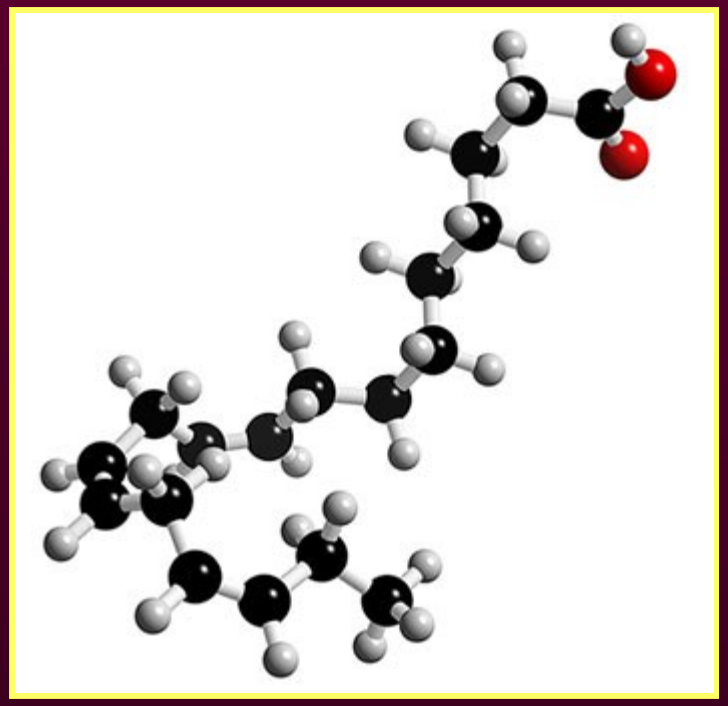
DEPRESSIONE ED OMEGA-3



Dott. Pierandrea Salvo

e

Dott.ssa Monica Baiano

Servizio per i Disturbi del Comportamento Alimentare e del Peso

ULSS 10 "Veneto Orientale", Portogruaro (VE)

Disturbi dell'umore

Disturbi depressivi

Disturbo depressivo maggiore ep. Singolo

Distrubo depressivo maggiore ricorrente

Disturbo distimico

Distrubo depressivo NAS

Epidemiologia della depressione

- Prevalenza lifetime 15%
- 4° causa di disabilità nel mondo
- Costo annuo in Europa 118 miliardi di Euro
- WHO indica che la DM causa il 6% del carico di malattia in Europa
- La fisiopatologia è poco nota
- I trattamenti non sono ancora mirati ai fattori causali

Soboki et al, 2006

Trattamento della depressione

Nome generico	Dose di partenza (mg/die)[a]	Dose usuale (mg/die)
Triciclici e tetraciclici		
• Triciclici con amine terziarie		
Amitriptilina	25-50	100-300
Clomipramina	25	100-250
Doxepina	25-50	100-300
Imipramina	25-50	100-300
Trimipramina	25-50	100-300
• Triciclici con amine secondarie		
Desipramina	25-50	100-300
Nortriptilina	25	50-200
Protriptilina	10	15-60
• Tetraciclici		
Amoxapina	50	100-400
Maprotilina	50	100-225
SSRI[b]		
Citalopram	20	20-60[c]
Fluoxetina	20	20-60[c]
Fluvoxamina	50	50-300[c]
Paroxetina	20	20-60[c]
Sertralina	50	50-200[c]
Inibitori del *reuptake* di dopamina e noradrenalina		
Bupropione[b]	150	300
Bupropione a rilascio prolungato	150	300
Inibitori del *reuptake* di serotonina e noradrenalina		
Venlafaxina[b]	37,5	75-225
Venlafaxina a rilascio prolungato	37,5	75-225
Modulatori della serotonina		
Nefazodone	50	150-300
Trazodone	50	75-300
Modulatori di noradrenalina e serotonina		
Mirtazapina	15	15-45
IMAO		
• Irriversibili, non selettivi		
Fenelzina	15	15-90
Tranilcipromina	10	30-60
• Reversibili IMAO-A		
Moclobemide	150	300-600
Inibitori selettivi del *reuptake* della noradrenalina		
Reboxetina	_d	_d

Efficacia dei trattamenti farmacologici nella depressione

- Meno del 60% dei paz depressi va in remissione di malattia con i trattamenti antidepressivi disponibili attualmente
- I benefici dei trattamenti attuali vs placebo hanno evidenza modesta

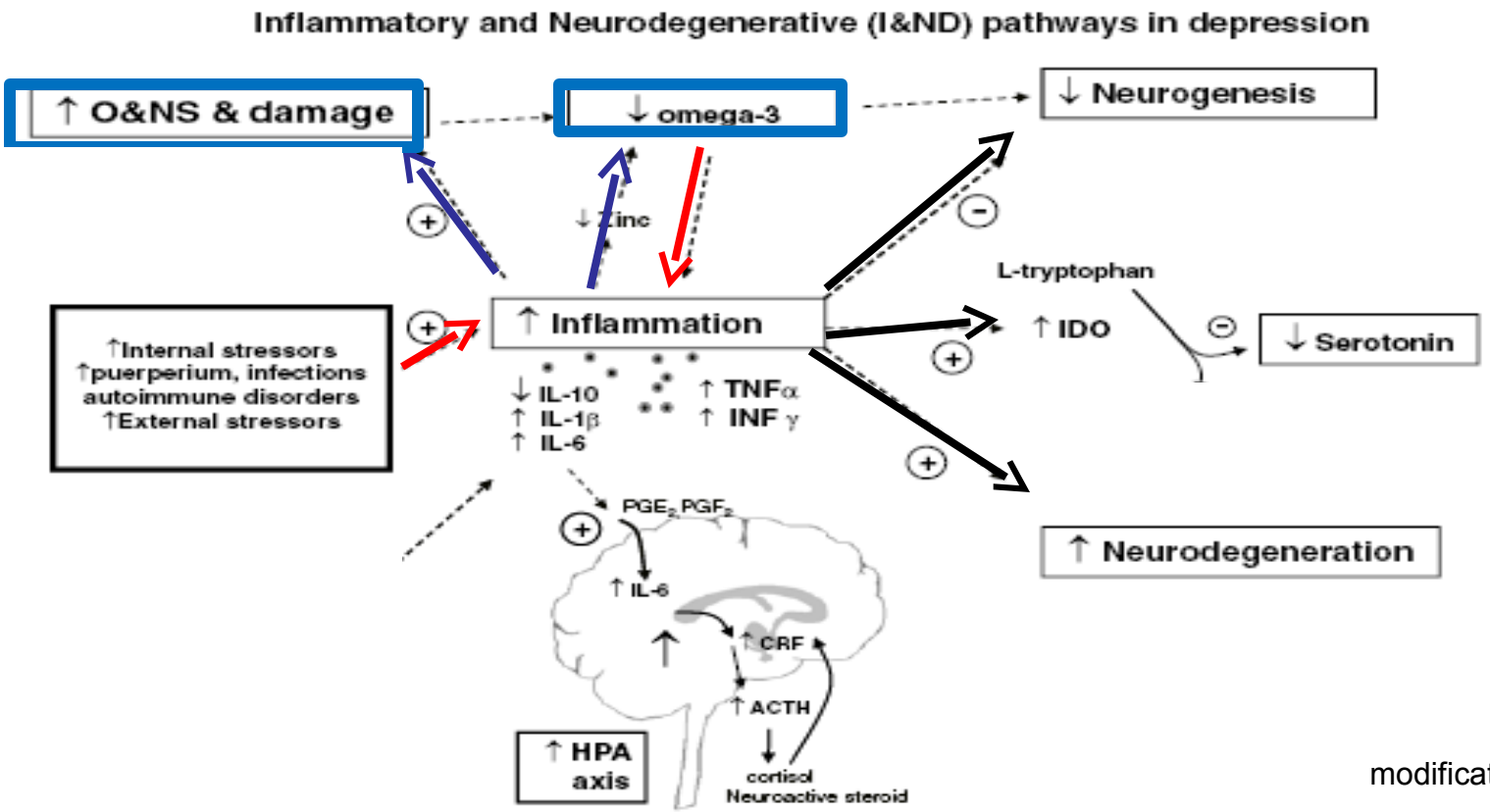
- **Bisogno di sviluppare nuove evidenze di eziopatogenesi e trattamento**

