Omega-3, Mood, Seafood Consumption, and Neuroimaging in Kids

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Disclosure Statement

Research Support

Inflammation Research Foundation
Royal DSM Nutritional Products, LLC
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Consulting

Inflammation Research Foundation (Scientific Advisory Board)
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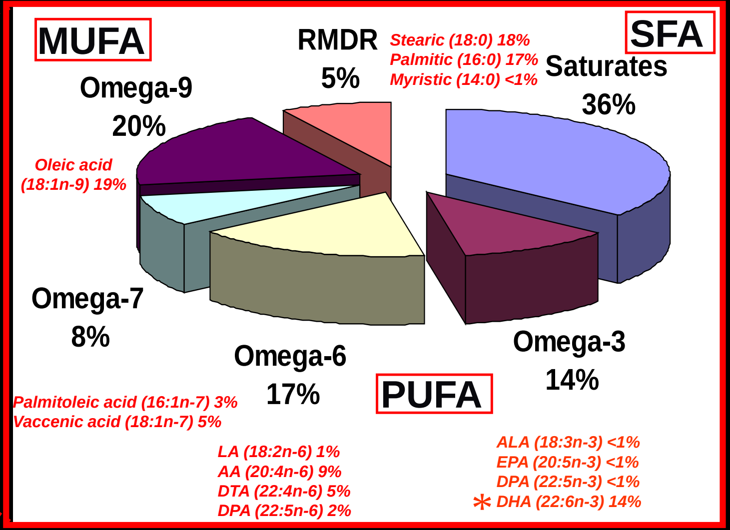
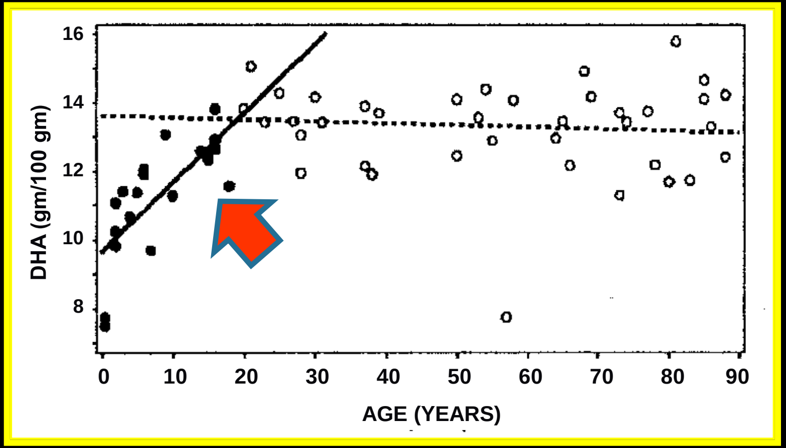
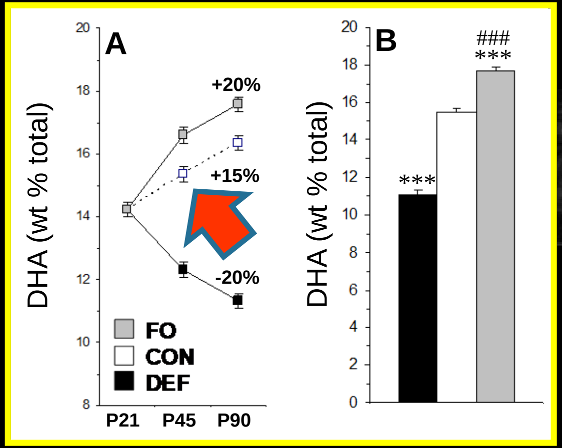
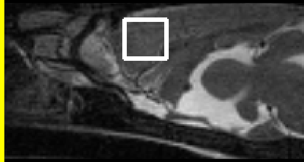
Fish/seafood are primary dietary sources of DHA which is the most abundant *n*-3 PUFA in the mammalian brain

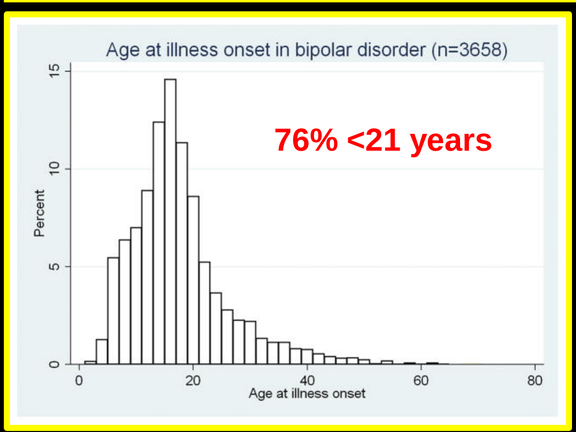


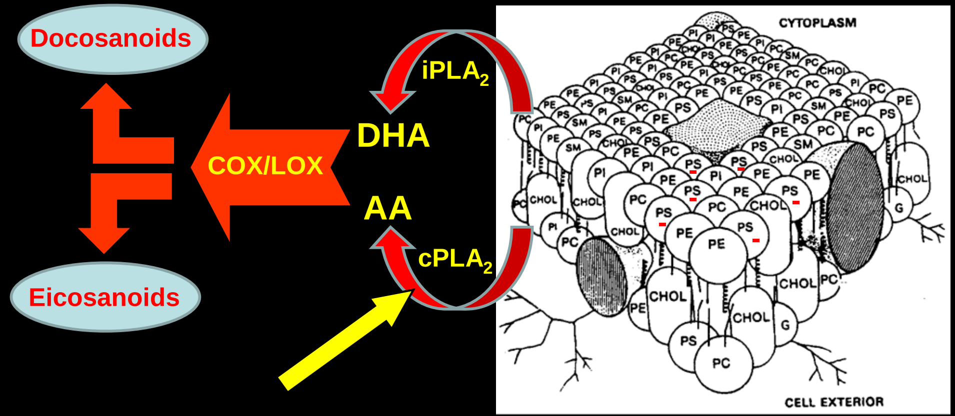
DHA levels increase sharply in the human and rat frontal cortex during adolescent development



