Complementary and alternative treatments

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Disclosures

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Definitions

• Complementary and Alternative Medicine (CAM)
• Complementary and Alternative Treatments (CATs)

– Group of diverse medical or other health care related practices or products that are not currently part of conventional medicine
– Complementary treatments, in conjunction with traditional medicine
– Alternative treatments, in place of traditional medicine
Complementary and Alternative Treatments

• Common targets:
  – Sleep
  – Anxiety
  – Attention symptoms
  – Irritability/aggression
  – OCD like symptoms
  – Social functions

• Biological vs non-biological treatments
Evdokia’s classification of CAT’s

- Likely effective, acceptable safety profile – encourage use but monitor

- Well tolerated, unknown/inconclusive efficacy: tolerate, encourage objective monitoring

- Well tolerated, no evidence of efficacy: discourage

- Unsafe/unknown safety, inconclusive or no efficacy: discourage
Common CATs with some evidence for their use
Omega 3 fatty acid supplements

- **EPA**: most common in the body
  - Mood regulation, antidepressant effects
- **DHA**: crucial for neurodevelopment
  - Important for vision, learning

- **Side effects**: Gastrointestinal distress, fishy odor, higher doses interfere with Vitamin K metabolism—may cause bleeding
  - Regulatory agencies have provided maximums:
    - >8 years, total EPA + DHA < 1 gr
    - >8 years, total EPA + DHA < 3 gr
Omega-3 Polyunsaturated Fatty Acids in Youths with Attention Deficit Hyperactivity Disorder (ADHD): A Systematic Review and Meta-analysis of Clinical Trials and Biological Studies

Jane Pei-Chen Chang\textsuperscript{a,b,c,*}, Kuan-Pin Su\textsuperscript{a,b,c,d}, Valeria Mondelli\textsuperscript{a}, and Carmine M. Pariante\textsuperscript{a}
### Omega 3s for ADHD - inattention

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>N3 Mean</th>
<th>SD</th>
<th>Total</th>
<th>Placebo Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Random, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gustafsson 2010</td>
<td>2.00</td>
<td>4.32088</td>
<td>46</td>
<td>1.5</td>
<td>4.788528</td>
<td>46</td>
<td>17.2%</td>
<td>0.11 [-0.30, 0.52]</td>
<td>2010</td>
</tr>
<tr>
<td>Perera 2012</td>
<td>0.46</td>
<td>0.617</td>
<td>48</td>
<td>0.15</td>
<td>0.093</td>
<td>46</td>
<td>16.7%</td>
<td>0.69 [0.27, 1.11]</td>
<td>2012</td>
</tr>
<tr>
<td>Widenhorn-Muller 2014</td>
<td>0.3</td>
<td>0.08</td>
<td>44</td>
<td>0.27</td>
<td>0.075498</td>
<td>48</td>
<td>16.9%</td>
<td>0.38 [-0.03, 0.80]</td>
<td>2014</td>
</tr>
<tr>
<td>Bos 2015</td>
<td>1.4</td>
<td>2.783682</td>
<td>19</td>
<td>-1.6</td>
<td>3.404490</td>
<td>19</td>
<td>7.4%</td>
<td>0.94 [0.27, 1.62]</td>
<td>2015</td>
</tr>
</tbody>
</table>

Subtotal (95% CI)

- Heterogeneity: $\tau^2 = 0.06; \chi^2 = 6.11, df = 3 (P = 0.11); I^2 = 51%$
- Test for overall effect: $Z = 2.87 (P = 0.004)$

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>N3 Mean</th>
<th>SD</th>
<th>Total</th>
<th>Placebo Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Random, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Richardson 2002</td>
<td>5.9</td>
<td>10.05471</td>
<td>15</td>
<td>1.1</td>
<td>9.236206</td>
<td>14</td>
<td>6.2%</td>
<td>0.48 [-0.26, 1.12]</td>
<td>2002</td>
</tr>
<tr>
<td>Sinn 2008</td>
<td>3.95</td>
<td>5.486155</td>
<td>77</td>
<td>0.59</td>
<td>8.622708</td>
<td>27</td>
<td>15.1%</td>
<td>0.52 [0.07, 0.96]</td>
<td>2008</td>
</tr>
<tr>
<td>Manor 2012</td>
<td>4.97</td>
<td>9.79</td>
<td>99</td>
<td>2.74</td>
<td>9.05</td>
<td>42</td>
<td>20.6%</td>
<td>0.23 [-0.13, 0.59]</td>
<td>2012</td>
</tr>
</tbody>
</table>

Subtotal (95% CI)

- Heterogeneity: $\tau^2 = 0.00; \chi^2 = 1.08, df = 2 (P = 0.58); I^2 = 0%$
- Test for overall effect: $Z = 2.71 (P = 0.007)$

Total (95% CI)

