

Brain Health, Mental Health, Depression

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*Every person with a brain
deserves good nutrition!*



Nutritional medicine as mainstream in psychiatry

Jerome Sarris, Alan C Logan, Tasnime N Akbaraly, G Paul Amminger, Vicent Balanzá-Martínez, Marlene P Freeman, Joseph Hibbeln, Yutaka Matsuoka, David Mischoulon, Tetsuya Mizoue, Akiko Nanri, Daisuke Nishi, Drew Ramsey, Julia J Rucklidge, Almudena Sanchez-Villegas, Andrew Scholey, Kuan-Pin Su, Felice N Jacka, on behalf of The International Society for Nutritional Psychiatry Research

Lancet Psychiatry, 2015

- The emerging and compelling evidence for nutrition as a crucial factor in the high prevalence and incidence of mental disorders suggests **that diet is as important to psychiatry as it is to cardiology, endocrinology, and gastroenterology.**
- Evidence is steadily growing for the relation between dietary quality (and potential nutritional deficiencies) and mental health, and for the select use of nutrient-based supplements to address deficiencies, or as monotherapies or augmentation therapies.
- **The members of the International Society for Nutritional Psychiatry Research advocate recognition of diet and nutrition as central determinants of both physical and mental health.**

2015-2020 Dietary Guidelines for Americans

“Emerging evidence also suggests that relationships may exist between eating patterns and some neurocognitive disorders and congenital anomalies.”

Mediterranean dietary patterns to reduce depression?

fish, olive oil and n-3 HUFAs as causal agents

1. Dietary patterns

Healthy
Mediterranean

2015 Dietary Guidelines for Americans Scientific committee evaluated **ONLY** data on dietary patterns for depression.

2. Specific foods

Fish
Olive oil

Fish consumption: a meta-analysis including **n=26** studies, **n=150,278** - lower risks of depression. **RR= 0.83** (95% CI 0.74 to 0.93)

[Li F, et al. J Epidemiol Community Health 2015;0:1–6](#)

3. Specific nutrients

n-3 HUFAs

Blood levels: a meta-analysis of **n=14** studies with **n=3,318** participants indicate higher blood levels of n-3 HUFAs are associated with lower risks of depression. **g= 0.85**, $p < 0.0000$ [Lin et al, Biol Psychiatry 2010;68:140–147](#)

4. RCTs

n-3 HUFAs vs.
placebo

Causal testing: a meta-analysis of **n=52** study conditions with **n=11,038** participants indicate **EPA rich**, n-3 HUFAs treat symptoms in major depressive disorders. **g=0.61** [Hallahan , Hibbeln et al, Br J Psychiatry, 2015](#)

5. Mechanistic basis

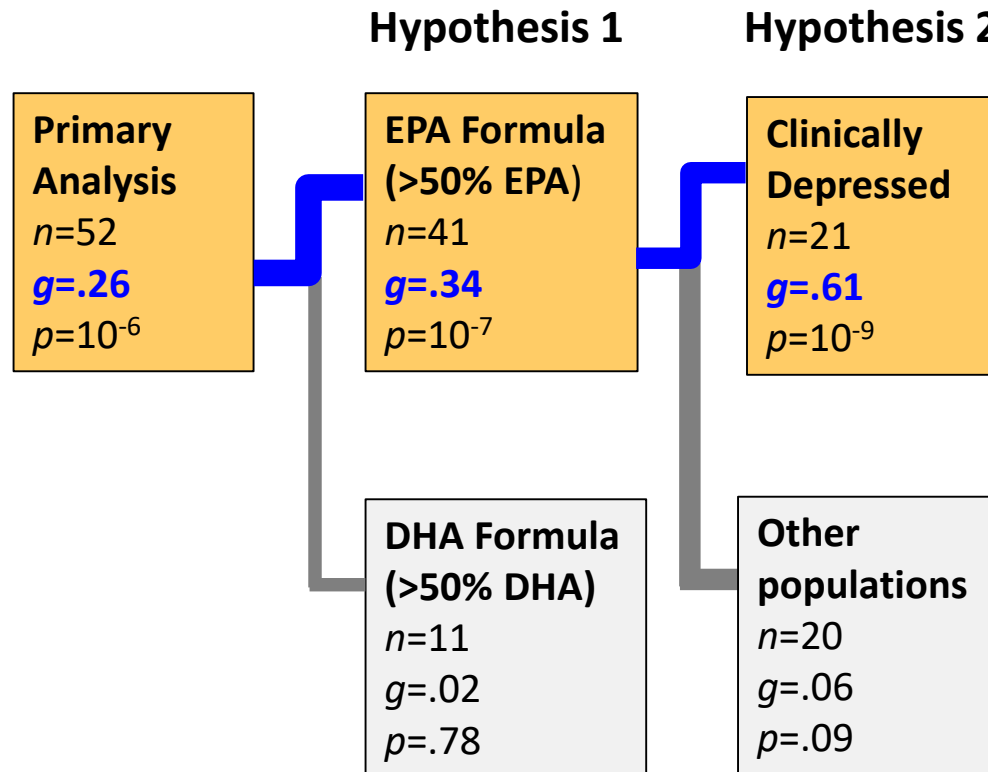
Multiple synergistic biological processes: n-3 HUFAs in neuroinflammation, dopaminergic and serotonergic function, neurogenesis and the stress axis

6. Olive oil

Olive oil, instead of vegetable oils, lowers intake of omega-6 fats and raises blood levels of **EPA** and is associated with lower risk of depression.