Metab Brain Dis (2009) 24:27–53
DOI 10.1007/s11011-008-9118-1

ORIGINAL PAPER

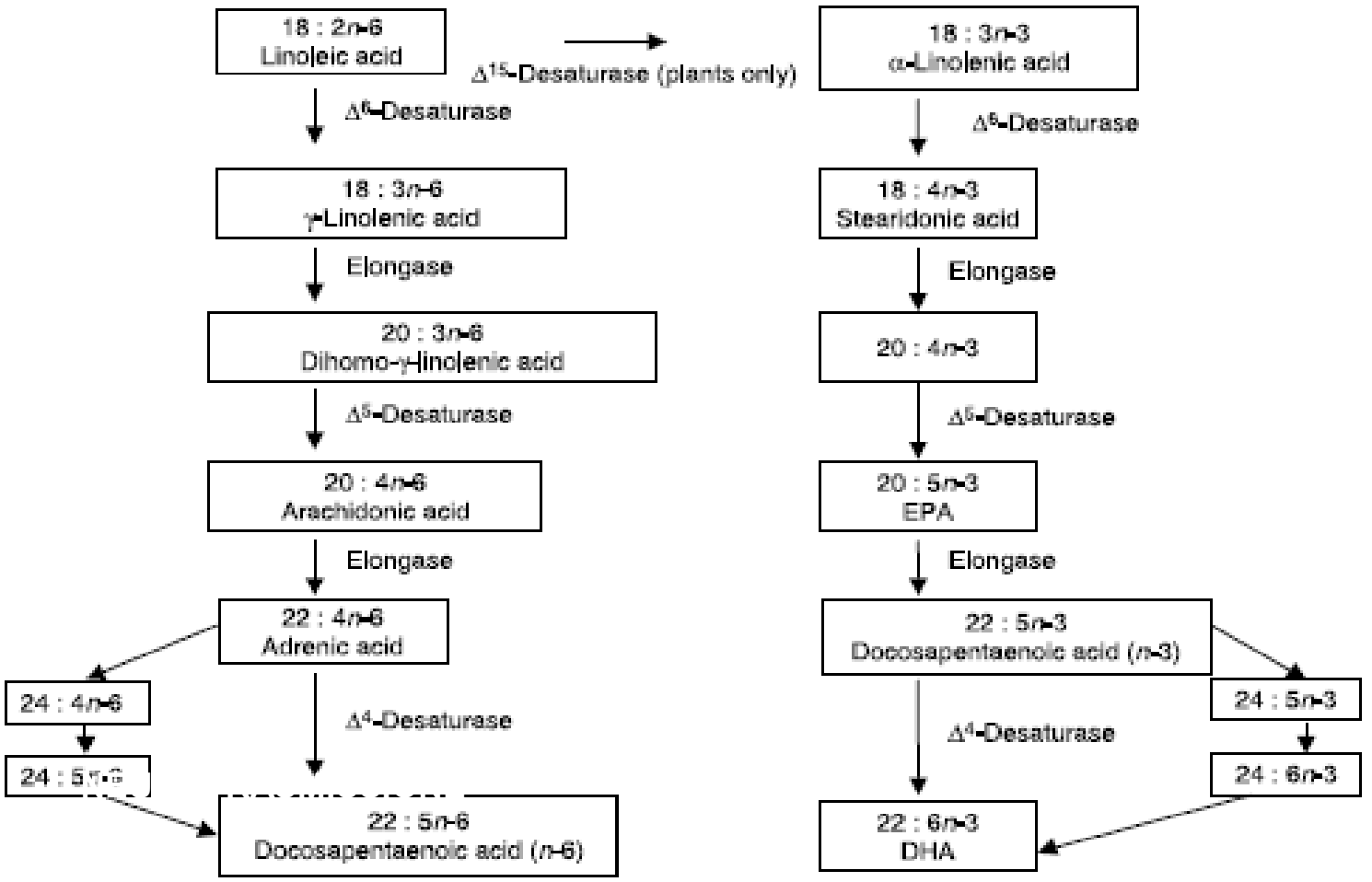
The inflammatory & neurodegenerative (I&ND) hypothesis of depression: leads for future research and new drug developments in depression

Michael Maes · Raz Yirmyia · Jens Noraberg · Stefan Brene · Joe Hibbeln · Giulia Perini · Marta Kubera · Petr Bob · Bernard Lerer · Mario Maj



modificata

Biosintesi degli ω-3 PUFA



Appleton et al. (2008), *Nutrition Research Reviews* 21: 13-41

Bartzokis (2011), *Frontiers in Bioscience* 16: 2695-2733

Fonti dietetiche

Acido cis linoleico ω6 serie

- Cereali
- Uova
- Pollami
- Olii vegetali

Acido α linoleico ω3 serie

- Pesce

Nelle diete occidentali il rapporto ω6 : ω3 è circa 10 : 1 (ottimale 1:1)

Cordain et al, 2005

ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

Journal of Psychiatric Research 43 (2009) 471–476

JOURNAL OF PSYCHIATRIC RESEARCH

www.elsevier.com/locate/jpsychires

Investigating the inflammatory phenotype of major depression: Focus on cytokines and polyunsaturated fatty acids

Timothy Dinan [a,*], Lee Siggins [b], Paul Scully [a], Sinead O'Brien [a], Paul Ross [b], Catherine Stanton [b]

[a] *Department of Psychiatry and Alimentary Pharmabiotic Centre, University College Cork, Wilton, Cork, Ireland*
[b] *Teagasc and Alimentary Pharmabiotic Centre, Moorepark, Cork, Ireland*

Received 17 April 2008; received in revised form 6 June 2008; accepted 10 June 2008

The findings of this study support our hypothesis that major depression is associated with a high ω-6:ω-3 ratio and elevation in the cytokine IL-6. Both parameters were found to be significantly correlated and overall the data indicate that depression is characterised by a peripheral pro-inflammatory phenotype. The inflammatory state persists when patients become normothymic as a result of SSRI therapy.