- Heterogeneity: $\tau^2 = 0.01; \chi^2 = 7.44, df = 6 (P = 0.28); I^2 = 19%$
- Test for overall effect: $Z = 4.30 (P < 0.0001)$
- Test for subgroup differences: $\chi^2 = 0.30, df = 1 (P = 0.58), I^2 = 0%$
Omega 3s for ADHD - hyperactivity
Omega 3s for ADHD - cognition
Omega 3 fatty acids in preschoolers with ASD

A randomized, placebo controlled trial of omega-3 fatty acids in the treatment of young children with autism

Deepali Mankad, Annie Dupuis, Sharon Smile, Wendy Roberts, Jessica Brian, Toni Lui, Lisa Genore, Dina Zaghoul, Alana Laboni, Peggy Margaret A Marcon and Evdokia Anagnostou
Figure 2 Omega-3 vs Placebo effects on the PDDBI and BASC-2. (a,b) Negative change reflects improvement, and (c,d) positive values favor Omega 3 over placebo. *Items are reversed so that negative change corresponds to an improvement across all PDDBI and BASC items.
N-acetyl-cysteine

- Important for glutathione biosynthesis, a very important antioxidant
  - Central effects at the NMDA receptor
Published in final edited form as. 

**A Randomized Controlled Pilot Trial of Oral N-Acetylcysteine in Children with Autism**

Antonio Y. Hardan, M.D.¹, Lawrence K. Fung, M.D., Ph.D.¹, Robin A. Libove, B.S.¹, Tetyana V. Obukhanych, Ph.D.², Surekha Nair, M.D.¹, Leonore A. Herzenberg, Ph.D.², Thomas W. Frazier, Ph.D.³, and Rabindra Tiouvaniam, Ph.D.¹

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**Figure 1.**
Significant improvements with NAC treatment for the primary outcome measures: Aberrant Behavior Checklist-Irritability subscale (ABC-Irritability) (F=8.80; p<0.001; d=0.96) with improvement being observed in week 4 and continuing through week 8 and Week 12. Error bars denote standard deviations. For clarity, positive error bars are shown for the placebo group, and negative error bars are shown for the NAC group.

José Paulo Couto, Ricardo Moreira

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Placebo Mean</th>
<th>Placebo SD</th>
<th>Placebo Total</th>
<th>NAC Mean</th>
<th>NAC SD</th>
<th>NAC Total</th>
<th>Weight IV, Random, 95% CI</th>
<th>Mean Difference IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarris 2015</td>
<td>21.05</td>
<td>9.31</td>
<td>22</td>
<td>21.77</td>
<td>8.04</td>
<td>22</td>
<td>21.9%</td>
<td>-0.72 [-5.86, 4.42]</td>
</tr>
<tr>
<td>Costa 2017</td>
<td>21.8</td>
<td>6</td>
<td>20</td>
<td>21.3</td>
<td>8.1</td>
<td>20</td>
<td>23.4%</td>
<td>0.50 [-4.26, 5.26]</td>
</tr>
<tr>
<td>Afshar 2012</td>
<td>-5.73</td>
<td>3.16</td>
<td>24</td>
<td>-10.87</td>
<td>2.94</td>
<td>24</td>
<td>36.8%</td>
<td>5.14 [3.41, 6.87]</td>
</tr>
<tr>
<td>Ghanizadeh 2016</td>
<td>19.7</td>
<td>9.7</td>
<td>11</td>
<td>11.3</td>
<td>5.7</td>
<td>11</td>
<td>17.8%</td>
<td>8.40 [2.09, 14.71]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>77</td>
<td></td>
<td></td>
<td>80</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>3.35 [-0.21, 6.91]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 8.19; Chi² = 8.64, df = 3 (P = 0.03); I² = 65%
Test for overall effect: Z = 1.84 (P = 0.07)

Fig. 5. Forest plot of mean difference (MD) by random effects model.
Hyperbaric oxygen therapy for the treatment of children and youth with Autism Spectrum Disorders: An evidence-based systematic review

