

Fish oil supplementation **may improve attention, working memory and ADHD symptoms in adults with autism spectrum disorder: A randomized crossover trial**

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Online Supporting Material

Supplemental Table 1. Baseline characteristics of completing participants and dropouts

	Dropouts (<i>n</i> = 4)	Completers (<i>n</i> = 22)	<i>P</i>
Age (y)	32.0 ± 9.1	27.0 ± 6.3	0.18
Height (m)	175 ± 8	177 ± 11	0.65
Weight (kg)	105 ± 42	80 ± 18	0.32
Women : Men (<i>n</i>)	2 : 2	11 : 11	>0.99
Education (y)	16.8 ± 8.2	14.0 ± 3.6	0.55
Married : Unmarried (<i>n</i>)	1 : 3	1 : 21	0.15
Dietary fatty fish (portions/mo)	2.2 [2.2; 6.4]	3.1 [1.9; 4.3]	0.52
Exercise (h/wk)	1.2 [0; 3.6]	0 [0; 1.4]	0.20
Number of psychiatric diagnoses	3.8 ± 1.0	3.5 ± 1.9	0.77
Number of psychiatric medications	2.3 ± 1.0	1.3 ± 1.1	0.087
Characters processed (<i>n</i>)	519 ± 50	476 ± 86	0.35
Processing variability (<i>n</i>)	11.5 ± 3.2	12.5 ± 5.8	0.75
Omission errors (<i>n</i>)	14 [14; 23]	11 [8; 22]	0.26
Commission errors (<i>n</i>)	0.5 [0; 1]	0 [0; 0]	0.096
Total d2 errors (%)	2.8 [2.5; 4.9]	2.3 [1.9; 4.9]	0.43
Word card (s)	41 ± 15	32 ± 5	0.32
Colour card (s)	44 ± 13	45 ± 9	0.78
Word-colour card (s)	71 ± 21	72 ± 21	0.98
Relative Stroop effect	0.8 ± 0.4	0.9 ± 0.4	0.53
Block span (<i>n</i>)	5.8 ± 1.8	6.6 ± 1.1	0.22
Total Corsi score	53 ± 28	65 ± 21	0.31
Total ADHD symptoms	24.4 ± 9.3	16.8 ± 9.7	0.12
Inattention	13.2 ± 5.5	9.6 ± 5.8	0.22
Hyperactivity & impulsivity	11.2 ± 4.9	7.2 ± 4.8	0.11
ADHD index	20.0 ± 5.1	13.8 ± 6.0	0.043
Global executive composite	144 ± 29	118 ± 19	0.020
Behavioural regulation index	58 ± 13	47 ± 8	0.019
Impulse inhibition	15.8 ± 2.3	11.2 ± 2.0	<0.001
Flexibility	12.0 ± 4.0	11.3 ± 3.0	0.73
Emotional control	20.6 ± 7.2	15.7 ± 3.6	0.21
Self-monitoring	9.6 ± 4.8	8.8 ± 2.0	0.54
Meta-cognition index	85 ± 16	70 ± 14	0.047
Cognitive initiation	18.4 ± 2.8	15.3 ± 3.7	0.080
Working memory	17.8 ± 4.7	13.3 ± 3.4	0.017
Planning/organising	19.8 ± 4.8	18.0 ± 4.5	0.43
Task-monitoring	11.4 ± 3.1	9.9 ± 2.0	0.17
Material organization	18.0 ± 2.8	14.0 ± 3.9	0.035
Total SRS-2 score	75 ± 39	65 ± 22	0.64
Communication & interaction	59 ± 32	52 ± 17	0.50
Social awareness	6.4 ± 5.0	7.3 ± 3.3	0.63
Social cognition	13.0 ± 7.9	11.6 ± 4.0	0.55
Social communication	24.6 ± 13.7	19.7 ± 8.8	0.32
Social motivation	15.2 ± 7.8	13.8 ± 5.1	0.62
RI&RB	15.4 ± 8.5	13.2 ± 5.7	0.49

Data are given as mean ± SD, median [25th; 75th percentile] or *n*. *P*-values for group differences are based on t-test (continuous variables), Mann-Whitney U-test (count variables), or Barnard's CSM test (categorical variables).

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; RI&RB, restricted interests and repetitive behaviour.

Supplemental Table 2: Whole-blood fatty acid composition after oil supplementation