Nell'uomo, bassi livelli di ω-3 PUFA sono stati associati ad un aumento dell'attività pro-infiammatoria nei soggetti con depressione (MDD)

Maes et al. (2009), *Metab Brain Dis* 24:27-53; Dinan et al. (2009), *J Psychiatry Res* 43: 471-476; Maes (2011), *Progr Neuropsychopharmacol Biol Psychiatry* 35:784-794; Jazayeri et al. (2010), *Psych Res* 178:112-115; Lu et al. (2010), *Neuropsychopharm* 35: 2238-2248

Nei pazienti affetti da MDD:

- la concentrazione sierica di ω-3 PUFA a catena lunga è < rispetto ai controlli;
- la concentrazione di eicosapentaenoic acid [EPA] e Docosahenoic acid [DHA]) è < nei RBC di pazienti rispetto ai controlli, soprattutto in coloro che hanno tentato il suicidio;
- gli ω-3 PUFA sono meno rappresentati anche nel tessuto adiposo e cerebrale;
- esiste una relazione inversa tra concentrazioni sieriche (o plasmatiche) di PUFA e sintomatologia depressiva.

Fattori causali:

-dieta

-stress

Assies et al. (2010), *PLoS ONE* 5 (5) e10635
Hibbeln (2009), *World Rev Nutr Diet* 99: 17-30

Disturbo depressivo nell'adulto e ω-3

STUDIO CARDIA

Colangelo et al. (2009), *Nutrition* 25(10): 1011-1019

In this observational study, we found that fish and omega-3 fatty acid intakes are inversely associated with risk of chronic depressive symptoms in women, but not in men. These relations were independent of other major lifestyle variables.

Disturbo depressivo nell'adulto e ω-3

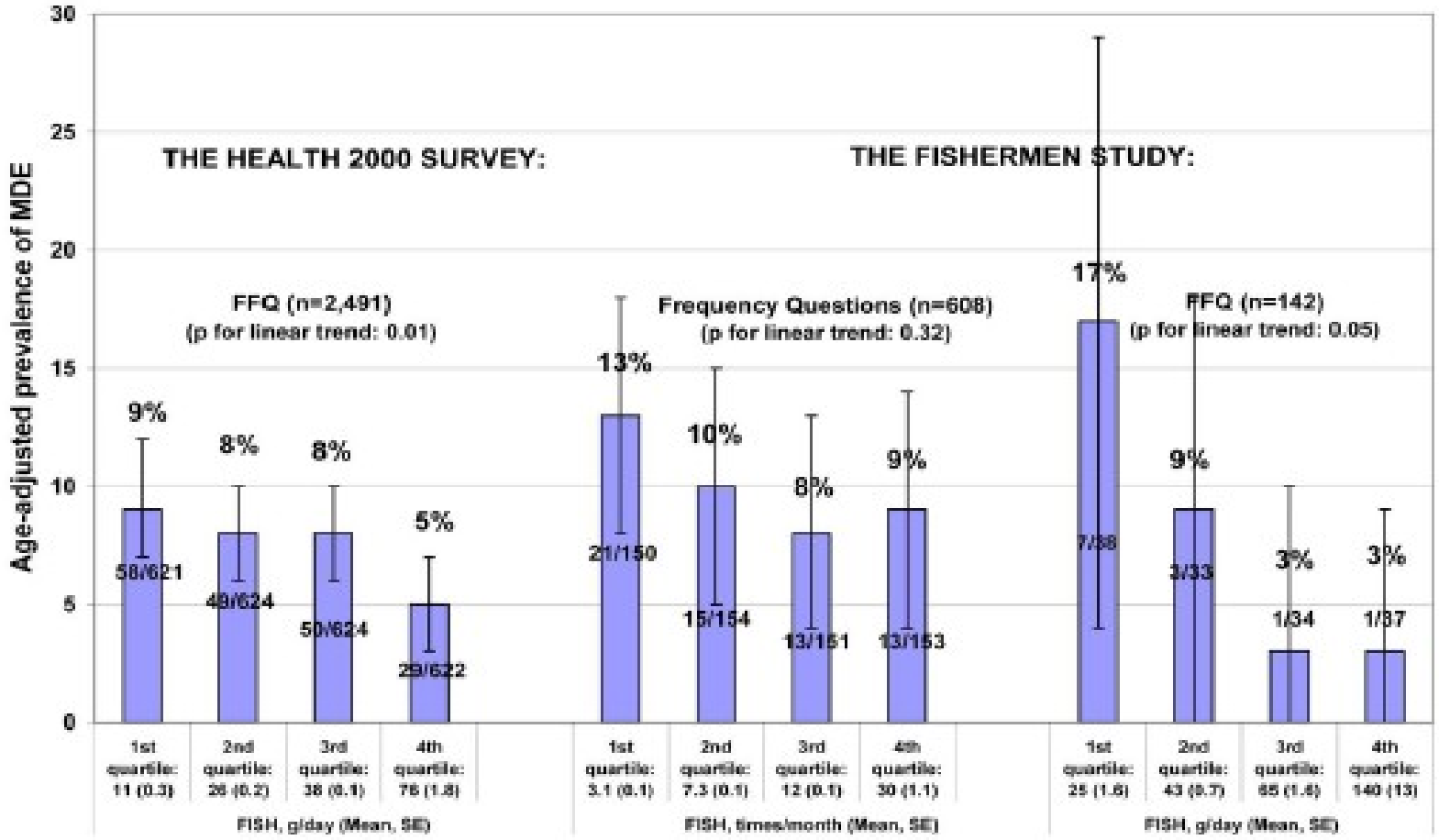


Figure 1. Age-adjusted 12-month-prevalence of depressive episodes in the men by quartiles of fish consumption.
doi:10.1371/journal.pone.0010530.g001

Fish Consumption and Omega-3 Polyunsaturated Fatty Acids in Relation to Depressive Episodes: A Cross- Sectional Analysis