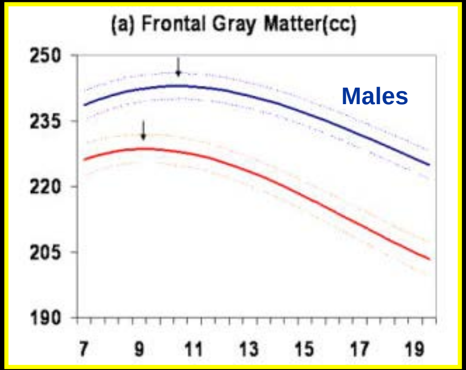


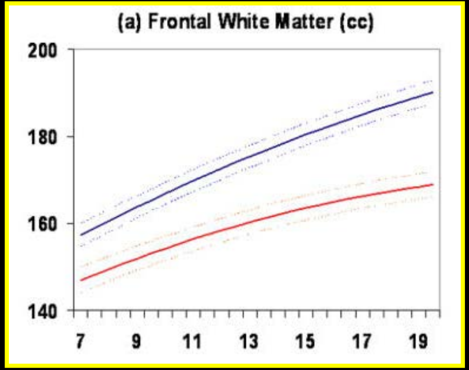




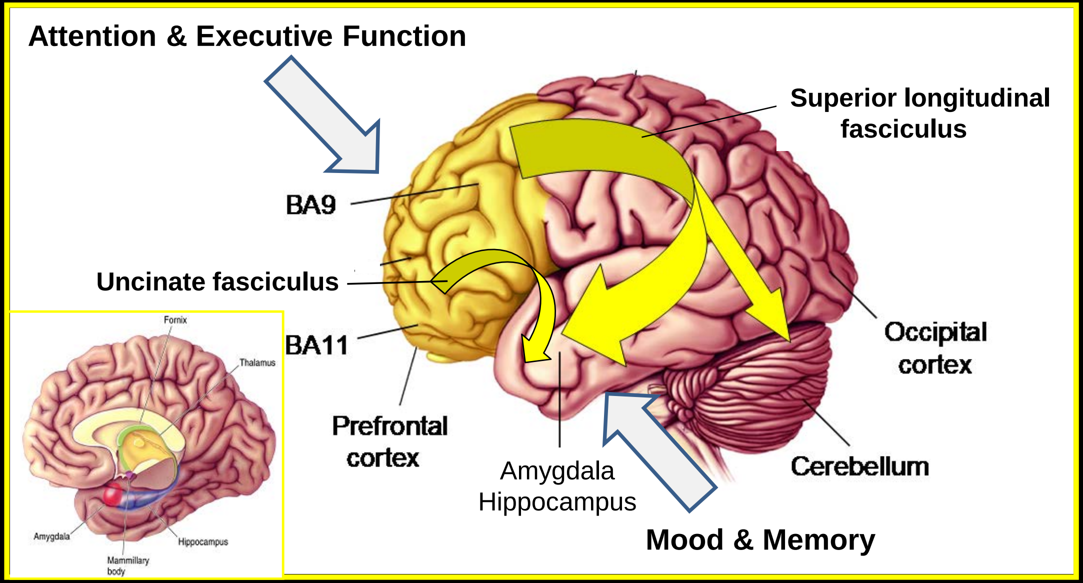


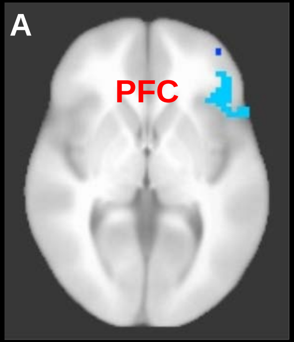
The frontal cortex regulates attention, executive function, and mood, and undergoes rapid maturational changes during adolescence

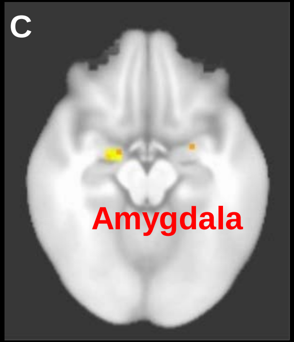




AGE (Years)

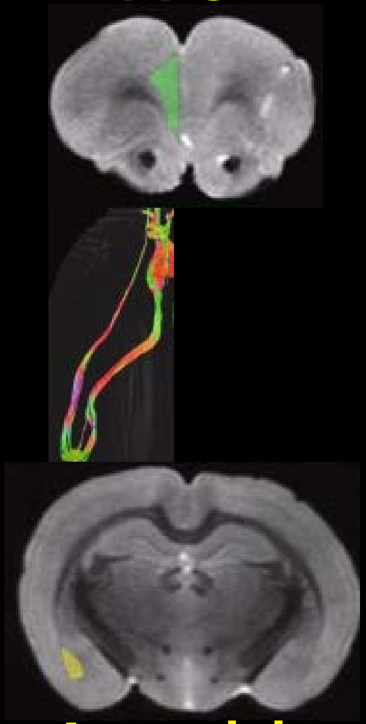


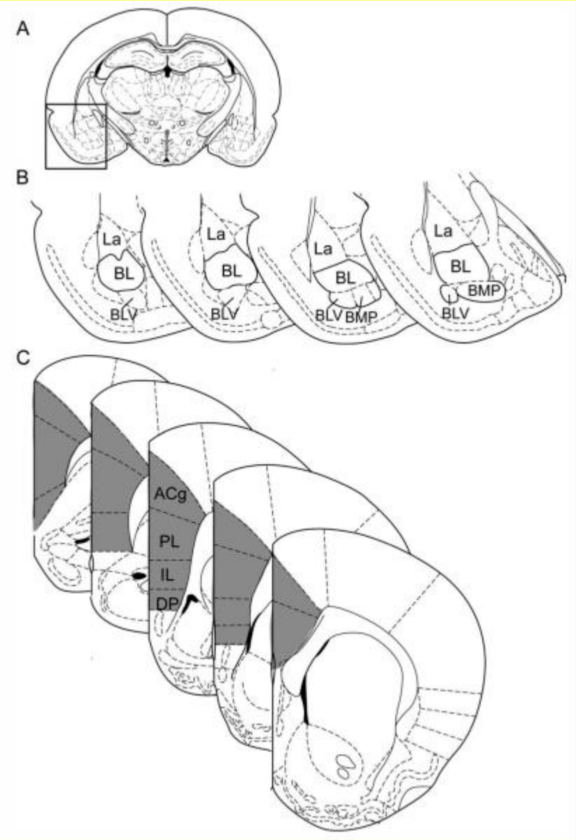


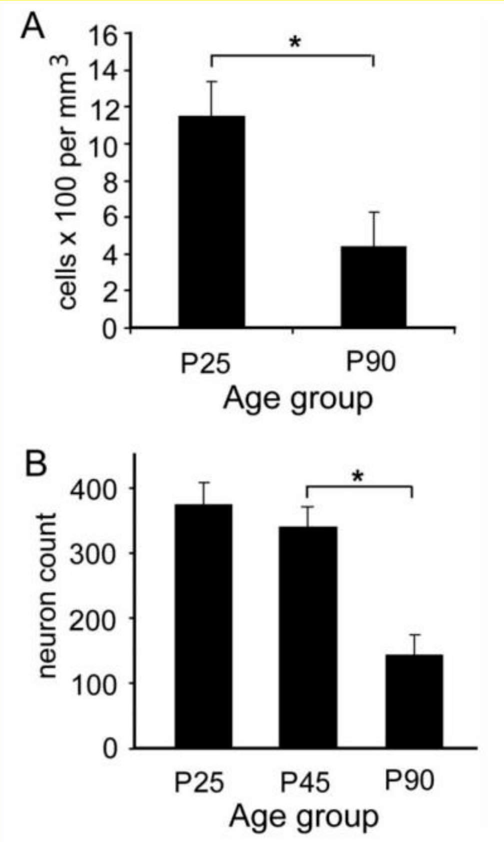


Geidd et al. (2009) *J Am Acad Child Adolesc Psychiatry.* 48:465-470

Robust frontal – amygdala pruning during adolescence in rats



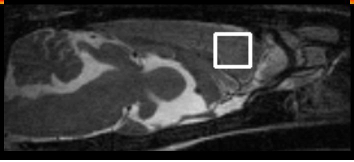




Cressman et al. (2010) *J Comp Neurol.* 518:2693-709

Rat neuroimaging:

P21



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Control *n*-3 (ALA+) — *n=20*