	Fish oil	Safflower oil	Estimated difference	P
14:0	0.85 ± 0.28	0.86 ± 0.28	0.02 (-0.13; 0.16)	0.85
16:0	24.7 ± 1.8	23.7 ± 1.8	-1.04 (-2.04; -0.04)	0.057
18:0	13.6 ± 1.0	13.1 ± 1.0	-0.44 (-1.06; 0.19)	0.19
22:0	0.90 ± 0.19	0.92 ± 0.19	0.02 (-0.08; 0.12)	0.70
24:0	1.59 ± 0.35	1.67 ± 0.35	0.08 (-0.15; 0.32)	0.46
Total SFA	42.8 ± 1.7	41.3 ± 1.7	-1.52 (-2.61; -0.42)	0.081
16:1 <i>n</i> -7	0.94 ± 0.25	1.01 ± 0.25	0.07 (-0.09; 0.23)	0.39
18:1 <i>n</i> -7	1.59 ± 0.12	1.56 ± 0.12	-0.04 (-0.10; 0.02)	0.25
18:1 <i>n</i> -9	18.5 ± 1.4	19.5 ± 1.4	0.99 (0.29; 1.68)	0.013
24:1 <i>n</i> -9	2.10 ± 0.47	2.13 ± 0.47	0.03 (-0.28; 0.34)	0.85
Total MUFA	23.8 ± 1.6	24.8 ± 1.6	1.07 (0.21; 1.92)	0.026
18:2 <i>n</i> -6	16.2 ± 1.6	19.0 ± 1.6	2.75 (1.83; 3.66)	<0.001
18:3 <i>n</i> -6	0.10 ± 0.05	0.18 ± 0.05	0.08 (0.05; 0.12)	<0.001
20:3 <i>n</i> -6	0.68 ± 0.18	1.05 ± 0.18	0.38 (0.28; 0.49)	<0.001
20:4 <i>n</i> -6	5.92 ± 0.75	5.96 ± 0.75	0.04 (-0.46; 0.53)	0.89
22:4 <i>n</i> -6	0.58 ± 0.13	0.61 ± 0.13	0.03 (-0.05; 0.11)	0.50
22:5 <i>n</i> -6	0.12 ± 0.03	0.12 ± 0.03	0.01 (-0.02; 0.02)	0.82
Total <i>n</i>-6 PUFA	23.9 ± 1.9	27.1 ± 1.9	3.28 (2.07; 4.48)	<0.001
18:3 <i>n</i> -3	0.34 ± 0.11	0.36 ± 0.11	0.03 (-0.04; 0.09)	0.45
20:5 <i>n</i> -3	2.50 ± 0.53	0.52 ± 0.53	-1.98 (-2.31; -1.66)	<0.001
22:5 <i>n</i> -3	0.92 ± 0.17	0.74 ± 0.17	-0.18 (-0.25; -0.11)	<0.001
22:6 <i>n</i> -3	2.35 ± 0.42	1.72 ± 0.42	-0.63 (-0.83; -0.44)	<0.001
Total <i>n</i>-3 PUFA	6.11 ± 0.97	3.35 ± 0.97	-2.77 (-3.29; -2.25)	<0.001
Total PUFA	30.0 ± 2.1	30.5 ± 2.1	0.51 (-0.83; 1.85)	0.47
<i>n</i>-6/<i>n</i>-3 PUFA	4.26 ± 1.38	9.42 ± 1.38	5.17 (4.38; 5.95)	<0.001
Total HUFA	13.1 ± 1.7	10.7 ± 1.7	-2.42 (-3.50; -1.35)	<0.001
<i>n</i>-3 HUFA%	42.8 ± 6.6	27.1 ± 6.6	-16 (-20; -12)	<0.001

Data are given as percent of fatty acids and presented as mean ± SD (*n* = 20). Estimated mean differences (95% CI) of fish oil relative to safflower oil are based on linear mixed models with participant ID as random effect and treatment, baseline, sequence, and period as fixed effects.

Abbreviations: Individual fatty acids are given as number of carbons : number of double bonds *n*-position of the last double bond from the methyl group; SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; *n*-3 HUFA%: *n*-3 long-chain PUFA (≥C20 : ≥3 *n*-3) of all long-chain PUFA

Supplemental Table 3. Effect of the oil intervention on whole-blood fatty acid composition and neurocognitive outcomes in the two crossover arms separately and combined

