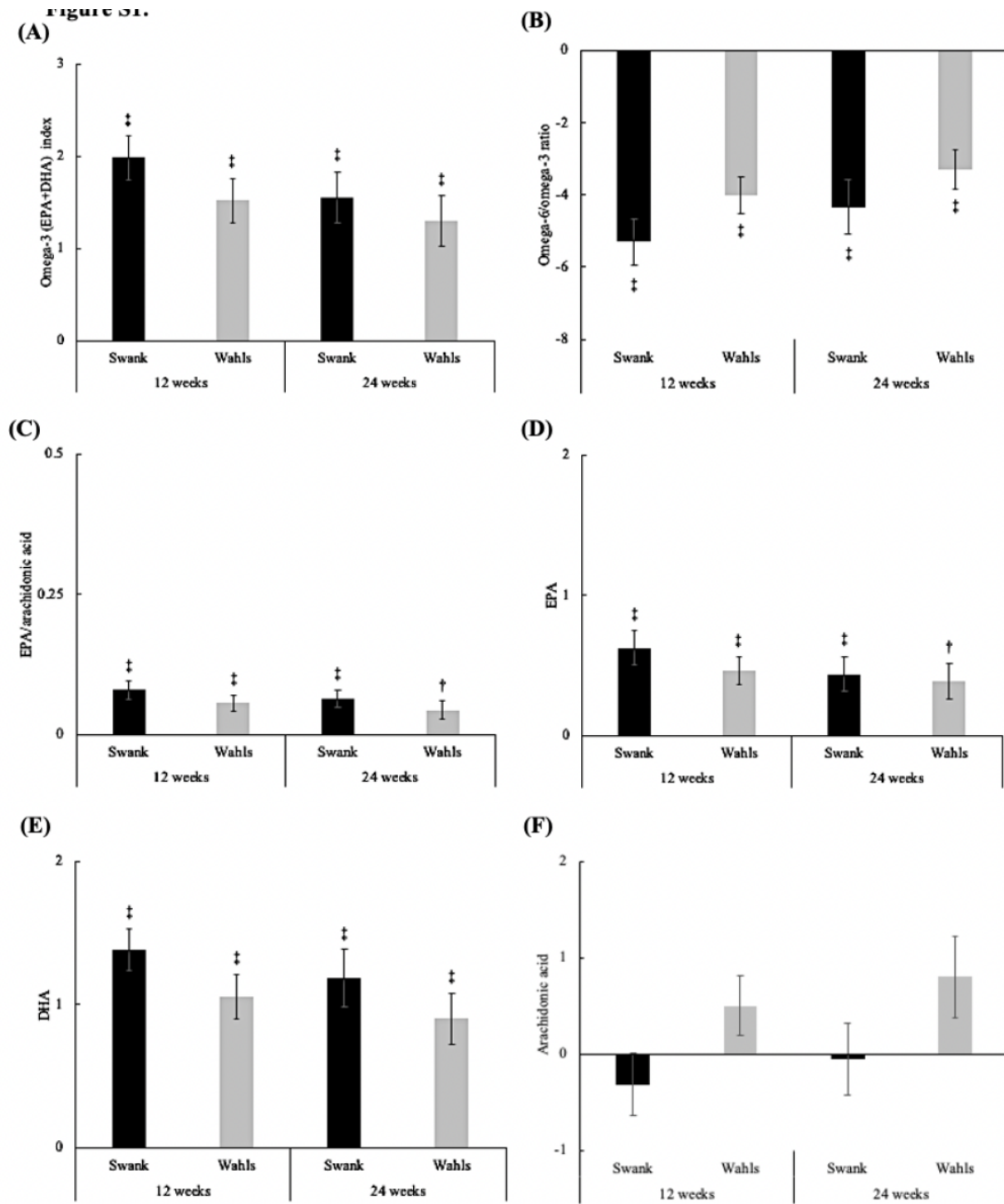


**Figure S1.** Mean Change of Baseline



A) Omega-3 (EPA + DHA) Index, (B) Omega-6/omega-3 ratio, (C) EPA/ARA ratio, (D) EPA, (E) DHA, and (F) ARA, arachidonic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; PDQ, Perceived Deficits Questionnaire; SDMT-O, Symbol Digit Modalities Test-Oral. Note: \* =  $P \leq .05$ ; † =  $P \leq .01$ ; ‡ =  $P \leq .001$

**Table S1.** Baseline Participant Characteristics at 12-Week Primary Study End Point

<b>Characteristics<sup>a</sup></b>	<b>Swank</b>	<b>Wahls</b>	<b>P value<sup>b</sup></b>
<b>N</b>	38	39	
<b>Age (y)</b>	46.9 ± 1.7	46.4 ± 1.5	.84
<b>Sex (female)</b>	35 (92.1)	32 (82.1)	.31
<b>MS duration (y)</b>	12.1 ± 1.6	9.3 ± 1.0	.14
<b>DMT use</b>			.83
None	13	10	
Oral	11	11	
Injectable	10	12	
Infused	4	6	
<b>Race (White)</b>	36 (94.7)	38 (97.4)	.99
<b>Education</b>			.32
High school	0 (0.0)	3 (7.7)	
Some college	12 (31.6)	10 (25.6)	
4-year degree	11 (28.9)	8 (20.5)	
Advanced degree	15 (39.5)	18 (46.2)	
<b>Smoking status</b>			.13
Never	29 (76.3)	23 (59.0)	
Former	3 (7.9)	2 (5.1)	
Current	6 (15.8)	14 (35.9)	
<b>Alcohol per month<sup>c</sup></b>			.99
None	6 (15.8)	7 (17.9)	
Within recommendations	29 (76.3)	29 (74.4)	
Above recommendation	3 (7.9)	3 (7.7)	
<b>PDQ total score</b>	32.4 (2.4)	35.9 (2.2)	.28
Attention	71.9 (2.9)	64.8 (3.5)	.12
Retrospective memory	9.15 (0.7)	9.5 (0.6)	.66
Prospective memory	8.00 (0.7)	8.9 (0.6)	.31
Planning	6.2 (0.6)	7.3 (0.6)	.22
<b>SDMT-O</b>	60.4 (1.5)	61.2 (1.5)	.71