Deficient *n*-3 (ALA-) — *n=20*

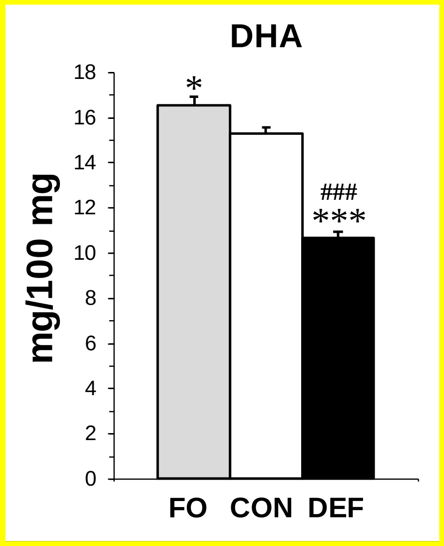
Fish Oil (EPA+DHA) — *n=20*

DTI
[1]H MRS
phMRI

Table 1. Diet Compositions

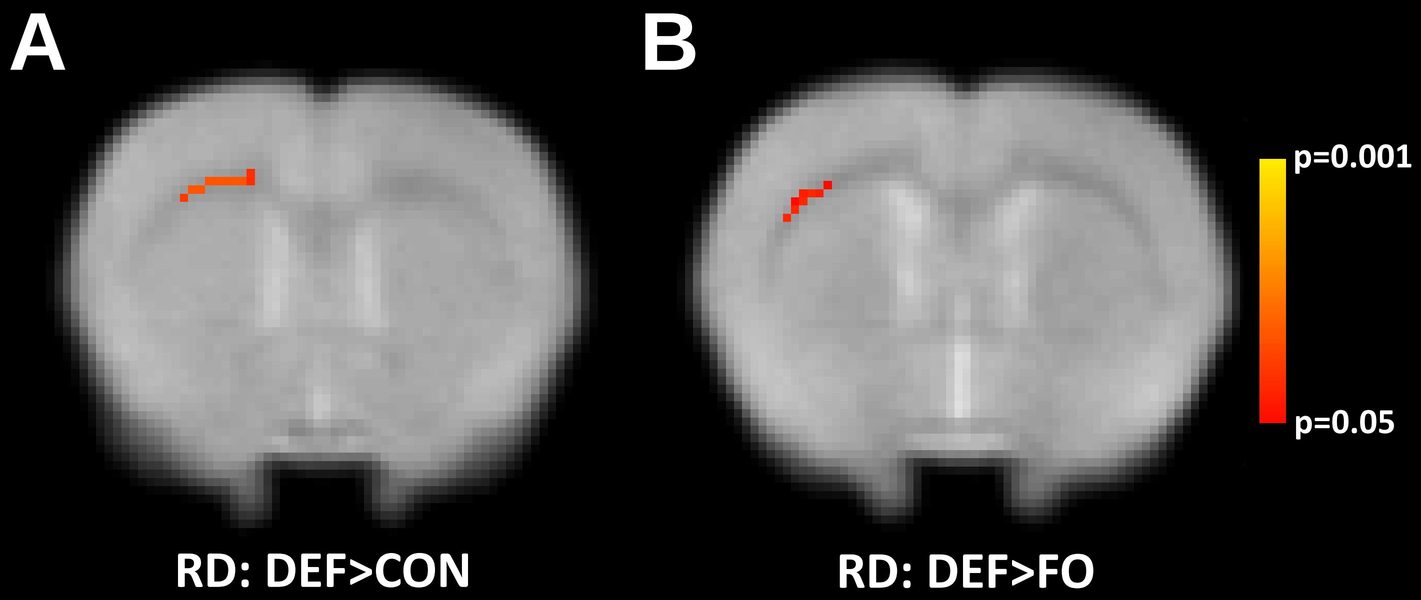
Ingredient[1]	Control (TD.04285)	Deficient (TD.04286)	Fish Oil (TD.110837)
Cornstarch	20	20	20
Sucrose	27	27	27
Dextrose	9.9	9.9	9.9
Maltose-dextrin	6	6	6
Cellulose	5	5	5
Mineral mix	3.5	3.5	3.5
Vitamin mix	1.0	1.0	1.0
L-Cystine	0.3	0.3	0.3
Choline bitartrate	0.25	0.25	0.25
TBHQ	0.002	0.002	0.002
Hydrogenated coconut oil	4.5	5.1	3.9
Safflower	1.9	1.9	1.9
Flaxseed	0.6	0	0
Fish oil	0	0	1.1
Fatty acid composition[2]			
C8:0	3.7	4.1	3.3
C10:0	3.3	3.7	3.0
C12:0	38	32.1	26.0
C14:0	11.5	12.9	11.8
C16:0	8.8	9.1	10.5
C18:0	10.7	11.7	10.4
16:1*n*-7	nd	nd	1.4
18:1*n*-9	6.7	5.1	6.3
18:1*n*-7	nd	nd	0.7
18:2*n*-6	22.5	21.3	22.6
20:4*n*-6	nd	nd	nd
18:3*n*-3	4.9	nd	nd
20:5*n*-3	nd	nd	2.2
22:5*n*-3	nd	nd	nd
22:6*n*-3	nd	nd	1.7

[1]g/100 g diet
[2]wt % of total fatty acids
nd = not detected



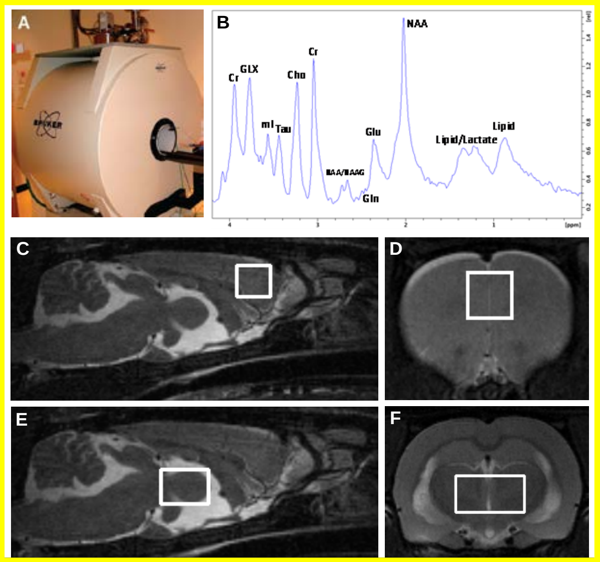
7 Tesla Brucker

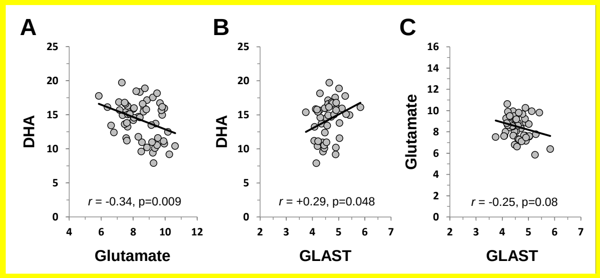
Adult forebrain white matter integrity is reduced by dietary omega-3 fatty acid deficiency during adolescent development

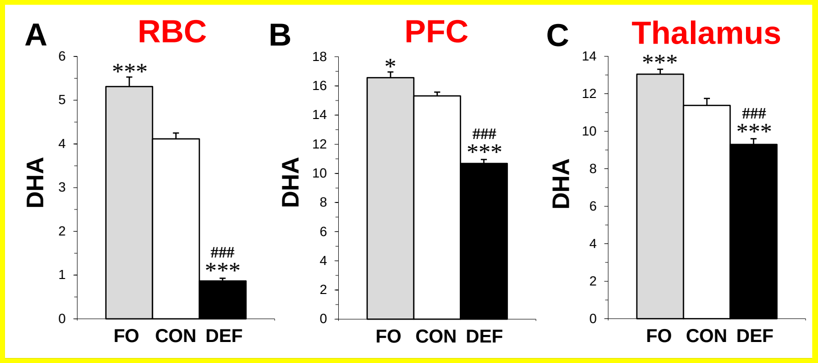


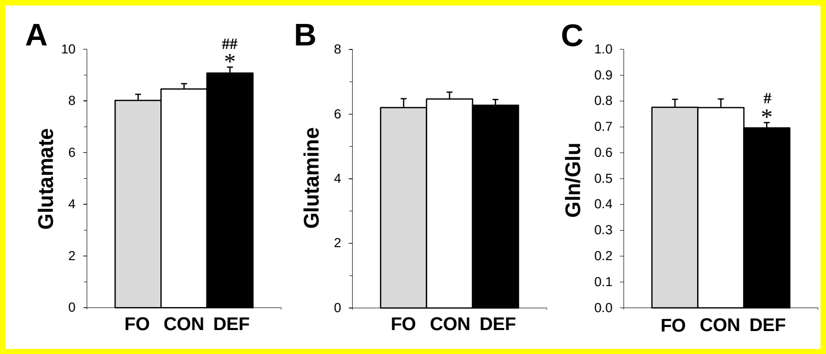
McNamara et al. (2018) *Dev Neurosci.* 40:84-92

Frontal glutamate homeostasis is modified by dietary omega-3 fatty acid intake during peri-adolescent development









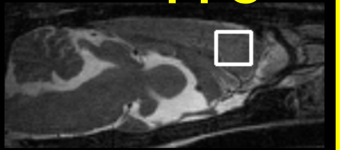
McNamara et al. (2017) *Psychiatry Res.* 270:39-45

