Flaxseed Oil Supplementation Increases Long-chain Omega-3 and Omega-6 Fatty Acids in Human Plasma

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Background

- Omega-3 (n-3) and omega-6 (n-6) fatty acids are integral to brain development, particularly during the prenatal and neonatal periods.
- Alpha-linolenic acid (LNA, 18:3 n-3) is an essential omega-3 fatty acid; humans must obtain LNA from the diet.
- Most supplementation studies have focused on docosahexaenoic acid (DHA, 22:6 n-3), a product of LNA that is synthesized in a series of desaturation and elongation steps (Figure 1).
- Sources of LNA (plants) are less expensive and more environmentally sustainable than sources of DHA (animals), which makes LNA consumption an attractive alternative to improving one's long-chain polyunsaturated fatty acid (LCPUFA) status.
- We (Niculescu et al, 2013) have demonstrated that supplementation with LNA alters methylation of the fatty acid desaturase-2 (*FADS2*) gene that codes for the delta-6 desaturase, the rate-limiting used in the essential fatty acid metabolic pathway.
- Further, LNA supplementation increased neurogenesis in the dentate gyri of mice pups, but only if gestational levels of LNA were adequate (Niculescu et al, 2011).
- We hypothesized that LNA supplementation would up-regulate LCPUFA production.

Participants and Method

- In the context of a larger study, typically-developing toddlers were enrolled at 16 months of age. They were randomly assigned to receive either 1288 mg corn oil or 1200 mg flaxseed oil per day for 120 days.
- Blood samples were collected at baseline and at endpoint using EDTA capillary tubes. Lipids were extracted from plasma and analyzed using gas capillary chromatography.

