OXIDATIVE STRESS SEVERITY PREDICTS OMEGA-3 FATTY ACID TREATMENT EFFICACY FOR IMMEDIATE RECALL IN CORONARY ARTERY DISEASE

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BACKGROUND

- Coronary artery disease (CAD) is associated with deficits in memory, which may increase the risk of mild cognitive impairment and dementia
- Oxidative stress damage to lipids (lipid peroxidation) is a pathophysiological feature of CAD and has been linked with mild cognitive impairment and dementia
- Omega-3 fatty acids (omega-3 FA) have antioxidant effects, which have been associated with improvements in memory
- Meta-analyses of clinical trials indicate that memory may be responsive to omega-3 FA treatment, but efficacy is heterogeneous and is presently unpredictable
- This study investigated the relationship between lipid peroxidation, omega-3 FA, and memory in the setting of a randomized, double-blind, placebo-controlled trial of omega-3 FA in CAD patients (NCT 00981383)

OBJECTIVE & HYPOTHESIS

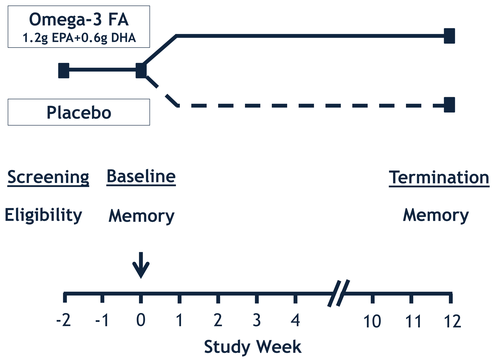
Objective: Investigate the relationship between baseline concentrations 4-hydroxynonenal (4-HNE), a widely-used marker of late-stage lipid peroxidation, and changes in memory over 12 weeks of omega-3 FA treatment, compared to placebo.

Hypothesis: Greater baseline 4-HNE concentrations will predict greater improvement in memory among patients in the omega-3 FA group, but not the placebo group.

METHODS

Inclusion Criteria

1. CAD patients (≥50% coronary artery stenosis)
2. Participating in cardiac rehabilitation
3. Absence of dementia/other cognitive disorder

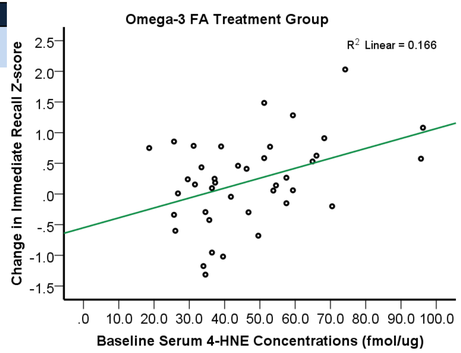


Memory Assessments
Verbal recall (immediate and delayed) California Verbal Learning Test II (CVLT)
Visuospatial recall (immediate and delayed) Brief Visuospatial Memory Test - Rev. (BVMT)
Composite Z-score from CVLT and BVMT was used
Serum 4-HNE Measurement (↓)
Fasting (12 hr overnight) blood
Standard Sandwich ELISA (Cell Biolabs, Inc.; STA-338)

RESULTS

Table 1. Participant Characteristics.

Variable, mean (SD)*	Omega-3 FA (n=40)	Placebo (n=46)	F/X²	P Value
Age	63.3 (8.7)	59.7 (8.0)	3.95	.05
Male, %	80	74	0.44	.51
Education, yrs	14.9 (3.5)	15.7 (3.3)	1.17	.28
sMMSE	28.6 (1.3)	29.0 (1.1)	3.31	.07
Vasc. RF, # of 5	3.1 (1.3)	2.8 (1.4)	0.89	.35
BL 4-HNE, fmol/ug	44.5 (16.8)	46.4 (14.7)	0.27	.60
Medications				
Antidiabetic, %	28	13	2.82	.09
Antihypertensive, %	85	70	2.86	.09
Anti-inflammatory, %	2	4	0.22	.64
ASA, %	80	93	3.48	.06
Beta-blocker, %	73	67	0.27	.61
Statin, %	98	100	1.16	.28



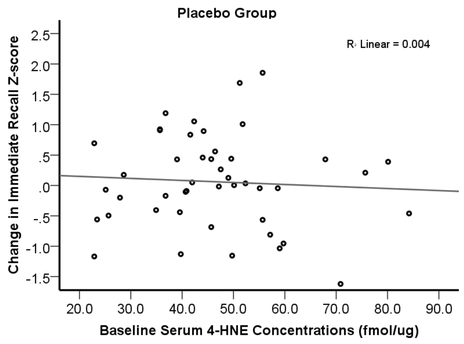


Table 2. Baseline 4-HNE Concentration and Change in Memory.

	Omega-3 FA (n=40)		Placebo (n=46)	
Baseline 4-HNE Predicting:	$F_{1,39}$ Value	P Value	$F_{1,45}$ Value	P Value
Composite memory	2.72	.11	0.89	.35
Immediate recall	6.49	*.02*	1.10	.30
Delayed recall	0.01	.94	2.45	.13

Table 3. Baseline 4-HNE Concentration and Covariates Predicting Change in Immediate Recall.

	Omega-3 FA (n=40)		Placebo (n=46)	
Predictor	$F_{1,39}$ Value	P Value	$F_{1,45}$ Value	P Value
Baseline 4-HNE	5.34	*.03*	0.21	.65
Age	0.09	.77	0.86	.36
Sex	0.50	.48	2.20	.15
Years of education	0.65	.43	4.33	*.04*

Notes: *Unless otherwise stated; ASA = acetylsalicylic acid; BL = baseline; SD = standard deviation; sMMSE = Standardized Mini-Mental State Examination; Vasc. RF = vascular risk factors

DISCUSSION & FUTURE DIRECTIONS

- Omega-3 FA treatment was not efficacious for improving any memory domain over 12 weeks compared to placebo (*not shown*)
- Higher baseline serum concentrations of 4-HNE were associated with greater improvement in immediate recall over 12 weeks in the omega-3 FA treated group, but not the placebo group
- Antioxidant effects of omega-3 FA may contribute to improved immediate recall among patients with greater oxidative stress severity
- This finding is exploratory and requires replication in a larger sample
- Future work may clarify the relationship between oxidative stress and omega-3 FA, as it pertains to cognitive performance

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