentrations at baseline did not differ between the control (2.51 ± 0.36 $\mu$mol/g of adipose triglyceride) and GLA groups (2.16 ± 0.14 $\mu$mol/g). The concentration did not change after 1 y in the control group (2.87 ± 0.36 $\mu$mol/g) but GLA accumulated in the adipose tissue of the GLA group compared with controls (5.39 ± 0.36 $\mu$mol/g, time × oil interaction, $P < 0.0001$). Continuing GLA supplementation for an additional 93 wk did not further increase the

**TABLE 1** Baseline characteristics of formerly obese men and women[1]

| | Control | | GLA | |
|---|---|---|---|---|
| Characteristic | All subjects | Completers[2] | All subjects | Completers |
| *n* | 22 | 17 | 23 | 13 |
| Male, *n* | 2 | 1 | 2 | 1 |
| Female, *n* | 20 | 16 | 21 | 12 |
| Age, *y* | 50.4 ± 1.90 | 52.6 ± 1.96 | 46.2 ± 2.03 | 44.2 ± 2.82* |
| Pre-VLED BMI, *kg/m²* | 35.9 ± 1.26 | 35.7 ± 1.53 | 36.4 ± 1.75 | 36.9 ± 2.71 |
| Weight loss with VLED, *kg* | 29.8 ± 2.56 | 28.8 ± 2.92 | 31.3 ± 4.66 | 34.1 ± 7.74 |
| Height, *m* | 1.68 ± 0.02 | 1.67 ± 0.02 | 1.68 ± 0.02 | 1.68 ± 0.02 |
| Weight, *kg* | 74.0 ± 2.57 | 73.7 ± 2.83 | 72.0 ± 2.45 | 70.7 ± 3.92 |
| Fat weight, *kg* | 23.3 ± 1.50 | 24.2 ± 1.58 | 22.8 ± 1.64 | 21.7 ± 2.37 |

[1] Values are means ± SEM. *Different from controls, $P < 0.01$ (*t* test).
[2] Completers are subjects completing a minimum of 50 wk during first year of study.

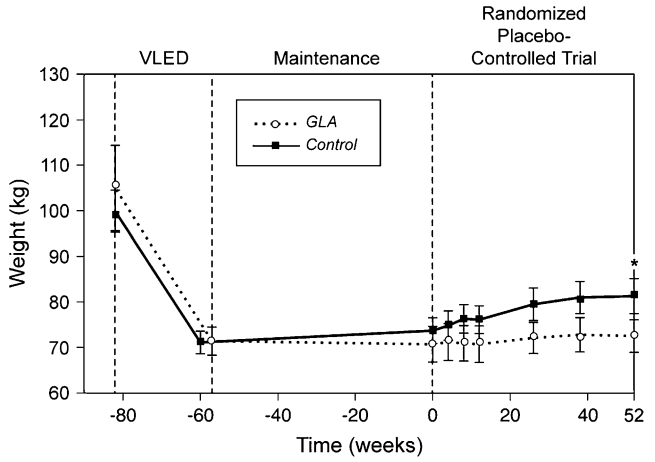


**FIGURE 1** Body weights prior to and during 52 wk of lipid supplementation in formerly obese men and women. Values are means ± SEM, $n = 13$ (GLA) and $n = 17$ (control). ANOVA (repeated measures) for weight change: *Different from $T_o$, $P < 0.001$; time × oil interaction, $P < 0.04$.

GLA concentration in adipose tissue of the GLA-GLA group (5.75 ± 0.72 μmol/g). Similar adipose GLA levels were attained in the Control-GLA group, which was supplemented with GLA from 15–33 mo of the study (6.11 ± 0.36 μmol/g). Dihomo-γ-linolenate (DGLA), the immediate elongation product of GLA, also increased in adipose tissue after 1 y of GLA supplementation from baseline concentrations of 9.79 ± 0.98 to 11.4 ± 0.98 μmol/g. In contrast, DGLA decreased from a baseline value of 10.4 ± 0.65 to 9.14 ± 0.33 μmol/g at 1 y in the control group (time × oil interaction, $P < 0.0001$). The adipose ARA concentration was not affected by 1 y of GLA supplementation. Although the proportions of both GLA and DGLA in the adipose triglycerides were small, they were well within the window of analytical precision previously demonstrated in this laboratory (7).

