Table H-11. Findings on omega-3 fatty acid supplementation for ADHD

| **Study**  **(Companion)**  **N**  **Qualitya**  **Design**  **Age Categoryb** | **Intervention** | **Comparison** | **Follow-up Times** | **Findings–Intervention** | **Findings–Comparison** | **Between group P value** |
| --- | --- | --- | --- | --- | --- | --- |
| **Behavior changes** | | | | | | |
| Manor, 201260  (Manor, 201361)  200  Good  RCT  b | Phospha-tidylserine enriched with omega-3 fatty acids | Placebo | 15 weeks | Euphoric  % patients with outcome = 38.9  Anxiety  % patients with outcome = 45  Irritable  % patients with outcome = 79.1  Prone Cry  % patients with outcome = 62.7  Talk Less  % patients with outcome = 31.8  Sad/Unhappy  % patients with outcome = 40  Irritability  % patients with outcome = 15.31 | Euphoric  % patients with outcome = 34.6  Anxiety  % patients with outcome = 63.5  Irritable  % patients with outcome = 84.6  Prone Cry  % patients with outcome = 57.7  Talk Less  % patients with outcome = 32.7  Sad/Unhappy  % patients with outcome = 34  Irritability  % patients with outcome = 11.63 | NR  NR  NR  NR  NR  NR  NR |
| **Changes in standardized symptom scores** | | | | | | |
| Anand, 201662  50  Good  RCT  c | Polyunsaturated fatty acids (300 mg/d) plus atomoxetine (0.5 mg/kg/d) | Atomoxetine (0.5 mg/kg/d) | 4 months | Conners Parent Rating Scale-Revised: Short Form  Mean = 36.6 (SD = 2.21) | Conners Parent Rating Scale-Revised: Short Form  Mean = 37.4 (SD = 2.18) | NS |
| Gustafsson, 201063  109  Good  RCT  b | Omega-3 fatty acid supplemen-tation (eico-sapentaenoic acid 500mg daily) | Placebo | 15 weeks | Total Conners Parent Rating Scale score  Mean = 43.8 (SD = 18.6)  Total Conners Rating Scale score  Mean = 43.1 (SD = 18.8) | Total Conners Parent Rating Scale score  Mean = 39.4 (SD = 18.4)  Total Conners Rating Scale score  Mean = 40.7 (SD = 17.9) | NS  NS |
| Johnson, 200964  (Johnson, 201265)  75  Good  RCT  b | Omega-3/6 fatty acid supplemen-tation (792mg daily) | Placebo | 3 months (double-blind phase)  6 months (open-label extension: continuous and naïve groups) | ADHD Rating Scale  Mean change = -3.78 (7.14)  ADHD Rating Scale  Mean change = -7.82 (8.07) | ADHD Rating Scale  Mean change = -1.65 (4.54)  ADHD Rating Scale  Mean change = -5.81 (7.16) | NS  NS |
| Manor, 201260  (Manor, 201361)  200  Good  RCT  b | Phospha-tidylserine enriched with omega-3 fatty acids | Placebo | 15 weeks  (treatment and placebo groups, N=162)  30 weeks (open-label extension: continuous and naïve groups, N=147) | CRS-P PS-Omega-3 continuous (30 weeks)  ADHD Index Mean = 64.05 (10.21)  CRS-T PS-Omega-3 continuous (30 weeks)  ADHD Index Mean= 62.35 (10.64)  CRS-P PS-Omega-3 continuous (30 weeks)  ADHD Index Mean Change = -0.95 (7.91)  CRS-T PS-Omega-3 continuous (30 weeks)  ADHD Index Mean Change = 0 (8.62) | CRS-P Placebo (weeks 1-15)  ADHD Index Mean = 65.67 (12.79)  CRS-T Placebo (weeks 1-15)  ADHD Index Mean = 64.44 (10.07)  CRS-P PS-Omega-3 (weeks 15-30)  ADHD Index Mean Change = -2.86 (8.51)  CRS-T PS-Omega-3 (weeks 15-30)  ADHD Index Mean Change = -1.72 (6.19) | NS  NS  NS  NS |
| Milte, 201266  (Milte, 201567)  90  Good  RCT  b | Fish oil rich in the omega-3 fatty acid, eico-sapentaenoic acid (EPA) | Fish oil rich in the omega-3 fatty acid, docosahexaenoiacid (DHA)  Placebo: Linoleic acid (LA) | 4 months | Conners Parent Rating Scale ADHD total  Mean between-group change (vs. placebo) = 1.56 (1.77) | Conners Parent Rating Scale ADHD total  Mean between-group change (vs. placebo) = 1.64 (1.9) | NR  EPA vs. placebo p=0.38  DHA vs. placebo p=0.39 |
| Raz, 200968  78  Fair  RCT  b | Omega-3 fatty acid supplemen-tation | Placebo | 1.75 months | Conners-ADHD (Teacher)  Mean = 3.64 (1.48)  Conners Mood (Teacher)  Mean = 2.76 (1.28)  Conners Mood (Parent)  Mean = 3.44 (1.42) | Conners-ADHD (Teacher)  Mean = 3.66 (1.12)  Conners Mood (Teacher)  Mean = 2.74 (1.30)  Conners Mood (Parent)  Mean = 4.03 (1.25) | NS  NS  NS |