	<i>Safflower oil → Fish oil</i>			<i>Fish oil → Safflower oil</i>			<i>Safflower oil → Fish oil + Fish oil → Safflower oil</i>					
	FO	SO	ΔOil (n = 8)	FO	SO	ΔOil (n = 12)	FO	SO	ΔOil (n = 20)	<i>P</i> _{period}	<i>P</i> _{sequence}	<i>P</i> _{interaction}
SFA (FA%)	40.9 ± 2.3	42.2 ± 2.5	-1.8 (-3.3; -0.2)	44.3 ± 1.7	39.6 ± 1.7	4.8 (3.6; 6.0)	42.6 ± 2.7	40.9 ± 2.5	1.5 (0.5; 2.5)	<0.001	0.51	0.008
MUFA (FA%)	23.1 ± 1.8	25.7 ± 1.7	-2.5 (-3.4; -1.5)	24.7 ± 1.9	24.3 ± 2.1	0.3 (-1.0; 1.7)	23.9 ± 2.0	25.0 ± 2.0	-1.1 (-1.9; -0.2)	0.005	0.42	0.025
PUFA (FA%)	32.3 ± 2.4	28.6 ± 2.1	4.0 (2.7; 5.4)	27.4 ± 2.6	32.4 ± 2.8	-5.0 (-7.1; -3.0)	29.8 ± 3.5	30.5 ± 3.1	-0.5 (-1.8; 0.8)	<0.001	0.95	0.46
18:2 n-6 (FA%)	16.5 ± 2.8	19.5 ± 2.2	-2.8 (-4.1; -1.6)	15.7 ± 2.5	18.4 ± 2.1	-2.6 (-3.9; -1.4)	16.1 ± 2.6	18.9 ± 2.2	-2.7 (-3.7; -1.8)	0.82	0.70	<0.001
20:5 n-3 + 22:6 n-3 (FA%)	5.6 ± 1.0	1.3 ± 0.3	4.4 (3.7; 5.0)	4.0 ± 1.2	3.0 ± 1.0	0.9 (0.2; 1.7)	4.8 ± 1.4	2.2 ± 1.1	2.7 (2.2; 3.1)	<0.001	0.96	<0.001
n-6/n-3 PUFA	3.7 ± 1.0	12.8 ± 2.9	-9.0 (-10.1; -7.9)	4.9 ± 1.5	6.2 ± 1.1	-1.3 (-2.4; -0.2)	4.3 ± 1.4	9.5 ± 4.0	-5.2 (-5.9; -4.4)	<0.001	0.008	<0.001
			ΔOil (n = 11)			ΔOil (n = 11)			ΔOil (n = 22)			
Characters processed (<i>n</i>)	550 ± 81	535 ± 81	16 (1; 31)	501 ± 77	511 ± 78	-10 (-27; 6)	526 ± 82	523 ± 78	3 (-8; 14)	0.035	0.98	0.63
Processing variability (<i>n</i>)	9.3 ± 5.1	10.2 ± 4.2	-0.9 (-2.5; 0.7)	10.4 ± 4.1	10.9 ± 5.3	-0.5 (-3.1; 2.0)	9.8 ± 4.5	10.5 ± 4.7	-0.7 (-2.2; 0.8)	0.81	0.61	0.35
Total d2 errors (%)	0.5 [0.2; 1.2]	1.3 [1.0; 3.0]	0.3 (0.1; 0.7)	1.6 [0.8; 3.7]	1.6 [0.7; 3.4]	1.3 (1.0; 1.8)	1.0 [0.4; 2.3]	1.4 [1.0; 3.2]	0.7 (0.5; 0.9)	0.001	0.42	0.016
Omission errors (<i>n</i>)	3.0 [1.0; 7.0]	7.0 [4.5; 17.5]	0.4 (0.2; 0.7)	8.0 [3.5; 18.5]	6.0 [3.5; 18.0]	1.2 (0.9; 1.7)	5.0 [2.3; 12.0]	7.0 [4.3; 18.5]	0.7 (0.5; 0.9)	0.002	0.34	0.012
Commission errors (<i>n</i>)	1.0 [0.5; 2.0]	1.0 [0.0; 3.0]	0.6 (0.3; 1.3)	1.0 [1.0; 1.0]	1.0 [0.0; 2.0]	0.9 (0.4; 2.2)	1.0 [1.0; 2.0]	1.0 [0.0; 2.0]	0.7 (0.4; 1.3)	0.54	0.79	0.28
Word card (s)	28.1 ± 6.1	31.2 ± 7.3	-3.1 (-4.6; -1.6)	29.6 ± 6.2	29.6 ± 5.6	0.0 (-1.6; 1.6)	28.8 ± 6.0	30.4 ± 6.4	-1.6 (-2.7; -0.5)	0.010	0.35	0.010
Colour card (s)	37.4 ± 7.2	42.1 ± 9.8	-4.7 (-8.0; -1.4)	42.9 ± 8.5	40.8 ± 6.9	2.1 (-1.4; 5.7)	40.1 ± 8.2	41.4 ± 8.3	-1.3 (-3.7; 1.1)	0.012	0.82	0.31
Word-colour card (s)	56.8 ± 12.2	63.5 ± 16.1	-6.7 (-11.1; -2.3)	71.5 ± 26.2	73.5 ± 30.1	-2.0 (-7.8; 3.8)	64.1 ± 21.4	68.5 ± 24.1	-4.4 (-8.2; -0.5)	0.24	0.14	0.037
Relative Stroop effect	0.7 ± 0.2	0.7 ± 0.3	0.0 (-0.1; 0.1)	0.9 ± 0.4	1.1 ± 0.7	-0.1 (-0.3; 0.1)	0.8 ± 0.3	0.9 ± 0.5	-0.1 (-0.2; 0.1)	0.30	0.22	0.31
Block span (<i>n</i>)	7.5 ± 0.9	6.9 ± 1.4	0.6 (0.0; 1.2)	7.4 ± 1.3	6.7 ± 1.1	0.6 (-0.2; 1.5)	7.5 ± 1.1	6.8 ± 1.3	0.6 (0.1; 1.2)	>0.99	0.35	0.030
Total Corsi score	91 ± 23	74 ± 32	17 (3; 31)	82 ± 26	71 ± 27	11 (-5; 27)	86 ± 24	73 ± 29	14 (2; 26)	0.64	0.35	0.032
			ΔOil (n = 10)			ΔOil (n = 11)			ΔOil (n = 21)			
Total ADHD symptoms	15.3 ± 8.9	18.4 ± 11.7	-3.1 (-6.6; 0.4)	13.5 ± 6.4	14.0 ± 7.2	-0.5 (-2.3; 1.2)	14.3 ± 7.6	16.1 ± 9.7	-1.8 (-3.7; 0.1)	0.20	0.85	0.073