[Wolfe et al Prog Neuropsychopharmacol Biol Psych. 2009 31;33\(6\):972-7](#)

Hierarchical meta-analysis for omega-3 HUFA trials in depression



Key to tree diagram:

When a branch's g or n approaches 0, no further analysis occurs

Grey boxes contain branches hypothesized to decrease effect size.

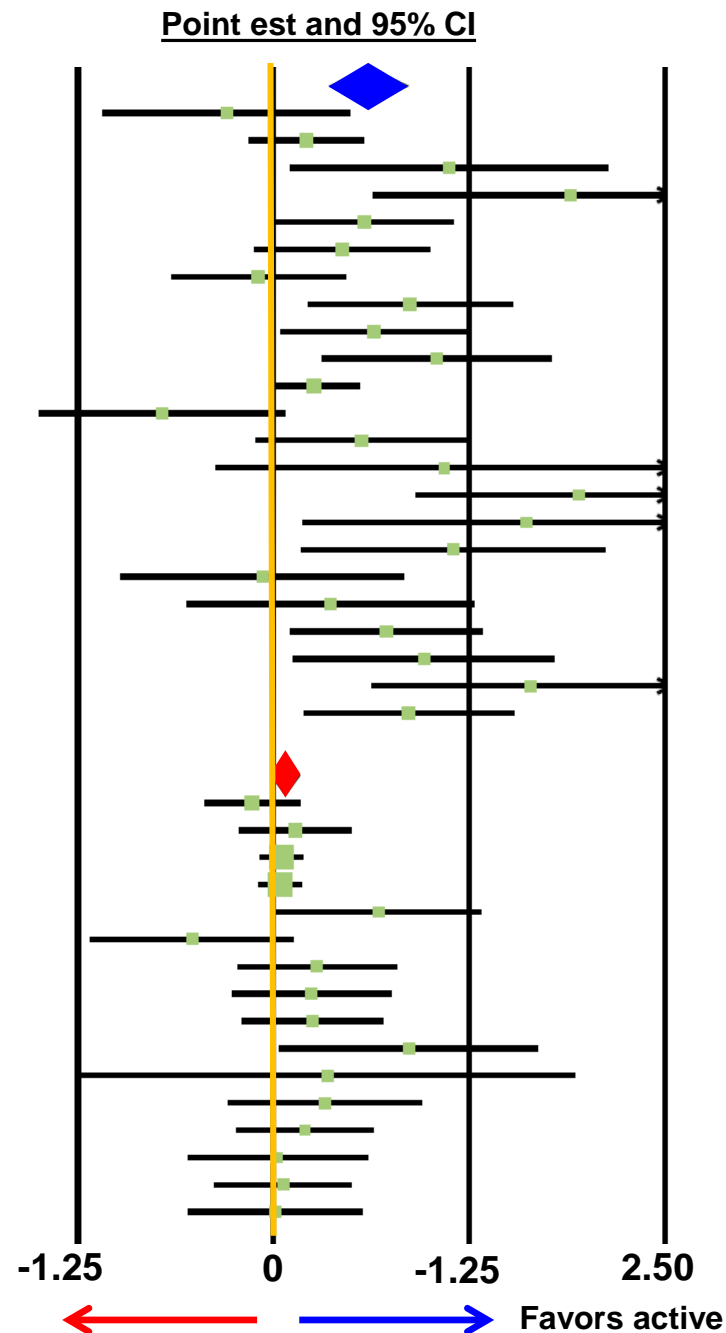
Orange boxes contain branches hypothesized to increase effect size.

RCTs for Depression Forrest Plot – EPA studies

Groups	Study name	Hedge's G	SE	wt	n
EPA/ Diagnosed depression					
	Bot et al., 2010	0.609	0.117		
	Carney et al., 2010	-0.300	0.397	4%	25
	da Silva et al., 2008 (Augmentation)	0.210	0.180	7%	122
	da Silva et al., 2008 (Monotherapy)	1.120	0.513	3%	13
	Frangou et al., 2006 (1g dose)	1.900	0.637	2%	16
	Frangou et al., 2006 (2g dose)	0.580	0.285	6%	37
	Frangou et al., 2006 (2g dose)	0.440	0.279	6%	38
	Freeman et al., 2008	-0.100	0.277	6%	51
	Gertsik et al., 2011	0.872	0.326	5%	40
	Hallahan et al., 2007	0.639	0.296	5%	49
	Jazayeri et al., 2008	1.040	0.369	5%	32
	Lesperance et al., 2011	0.259	0.140	7%	204
	Lucas et al., 2009 (MDE Diagnosis)	-0.715	0.394	4%	29
	Mischoulon et al., 2009	0.560	0.338	5%	35
	Mozaffari et al., 2013 (EPA)	0.560	0.338	5%	35
	Mozaffari et al., 2013 (EPA)	1.090	0.737	2%	31
	Nemets et al., 2002	1.950	0.528	3%	20
	Nemets et al., 2006	1.615	0.721	2%	20
	Peet & Horrobin et al., 2002 (1g)	1.150	0.488	3%	23
	Peet & Horrobin et al., 2002 (2g)	-0.070	0.455	4%	24
	Peet & Horrobin et al., 2002 (4g)	0.360	0.461	4%	23
	Rondanelli et al., 2010	0.720	0.305	5%	46
	Stoll et al., 1999	0.960	0.418	4%	30
	Su et al., 2003	1.640	0.509	3%	28
	Su et al., 2008	0.862	0.335	5%	33