Cynthia Goldfarb\textsuperscript{a,b,*}, Lisa Genore\textsuperscript{b}, Carolyn Hunt\textsuperscript{a}, Janine Flanagan\textsuperscript{a}, Mark Handley-Derry\textsuperscript{a}, Anita Jethwa\textsuperscript{a}, Nicola Jones-Stokreef\textsuperscript{a}, S.M.L. Kirkpatrick\textsuperscript{a}, A. Richards\textsuperscript{a}, Lillian Rojnica\textsuperscript{a}, Clive Schwartz\textsuperscript{a}, David Shaw\textsuperscript{a}, Diann Superina-Bell\textsuperscript{a}, Elizabeth Young\textsuperscript{a}, Evdokia Anagnostou\textsuperscript{a,b}
<table>
<thead>
<tr>
<th>Citation</th>
<th>Design</th>
<th>Participants (completers)</th>
<th>Intervention</th>
<th>Outcomes</th>
<th>Adverse Events</th>
<th>Class of Evidence: HBOT impact on ASD SX/Behavior/skills</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roasignol et al. (2007)</td>
<td>Prospective Open-label pilot study, no control group</td>
<td>N = 18 Ages 3–16 years</td>
<td>40 × 45 min sessions HBOT (1.3/1.5 ATA)</td>
<td>Decrease ATEC (p=0.02)</td>
<td>None reported</td>
<td>Class IV</td>
</tr>
<tr>
<td>Rossignol et al. (2009)</td>
<td>RCT</td>
<td>N = 56 Autism Age 2–7 years</td>
<td>N = 26 HBOT-30 Control-26 Autism Age 2–7 yrs</td>
<td>Decrease SRS motivation subscale (p=0.018)</td>
<td>Improved ABC—C social withdrawal (p=0.008)</td>
<td>Class I (Physician CGI) (ABC, ATEC)</td>
</tr>
<tr>
<td>Granpeesheh et al. (2010)</td>
<td>Randomized control trial</td>
<td>N = 34 Autism HBOT = 18 Control = 16 Autism Age 2–7 yrs</td>
<td>80 × 1 h HBOT (1.3 ATA) Control: 80 × 1 h room air</td>
<td>Clinician CGI “responder”: 9/30 vs. 2/26 (p=0.047) favouring treatment group</td>
<td>No change on ABC, ATEC</td>
<td>Class I</td>
</tr>
<tr>
<td>Jepson et al. (2011)</td>
<td>Non-concurrent multiple-baseline-across participants</td>
<td>N = 16 Autism, PDD-NOS, Aspergers Age 3–9 yrs</td>
<td>40 × 1 h HBOT (1.3 ATA)</td>
<td>No group differences on any of numerous standardized test/behavioural observation</td>
<td>1 case UTI and rash</td>
<td>Class III</td>
</tr>
<tr>
<td>Sampanthavivat et al. (2012)</td>
<td>Randomized control trial</td>
<td>N = 58 Autism Age 3–9 years</td>
<td>20 × 1 h HBOT (1.5 ATA) Control: 20 × 1 h 115 ATA, room air</td>
<td>No group differences on any of numerous standardized test/behavioural observation</td>
<td>Minor-grade ear barotrauma</td>
<td>Class I</td>
</tr>
</tbody>
</table>
Chelation Therapy

Chelation for autism spectrum disorder (ASD) (Review)

James S, Stevenson SW, Silove N, Williams K

- No evidence of benefit
- Evidence of harm
Related questions we received in advance

- Stem cell therapies
  - No RCT to-date, but active program at Duke U
  - Potential for harm

- Cannabis

Adi Aran¹ID, Hanoch Cassuto², Asael Lubotzky¹, Nadia Wattad¹, Esther Hazan¹

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Is Cannabis Use Associated With the Worst Inpatient Outcomes in Attention Deficit Hyperactivity Disorder Adolescents?

Rikinkumar S. Patel¹, Priya Patel², Kaushal Shah³, Mandeep Kaur⁴, Zeeshan Mansuri⁵, Ramkrishna Makani⁶

Cannabinoids in attention-deficit/hyperactivity disorder: A randomised-controlled trial

Ruth E. Cooperᵃ,b, Emma Williamsᵃ, Seth Seegobinᵃ,c, Charlotte Tyeᵃ, Jonna Kuntsiᵃ, Philip Ashersonᵃ,*
Evdokia’s classification of CAT’s

- Likely effective, acceptable safety profile – encourage use but monitor
  - Melatonin, omega 3s for ADHD, some antioxidants (NAC), meditation practices, sensory interventions

- Well tolerated, unknown/inconclusive efficacy: tolerate, encourage objective monitoring
  - Most vitamin supplementation, including Vit C, B6, B12 /Most antioxidants
  - Gluten/casein free diets (Caveat: associated with nutritional deficiencies)
  - Carnosine (amino-acids), digestive enzymes / Omega3 fatty acids
  - Variety of non biological interventions (listening, vision therapies, manual therapies, acupuncture etc)
  - Neurofeedback
  - Animal assisted therapies, music therapy and exercise
  - probiotics

- Well tolerated, no evidence of efficacy: discourage
  - HBOT, secretin, listening therapies (AIT)

- Unsafe/unknown safety, inconclusive or no efficacy: discourage
  - Chelation, Chlorine Dioxide (DO) – MMS-Bleach therapies, certain herbs (e.g. kava)
Useful resources

- National Institutes of Health National Center for Complementary and Alternative Medicine (http://nccam.nih.gov.myaccess.library.utoronto.ca/)
- Toolkits (http://nccam.nih.gov.myaccess.library.utoronto.ca/timeto talk/)
From disability to possibility