Inattention	9.4 ± 5.9	11.1 ± 6.5	-1.7 (-3.7; 0.3)	7.8 ± 4.6	9.3 ± 5.4	-1.5 (-3.0; 0.1)	8.6 ± 5.2	10.1 ± 5.9	-1.6 (-2.8; -0.3)	0.85	0.65	0.023
Hyperactiv & impulsiv	5.9 ± 4.4	7.3 ± 6.1	-1.4 (-3.3; 0.5)	5.6 ± 2.5	4.7 ± 2.6	0.9 (-0.2; 2.0)	5.8 ± 3.4	6.0 ± 4.7	-0.2 (-1.3; 0.8)	0.045	0.93	0.65
ADHD Index	12.2 ± 5.4	14.2 ± 7.0	-2.0 (-4.4; 0.4)	11.7 ± 4.1	10.8 ± 3.7	0.9 (-0.5; 2.4)	12.0 ± 4.7	12.4 ± 5.6	-0.5 (-1.9; 0.8)	0.051	0.70	0.45
BRIEF GEC	114 ± 19	118 ± 23	-4.2 (-10.5; 2.1)	115 ± 17	108 ± 19	7.1 (0.8; 13.4)	114 ± 18	113 ± 21	1.4 (-3.0; 5.9)	0.023	0.48	0.53
Behavioural regulatory index	46 ± 11	50 ± 13	-4.1 (-7.7; -0.5)	44 ± 6	41 ± 5	2.8 (0.4; 5.3)	45 ± 8	45 ± 10	-0.6 (-2.8; 1.5)	0.005	0.24	0.57
Impulse inhibition	10.9 ± 2.7	12.2 ± 3.9	-1.3 (-2.4; -0.2)	10.5 ± 1.5	10.4 ± 1.7	0.2 (-0.7; 1.1)	10.7 ± 2.1	11.2 ± 3.0	-0.6 (-1.2; 0.1)	0.046	0.093	0.12
Cognitive flexibility	11.5 ± 3.4	11.7 ± 3.1	-0.2 (-1.2; 0.8)	10.5 ± 1.9	9.5 ± 1.8	1.0 (-0.4; 2.4)	11.0 ± 2.7	10.6 ± 2.7	0.4 (-0.5; 1.3)	0.20	0.13	0.39
Emotional control	15.0 ± 4.5	15.7 ± 4.2	-0.7 (-2.4; 1.0)	14.9 ± 3.8	13.8 ± 2.9	1.1 (0.0; 2.2)	15.0 ± 4.1	14.7 ± 3.6	0.2 (-0.8; 1.2)	0.091	>0.99	0.70
Self-monitoring	8.1 ± 2.3	10.0 ± 3.2	-1.9 (-3.3; -0.5)	7.9 ± 1.6	7.4 ± 1.6	0.5 (0.0; 1.1)	8.0 ± 1.9	8.6 ± 2.8	-0.7 (-1.4; 0.0)	0.004	0.22	0.081
Meta-cognition index	68 ± 13	68 ± 12	-0.1 (-4.0; 3.8)	71 ± 14	67 ± 15	4.3 (0.1; 8.4)	70 ± 14	68 ± 14	2.1 (-0.8; 5.0)	0.15	0.86	0.17
Cognitive initiation	14.5 ± 3.2	14.6 ± 2.9	-0.1 (-1.3; 1.1)	15.7 ± 4.4	15.2 ± 4.2	0.5 (-0.6; 1.7)	15.1 ± 3.8	14.9 ± 3.5	0.2 (-0.7; 1.1)	0.49	0.77	0.64
Working memory	13.7 ± 3.8	13.4 ± 3.8	0.3 (-1.8; 2.4)	13.1 ± 2.4	12.1 ± 2.3	1.0 (-0.1; 2.1)	13.4 ± 3.1	12.7 ± 3.1	0.6 (-0.5; 1.8)	0.56	0.27	0.29
Planning/organising	17.2 ± 3.6	17.0 ± 2.4	0.2 (-2.0; 2.4)	18.4 ± 3.6	17.3 ± 4.5	1.1 (-0.5; 2.7)	17.8 ± 3.5	17.1 ± 3.6	0.6 (-0.7; 2.0)	0.52	0.64	0.36
Task-monitoring	10.2 ± 2.4	10.0 ± 2.4	0.2 (-0.6; 1.0)	9.6 ± 2.2	9.2 ± 3.2	0.5 (-0.9; 1.8)	9.9 ± 2.3	9.6 ± 2.8	0.3 (-0.5; 1.2)	0.77	0.31	0.45
Material organization	12.6 ± 4.0	13.3 ± 3.8	-0.7 (-1.8; 0.4)	14.4 ± 4.6	13.2 ± 4.3	1.2 (-0.1; 2.5)	13.5 ± 4.3	13.2 ± 4.0	0.2 (-0.6; 1.1)	0.044	0.51	0.59
Total SRS-2 Score	61 ± 24	61 ± 22	-0.5 (-9.3; 8.3)	58 ± 21	55 ± 21	2.7 (-2.3; 7.7)	59 ± 22	58 ± 21	1.1 (-4.4; 6.7)	0.58	0.33	0.70
Communicat & interact.	49 ± 20	49 ± 17	-0.8 (-8.1; 6.5)	47 ± 18	45 ± 17	2.5 (-2.2; 7.1)	48 ± 18	47 ± 17	0.8 (-4.0; 5.6)	0.51	0.26	0.74
Social awareness	6.1 ± 3.4	6.5 ± 3.1	-0.4 (-1.6; 0.8)	6.6 ± 2.5	6.1 ± 2.6	0.5 (-0.4; 1.5)	6.4 ± 2.9	6.3 ± 2.8	0.1 (-0.8; 0.9)	0.28	0.53	0.87
Social cognition	12.0 ± 5.1	11.1 ± 5.0	0.9 (-1.1; 2.9)	9.5 ± 4.2	9.0 ± 4.2	0.5 (-1.2; 2.1)	10.7 ± 4.7	10.0 ± 4.6	0.7 (-0.7; 2.1)	0.76	0.86	0.36
Social communication	18.5 ± 9.5	19.1 ± 9.0	-0.6 (-4.9; 3.7)	17.9 ± 8.2	16.2 ± 7.3	1.7 (-1.1; 4.5)	18.2 ± 8.6	17.6 ± 8.1	0.6 (-2.0; 3.1)	0.38	0.66	0.67
Social motivation	11.9 ± 4.5	12.6 ± 4.4	-0.7 (-2.9; 1.5)	13.1 ± 5.7	13.4 ± 5.4	-0.3 (-1.7; 1.2)	12.5 ± 5.1	13.0 ± 4.9	-0.5 (-1.8; 0.8)	0.75	0.056	0.47
RI&RB	12.1 ± 5.0	11.8 ± 6.2	0.3 (-1.7; 2.3)	10.7 ± 5.5	10.5 ± 5.8	0.3 (-1.6; 2.1)	11.4 ± 5.2	11.1 ± 5.8	0.3 (-1.1; 1.6)	0.98	0.94	0.68