Anna Liisa Suominen-Taipa

Disturbo depressivo nell'adulto e ω-3

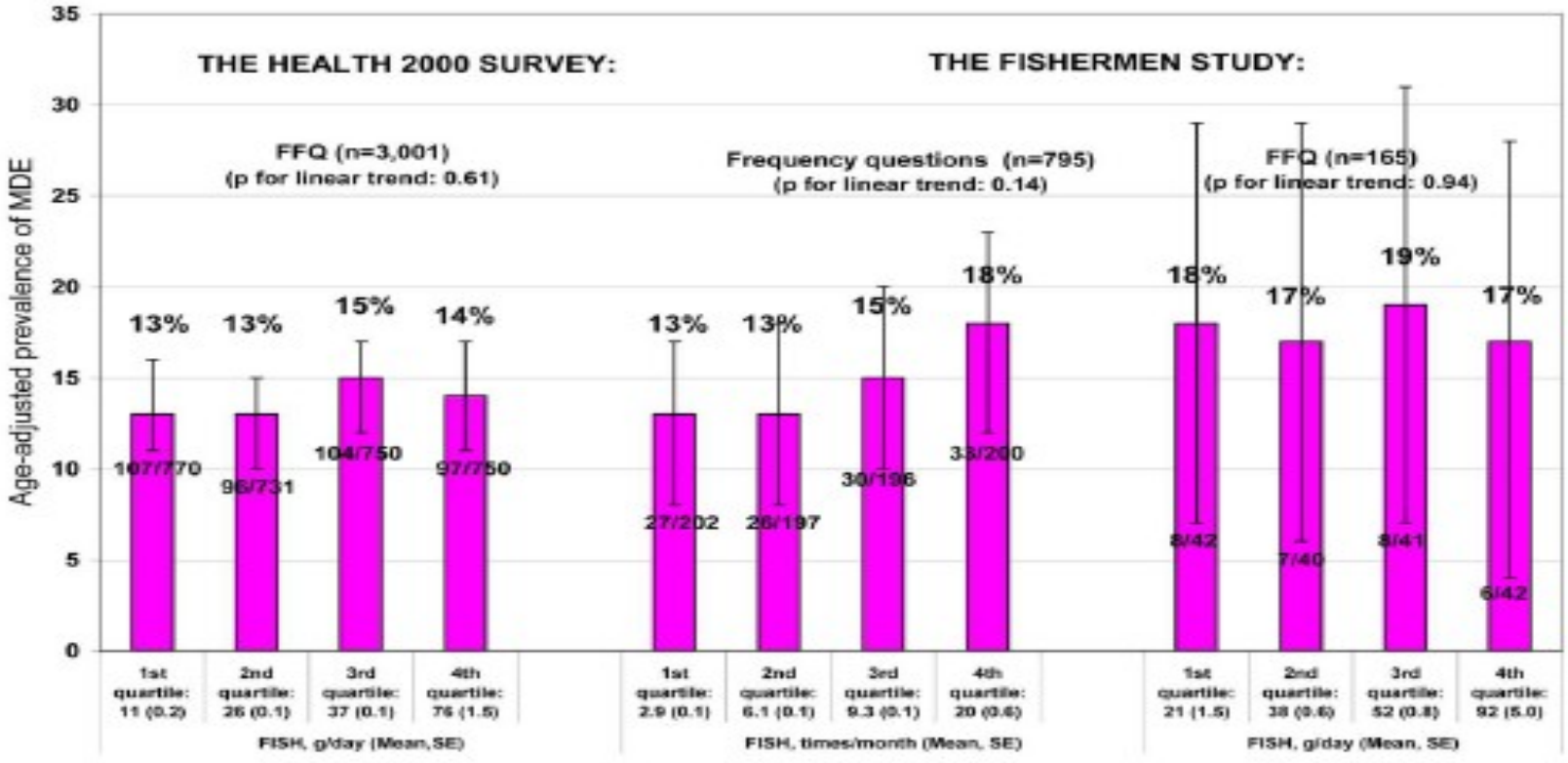
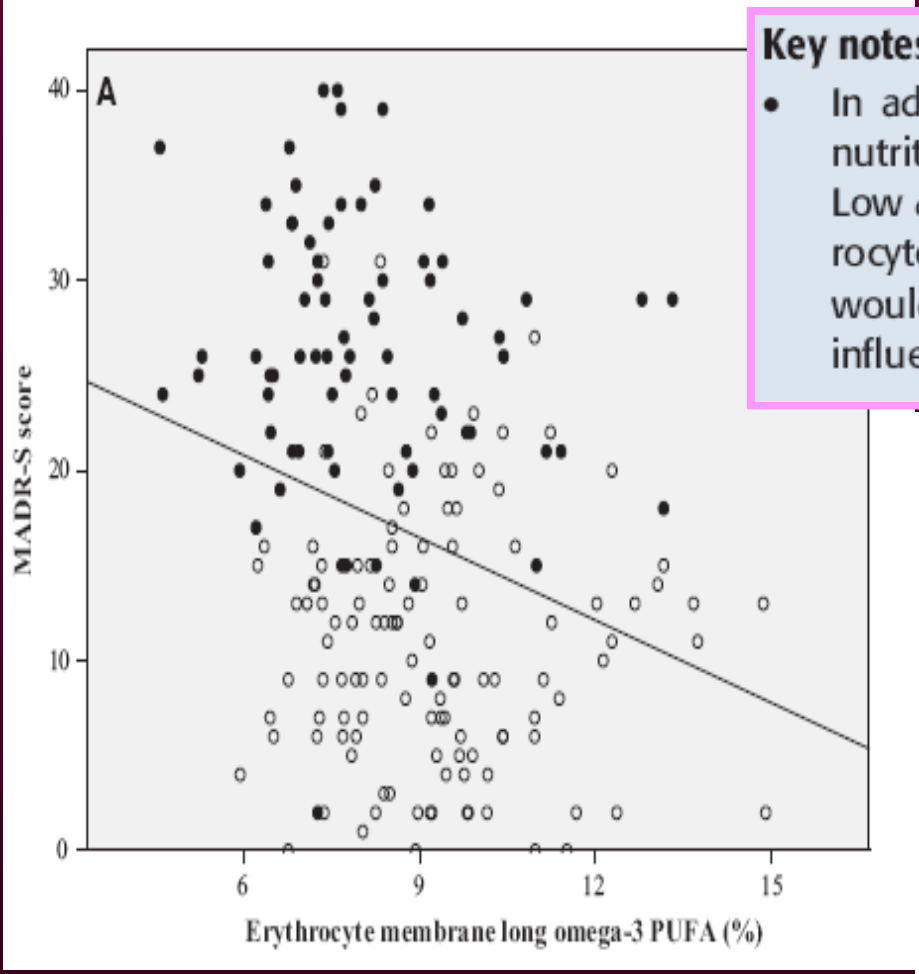


Figure 2. Age-adjusted 12-month-prevalence of depressive episodes in the women by quartiles of fish consumption.
doi:10.1371/journal.pone.0010530.g002

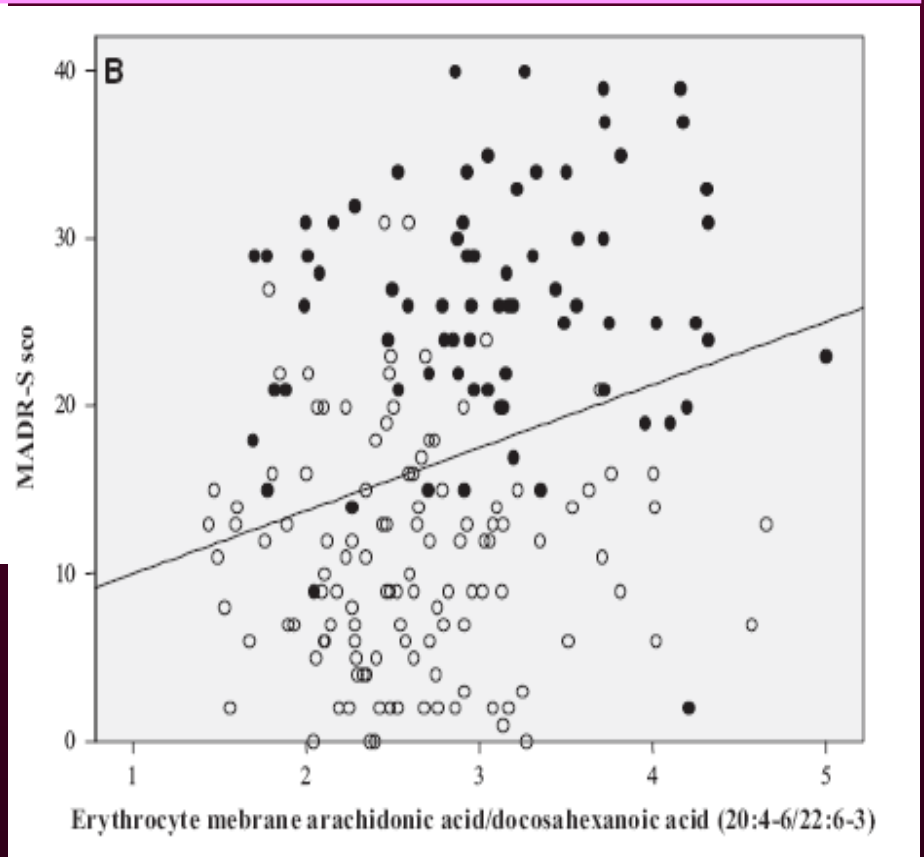
It is also possible that the lack of protective effect of fish in women is related to reverse causality. Depression may cause changes in overall food consumption in women masking the beneficial effects of fish. Another possible explanation for the gender difference may be that women are more prone to depression than men.