EPA/ No Diagnosis

		0.076	0.041		
	Andreeva et al., 2012 (Men)	-0.136	0.148	7%	1,604
	Andreeva et al., 2012 (Women)	0.137	0.176	5%	396
	Giltay et al., 2011 (EPA+ALA Mono)	0.053	0.064	31%	1,304
	Giltay et al., 2011 (EPA Mono)	0.043	0.064	31%	1,301
	Giltay et al., 2011 (EPA Aug)	0.673	0.326	2%	49
	Giltay et al., 2011 (EPA+ALA Aug)	-0.521	0.324	2%	48
	Keicolt-Glaser et al., 2012 (1.25g)	0.277	0.254	3%	69
	Keicolt-Glaser et al., 2012 (2.5g)	0.240	0.253	3%	69
	Lucas et al., 2009 (No MDE Diag.)	0.250	0.223	3%	91
	Sinn et al., 2012 (EPA)	0.863	0.413	1%	24
	Tajalizadekhoob et al., 2011 (Aug)	0.349	0.797	0%	11
	Tajalizadekhoob et al., 2011 (Mono)	0.328	0.307	2%	55
	Van de Rest et al., 2008 (1.8g L2/3*)	0.200	0.216	4%	98
	Van de Rest et al., 2008 (1.8g H1/3*)	0.024	0.286	2%	55
	Van de Rest et al., 2008 (.4g L2/3*)	0.060	0.216	4%	100
	Van de Rest et al., 2008 (.4g H1/3*)	0.010	0.279	2%	49



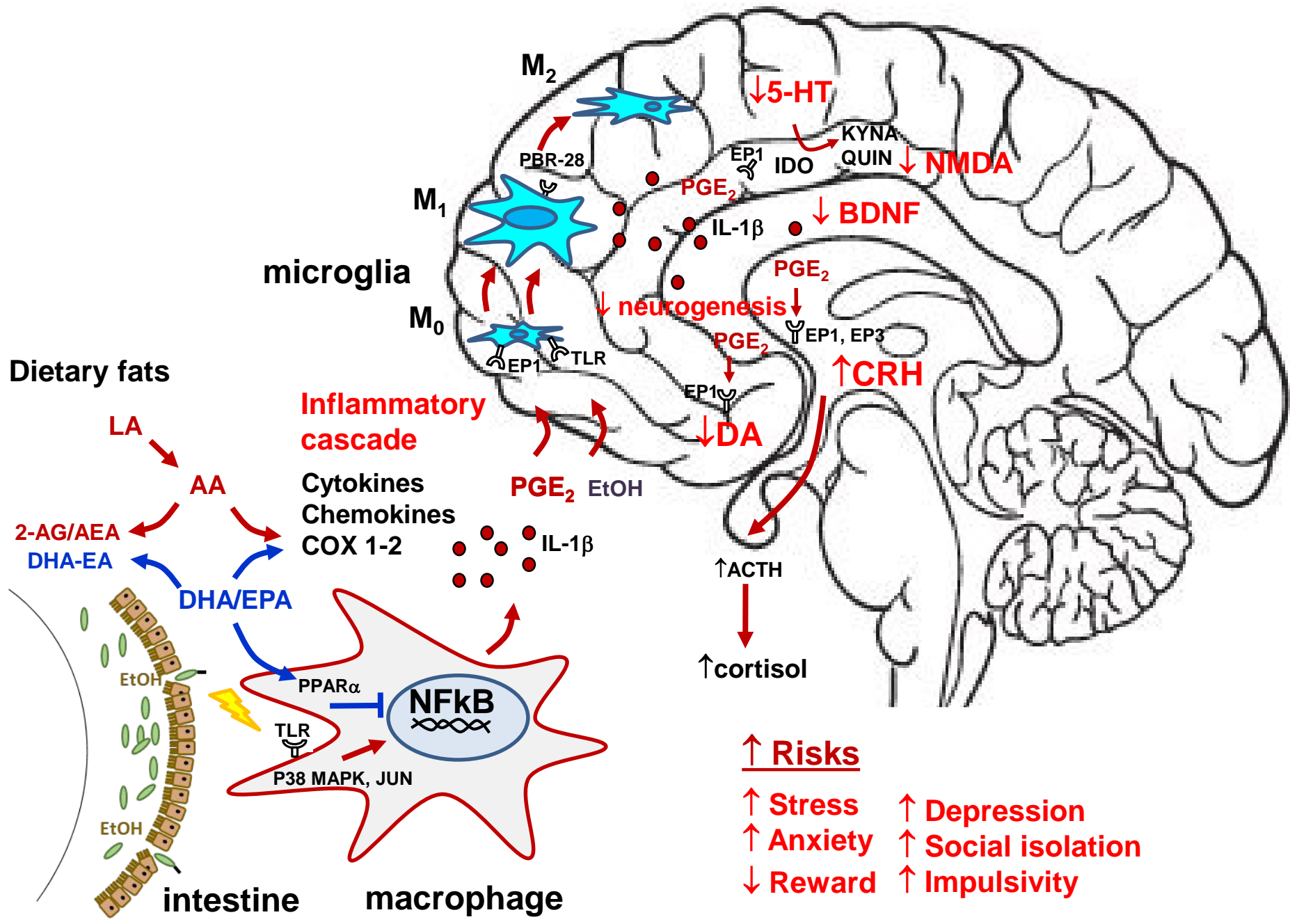
Omega-3 HUFAs - Summary of RCTs for Depression