Data are given as mean ± SD or median [25th; 75th percentile] and estimated mean difference (95% CI) between oil treatments. Effect estimates in the individual arms are from linear mixed models with participant ID as random effect and baseline, period and sequence as fixed effects. Models for combined effects included a period × sequence-interaction term. Estimates for omission + commission errors and total d2 error% are IR and OR from generalized linear mixed models (Poisson and binomial, respectively) with the same factors and covariates.

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; FA%, percent of all fatty acids; GEC, global executive function composite; RI&RB, restricted interests and repetitive behaviour.

Supplemental Table 4. Effect of the oil intervention on neurocognitive test performance

	Baseline	Fish oil	Safflower oil	Estimated difference <i>Primary analysis</i>	<i>P</i>	Estimated difference <i>Secondary analysis</i>	<i>P</i>	Estimated difference <i>Tertiary analysis</i>	<i>P</i>
d2 test									
Characters processed (<i>n</i>)	482 ± 82	527 ± 82	523 ± 78	3 (-8; 14)	0.63	-0.5 (-10; 9)	0.91	1 (-9; 10)	0.86
Processing variability (<i>n</i>)	12.4 ± 5.4	9.8 ± 4.5	10.5 ± 4.7	-0.7 (-2.2; 0.8)	0.35	-1.1 (-2.5; 0.3)	0.13	-0.8 (-2.2; 0.5)	0.23
Omission errors (<i>n</i>)	12 [3; 22]	5 [2, 12]	7 [4, 19]	0.7 (0.5; 0.9)	0.012	0.8 (0.6; 1.0)	0.088	0.7 (0.6; 1.0)	0.024
Commission errors (<i>n</i>)	0 [0; 1]	10 [0, 2]	1 [0, 2]	0.7 (0.4; 1.3)	0.31	0.8 (0.5; 1.5)	0.57	0.8 (0.5; 1.5)	0.57
Total errors (%)	2.5 [1.9; 4.8]	1.0 [0.4, 2.3]	1.4 [1.0, 3.2]	0.7 (0.5; 0.9)	0.016	0.8 (0.6; 1.0)	0.088	0.7 (0.6; 1.0)	0.030
Stroop test									
Word card (s)	34 ± 8	29 ± 6	30 ± 6	-1.6 (-2.7; -0.5)	0.010	-1.8 (-2.8; -0.8)	0.002	-1.6 (-2.6; -0.6)	0.005
Colour card (s)	45 ± 9	40 ± 8	41 ± 8	-1.3 (-3.7; 1.1)	0.31	-1.7 (-4.1; 0.7)	0.17	-1.4 (-3.8; 1.0)	0.26
Word-colour card (s)	72 ± 21	64 ± 21	69 ± 24	-4 (-8; -1)	0.037	-5 (-8; -1)	0.024	-5 (-9; -2)	0.013
Relative Stroop effect	0.8 ± 0.3	0.8 ± 0.3	0.9 ± 0.5	-0.1 (-0.2; 0.1)	0.31	0.0 (-0.1; 0.1)	0.64	0.0 (-0.1; 0.1)	0.76
Corsi Block test									
Block span (<i>n</i>)	6.4 ± 1.2	7.5 ± 1.1	6.8 ± 1.3	0.6 (0.1; 1.2)	0.030	0.6 (0.1; 1.1)	0.030	0.8 (0.3; 1.3)	0.003
Total score	62 ± 22	86 ± 24	73 ± 29	14 (2; 26)	0.032	15 (3; 24)	0.023	12 (1; 23)	0.039

Data are given as mean ± SD or median [25th; 75th percentile] at baseline (*n* = 26) and at the end of each oil intervention period (*n* = 22). The estimated mean differences (95% CI) between the oils (fish oil vs safflower oil) are based on linear mixed models with participant ID as random effect and treatment, baseline, sequence, and period as fixed effects. Count variables were analysed by generalized linear mixed models (Poisson or binomial) adjusting for the same factors and covariates and the results are shown as incidence ratio (omission and commission errors) or odds ratio (total errors). The primary analysis includes all 22 subjects and the secondary and tertiary sensitivity analysis are performed with exclusion of the most or the two most influential outliers, respectively.

Supplemental Table 5. Effect of the oil intervention on neurocognitive scale scores