Disturbo depressivo nell'adolescente e ω-3



Key notes

- In adolescents with eating disorders (ED), the altered nutritional intake influences essential fatty acid status. Low $\omega 3$ polyunsaturated fatty acid proportions in erythrocyte membranes are associated with depression. This would indicate that specific nutritional deficiencies influence the expression of psychopathology in ED.



Swenne et al. (2011), *Acta Paediatrica* DOI: 10.1111/j1651-2227.2011.02400.x

Disturbo depressivo nell'adolescente e ω-3

Assunzione di n-3 PUFA e rischio di MDD nell'adolescente

TABLE 3. Spearman correlation coefficients between the BDI-Y scores at 14 and 17 years, and dietary intake (g/day) of fatty acids measured by FFQ at 14 years

Food Frequency Questionnaire

Fats and fatty acids at 14 years	Year 14 BDI-Y ($N = 1,407$) r	Year 14 BDI-Y ($N = 1,407$) P	Year 17 BDI-Y ($N = 995$) r	Year 17 BDI-Y ($N = 995$) P
Total fat	−.054	.04**	−.099	<.01***
Saturated fat	−.058	.03**	−.098	<.01***
Monounsaturated fat	−.055	.04**	−.097	<.01***
Polyunsaturated fat	−.002	.94	−.041	.19
Total n-3 PUFA	−.035	.19	−.066	.04**
ALA 18:3(n-3)	−.035	.19	−.089	<.01***
EPA 20:5(n-3)	−.067	.01**	−.062	.05**
DPA 22:5(n-3)	−.070	<.01***	−.075	.02**
DHA 22:6(n-3)	−.042	.11	−.038	.23
n-3 LCPUFA (EPA+DPA+DHA)	−.063	.02**	−.069	.03**
Total n:6 PUFA	.003	.91	−.037	.24
LA 18:2(n-6)	.005	.86	−.036	.25
Eicosadienoic acid 20:2(n-6)	−.041	.12	−.062	.05**
dGLA 20:3(n-6)	−.063	.02**	−.066	.04**
Arachidonic acid AA 20:4(n-6)	−.062	.02**	−.067	.04**
Bosseopentaenoic acid 20:5(n-6)	−.039	.14	−.006	.85
Adrenic acid 22:4(n:6)	−.060	.02**	−.078	.01**
AA:EPA	.025[a]	.34	.009[b]	.77
AA:DHA	.020	.46	.004	.90
Total n-6:total n:3	.028	.30	.032	.32

…. it is likely that while an inverse relationship exists between n-3 PUFA intake and depressive symptoms in adolescents, much of this relationship may be accounted for by overall energy intake, and other confounders.

Oddy et al. (2011), *Depr Anx* 28 : 582–588 (2011)

Disturbo depressivo nell'anziano e ω-3

- Tende ad essere una condizione persistente o ricorrente che può comportare frequenti accessi ospedalieri, aumentare la lunghezza della degenza, incrementare l'uso di farmaci, fino all'abuso.
- Incide negativamente sul funzionamento cognitivo e accresce il rischio di eventi cerebro e cardiovascolari e diabete.
- Le forme subsindromiche condizionano altrettanto profondamente la qualità di vita.

Necessita' di nuovi trattamenti:

- Privi di effetti avversi
- Efficaci
- Profilo farmacocinetico e farmacodinamico mirato

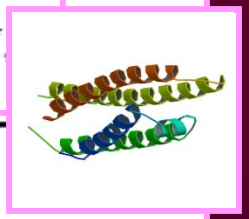
Disturbo depressivo nell'anziano e ω-3

Table

Omega-3 fatty acids and cognitive decline: modulation by ApoEε4 allele and depression

Cécilia Samieri[a,d,*], Catherine Féart[a,d], Cécile Proust-Lima[c,d], Evelyne Peuchant[e,f], Jean-François Dartigues[b,d], Hélène Amieva[b,d], Pascale Barberger-Gateau[a,d]

Neurobiology of Aging 32 (2011) 2317.e13–2317.e22



pEPA + ApoE carriers/sintomi depressivi

=

Rallentato decadimento cognitivo

pDHA+ApoE carriers

=

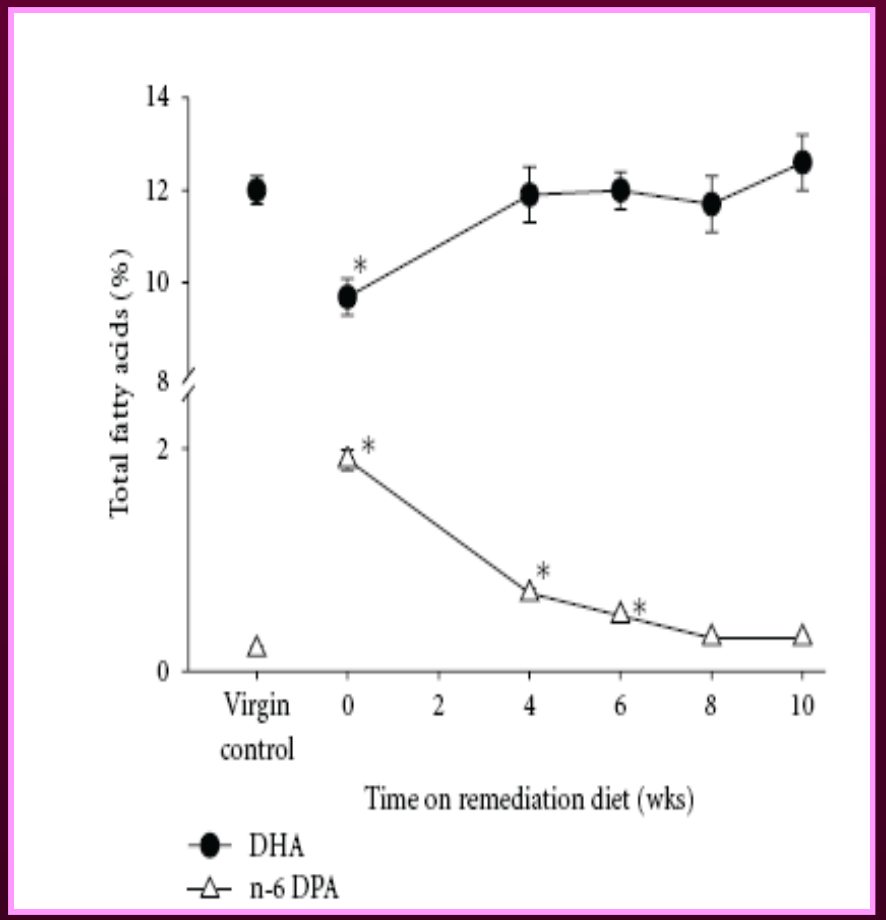
Rallentato decadimento cognitivo

Geriatric depression scale-15										
Baseline										
All pa								0.		
Non-a								−0.		
Final										
All pa								0.		
Non-a								−1.		
Change										
All participants	32	−1.24	2.50	29	−0.30	2.77	−1.64	0.10[b]	5.35	0.03[d]
Non-antidepressant	28	−1.47	2.51	23	−0.08	3.05	−1.76	0.08[b]	7.96	0.00[d]
Fish oil group										
All participants	32						2.82	0.00[g]		
Non- antidepressant	28						3.07	0.00[g]		
Placebo group										
All participants	29						0.26	0.79[g]		
Non-antidepressant	23						0.13	0.89[g]		