- EPA enriched formulations appear to be effective for clinical depressions.
- Participants must have clinically significant depressive symptoms.
- Publication bias in small studies and heterogeneity is evident.
- Larger, appropriately designed studies are indicated.
- Effect sizes are good in comparison to other therapies.

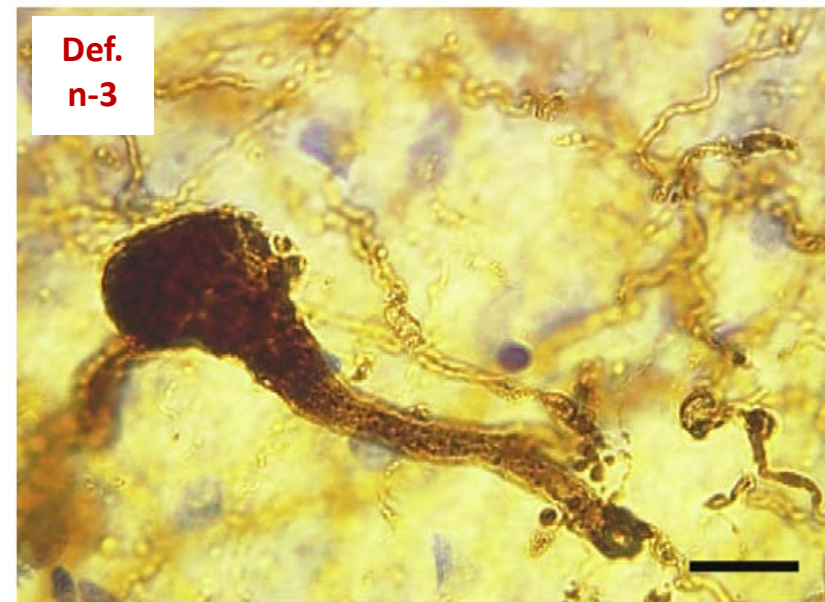
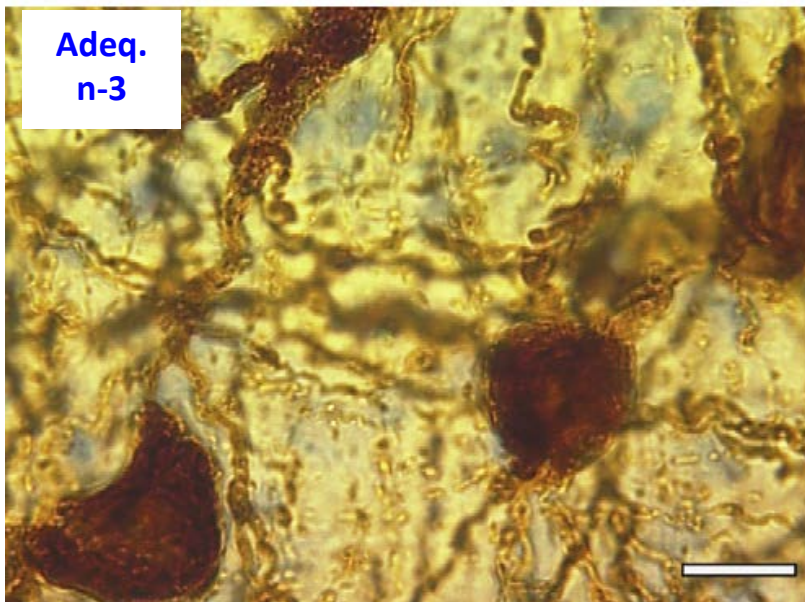
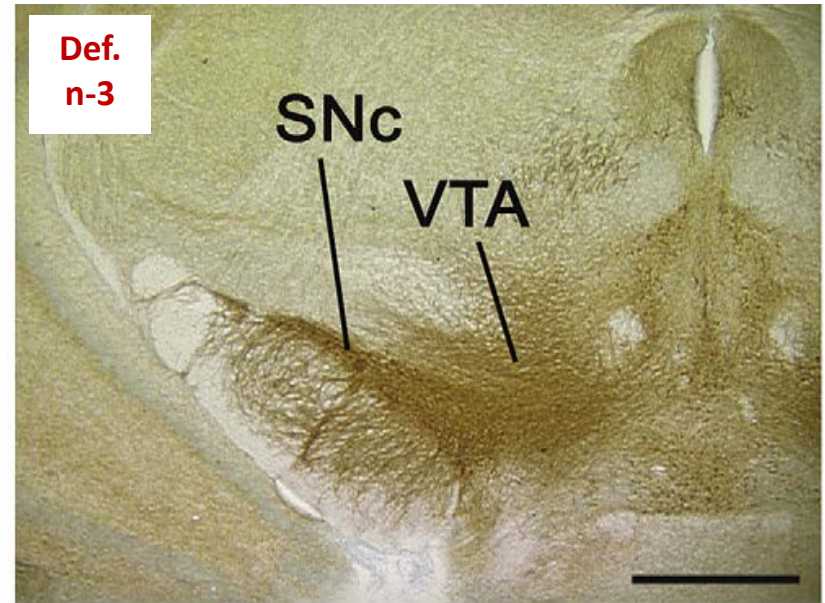
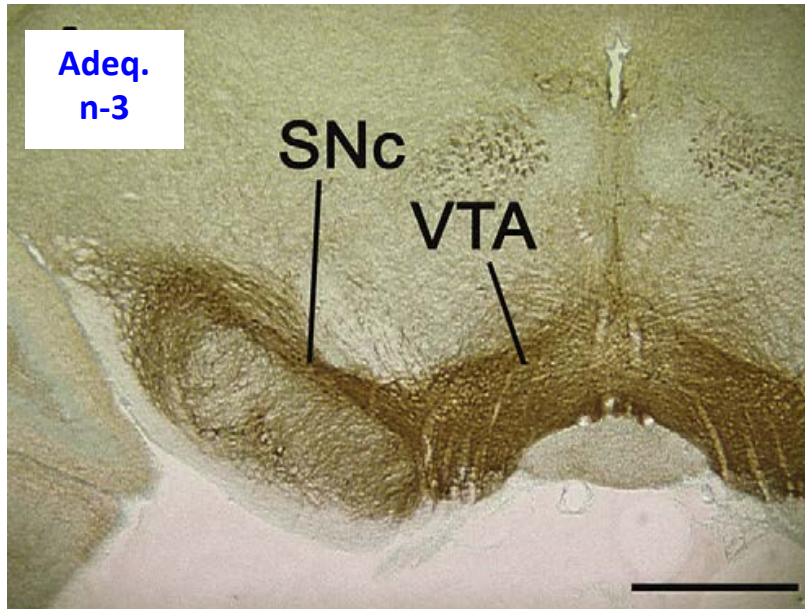
Therapies for Adult Major Depression - Effect sizes (Cohens *d*)