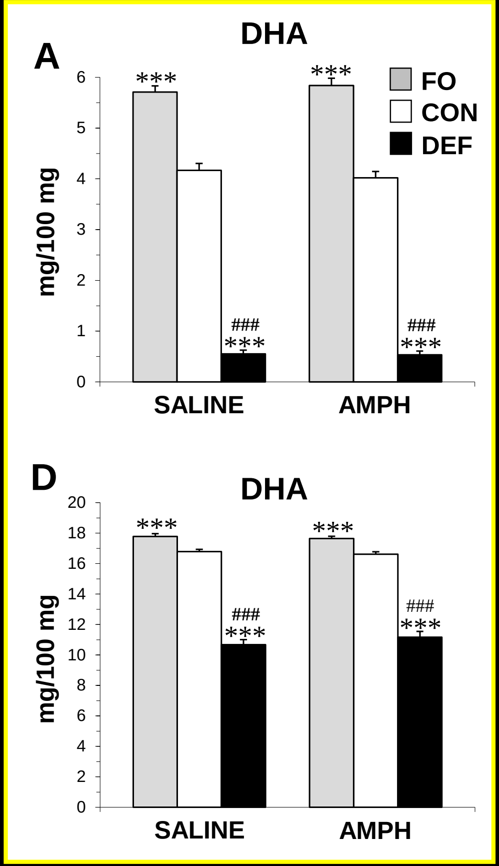
Adolescent omega-3 fatty acid deficiency impairs frontostriatal recruitment following repeated amphetamine treatment

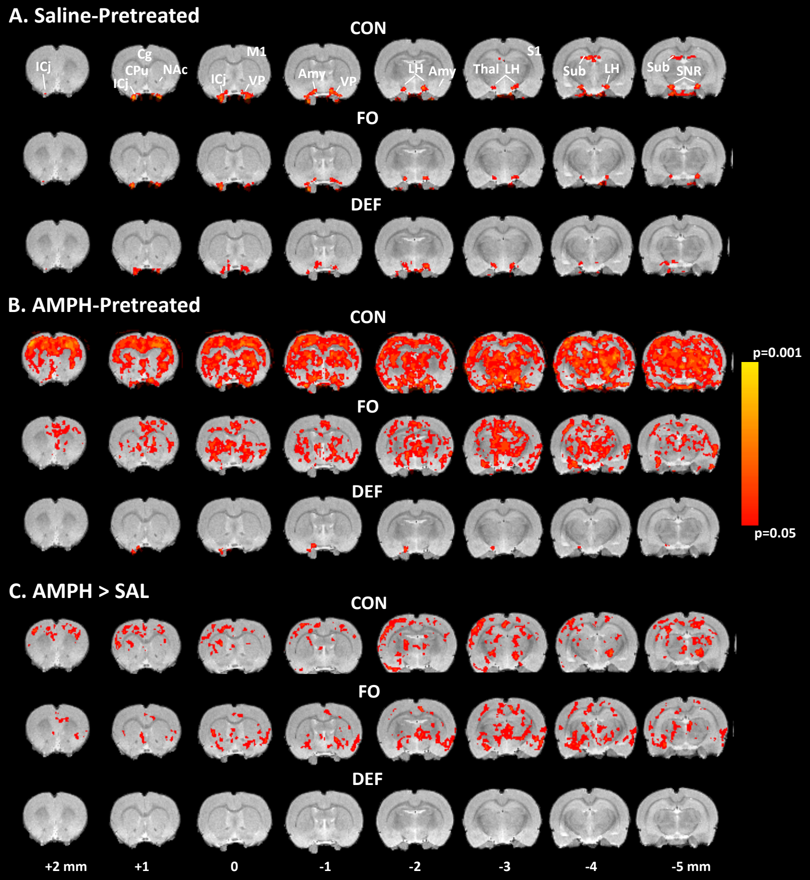
RBC

r = +0.95, p≤0.0001

PFC

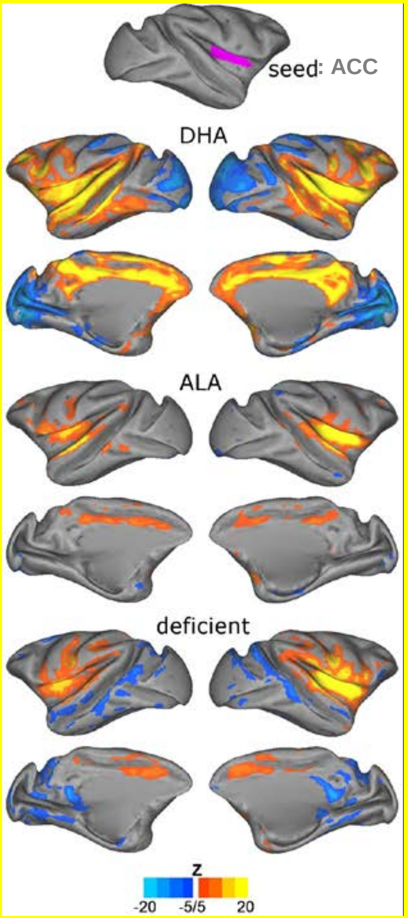


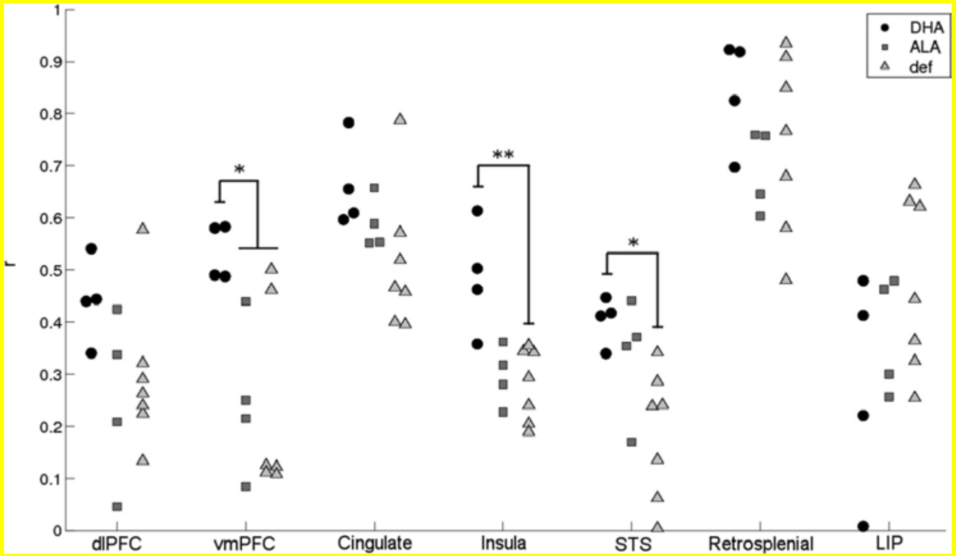




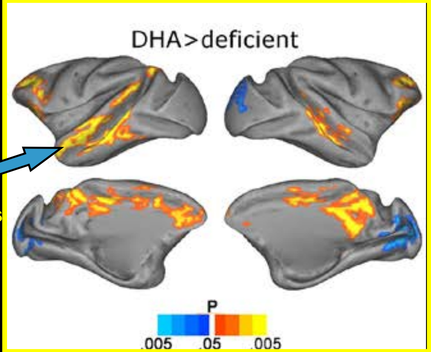
McNamara et al. (2018) *Nutr Neurosci.* [Epub ahead of print]

Reduced frontal connectivity in DHA-deficient monkeys





Superior Temporal Sulcus



Grayson et al. (2014) *J Neurosci.* 34:2065-2074

Reduced frontal connectivity in children with low vs. high RBC DHA

RBC DHA was positively correlated with weekly fish intake frequency (r=+0.57, P = 0.0002).