*Laboratory measurements.* Administration of GLA over a period of time would be expected to increase both the DGLA and ARA contents of membranes, which could have measurable physiological effects. To assess for these, bleeding time, blood pressure, and fasting serum glucose were monitored at 0, 3, and 12 mo, but significant effects were not observed. However during the first year, WBC decreased in the completer GLA group compared with the control group (**Table 3**; time × oil interaction, $P < 0.05$). Within the WBC differential, there tended to be a reduction in the proportion of neutrophils in the GLA group (time × oil interaction, $P < 0.06$), and was significant when expressed as absolute neutrophil count (time × oil interaction, $P < 0.05$). Of note, however, is that all of the group means for the WBC variables were within normal range during the study. Differences were not significant when comparisons were made between baseline and the 33 mo time point in the GLA-GLA and Control-GLA groups. Routine clinical chemistry results also did not differ between the 2 groups.

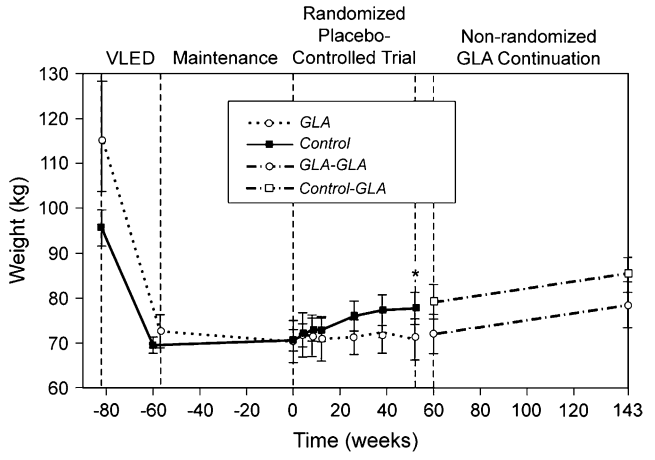


**FIGURE 2** Body weights for continuation subgroup subjects during randomized placebo-controlled trial and nonrandomized GLA continuation. Values are means ± SEM, $n = 9$ (GLA-GLA) and $n = 14$ (Control-GLA). ANOVA (repeated measures) contrast analysis, $P < 0.01$; time × oil interaction, $P < 0.03$.

*Step-wise regression analysis.* The unadjusted difference in weight change between baseline and 1 y for the 2 groups was 5.8 ± 2.8 kg (**Table 4**). Predictors of weight change that met the $P < 0.15$ threshold criterion were: *1*) time since weight loss prior to randomization ($P < 0.09$); *2*) percentage of weeks that food records were kept during the study ($P < 0.06$); and *3*) maximum BMI ($P < 0.11$). When these 3 independent variables were entered into the model, the adjusted difference in weight change attributable to GLA supplementation was 5.2 ± 2.6 kg ($P < 0.03$, $R^2 = 0.36$).

Concurrent use of anorexigenic medications could influence weight regain. The durations of anorexigenic agent use were 8.73 ± 0.75 mo and 6.92 ± 0.95 mo for the GLA ($n = 10$) and control ($n = 9$) groups, respectively, for the first year of the study and 8.17 ± 1.53 mo and 6.00 ± 1.38 mo for the GLA-GLA ($n = 6$) and Control-GLA ($n = 5$) groups, respectively, for the second year of the study. These durations did not differ and stepwise regression indicated that anorexigenic medication use was not a contributor to outcome. The recorded minutes of exercise per week was 163 min for both groups and also did not contribute to weight regain. Other potential predictors that entered into the step-wise regression analysis included: weeks in the study, number of contacts with a behaviorist during the study year, recorded minutes of exercise per week, weeks during the study year in which subject followed another VLED regimen, kg of body fat, age at beginning of study, pre-VLED BMI, BMI at randomization, kg of weight lost prior to the study, percentage of initial weight lost during the VLED, and number of times the subject reported losing >10% of body weight. None of these variables were significant. A step-wise regression analysis at 33 mo found no other independent variables influencing weight regain.

## Discussion

The primary observation of this study is that γ-linolenate administered as borage oil reduces weight regain in formerly obese humans. The >9-mo delay in onset for this effect in this group of subjects is consistent with the dilution of GLA into adipose triglycerides. The precise mechanism by which GLA suppresses weight regain needs to be determined but is most likely due to increased ARA production and incorporation into tissue lipid pools. Potential pathways through which ARA might influence cellular disposition of dietary fuel are many and include improved peripheral glucose disposal via enhanced insulin sensitivity (3), downregulation of lipogenesis (1,2), upregulation of lipid oxidation (17), and increased leptin secretion (18). In addition, modification of the FA composition of PL could affect the