Psychotherapy	0.22
Antidepressants	0.30-0.31
EPA enriched omega-3 HUFAs	0.61

Dietary fats and neuro-inflammation in mental ill health



n-3 HUFA deficient diets cause a 50% loss of dopaminergic neurons

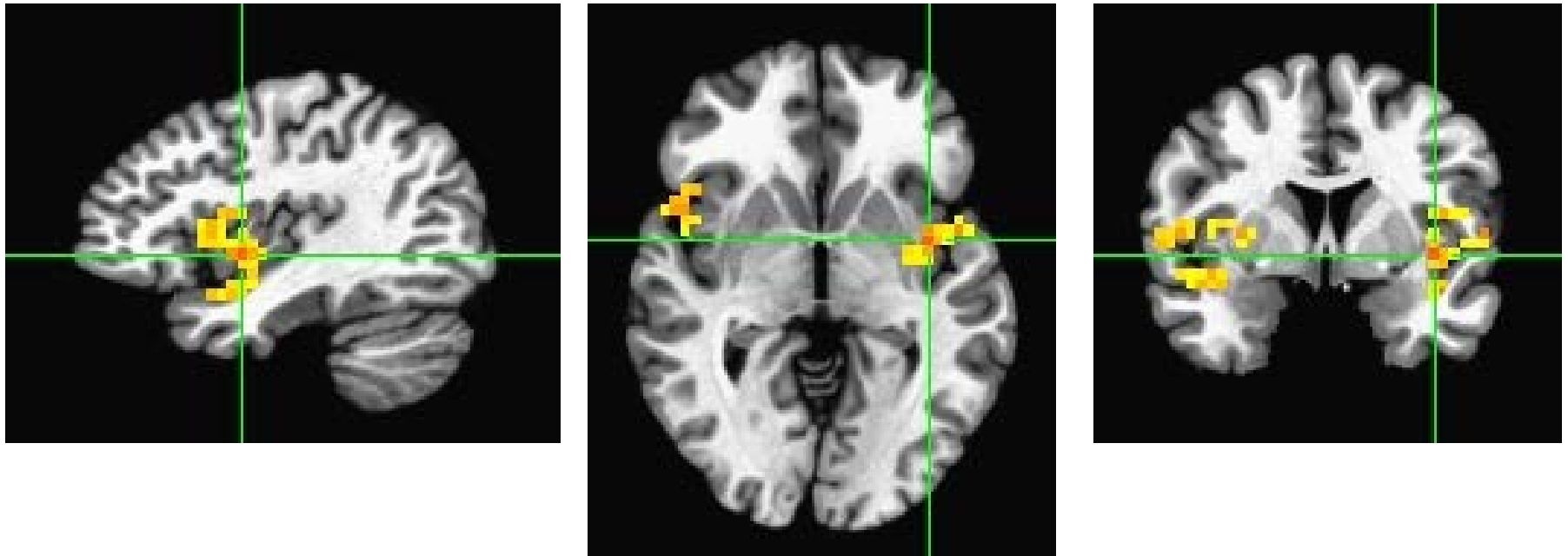


Tyrosine hydroxylase staining

n-3 HUFAs increase anticipation of total reward in Adult ADHD

Final (16 w) minus baseline, active minus placebo, MID task

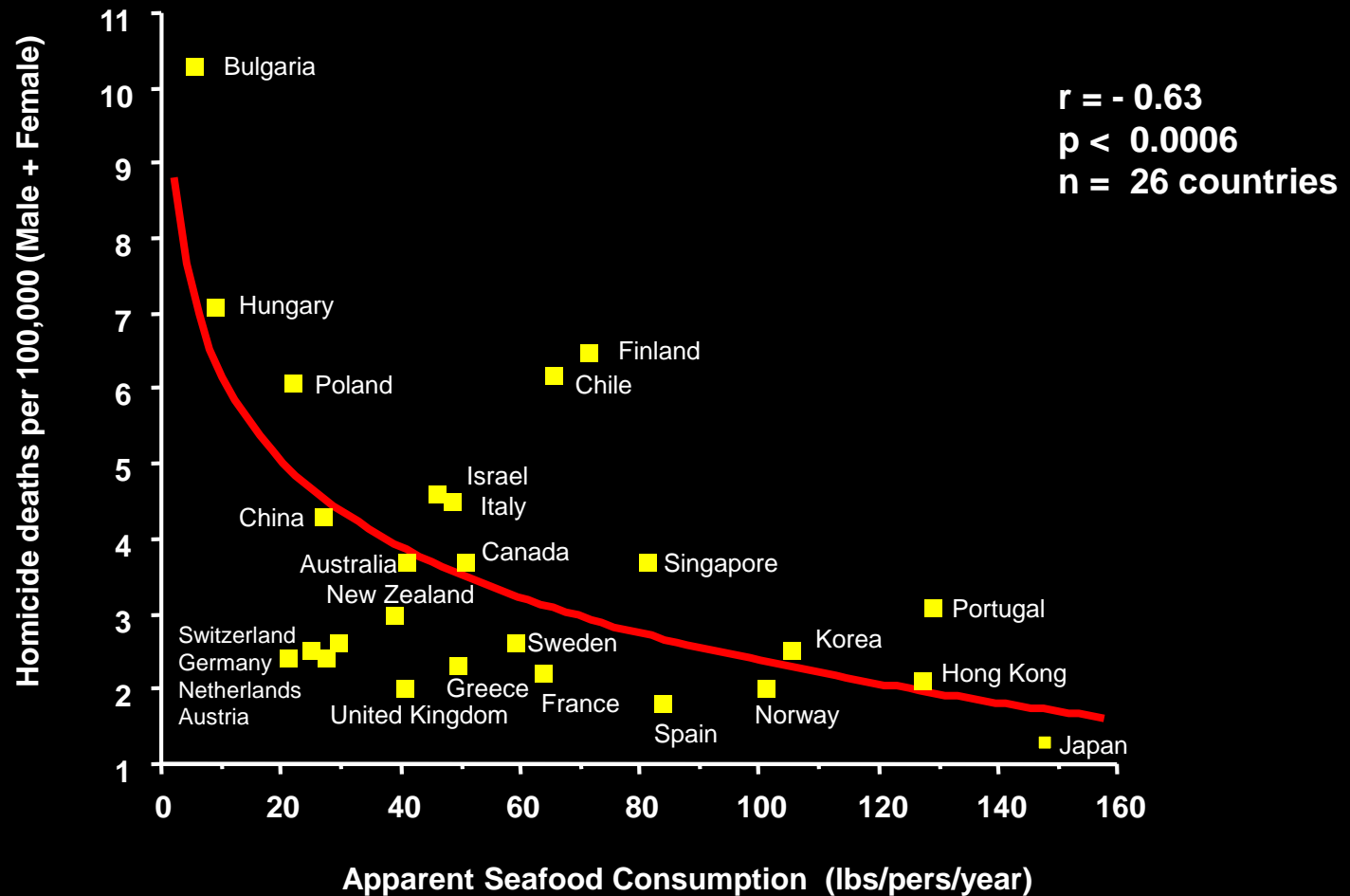
Bilateral insula and superior temporal cortex



Peak areas($\alpha < 0.01$): Rt. Superior temporal gyrus and Lt. Insula

Contiguous areas (< 0.05): R/L Insula, R/L Lentiform Nucleus, R/L Claustrum, R/L Precentral Gyrus, R/L Inferior Frontal Gyrus, Rt. Inferior Frontal Gyrus, Lt. Inferior Temporal Gyrus

Homicide Mortality Rates¹ and Seafood Consumption



¹World Health Statistics Annual 1995, WHO, Geneva Switzerland Hibbeln, JR World Rev Nutr Diet, 2001; 88; 41-46