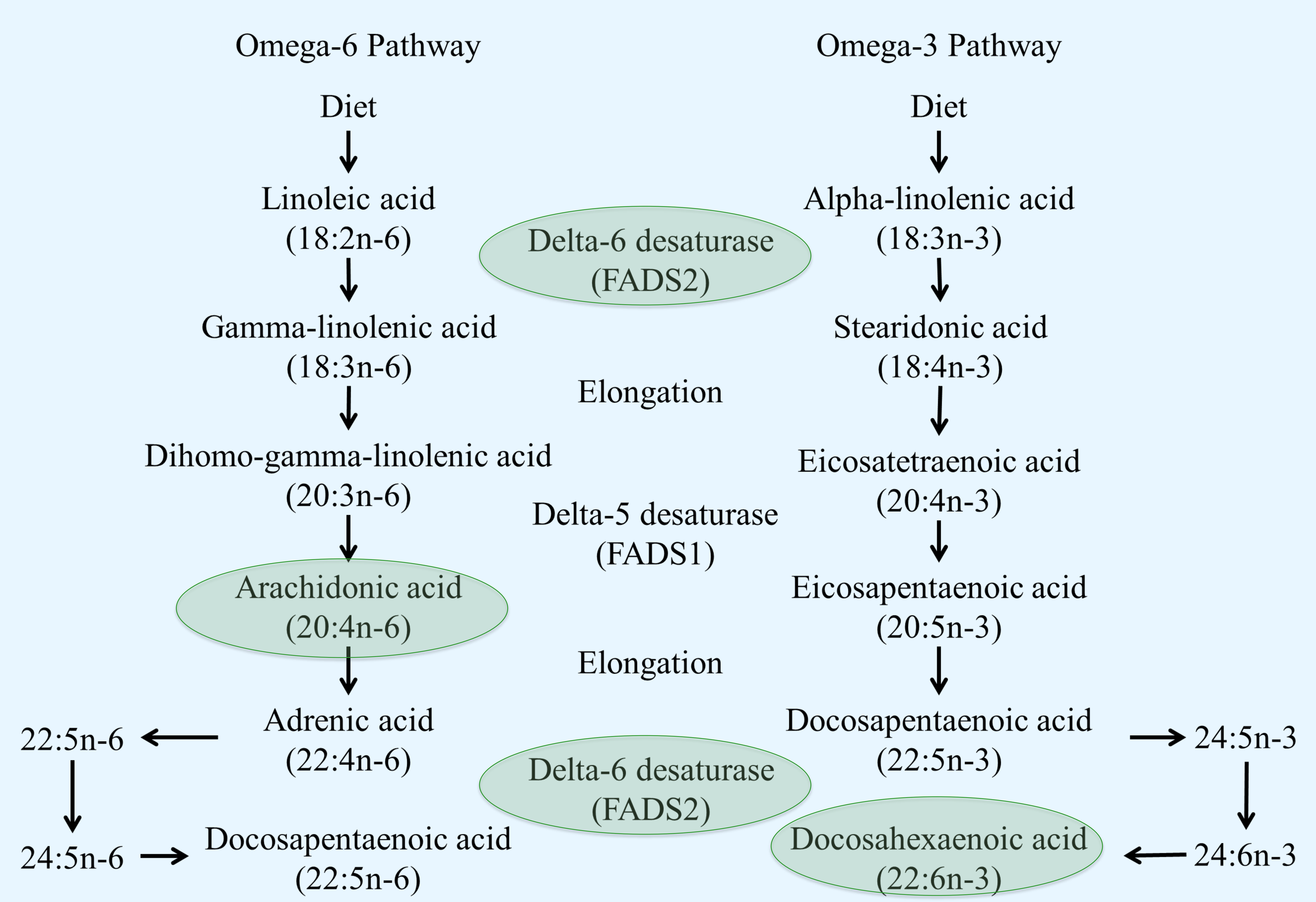
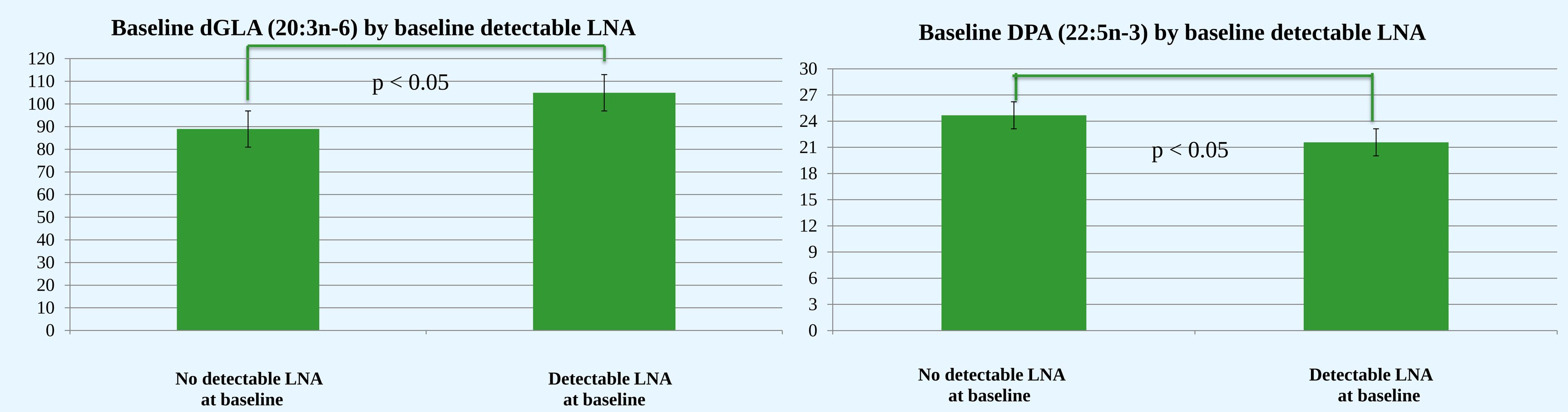


Figure 1. Essential fatty acid metabolic pathway

Data Analyses

- difference scores = fatty acid levels after 120 day supplementation - baseline fatty acid levels
- n-6 to n-3 ratio = sum of n-6 / sum of n-3
- 53.6% of toddlers did not have any detectable levels of LNA at baseline, suggesting efficient conversion of LNA into LCPUFAs. Data were split by this variable.
- Baseline fatty acid levels were assessed in a one-way ANOVA with LNA group as the between subjects factor.
- Endpoint fatty acid levels were assessed in a 2 (Flaxseed, Corn oil) X 2 (LNA, No LNA) ANOVA.
- Difference scores were assessed in a 2 (Flaxseed, Corn oil) X 2 (LNA, No LNA) ANOVA.