	Baseline	Fish oil	Safflower oil	Estimated difference <i>Primary analysis</i>	P	Estimated difference <i>Secondary analysis</i>	P	Estimated difference <i>Tertiary analysis</i>	P
Conners scale									
Total ADHD symptoms	18.2 ± 9.9	14.3 ± 7.6	16.1 ± 9.7	-1.8 (-3.7; 0.1)	0.073	-2.3 (-4.1; -0.6)	0.016	-2.0 (-3.7; -0.3)	0.037
Inattention	10.3 ± 5.8	8.6 ± 5.2	10.1 ± 5.9	-1.6 (-2.8; -0.3)	0.023	-1.9 (-3.1; -0.7)	0.005	-1.6 (-2.7; -0.5)	0.011
Hyperactivity & impulsivity	7.9 ± 5.0	5.8 ± 3.4	6.0 ± 4.7	-0.2 (-1.3; 0.8)	0.65	0.1 (-0.9; 1.0)	0.89	-0.1 (-1.0; 0.8)	0.82
ADHD index	15.0 ± 6.3	12.0 ± 4.7	12.4 ± 5.6	-0.5 (-1.9; 0.8)	0.45	-0.4 (-1.9; 1.0)	0.54	-0.6 (-2.1; 0.9)	0.47
BRIEF-A									
GEC	122 ± 23	114 ± 18	113 ± 21	1.4 (-3.0; 5.9)	0.53	0.3 (-3.9; 4.4)	0.90	0.0 (-4.4; 4.3)	0.99
BRI	49 ± 10	45 ± 8	45 ± 10	-0.6 (-2.8; 1.5)	0.57	-0.4 (-2.7; 1.8)	0.71	-0.7 (-3.0; 1.7)	0.59
Impulse inhibition	12.1 ± 2.7	10.7 ± 2.1	11.2 ± 3.0	-0.6 (-1.2; 0.1)	0.12	-0.5 (-1.2; 0.2)	0.21	-0.5 (-1.3; 0.2)	0.17
Flexibility	11.4 ± 3.1	11.0 ± 2.7	10.6 ± 2.7	0.4 (-0.5; 1.3)	0.39	0.3 (-0.6; 1.2)	0.53	0.6 (-0.2; 1.4)	0.17
Emotional control	16.6 ± 4.7	15.0 ± 4.1	14.7 ± 3.6	0.2 (-0.8; 1.2)	0.70	-0.1 (-1.0; 0.7)	0.78	0.1 (-0.8; 0.9)	0.92
Self-monitoring	8.9 ± 2.6	8.0 ± 1.9	8.6 ± 2.8	-0.7 (-1.4; 0.0)	0.081	-0.6 (-1.3; 0.2)	0.15	-0.4 (-1.1; 0.3)	0.28
MI	73 ± 16	70 ± 14	68 ± 14	2.1 (-0.8; 5.0)	0.17	1.5 (-1.3; 4.2)	0.31	2.2 (-0.2; 4.6)	0.095
Cognitive initiation	15.9 ± 3.6	15.1 ± 3.8	14.9 ± 3.5	0.2 (-0.7; 1.1)	0.64	0.4 (-0.4; 1.3)	0.33	0.4 (-0.5; 1.3)	0.40
Working memory	14.1 ± 3.9	13.4 ± 3.1	12.7 ± 3.1	0.6 (-0.5; 1.8)	0.29	0.2 (-0.6; 1.0)	0.68	0.1 (-0.7; 1.0)	0.77
Planning/organization	18.4 ± 4.5	17.8 ± 3.5	17.1 ± 3.6	0.6 (-0.7; 2.0)	0.36	0.2 (-0.9; 1.2)	0.77	0.1 (-1.0; 1.2)	0.85
Task-monitoring	10.2 ± 2.2	9.9 ± 2.3	9.6 ± 2.8	0.3 (-0.5; 1.2)	0.45	0.1 (-0.6; 0.8)	0.79	0.3 (-0.4; 0.9)	0.45
Material organization	14.7 ± 4.0	13.5 ± 4.3	13.2 ± 4.0	0.2 (-0.6; 1.1)	0.59	0.0 (-0.7; 0.7)	>0.99	-0.1 (-0.8; 0.7)	0.81
SRS-2									
Total score	67 ± 25	59 ± 22	58 ± 21	1.1 (-4.4; 6.7)	0.70	2.8 (-2.1; 7.7)	0.29	3.2 (-1.8; 8.3)	0.22
Communication & interaction	54 ± 20	48 ± 18	47 ± 17	0.8 (-4.0; 5.6)	0.74	2.1 (-2.3; 6.5)	0.35	1.5 (-3.0; 6.0)	0.53
Social awareness	7.1 ± 3.5	6.4 ± 2.9	6.3 ± 2.8	0.1 (-0.8; 0.9)	0.87	0.1 (-0.8; 1.0)	0.82	-0.1 (-0.9; 0.7)	0.84
Social cognition	11.8 ± 4.8	10.7 ± 4.7	10.0 ± 4.6	0.7 (-0.7; 2.1)	0.36	0.6 (-0.9; 2.1)	0.43	0.5 (-0.9; 1.8)	0.53
Social communication	20.6 ± 9.8	18.2 ± 8.6	17.6 ± 8.1	0.6 (-2.0; 3.1)	0.67	1.3 (-1.0; 3.5)	0.30	1.1 (-1.4; 3.5)	0.40
Social motivation	14.0 ± 5.5	12.5 ± 5.1	13.0 ± 4.9	-0.5 (-1.8; 0.8)	0.47	-0.4 (-1.7; 1.0)	0.61	-0.1 (-1.5; 1.2)	0.85
RI&RB	13.6 ± 6.2	11.4 ± 5.2	11.1 ± 5.8	0.3 (-1.1; 1.6)	0.68	-0.1 (-1.3; 1.1)	0.87	0.3 (-0.7; 1.2)	0.63

Data are given as mean ± SD ($n = 26$ at baseline and $n = 21$ at the end of the two oil intervention periods) and estimated mean differences (95% CI) between the oil treatments (fish oil vs safflower oil). Analyses were performed linear mixed models with participant ID as random effect and treatment, baseline, sequence, and period as fixed effects. The primary analysis includes all 21 subjects and the secondary and tertiary sensitivity analysis are performed with exclusion of the most or the two most influential outliers, respectively.

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; RI&RB, restricted interests and repetitive behaviour; BRI, behavioural regulatory index; GEC, global executive function composite; MI, meta-cognition index.

Supplemental Table 6. Baseline characteristics of participants with and without ADHD

	With ADHD	Without ADHD
Gender (Women:Men) (<i>n</i>)	5 : 6	6 : 5
Age (y)	26.6 ± 5.5	27.3 ± 7.2
Education (y)	13.2 ± 3.3	14.8 ± 3.8
Employment (Full:Partly:None:Student) (<i>n</i>)	1 : 2 : 4 : 4	1 : 2 : 2 : 6
Residence (Institution:Family:Alone) (<i>n</i>)	6 : 1 : 4	4 : 3 : 4
Number of psychiatric diagnoses	4.5 ± 1.5 *	2.5 ± 1.7
Asperger's : other (<i>n</i>)	6 : 5	10 : 1
ADHD diagnosis, HI-C : PI (<i>n</i>)	6 : 5	0 : 0
Anxiety : Depression (<i>n</i>)	4 : 7	4 : 3
Number of psychiatric medications	1.5 ± 1.0	1.0 ± 1.1
Psychostimulants	5 (45.5 %) *	0 (0.0 %)
Antipsychotics	1 (9.1 %)	3 (27.3 %)
Anticonvulsants	1 (9.1 %)	3 (27.3 %)
Hypnotics	1 (9.1 %)	2 (18.2 %)
Antidepressants	4 (36.4 %)	4 (36.4 %)
Miscellaneous	2 (18.2 %)	0 (0.0 %)
Characters processed (<i>n</i>)	485 ± 77	467 ± 96
Processing variability (<i>n</i>)	11.9 ± 4.4	13.1 ± 7.1
Total d2 errors (%)	2.0 [1.8; 3.9]	2.5 [1.9; 8.8]
Omission errors (<i>n</i>)	10 [9; 17]	11 [8; 42]
Commission errors (<i>n</i>)	1 [1; 2]	0 [0; 2]
Word card (s)	31.1 ± 4.4	33.4 ± 5.9
Colour card (s)	42.3 ± 6.3	48.2 ± 9.9
Word-colour card (s)	64 ± 11 (*)	80 ± 26
Relative Stroop effect	0.7 ± 0.2	0.9 ± 0.4
Block span (<i>n</i>)	6.5 ± 1.1	6.5 ± 1.0
Total Corsi score	67 ± 23	64 ± 20
Total ADHD symptoms	21.4 ± 10.3 *	12.5 ± 6.8
Inattention	12.5 ± 5.9 *	6.9 ± 4.4
Hyperactivity & impulsivity	8.9 ± 5.5	5.5 ± 3.5
ADHD index	15.9 ± 6.4	11.8 ± 5.1
BRIEF Global executive composite score	120 ± 21	115 ± 18
Behavioural regulation index	46.8 ± 9.0	47.0 ± 6.8
Impulse inhibition	11.5 ± 1.9	10.9 ± 2.1
Flexibility	11.5 ± 3.1	11.1 ± 2.8
Emotional control	15.1 ± 4.3	16.2 ± 2.9
Self-monitoring	8.7 ± 2.1	8.8 ± 2.0
Meta-cognition index	73 ± 14	68 ± 14
Cognitive initiation	16.5 ± 3.3	14.1 ± 3.6
Working memory	14.2 ± 3.5	12.4 ± 3.0
Planning/organization	18.3 ± 4.9	17.7 ± 4.2
Task-monitoring	9.8 ± 1.8	9.9 ± 2.2
Material organization	14.5 ± 4.2	13.4 ± 3.5
Total SRS score	66 ± 27	65 ± 17
Communication & interaction	53 ± 22	51 ± 13
Social awareness	8.0 ± 3.4	6.6 ± 3.0
Social cognition	11.0 ± 4.9	12.0 ± 3.0
Social communication	18.8 ± 11.0	20.4 ± 6.6
Social motivation	15.3 ± 6.0	12.4 ± 3.8
RI&RB	12.6 ± 6.0	13.7 ± 5.6