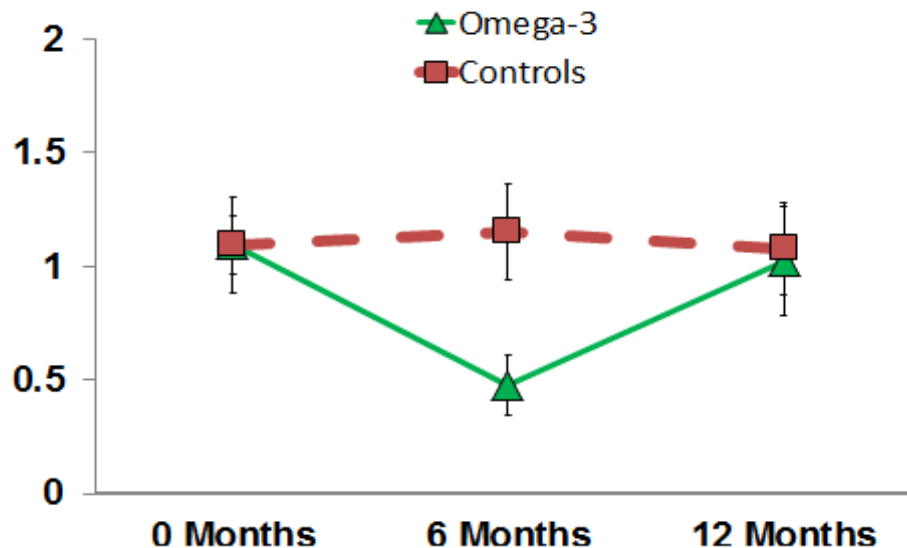
Mauritius Child Health Project

Age 8-16,
Randomized, stratified by age, gender
Blinded, 38.7% Creole, 61.3% Indian

n=95 omega-3, n= 89 placebo

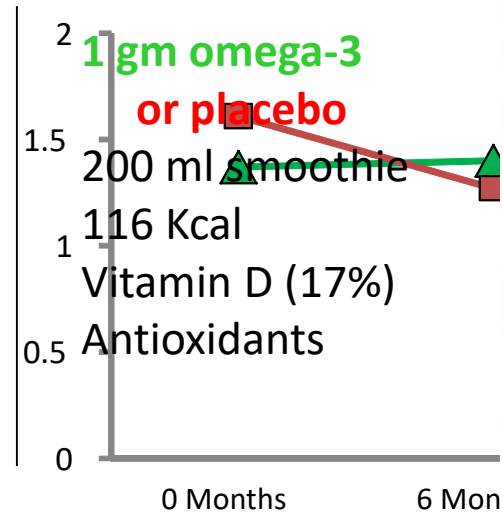
6 mo. intervention, 6 mo. follow up
Child Behavior Checklist (parent)