Tajalizadekhoob et al. (2011), *Eur Arch Psychiatry Clin Neurosci* DOI 10.1007/s00406-011-0191-9

Disturbo depressivo in gravidanza e ω-3

Effetti della dieta correttiva sulla composizione di fosfolipidi cerebrali DHA e n-6-DPA nella fase post-partum di ratti deprivati di n-3PUFA



Levant (2011) *Depression Research and Treatment*

doi: 10.1155/2011/467349

Disturbo depressivo in gravidanza e ω-3

TABLE 3. Unadjusted[a] and Adjusted[b] Associations of Maternal High Levels of Depressive Symptoms at 32 Weeks' Gestation by Omega-3 Intake From Seafood (n = 9960)

Omega-3 Intake (g/wk)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
None	1.97 (1.63–2.38)	1.54 (1.25–1.89)
0.1–0.4	1.64 (1.37–1.96)	1.37 (1.13–1.66)
0.4–1.5	1.31 (1.13–1.52)	1.20 (1.03–1.41)
>1.5[c]	1.00	1.00
P for trend	<0.0001	<0.0001

[a]Data restricted to those mothers with complete data on confounders.

[b]Adjusted for estimated energy intake, maternal age, maternal education, maternal smoking, maternal ethnic background, housing tenure, crowding, childhood life events, recent life events, chronic stress (FAI), parity, and outcome of immediately preceding pregnancy.

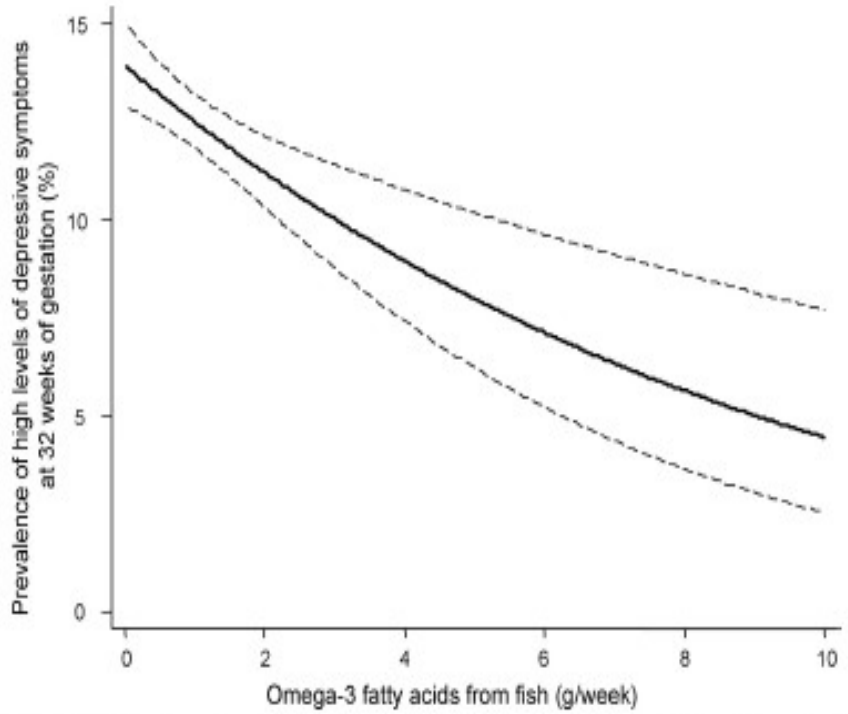


FIGURE 1. Results of model to show the prevalence of high levels of depressive symptoms with increasing omega-3 intake from seafood.

Golding et al. (2009), *Epidemiology* 20(4) 598-602

Disturbo depressivo in gravidanza e ω-3

				Baseline score (HAM-D)		End point score (HAM-D)	
Study design	Sample size	Daily dose (g)	Study duration	ω3	PBO	ω3	PBO
OL	15	0.93-2.8	8.3	18.4±3.8	-	12±5.5	-
DB-RCT	24	3.4	8	22.1±5.0	21.8±3.9	9.0±4.0	13.8±5.3
DB-RCT	51	1.9	8	18.86±3.43	17.43±2.19	2.82 ±5.48	9.91±4.74
DB-RCT	26	2.05	6	19.7± 4.8	•19.0±3.5	7.9±5.1	9.7±5.1
OL	16	0.5, 1.4, 2.8	8	19.1	-	10.0	-
DB-RCT	89	~0.2	4	7.1±4.7*	6.5±4.2*	5.8±7.1*	4.8±5.9*

OL=open label; DB-RCT=double blind Randomized controlled trial; *BDI

Modificato da: Boria & Marino (2010), *Pharmacotherapy* 30(2): 210-216

Depressione unipolare e bipolare ed ω-3

The role of omega-3 fatty acids in mood disorders

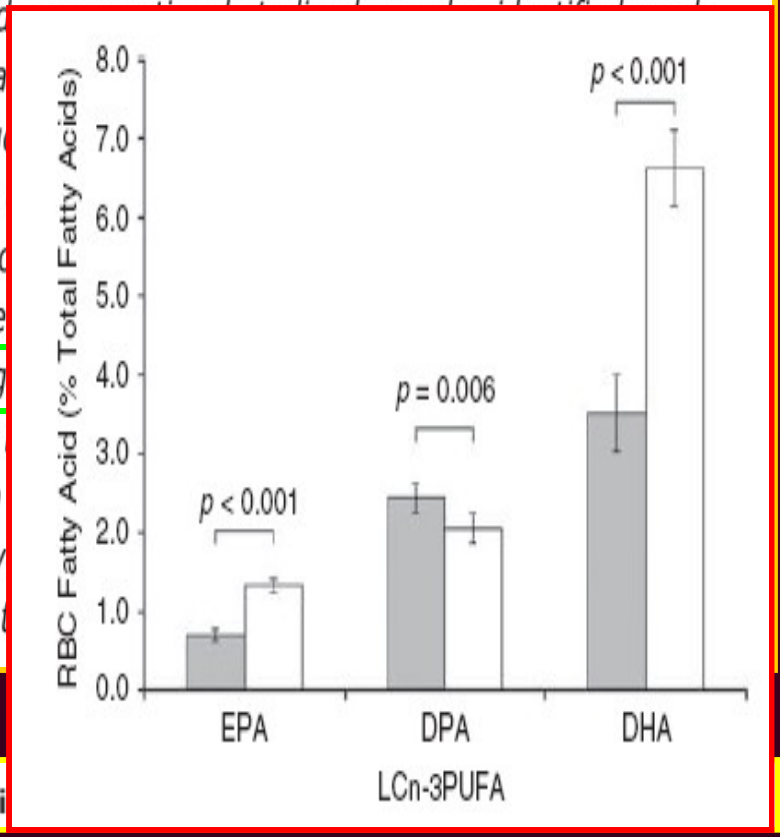
Lauren A Stahl[1], Denovan P Begg[1], Richard S Weisinger[1] & Andrew J Sinclair[2]*