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DMT, disease-modifying therapy; MS, multiple sclerosis; PDQ, Perceived Deficits Questionnaire; SDMT-O, Symbol Digit Modalities Test-Oral.

<sup>a</sup>All values shown in mean  $\pm$  SEM or N (%). Data adapted.<sup>6</sup>

<sup>b</sup>Significance determined by Fisher's exact test or generalized linear models.

<sup>c</sup>Alcohol recommendations are less than or equal to 1 standard drink for women and less than or equal to 2 standard drinks for men.

**Table S2.** Association of 12-Week Serum Fatty Acid Changes with PDQ Subscore Changes

	PDQ attention		PDQ retrospective memory		PDQ prospective memory		PDQ planning memory	
	$\beta$ -coefficient <sup>a</sup> (95% CI)	<i>P</i> value	$\beta$ -coefficient (95% CI)	<i>P</i> value	$\beta$ -coefficient (95% CI)	<i>P</i> value	$\beta$ -coefficient (95% CI)	<i>P</i> value
Omega-3 (EPA +DHA) index	-2.18 (-7.00, 2.63)	0.37	-0.07 (-5.65, 5.79)	0.98	0.43 (-3.60, 4.47)	0.83	-0.89 (-6.58, 4.81)	0.76
Omega-6/omega-3 ratio	1.71 (-0.81, 4.23)	0.18	0.47 (2.42, 3.46)	0.75	0.21 (-1.87, 2.30)	0.84	0.38 (-2.55, 3.32)	0.80
EPA	-5.60 (-16.1, 4.90)	0.29	3.35 (-8.92, 15.6)	0.59	2.29 (-6.30, 10.9)	0.60	0.54 (-11.8, 12.9)	0.93
DHA	-2.96 (-10.8, 4.91)	0.46	-1.22 (-10.1, 7.70)	0.79	3.21 (-5.19, 7.61)	0.71	-0.95 (-9.88, 7.98)	0.83
EPA/ARA ratio	-54.67 (-133, 23.3)	0.17	-6.74 (-97.0, 83.5)	0.88	-0.00 (-64.8, 64.8)	1	-26.3 (-113, 60.8)	0.55
ARA	-0.38 (-4.47, 3.71)	0.85	-0.36 (-4.2, 4.9)	0.87	0.77 (-2.6, 4.1)	0.65	0.32 (-4.40, 5.05)	0.89

ARA, arachidonic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; PDQ, Perceived Deficits Questionnaire.

<sup>a</sup>The  $\beta$ -coefficient is the degree of change in the outcome variable for every 1 unit of change in the independent variable. The *t* test assesses whether the beta coefficient is statistically and significantly different from zero.

**Table S3.** Mediation Effect of 12-Week Serum Fatty Acid Changes on PDQ Subscores

	<b>PDQ attention</b>		<b>PDQ retrospective memory</b>		<b>PDQ prospective memory</b>		<b>PDQ planning memory</b>	
	Percent mediated (95% CI)	<i>P</i> value	Percent mediated (95% CI)	<i>P</i> value	Percent mediated (95% CI)	<i>P</i> value	Percent mediated (95% CI)	<i>P</i> value
Omega-3 (EPA + DHA) index	11.9 (-33.9, 57.6)	0.61	5.35 (-45.3, 56.0)	0.84	-0.04 (-55.4, 55.3)	0.99	-1.35 (-49.8, 47.1)	0.96
Omega-6/omega-3 ratio	38.5 (-30.9, 108)	0.28	22.6 (-56.5, 101.7)	0.58	18.5 (-66.3, 103.3)	0.67	9.59 (-61.8, 81.0)	0.79
EPA	6.99 (-25.4, 39.4)	0.67	2.36 (-35.7, 40.4)	0.90	-4.53 (-45.7, 36.6)	0.83	1.87 (-33.03, 36.8)	0.92
DHA	17.3 (-32.7, 67.2)	0.50	22.4 (-37.3, 82.2)	0.46	3.62 (-58.6, 65.8)	0.91	-2.14 (-55.1, 50.8)	0.94
EPA/ARA ratio	15.6 (-13.4, 44.6)	0.29	15.8 (-16.2, 47.9)	0.33	8.68 (-28.8, 46.2)	0.65	12.50 (-18.5, 43.5)	0.43
ARA	-0.34 (-4.42, 3.74)	0.87	-0.47 (-6.08, 5.13)	0.87	-0.37 (-4.85, 4.11)	0.87	-3.39 (-5.08, 4.30)	0.87

ARA, arachidonic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; PDQ, Perceived Deficits Questionnaire.