**TABLE 2** Measures of body and fat weight in formerly obese men and women prior to and following 9–12 mo of lipid supplementation[1]

| | Baseline | | | | 9–12 Mo | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Control | | GLA | | Control | | GLA | | |
| | All | Completers[2] | All | Completers | All | Completers | All | Completers | *P*-Value[3] |
| *n* | 22 | 17 | 23 | 13 | 22 | 17 | 23 | 13 | |
| Body weight, *kg* | 74.0 ± 2.57 | 73.7 ± 2.83 | 72.0 ± 2.45 | 70.7 ± 3.92 | 81.6 ± 3.61** | 81.3 ± 3.86** | 76.6 ± 2.91* | 72.5 ± 3.59 | <0.04 |
| Fat weight, *kg* | 23.3 ± 1.50 | 24.2 ± 1.58 | 22.8 ± 1.64 | 21.7 ± 2.37 | 29.2 ± 2.25 | 30.3 ± 2.47* | 26.3 ± 2.28 | 22.6 ± 2.51 | <0.05 |

[1] Values are means ± SEM. Asterisks indicate different from baseline, $*P < 0.01$, $**P < 0.001$.
[2] Completers are subjects completing a minimum of 50 wk during first year of study.
[3] Repeated measures ANOVA.

functioning of membrane proteins including G protein-coupled receptors (19), the insulin receptor (20,21), and the $\beta$-adrenergic receptor (22), all with potential effects on energy metabolism. Furthermore, the recent evidence linking variations in the expression of the Δ6 desaturase (FADS2) gene, membrane ARA, and serum triacylglycerol levels (11–13) in humans is consistent with our observations in this study.

The results of this human study confirm 2 prior studies of Zucker rats in which administration of GLA to juveniles suppressed food intake and weight gain in the obese genotype, whereas the same dose had no effect on food intake or weight in the lean genotype (7,9). In both of these animal studies, we demonstrated a measurable throughput of GLA to ARA in liver PL in the obese genotype but not in the lean genotype. This apparent genotypic specificity for net conversion of GLA to ARA may explain why others have not observed a rise in ARA following GLA administration in animals (23,24) or humans (25). The other variable that differentiated our study from others was duration, because, to our knowledge, no prior published human studies have monitored the effects of GLA administration for longer than 12 mo. In a study of humans, Johnson et al. (26) found that GLA supplementation increased PL ARA, but the dose used was 3–6 g/d.

There is also the possibility that the mechanism of action of GLA on weight change involves its immediate elongation product, DGLA, which also increased significantly in adipose due to GLA supplementation. DGLA is not known to have direct effects on pathways influencing lipid oxidation or storage. However, it has antiinflammatory effects (20) which may have been operative in weight gain suppression, especially in view of recent studies suggesting an association between obesity and markers of inflammation. Elevated levels of plasma C-reactive protein (CRP) (27) and WBC (28,29) have been observed in obese adults when compared with normal-weight counterparts. Other studies have found positive and significant correlations between plasma CRP concentrations and indices of adiposity such as body fat mass (30–32), waist girth (30,31,33), and visceral fat (31–33), suggesting that adiposity contributes to low-grade chronic inflammation. Interestingly, serum CRP (31–35) and WBC (36,37) levels in obese subjects have been shown to decrease with weight loss. Valerio et al. (38) demonstrated that increased TNF$\alpha$ reduces mitochondrial biogenesis and fat oxidation in mice. In our study, the WBC number was reduced by GLA supplementation. The potential for a causal relation between a reduction in inflammatory markers and suppression of weight regain deserves further investigation.

As in any human research, there were a number of potentially confounding variables in this study. This was particularly true because we chose to administer GLA as an adjunct to ongoing multidisciplinary treatment. Step-wise regression analysis was used to test for significant contributions by other variables. Potentially significant variables included time since weight loss prior to randomization, percentage of weeks that food records were maintained, and maximum BMI. None of these variables, however, were significant after entry into the model (two-tailed test). Other variables, such as concurrent use of anorexigenic medication, amount of weight lost, and age, also did not diminish the contribution of GLA to weight maintenance following weight loss.

Another practical issue that had to be decided in this human study was whether to stop the study when the primary endpoint differed significantly between the groups. In the end, this decision pivoted on the question of whether to regard obesity as a disease that contributes to health risk in humans. With the continuing emergence of information indicating that excess weight is an independent contributor to morbidity and mortality (39),

**TABLE 3** Selected hematologic variables in formerly obese men and women prior to and after 1 y of lipid supplementation[1]

| | Baseline | | 1 Y | | |
|---|---|---|---|---|---|
| | Control | GLA | Control | GLA | *P*-Value[2] |
| White blood cells, $\times 10^9$/*L* | 4.87 ± 0.27 | 5.70 ± 0.41 | 5.22 ± 0.31 | 5.13 ± 0.24 | <0.05 |
| Lymphocytes, *%* | 32.9 ± 1.66 | 34.7 ± 2.54 | 31.2 ± 2.09 | 35.9 ± 1.76 | NS[3] |
| Neutrophils, *%* | 56.5 ± 1.76 | 54.3 ± 3.23 | 57.6 ± 2.31 | 52.4 ± 2.31 | NS |
| Neutrophils, $\times 10^9$/*L* | 2.78 ± 0.21 | 3.22 ± 0.39 | 3.04 ± 0.24 | 2.73 ± 0.23 | <0.05 |

[1] Values are means ± SEM.
[2] Repeated measures ANOVA.
[3] NS, not signficant, $P > 0.05$.