Table 1 Clinician and parent ratings of mood and behaviour before and after the consumption of 360 mg per day EPA and 1560 mg per day DHA for 6 weeks by children and adolescents diagnosed with JBD

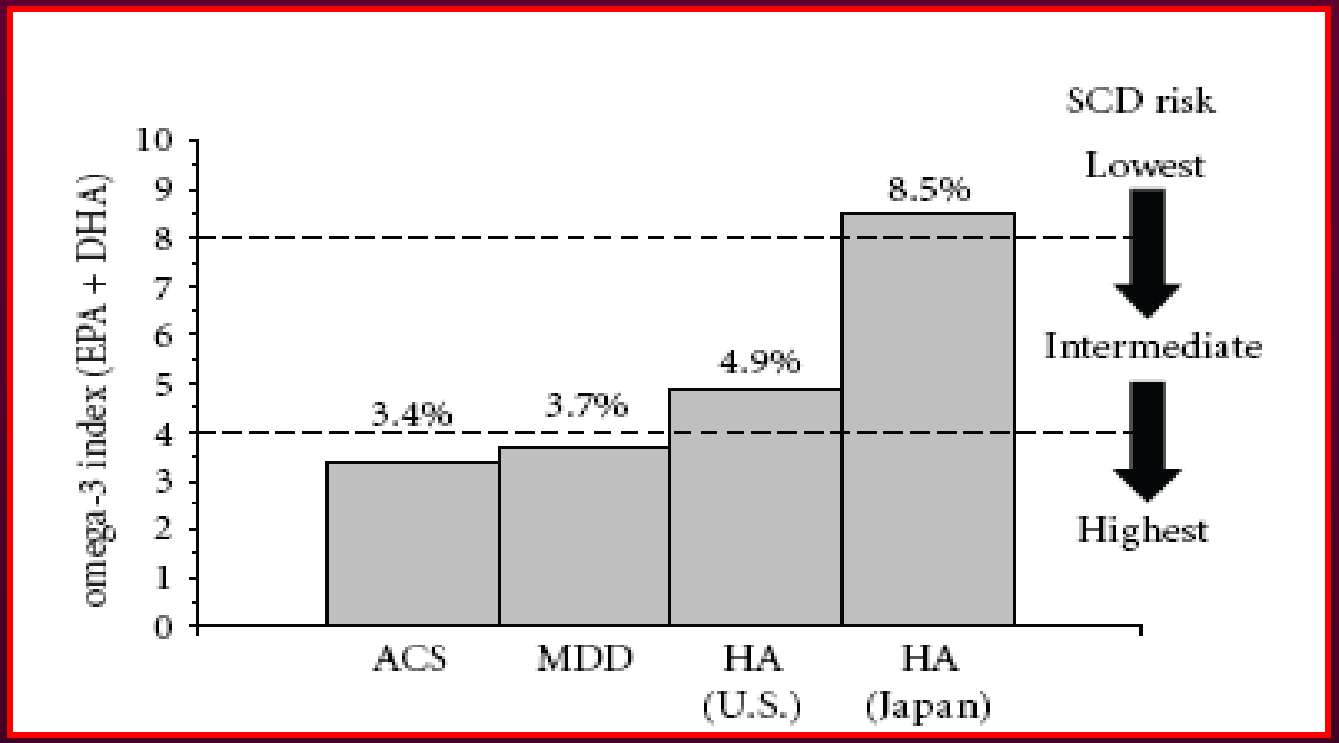
Scale/subscale[a]	*Baseline*	*Post intervention*	*P-value*
Clinician ratings			
Mania	13.1 (±1.66)	6.3 (±1.82)	0.004
Depression	12.0 (±1.52)	5.6 (±1.64)	0.002
Global functioning	50.8 (±2.20)	65.0 (±2.41)	<0.001
Parent ratings			
CBCL-PR—internal	71.2 (±2.67)	65.7 (±2.80)	0.009
CBCL-PR—external	67.3 (±2.50)	62.5 (±2.60)	0.014
CBCL-PR—total	71.6 (±2.67)	64.8 (±2.87)	0.010

Abbreviation: CBCL-PR, Child Behaviour Checklist—Parent Report.
[a]Mania, Young Mania Rating Scale (YMRS); Depression, Hamilton Depression Rating Scale (HAM-D); Global functioning, Global Assessment Scale for Children (C-GAS).

ain omega-3 polyunsaturated fatty acid (PUFA), plays



Disturbo depressivo, eventi CV e ω-3



Il rischio di morte cardiaca improvvisa (SCD) è comparabile nei pazienti con sindrome coronarica acuta (ACS) e pazienti con MDD

McNamara (2009), *Cardiovascular Psychiatry and Neurology* doi:10.1155/2009/362795

Chang et al. (2009), *Cardiovascular Psychiatry and Neurology* doi: 10.1155/2009/725310

Studi epidemiologici ed evidenze sperimentali suggeriscono che gli ω-3 PUFA possono avere un ruolo nella prevenzione e nel miglioramento clinico dei disturbi dell'umore, in particolare disturbo depressivo (MDD), depressione post-partum (DPP) e disturbo bipolare (DB)

Behavioural Brain Research 219 (2011) 116–122

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Research report

Chronic ω-3 fatty acids supplementation promotes beneficial effects on anxiety, cognitive and depressive-like behaviors in rats subjected to a restraint stress protocol

Anete Curte Ferraz[a,*], Ana Marcia Delattre[a], Rhiana G. Almendra[a], Marina Sonagli[a], Conrado Borges[a], Paula Araujo[b], Monica L. Andersen[b], Sergio Tufik[b], Marcelo M.S. Lima[a]

Psychoneuroendocrinology (2009) 34, 199–211

available at www.sciencedirect.com

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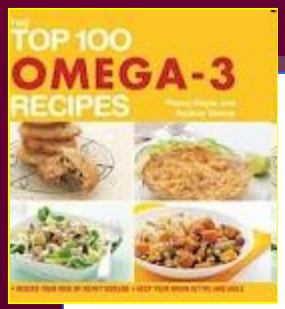
journal homepage: www.elsevier.com/locate/psyneuen

PUFA induce antidepressant-like effects in parallel to structural and molecular changes in the hippocampus

Venugopal Reddy Venna[a,1], Dominique Deplanque[a,1], Cécile Allet[b,2], Karim Belarbi[b,2], Malika Hamdane[b,2], Régis Bordet[a,*]



Complementary Therapies in Clinical Practice 17 (2011) 107–112

Contents lists available at ScienceDirect

Complementary Therapies in Clinical Practice

journal homepage: www.elsevier.com/locate/ctcp

Food as medicine in psychiatric care: Which profession should be responsible for imparting knowledge and use of omega-3 fatty acids in psychiatry