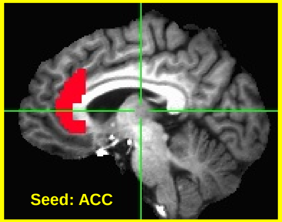


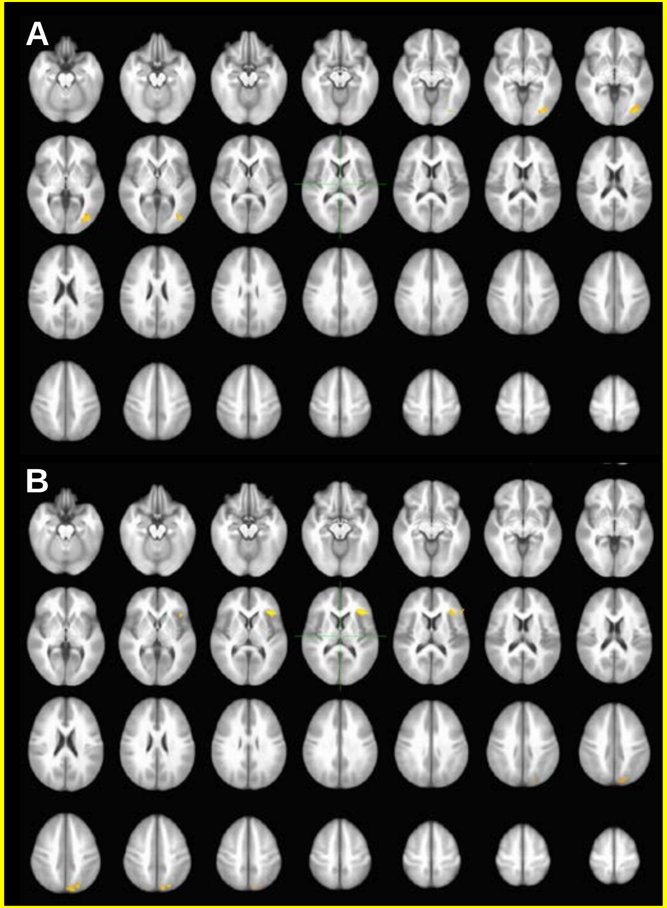
Table 2. Fish Intake Frequency and Erythrocyte LC*n*-3 Fatty Acid Composition

Variable[1]	Low-DHA (n=18)	High-DHA (n=18)	*P*-value[2]
Fish intake (times/week)	0.5 ± 0.6	1.3 ± 0.9	**0.003**
Docosapentaenoic acid (22:5*n*-3)	1.6 ± 1.1	1.9 ± 1.1	0.28
Eicosapentaenoic acid (EPA, 20:5*n*-3)	0.2 ± 0.2	0.7 ± 0.6	**0.008**
Docosahexaenoic acid (DHA, 22:6*n*-3)	2.6 ± 0.85	4.1 ± 1.1	**0.0001**
Omega-3 Index (EPA+DHA)	2.7 ± 0.9	4.7 ± 1.3	**0.0001**

[1]Fatty acid values are group mean weight percent of total fatty acids ± S.D.
[2]Two-tailed *t*-tests

Table 4. Regions exhibiting reduced functional connectivity in the low-DHA group relative to the high-DHA group

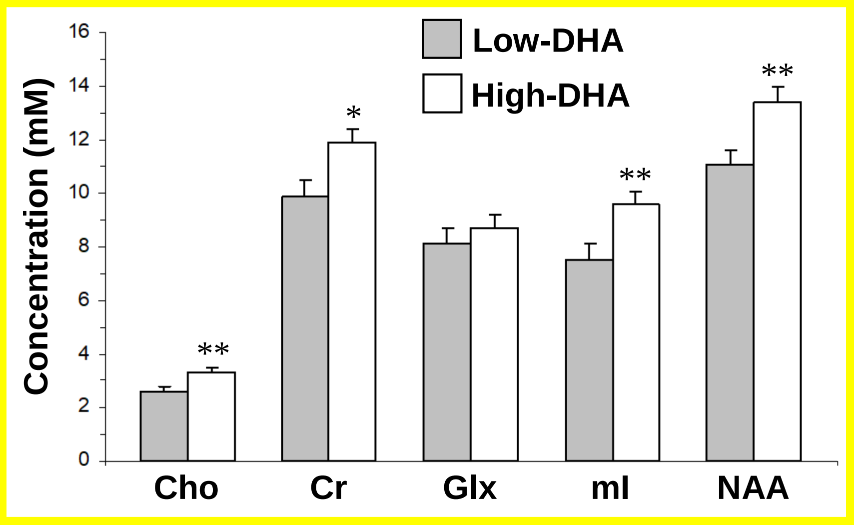
Brain region (Brodmann's Area)	Talairach coordinates (mm) *x*	*y*	*z*	Cluster Size (Voxels)
Right ACC Seed-Region				
Right Insula (BA13)	-39.3	-26.2	10.9	46
Right Inferior frontal gyrus (BA45)				
Right Inferior frontal gyrus (BA46)				
Right Precuneus (BA19)	-14.4	75.5	44.8	38
Right Superior parietal lobule (BA7)				
Left ACC Seed-Region				
Right Lingual gyrus (BA18)	-35.8	74.4	0.5	53
Right Inferior occipital gyrus (BA19)				
Right Middle occipital gyrus (BA19)				
Right Inferior temporal gyrus (BA20)				

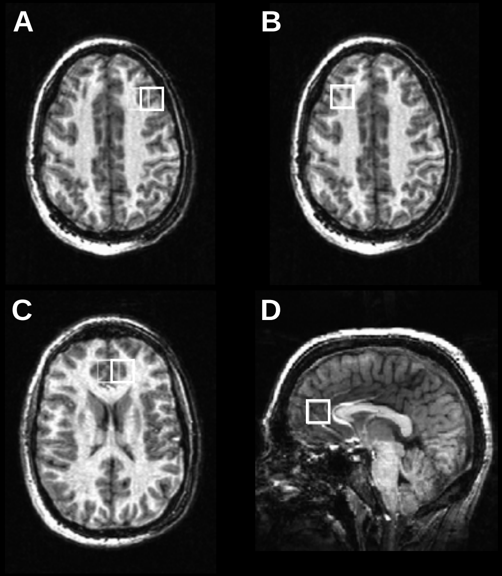


Almeida et al. (2017) *Nutr Neurosci.* 20:246-254

Reduced biochemical indices of cortical integrity in children with low vs. high RBC DHA

Low DHA (n=19) 2.5±0.2 wt % TTL
High DHA (n=19) 4.1±0.2 wt % TTL





Reaction Time (CPT-IP)
Low DHA 693±13 ms
High DHA 638±14 ms
p=0.007

McNamara et al. (2013) *Nutr Neurosci.* 16:183-190

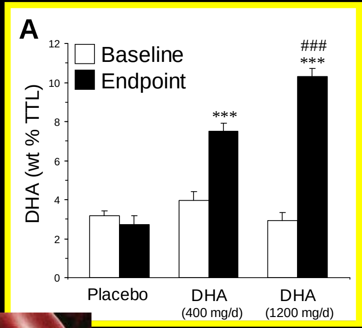
Effect of algal DHA supplementation on attention-induced frontal cortex activity in healthy children

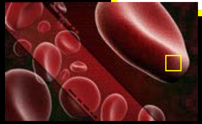
Baseline — **8 weeks**

Placebo (n=10)

DHA 400 mg/d (n=10)

DHA 1,200 mg/d (n=12)