**TABLE 4** Results of stepwise regression for dependent variable weight change[1]

| Steps | Predictor in model | Regression coefficient | *P*-Value[2] |
|---|---|---|---|
| Unadjusted difference in weight change | | 5.81 ± 2.83 | 0.03 |
| 1 | Time between VLED end and study enrollment, *wk* | −0.03 ± 0.02 | 0.09 |
| 2 | Number of weeks food records kept, *%* | −0.08 ± 0.04 | 0.06 |
| 3 | Maximum BMI, $kg/m^2$ | 0.27 ± 0.16 | 0.11 |
| Adjusted difference in weight change | | 5.19 ± 2.61 | 0.03 |

[1] Values are means ± SEM.
[2] Values for dependent variable, difference in weight changes, are one-tailed, and values for independent variables are two-tailed.

in addition to the results of this current line of research that links weight gain to a biochemical abnormality of EFA metabolism, we concluded that it was unethical to continue subjects in the control group once the primary endpoint was achieved. Thus, some of the enrolled subjects did not complete the full 12-mo protocol, truncating the study by as much as 3 mo for some subjects.

The advantage of performing this study in the context of a practical outpatient weight management program is apparent from the overall success of the treatment, which provided a positive environment within which excellent subject retention over a relatively long study period was possible. GLA administered as borage oil appeared to be effective in weight maintenance, as the total weight gained during the 196 ± 15.9 wk following the VLED was 5.87 ± 3.44 kg and 15.7 ± 2.70 kg for the GLA-GLA and Control-GLA groups, respectively. These results compare favorably to the weight regain of 20.1 ± 2.21 kg ($P < 0.02$) during the 160 ± 3.28 wk following the VLED for a comparable population ($n = 65$) that lost weight at this same center but did not participate in the study. These results highlight the potential for this combination of treatment modalities, including the use of GLA for membrane fatty acid modification, in the practical management of severe adult obesity.

This observation notwithstanding, however, both the clinical utility and safety of this approach to treat human obesity through membrane modification needs to be determined. Naturally occurring sources of GLA include borage, black currant, and evening primrose oils; but all are relatively dilute sources (<20% of constituent fatty acids as GLA) that require a sizeable dose and prolonged administration to achieve a measurable effect. Although more concentrated sources of GLA can be found (40), cost and safety issues remain. In particular, given its demonstrated throughput to PL ARA in our subjects, and the observation that a not uncommon genetic variation in ARA metabolism in humans is associated with an increased inflammatory response (41), an intervention that enhances the tissue ARA pool cannot be assumed to be safe for the general population.

In this study, in which 23 formerly obese humans were given ~1 g/d of GLA as borage oil for >9 mo, no overt side effects were observed and no subjects dropped out for reasons attributed to the supplement. Differences were not observed between the groups over time for systolic or diastolic blood pressure, bleeding time, or fasting serum glucose concentration. During the first year, small but significant reductions within the normal range occurred for total WBC and total neutrophils in the GLA group compared with controls, consistent with the previously reported antiinflammatory effect of GLA (26). However, when comparisons were made between baseline and 33 mo, the differences were not significant, probably because the populations groups were slightly different, and because the number of participating subjects was reduced by attrition. Theis et al. (42) also found no significant changes in the total number of leukocytes and neutrophils in subjects supplemented with GLA (770 mg/d) for 12 wk. The increase in the GLA concentrations of adipose tissue reached a maximum by 50 wk, and GLA supplementation for an additional 93 wk did not increase it further. The accumulation of GLA in body lipid pools has the potential for greater throughput into ARA pools as well. Because ARA has many effects, including mediating inflammation, platelet aggregation, and cell proliferation, more careful studies with extended duration of GLA supplementation must be done before this substance can be recommended for use in the treatment of human obesity.

Perhaps more important than its potential therapeutic value, the fact that GLA supplementation effectively suppressed weight regain in this human study is consistent with abnormal EFA metabolism being a common problem among severely obese humans. Our prior animal studies observed distorted EFA metabolism as a common event downstream of multiple known or putative obesity genes (7–9), and two of these were intervention studies linking this EFA disturbance to the phenotypic accumulation of excess body fat. That the current study results run parallel with our prior studies in genetically obese rats provides strong support for further evaluation of this abnormality in EFA metabolism and its role as an intermediary between prevalent genes and obesity in humans.


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