Berit Johannessen*, Ingjerd Skagestad, Anne Mari Bergkaasa

University of Agder, Faculty of Health and Sports, Institute of Health and Nursing Science, Norway

Disturbo depressivo, eventi CV e ω-3

Association between Omega-3 Fatty Acids and Depressive Symptoms among Patients with Established Coronary Artery Disease: Data from the Heart and Soul Study

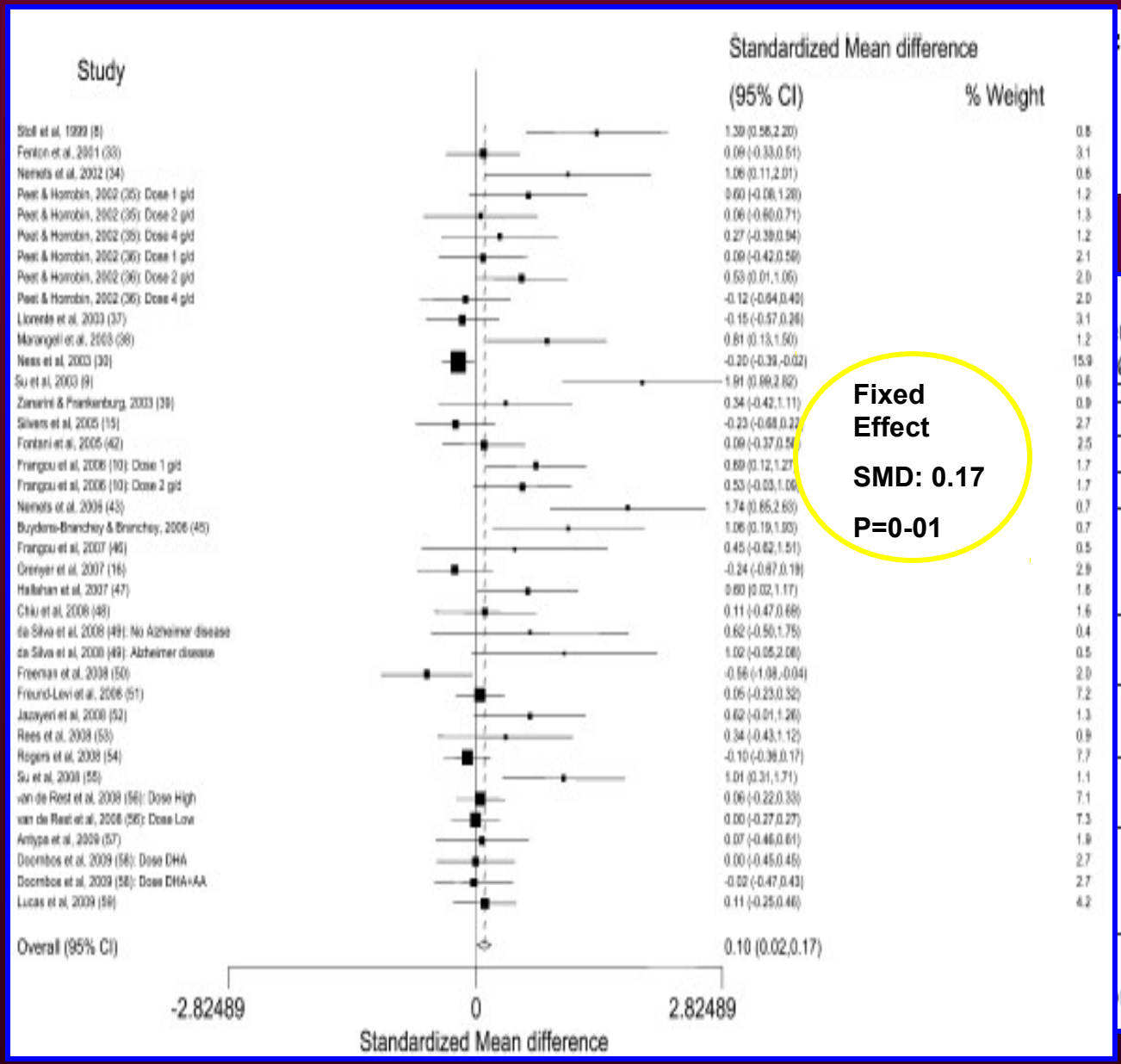
Sadia Ali[a], Sachin K. Garg[d], Beth E. Cohen[a,b], Prashant Bhave[b], William S. Harris[e], and Mary A. Whooley[a,c]

- Studio di coorte prospettico condotto su 987 pz con diagnosi di patologia coronarica
- Misurazione dei PUFA nelle plasmamembrane di RBC e determinazione di sintomatologia depressiva mediante PHQ-9 (cut-off: >10)
- Relazione inversa tra concentrazione di PUFA e sintomi depressivi

Uso di supplementi a base di n-3 PUFA in pz con patologia coronarica e MDD?

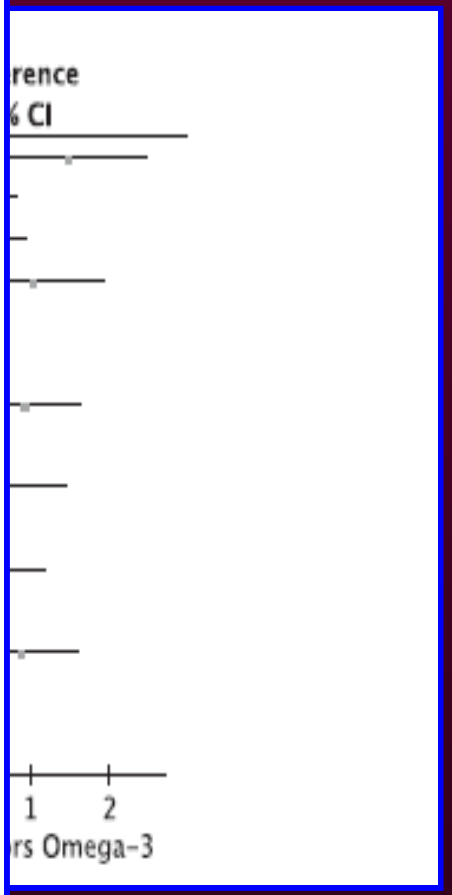
Psychother Psychosom. 2009 ; 78(2): 125–127. doi:10.1159/000203118.

In conclusione...



Appleton et. Al (2010)

Am J Clin Nutr 91:757-770



Review

Adjuvant use of nutritional and herbal medicines with antidepressants, mood stabilizers and benzodiazepines

Jerome Sarris [a,*], David J. Kavanagh [b], Gerard Byrne [a]

TAKE HOME MESSAGES

- ✓ **Gli ω-3 PUFA sembrano avere un effetto timo-modulatore ed antidepressivo quando associati a terapie farmacologiche ben consolidate (potenziamento?)**
- ✓ **L'impiego degli ω-3 PUFA in monoterapia potrebbe essere indicato nella MDD infantile**
- ✓ **Le evidenze a sostegno di un uso razionale degli ω-3 PUFA nel DB e nella DPP non sono ancora robuste**

Freeman & Rapaport (2011), *J Clin Psychiatry* 72:2; Owen et al. (2008), *Curr Opin Psych* 21:19-24; Pawels et al., (2008), Drug New Perspectives 21(8):446-451; Sarris et al. (2010), J Psych Res 44: 32-41