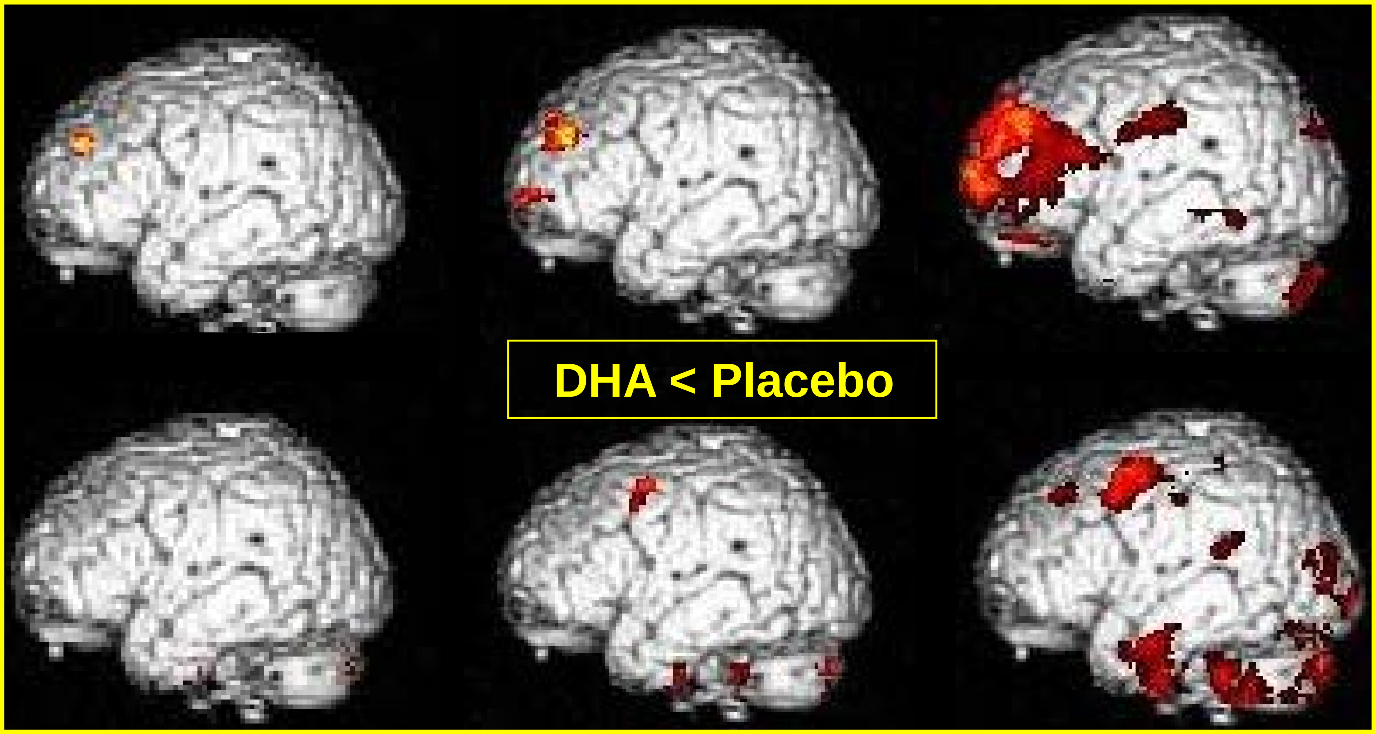
4 Tesla Varian

fMRI (CPT-IP)

McNamara et al. (2010) *Am J Clin Nutr* 91:1060-1067

8-week DHA: 1,200 mg/d

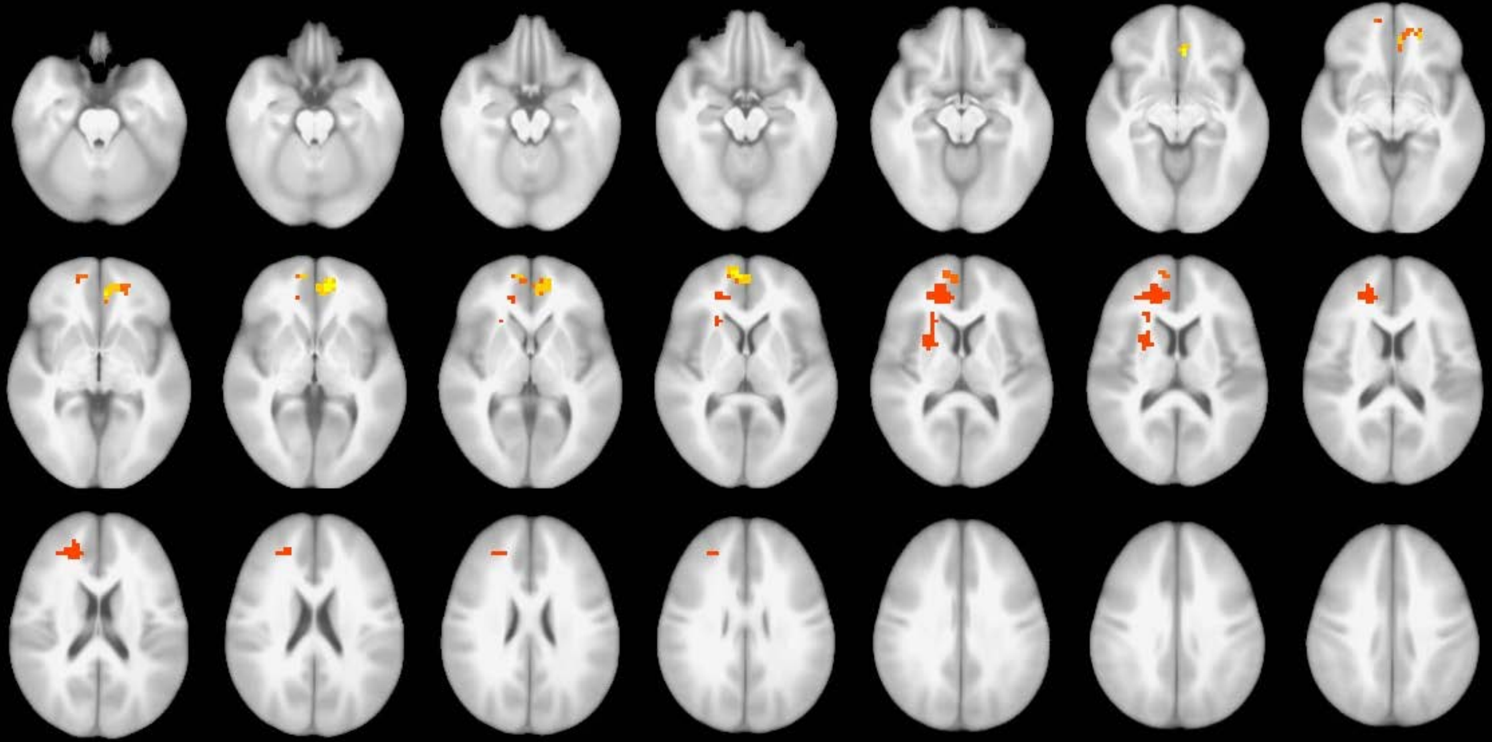
DHA > Placebo



P<0.005 (T25) | *P<0.01 (T25)* | *P<0.05 (T25)*

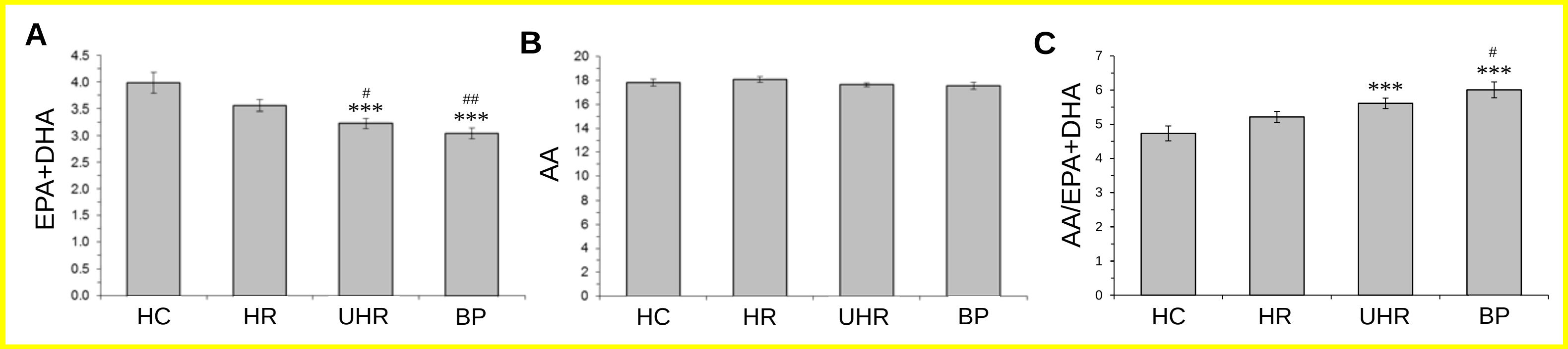
McNamara et al. (2010) *Am J Clin Nutr* 91:1060-1067