Data are given as mean ± SD, median [25th; 75th percentile] or *n* based on 11 participants in each subgroup. Comparisons were performed by t-test, Mann-Whitney U-test, or Barnard's CSM test (categorical variables) and the statistical significance the subgroups are indicated by * $P < 0.05$ and (*) $P < 0.10$.

Abbreviations: ADHD, attention- deficit/hyperactivity disorder including the predominantly inattentive (PI) and predominantly hyperactive-impulsive and combined (HI-C) subtypes; RI&RB, restricted interests and repetitive behaviour.

Supplemental Table 7. Effect of the oil intervention on neurocognitive questionnaire scores in participants with and without ADHD

	<u>With ADHD</u>				<u>Without ADHD</u>			
	Fish Oil	Safflower oil	Estimated difference	P	Fish oil	Safflower oil	Estimated difference	P
Total ADHD symptoms	16.9 ± 7.9	20.4 ± 10.6	-3.5 (-6.0; -1.0) ^(*)	0.026	12.0 ± 6.8	12.2 ± 7.1	-0.2 (-2.5; 2.2)	0.89
Inattention	10.8 ± 5.4	12.9 ± 6.6	-2.1 (-4.0; -0.2)	0.059	6.5 ± 4.3	7.6 ± 3.9	-1.0 (-2.7; 0.6)	0.25
Hyper & impulsivity	6.1 ± 3.0	7.5 ± 4.6	-1.4 (-2.8; -0.1) *	0.077	5.5 ± 3.9	4.5 ± 4.5	0.9 (-0.4; 2.2)	0.22
GEC	115 ± 20	119 ± 22	-3.4 (-9.3; 2.5) *	0.29	114 ± 16	107 ± 19	5.9 (0.0; 11.8)	0.080
BRI	43 ± 9	47 ± 11	-3.3 (-5.3; -1.3) *	0.011	46 ± 8	44 ± 10	1.9 (-0.9; 4.8)	0.21
Impulse inhibition	10.7 ± 2.4	12.1 ± 3.6	-1.4 (-2.5; -0.3) *	0.034	10.7 ± 2.0	10.5 ± 2.3	0.2 (-0.4; 0.8)	0.51
Flexibility	10.9 ± 3.2	11.0 ± 2.6	-0.1 (-1.2; 1.0)	0.86	11.1 ± 2.3	10.2 ± 2.8	0.9 (-0.6; 2.3)	0.27
Emotional control	14.2 ± 4.3	14.8 ± 3.8	-0.6 (-1.8; 0.6)	0.36	15.6 ± 3.9	14.6 ± 3.7	1.0 (-0.1; 2.2)	0.12
Self-monitoring	7.4 ± 1.8	8.6 ± 2.8	-1.2 (-2.2; -0.2)	0.051	8.5 ± 1.9	8.6 ± 2.9	-0.2 (-1.1; 0.8)	0.74
MI	72 ± 14	72 ± 14	-0.1 (-4.4; 4.2)	0.96	68 ± 13	63 ± 12	4.0 (0.3; 7.7)	0.064
Cognitive initiation	16.5 ± 3.1	17.0 ± 3.0	-0.5 (-1.9; 0.9)	0.51	13.9 ± 4.1	13.0 ± 2.9	0.8 (-0.2; 1.9)	0.15
Working memory	13.4 ± 3.0	13.7 ± 3.9	-0.3 (-1.5; 0.9)	0.64	13.4 ± 3.3	11.8 ± 1.8	1.5 (-0.4; 3.5)	0.15
Planning/organization	17.8 ± 4.1	17.3 ± 3.2	0.5 (-1.9; 2.9)	0.69	17.8 ± 3.1	17.0 ± 4.0	0.7 (-0.7; 2.1)	0.35
Task-monitoring	10.4 ± 2.4	10.5 ± 2.6	-0.1 (-1.4; 1.2)	0.88	9.5 ± 2.1	8.7 ± 2.7	0.7 (-0.4; 1.8)	0.24
Material organization	14.0 ± 5.1	13.7 ± 4.6	0.3 (-0.8; 1.4)	0.59	13.1 ± 3.8	12.8 ± 3.5	0.3 (-1.0; 1.5)	0.71

The results are presented as mean ± SD and estimated mean differences (95% CI) between fish oil vs safflower oil based on 10 participants in the ADHD strata and $n = 11$ without ADHD. Data were analysed by linear mixed models with participant ID as random effect and treatment, baseline, sequence, and period as fixed effects. Omission and commission errors were analysed by generalized linear mixed models (Poisson) including the same adjustments and the results are shown as incidence ratio except for commission errors in the participants with ADHD due to lack of fit with the model. Potential differences in oil effects in the strata were also examined by inclusion of a subgroups × treatment-interaction term in analyses in the combined group and effect modification by ADHD diagnosis is indicated by ^(*) $P < 0.1$; * $P < 0.05$.