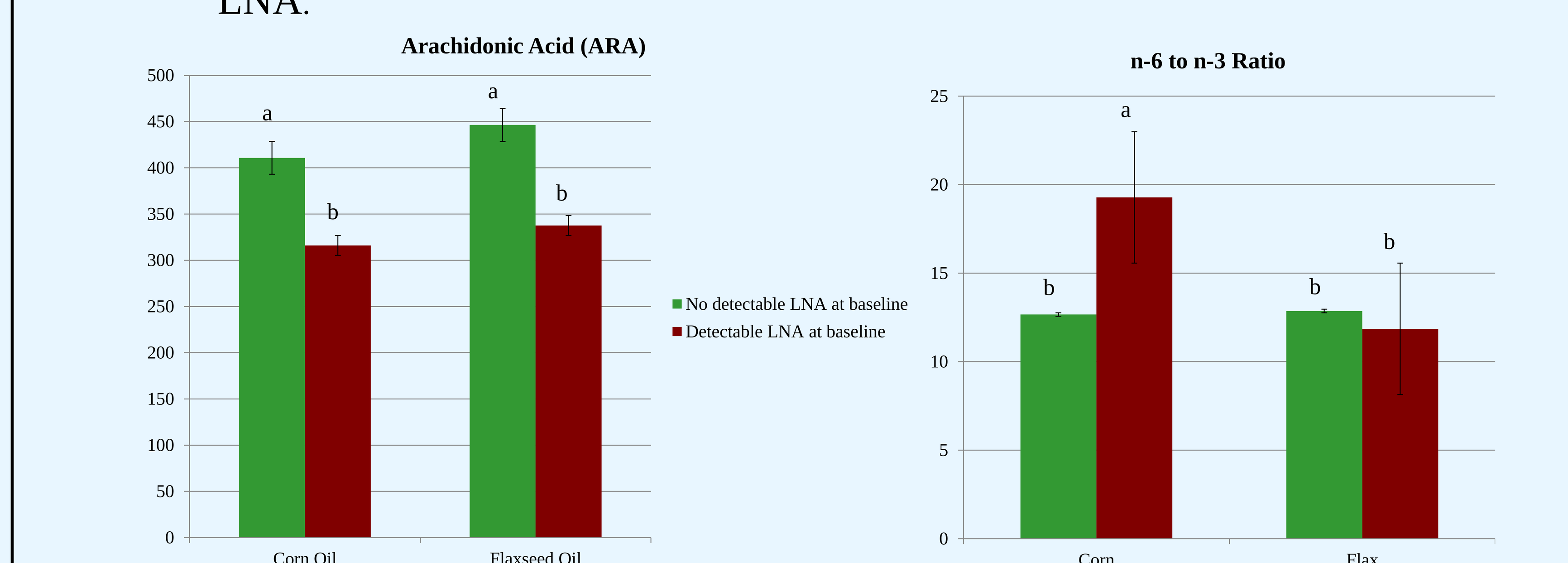
Figure 2. Baseline fatty acid levels by baseline LNA.