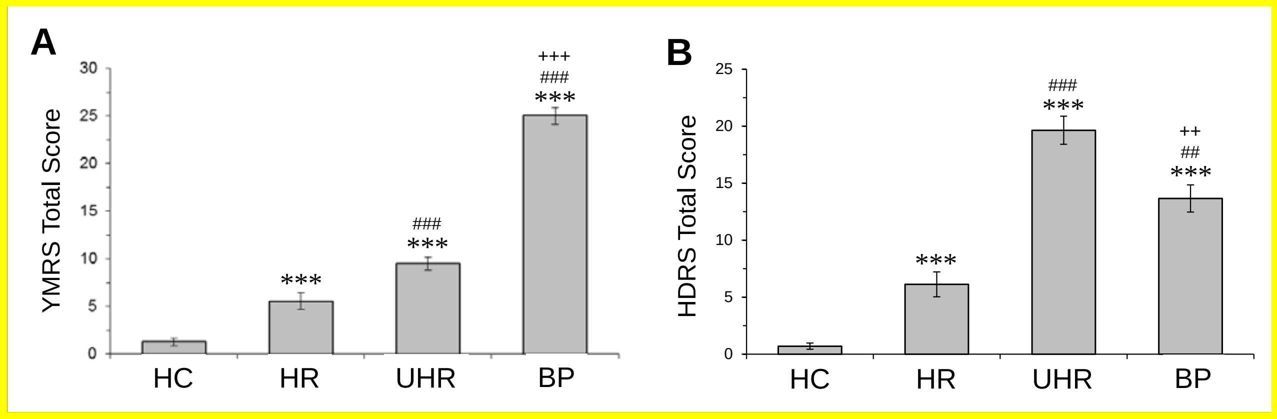
Positive relationship between RBC DHA levels and frontal cortical activity in adolescents with MDD



McNamara et al. unpublished data

Mood symptom severity in adolescents is inversely associated with RBC EPA+DHA levels





RBC EPA+DHA (*n=130*)

YMRS

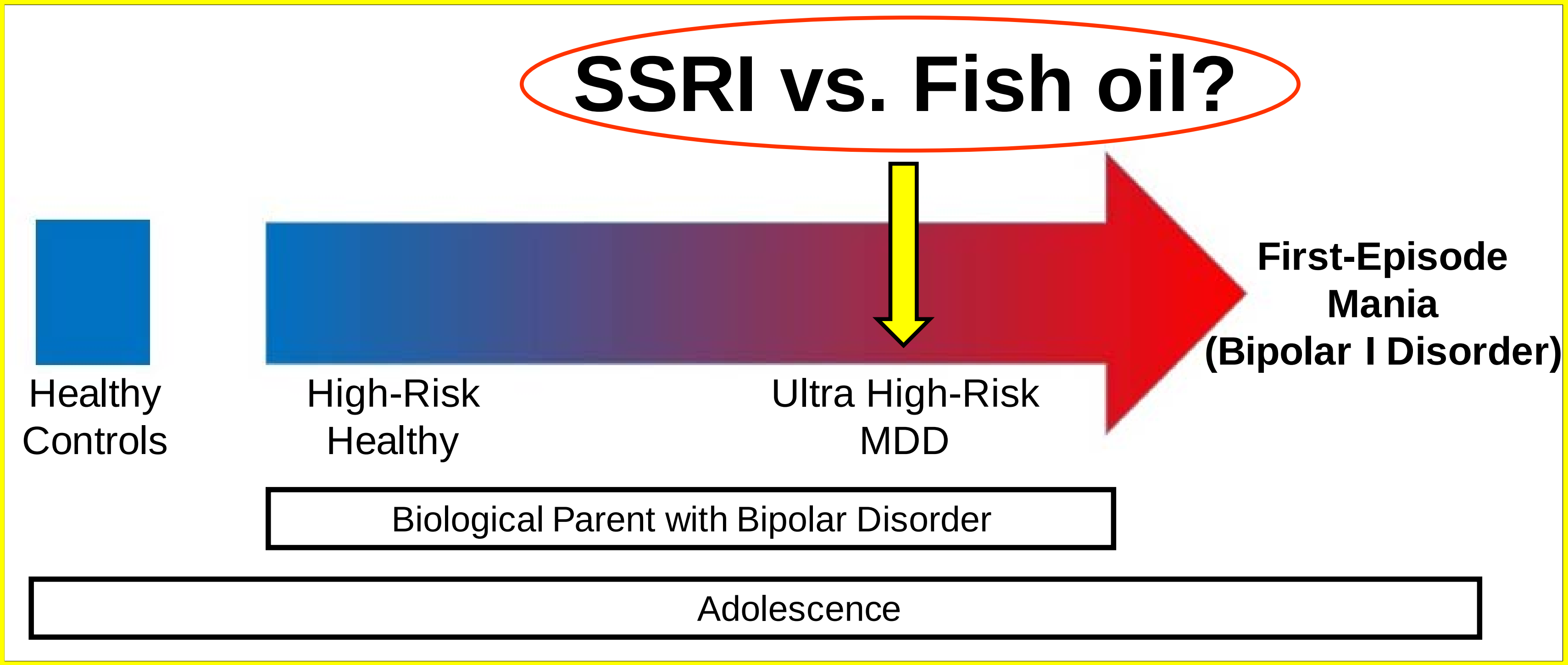
r = -0.29, *p*=0.0008

HDRS

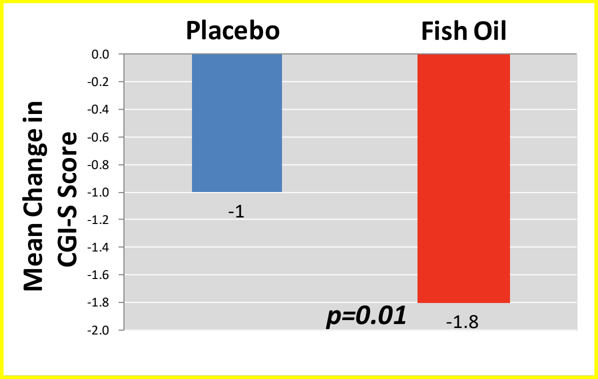
r = -0.28, *p*=0.003

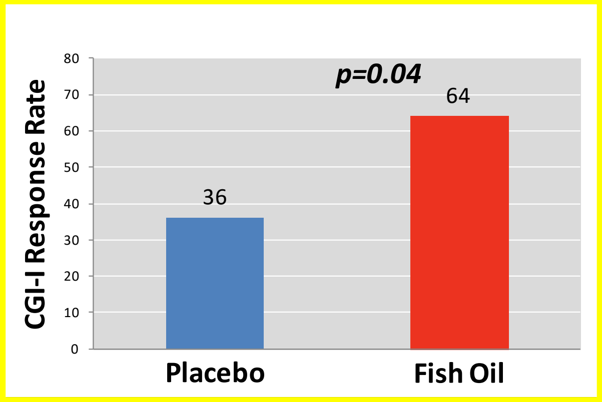
McNamara et al. (2016) *Early Interv Psychiatry.* 10:203-211

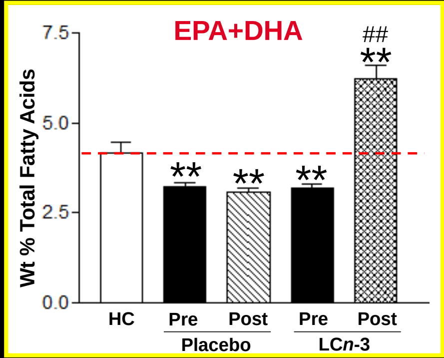
Risk Progression in Bipolar Disorder

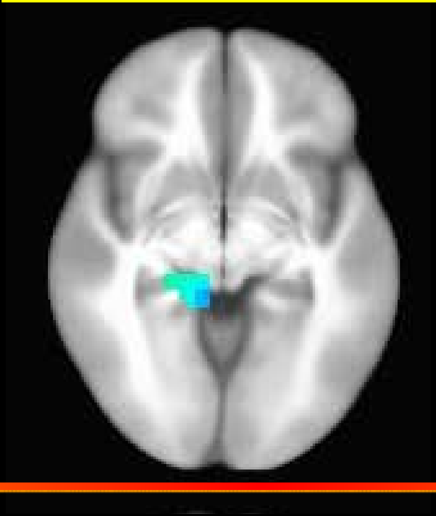


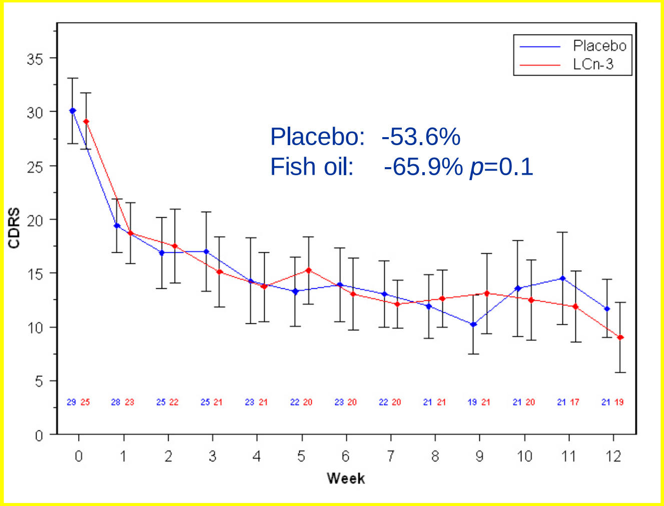
Fish oil (2.1 g/d) improves global functioning and reduces emotion-induced limbic activation in high-risk youth