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; BRI, behavioural regulatory index; GEC, global executive function composite; MI, meta-cognition index.

Supplemental Table 8. Differences in the effect of the oil intervention on ASD symptoms depending on comorbidities and gender

	Fish oil	Safflower oil	ΔOil	<i>P</i>	Fish oil	Safflower oil	ΔOil	<i>P</i>
	ADHD (<i>n</i> = 11)				No ADHD (<i>n</i> = 11)			
Total SRS score	59 ± 26	58 ± 22	0.8 (-7.6; 9.2)	0.86	59 ± 19	58 ± 22	1.3 (-6.8; 9.4)	0.77
Communication & interaction	48 ± 22	47 ± 18	0.2 (-7.0; 7.4)	0.96	48 ± 15	46 ± 17	1.2 (-5.6; 8.0)	0.74
Social awareness	6.4 ± 2.7	6.5 ± 2.5	-0.1 (-1.3; 1.1)	0.88	6.4 ± 3.2	6.1 ± 3.1	0.2 (-1.0; 1.4)	0.74
Social cognition	9.8 ± 5.9	9.1 ± 5.3	0.7 (-0.7; 2.1)	0.37	11.5 ± 3.4	10.8 ± 4.1	0.7 (-1.9; 3.2)	0.63
Social communication	18.5 ± 10.7	18.5 ± 9.1	0.0 (-3.1; 3.1)	>0.99	17.9 ± 6.6	16.7 ± 7.4	1.0 (-2.6; 4.6)	0.61
Social motivation	12.9 ± 5.9	13.3 ± 4.9	-0.4 (-2.8; 2.0)	0.75	12.2 ± 4.5	12.7 ± 5.1	-0.6 (-1.9; 0.7)	0.36
RI&RB	11.6 ± 5.3	11.0 ± 5.7	0.6 (-1.6; 2.8)	0.61	11.2 ± 5.3	11.2 ± 6.3	0.1 (-1.7; 1.8)	0.94
	Depression (<i>n</i> = 9)				No depression (<i>n</i> = 12)			
Total SRS score	55 ± 18	53 ± 16	1.5 (-7.2; 10.1)	0.75	63 ± 25	62 ± 25	0.9 (-5.9; 7.8)	0.91
Communication & interaction	42 ± 15	42 ± 13	0.8 (-6.4; 8.0)	0.84	52 ± 20	51 ± 19	0.9 (-5.1; 6.9)	0.80
Social awareness	6.4 ± 1.7	6.1 ± 2.5	0.2 (-1.4; 1.9)	0.77	6.3 ± 3.6	6.4 ± 3.1	-0.1 (-1.0; 0.8)	0.43
Social cognition	9.1 ± 4.3	8.8 ± 3.7	0.4 (-1.5; 2.2)	0.72	11.8 ± 4.8	10.9 ± 5.2	0.9 (-1.3; 3.1)	0.84
Social communication	15.6 ± 6.8	14.6 ± 7.2	1.0 (-2.5; 4.6)	0.59	20.2 ± 9.5	19.8 ± 8.2	0.3 (-2.8; 3.5)	0.74
Social motivation	11.3 ± 5.2	12.1 ± 4.2	-0.9 (-3.4; 1.7)	0.54	13.4 ± 5.1	13.7 ± 5.4	-0.3 (-1.7; 1.2)	>0.99
RI&RB	12.2 ± 4.4	11.6 ± 4.6	0.7 (-2.1; 3.5)	0.65	10.8 ± 5.8	10.8 ± 6.8	0.0 (-1.4; 1.4)	0.77
	Women (<i>n</i> = 10)				Men (<i>n</i> = 11)			
Total SRS score	59 ± 24	61 ± 22	-0.2 (-12.6; 12.3)	0.98	59 ± 21	55 ± 21	6.8 (-0.4; 14.1)	0.097
Communication & interaction	48 ± 20	49 ± 17	-0.1 (-9.3; 9.0)	0.98	48 ± 17	45 ± 17	4.7 (-1.9; 11.4)	0.20
Social awareness	6.2 ± 3.4	6.9 ± 2.6	-0.4 (-2.0; 1.1)	0.60	6.5 ± 2.5	5.7 ± 2.9	1.1 (-0.3; 2.4)	0.15
Social cognition	11.8 ± 4.9	11.3 ± 4.7	1.3 (-1.1; 3.6)	0.33	9.6 ± 4.4	8.8 ± 4.5	2.3 (0.3; 4.2)	0.054
Social communication	18.6 ± 9.4	19.4 ± 8.6	-0.5 (-5.9; 4.9)	0.86	17.8 ± 8.2	15.9 ± 7.6	1.6 (-2.6; 5.7)	0.48
Social motivation	11.1 ± 4.1	11.8 ± 4.3	-0.4 (-2.9; 2.0)	0.74	13.8 ± 5.7	14.1 ± 5.3	-0.2 (-2.2; 1.9)	0.88
RI&RB	11.4 ± 5.4	11.8 ± 6.2	-0.1 (-2.2; 2.0)	0.95	11.4 ± 5.2	10.5 ± 5.8	2.1 (-0.4; 4.7)	0.14

Data are given as mean ± SD and estimated differences between fish oil vs safflower oil are shown as mean (95% CI). Stratified analyses were performed by linear mixed models with participant ID as random effect and treatment, baseline, sequence, and period as fixed effects.

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; RI&RB, restricted interests and repetitive behaviour.