| Widenhorn-Muller, 201469  110  Fair  RCT  b | Omega-3 fatty acid supplementation (720 mg daily) plus 15 mg vitamin E | Placebo | 4 | CBCL total problems  Mean = 62.36 (SE = 1.47)  Teacher Report Form--total problems  Mean = 55.8 (SE = 1.09) | CBCL total problems  Mean = 60.15 (SE = 1.38)  Teacher Report Form--total problems  Mean = 56.82 (SE = 1.16) | P=0.98  P=0.62 |
| Hariri, 201270  120  Poor  RCT  b | Omega-3 fatty acid supplemen-tation (900 mg daily) | Placebo | 8 weeks | Conners Abbreviated  Mean = 21.03 (3.98) | Conners Abbreviated  Mean = 24.02 (4.22) | P=0.251 |
| **Elevated blood pressure** | | | | | | |
| Manor, 201260  (Manor, 201361)  200  Good  RCT  b | Phospha-tidylserine enriched with omega-3 fatty acids | Placebo | 15 weeks | Systolic  Mean = 103.6 (SD = 14.82)  Diastolic  Mean = 64.66 (SD = 11.39) | Systolic  Mean = 100.25 (SD = 12.95)  Diastolic  Mean = 63.89 (SD = 10.28) | P=0.955  P=0.342 |
| **Functional impairment** | | | | | | |
| Johnson, 200964  (Johnson, 201265)  75  Good  RCT  b | Omega-3/6 fatty acid supplementation (792 mg daily) | Placebo | 3 months (double-blind phase)  6 months (open-label extension: continuous and naïve groups) | Clinical Global Impression score  Mean change = -0.58 (0.87)  Clinical Global Impression score  Mean change = -1.24 (1.07) | Clinical Global Impression score  Mean change = -0.13 (0.50)  Clinical Global Impression score  Mean change = -0.93 (0.92) | NS  NS |
| **Sleep disturbance** | | | | | | |
| Manor, 201260  (Manor, 201361)  200  Good  RCT  b | Phospha-tidylserine enriched with omega-3 fatty acids | Placebo | 15 weeks | Insomnia  % patients with outcome = 38.2  Severe insomnia  % patients with outcome = 2.04  Nightmares  % patients with outcome = 29.1 | Insomnia  % patients with outcome = 53.9  Severe insomnia  % patients with outcome = 6.98  Nightmares  % patients with outcome = 34.6 | NR  NR  NR |
| **Tics or other movement disorders** | | | | | | |
| Manor, 201260  (Manor, 201361)  200  Good  RCT  b | Phospha-tidylserine enriched with omega-3 fatty acids | Placebo | 15 weeks | Tics  % patients with outcome = 22.7 | Tics  % patients with outcome = 32.7 | NR |
| **Gastrointestinal symptoms** | | | | | | |
| Manor, 201260  (Manor, 201361)  200  Good  RCT  b | Phospha-tidylserine enriched with omega-3 fatty acids | Placebo | 15 weeks | Stomachaches  % patients with outcome = 39.5  Decreased appetite  % patients with outcome = 32.7  Severely decreased appetite  % patients with outcome = 4.08 | Stomachaches  % patients with outcome = 46.2  Decreased appetite  % patients with outcome = 32.7  Severely decreased appetite  % patients with outcome = 4.65 | NR  NR  NR |
| **Growth suppression** | | | | | | |
| Manor, 201260  (Manor, 201361)  200  Good  RCT  b | Phospha-tidylserine enriched with omega-3 fatty acids | Placebo | 15 weeks | Height in cm  Mean = 135.25 (SD = 13.35) | Height in cm  Mean = 136.77 (SD = 12.26) | P=0.196 |
| **Increased heart rate** | | | | | | |
| Manor, 201260  (Manor, 201361)  200  Good  RCT  b | Phospha-tidylserine enriched with omega-3 fatty acids | Placebo | 15 weeks | Increased Heart Rate  Mean = 79.72 (SD = 12.03) | Increased Heart Rate  Mean = 81.18 (SD = 13.24) | p=0.825 |
| **Personality change** | | | | | | |
| Manor, 201260  (Manor, 201361)  200  Good  RCT  b | Phospha-tidylserine enriched with omega-3 fatty acids | Placebo | 15 weeks | Uninterested  % patients with outcome = 32.7 | Uninterested  % patients with outcome = 38 | NR |
| **Weight decrease** | | | | | | |
| Manor, 201260  (Manor, 201361)  200  Good  RCT  b | Phospha-tidylserine enriched with omega-3 fatty acids | Placebo | 15 weeks | Weight (kg)  Mean = 33.39 (SD = 10.61) | Weight (kg)  Mean = 33.06 (SD = 8.42) | P=0.980 |

a See Methods section “Quality Assessment of Individual Studies” for definitions of quality assessment ratings.

b Age categories: a = children aged ≤6 years, b = children aged 7-17, c = children of all ages ≤17.

Abbreviations: ADHD=attention deficit hyperactivity disorder; CRS-P=Conners Rating Scale-Parent; CRS-T=Conners Rating Scale-Teacher; NR=not reported; SE=standard error; SD=standard deviation; RCT=randomized controlled trial