Results

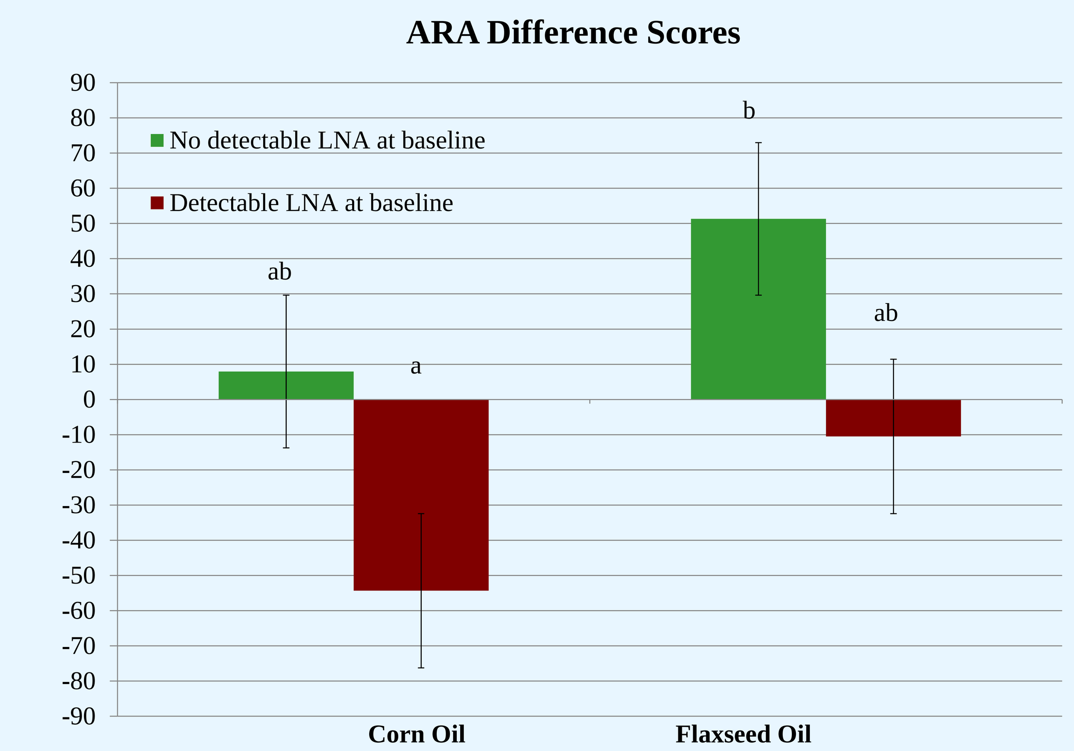
- Baseline (Figure 2): Toddlers with no detectable baseline LNA had higher levels of docosapentaenoic acid (DPA n-3), $F(1, 66) = 4.05$, $p < 0.05$, and lower levels of dihommo-gamma-linolenic acid (dGLA n-6), $F(1, 67) = 6.53$, $p < 0.05$, compared to toddlers with detectable baseline LNA.
- Endpoint (Figure 3, left): Toddlers with no detectable baseline LNA had higher levels of arachidonic acid (ARA n-6) after supplementation, $F(2, 38) = 3.78$, $p < 0.05$, compared to toddlers with detectable baseline LNA, despite no differences in ARA levels at baseline.
- Ratio (Figure 3, right): Children with no detectable LNA at baseline had no change in their ratio whether they received corn oil or flaxseed oil. Children with detectable baseline LNA who received corn oil had significantly higher ratios than children who consumed flaxseed oil, $F(3, 34) = 2.81$, $p < 0.05$.

Figure 3. Fatty acid levels after 120-day supplementation by experimental group and baseline LNA.



Bars with different letters are significantly different

Figure 4. Difference scores by experimental group and baseline LNA.



Bars with different letters are different at $p < 0.1$ level

Results

- Difference Scores (Figure 4):
  - The corn oil group with no detectable baseline LNA and the flaxseed group with detectable LNA evidenced no change in ARA levels after the 120-day intervention, *ns*.
  - Corn oil with detectable LNA compared to flax oil with no detectable LNA, $t(13) = -1.53$, $p < 0.1$

Discussion

- Supplementation with LNA for four months altered fatty acid levels in toddlers contingent on baseline levels of LNA, which is similar to results shown in animal work.
- There were no differences in ARA levels at the beginning of the study. Over 120 days of supplementation, children's levels of ARA became differentially predicted by intervention group membership.
- Interestingly, after the intervention, the corn oil group with detectable baseline LNA showed a very large decrease in ARA despite the high amount of omega-6 fatty acids in corn oil, and the flaxseed oil group with no detectable baseline LNA evidenced a large increase in ARA. This may indicate a preferential use of the desaturase.
- Baseline LNA affected omega-6 fatty acids as well, likely due to the competition for desaturase and elongase.
- Supplementation with LNA may be a viable option for those who can efficiently convert LNA to LCPUFAs. A better understanding of individual differences in fatty acid metabolism would allow recommendations for optimal individualized consumption.

References

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