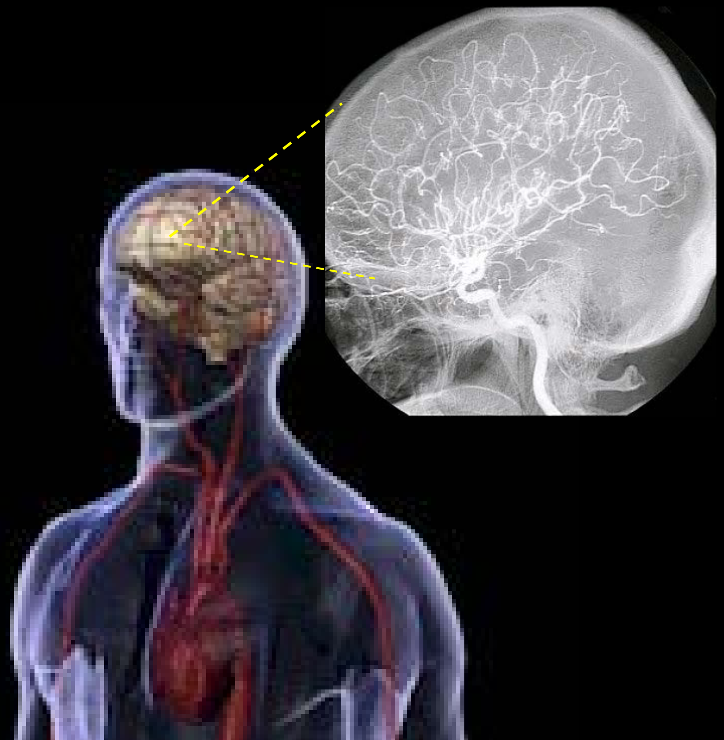
Response rates:

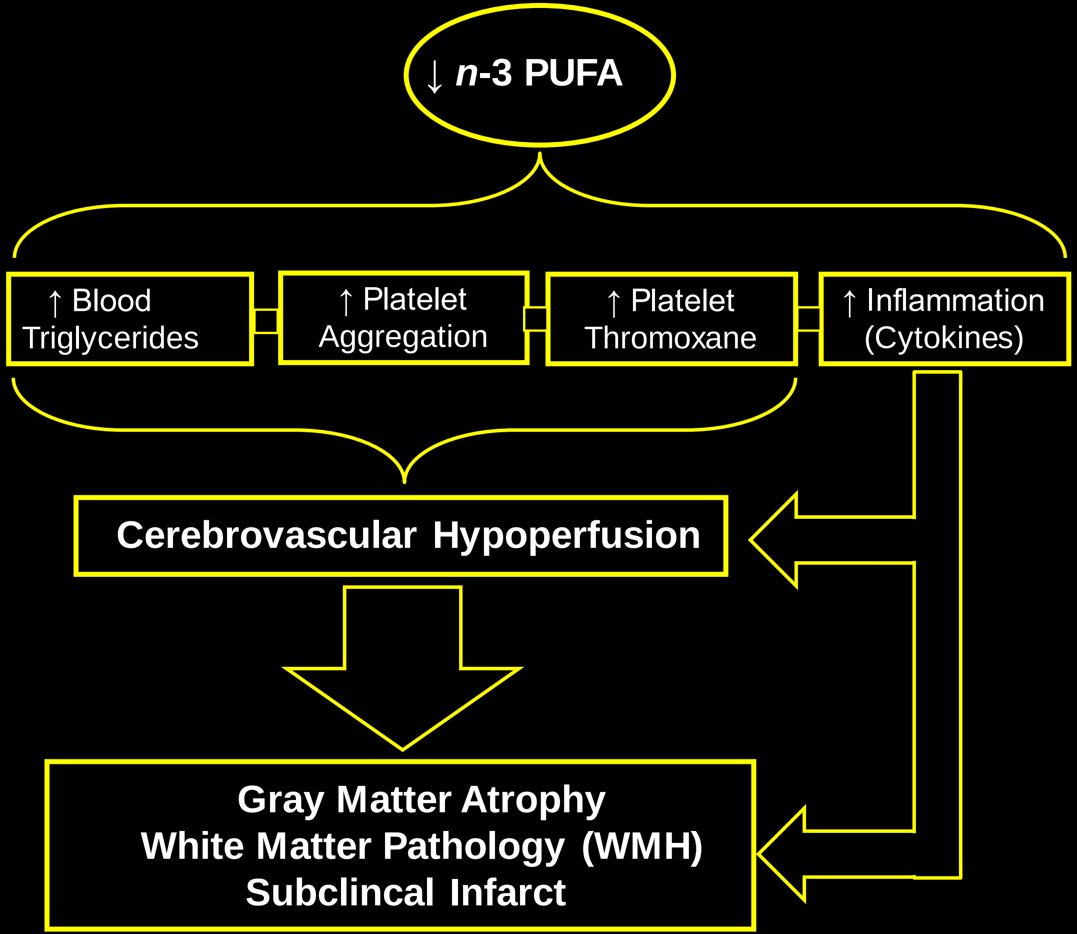
61% (Fish oil) vs. 55% (Placebo)(p=0.4)

Remission rates:

52% (Fish oil) vs. 54% (Placebo)(p=0.1)

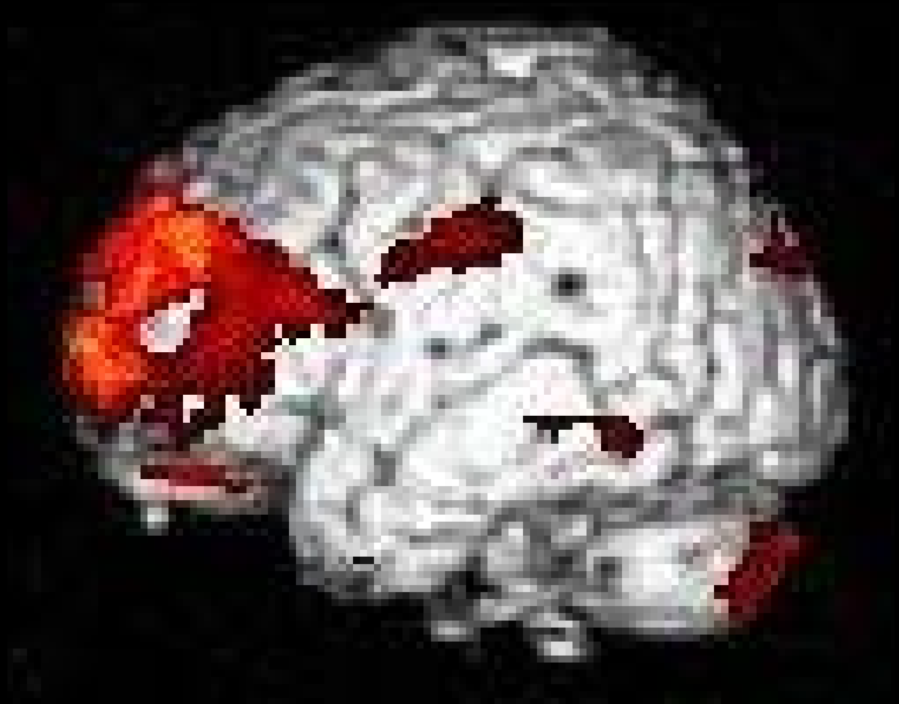
Mediating mechanisms





McNamara et al. (2018) *PLEFA* [Epub ahead of print]

This is Your (child's) Brain on DHA



Any Questions?