Child Proactive Aggression

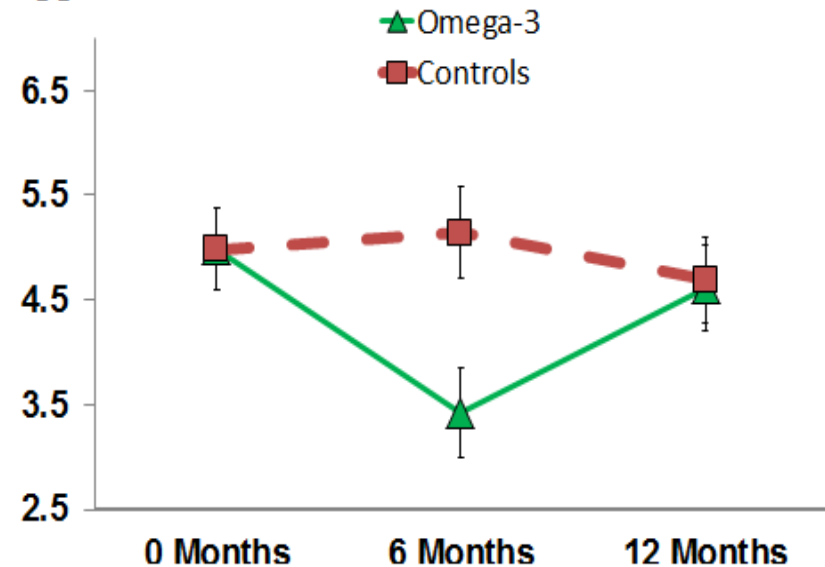


Omega-3 specific

Delinque

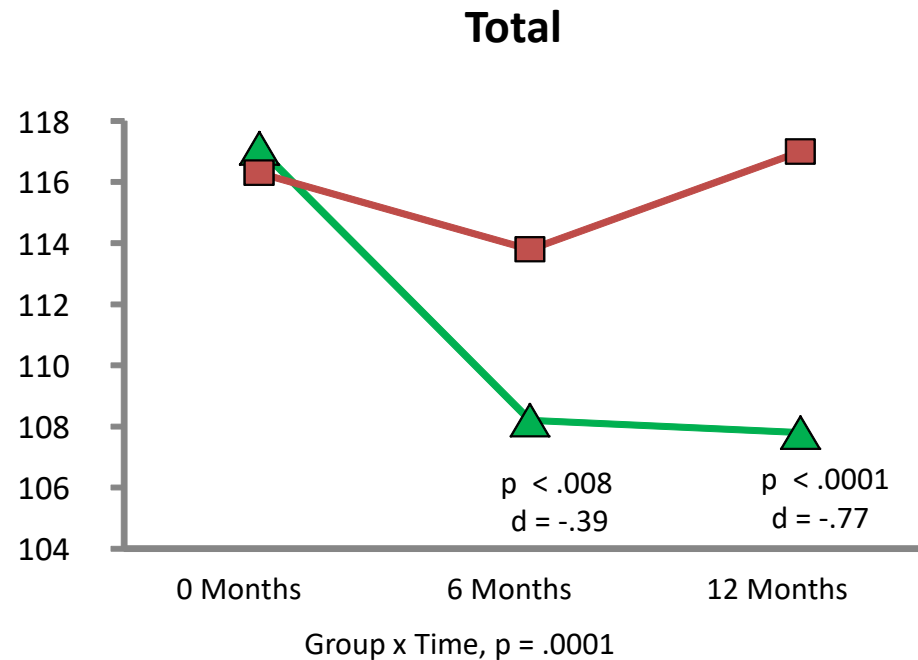


Child Reactive Aggression

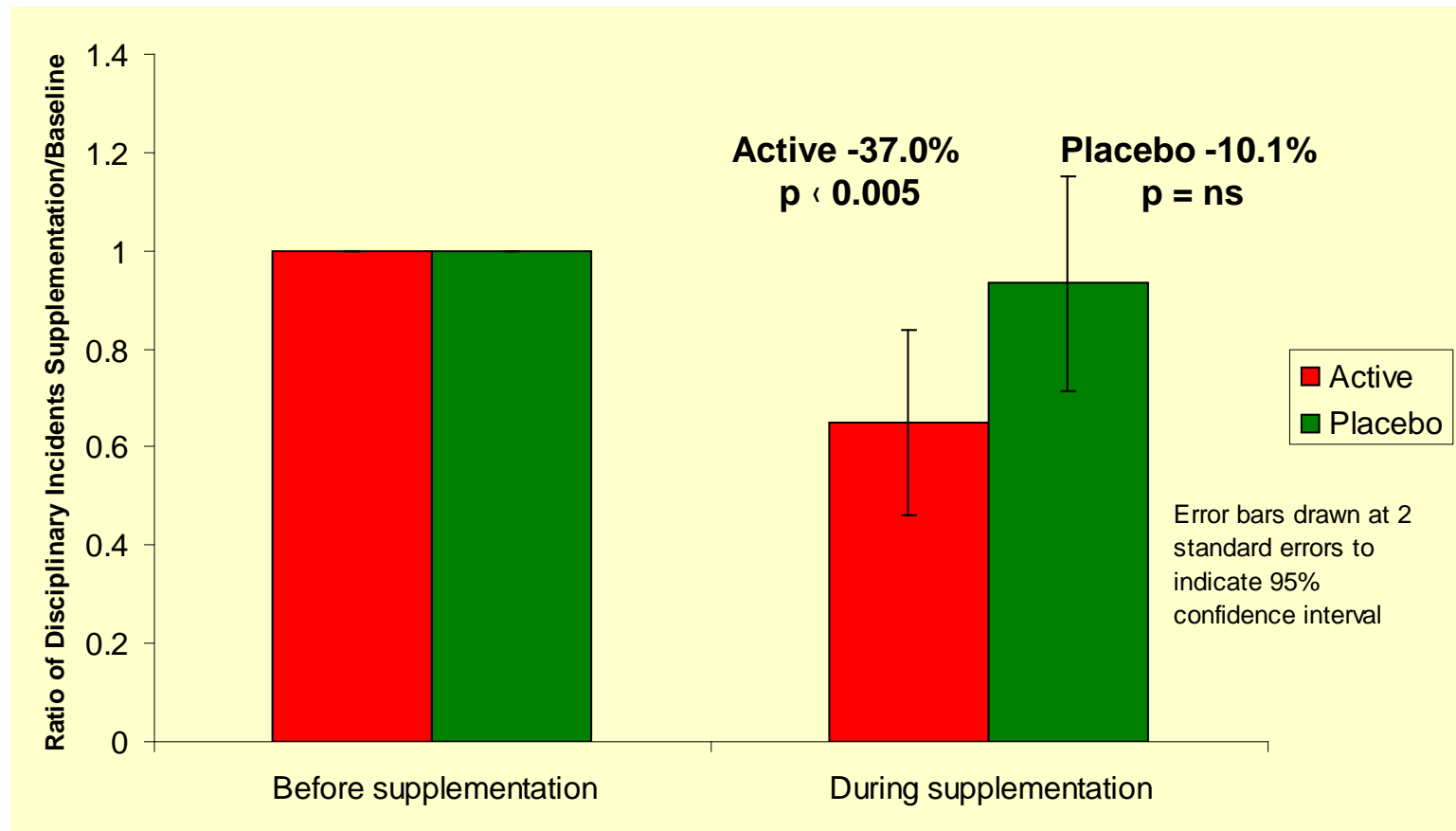


Parents were less psychopathic when their children took omega-3's

Parent Psychopathic Personality Inventory



Reduced Felony Violent Offences Among Prisoners with recommended daily amounts of vitamins, minerals and essential fatty acids



**UK maximum security prison - 338 offences among 172 prisoners
over 9 months treatment in a compared to 9 months baseline.**

***“Unless we prioritize brain nutrition,
we will become a race of morons.
The future health and intelligence of
humanity is at stake, and it’s the most
serious threat of our times”
- 1972 -***



Prof. Michael Crawford. PhD, FRSB, FRCPath,

Order of the Rising Sun, 2015, Tokyo, Japan.

Chevreur Medal, 2015, Paris, France.

Alexander Leaf Distinguished Scientist Award for
Lifetime Achievement. ISSFAL, 2016

Thank you

