Brain-Specific Effects of Ambrotose® Products: A Preliminary Animal Study to Investigate Cognitive Benefits Found in Humans

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BACKGROUND: Saccharides play important roles in the brain, where they are largely glycoconjugated to proteins or lipids to assist in structural development, synaptogenesis and synaptic transmission. Saccharides can also be a source for energy and neurotransmitter production. There is considerable interest in better understanding the health benefits of orally administered naturally derived polysaccharides and exploring their potential to influence neurologic function and health. A number of clinical studies have demonstrated that intake of a mixed saccharide prebiotic glyconutritional dietary supplement, Ambrotose® complex (AMB), can improve various aspects of learning, memory, and mood in healthy adults.

OBJECTIVES: To review the current literature on the cognitive benefits of Ambrotose complex consumption and explore possible mechanisms by which it and a similar formulation enhanced with Undaria pinnatifida fucoidans, Advanced Ambrotose® powder (AA), might influence brain function.

METHODS: C57BL/6 male mice (5/group) were fed a normal diet and received daily 57.4 mg/kg of Ambrotose complex or Advanced Ambrotose powder, or water (control) by oral gavage for 28 days. On day 29 animals were sacrificed by CO₂ asphyxiation and the hippocampus and prefrontal cortex were immediately removed and flash frozen in liquid nitrogen. Total RNA was extracted and quantitative RT-PCR was used to measure levels of brain-derived neurotrophic factor (BDNF), interleukin (IL)-6, IL-1β, and tumor necrosis factor (TNF)-α mRNA.

RESULTS: Six randomized, double-blind, placebo-controlled human clinical trials indicate that oral intake of Ambrotose® complex exerts positive effects on cognitive function and mood in healthy adults (Table 2). Intake by mice of a dose of Advanced Ambrotose w/w equivalent to the 4 g daily dosage recommendation for adults for 28 days significantly increased gene expression of BDNF in the hippocampus and decreased expression of IL-6 in the cortex (Figure).

DISCUSSION: A number of clinical studies suggest that Ambrotose complex shows promise, when taken orally, in supporting neurologic health and function. BDNF is a commonly studied protein associated with a variety of brain functions, including learning, memory, and stress. An increase in BDNF has been shown to be associated with better performance on simple working memory task [Reading span, first session].

Table 1. Ambrotose product formulations

<table>
<thead>
<tr>
<th>Ambrotose complex powder</th>
<th>Aloe vera gel powder</th>
<th>Aloe vera gel extract</th>
<th>Larch arabinogalactan</th>
<th>Gum ghatti</th>
<th>Gum tragacanth</th>
<th>Glucosamine</th>
<th>Undaria pinnatifida</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced Ambrotose powder</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Table 2. Ambrotose complex improves cognitive function and mood in healthy adults

<table>
<thead>
<tr>
<th>Study design</th>
<th>Population</th>
<th>N</th>
<th>Dose</th>
<th>Duration</th>
<th>Cognitive tests performed</th>
<th>Significant effects</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized, double-blind, placebo-controlled</td>
<td>Healthy middle-aged adults</td>
<td>109</td>
<td>3.6 g/day</td>
<td>12 weeks</td>
<td>Rey Auditory-Verbal Learning Test (RA VLT); Visual Pattern Span Recall; Visual Pattern Span Recognition Reading Span; Computation Span; Stroop; Letter Cancellation; Digit Symbol Coding, Boxes test, Matrix Reasoning &amp; Spot the Word [Weschler Adult Intelligence Scale III]; POMS; Depression Anxiety and Stress Scale; Perceived Stress Scale-10</td>
<td>Better performance on immediate recall tasks [RA VLT trials 2 &amp; 5] and recognition memory task [RA VLT Recognition]; lower depression-dejection and anger-hostility scores [POMS]</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>73</td>
<td>4 g</td>
<td>2 hr</td>
<td>RA VLT; Cognitive Demand battery (Serial Threes; Serial Sevens, Rapid Visual Information Processing (RVIP), Visual analogue mental fatigue scale); POMS; Short-form health survey (SF-36); State-trait anxiety questionnaire; Bond-Lader visual analogue scale</td>
<td>Better performance on recognition memory task [RA VLT recognition A &amp; B] and working memory task [Serial Sevens] during mental fatigue. Effects were independent of blood glucose response.</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>45</td>
<td>7 g</td>
<td>10 min</td>
<td>RA VLT; Self-Ordered Pointing; Digit Span forwards; Digit Span backwards; Matrix Reasoning [Weschler Adult Intelligence Scale III]</td>
<td>No effects. 25 g glucose also showed no effects.</td>
<td>12</td>
</tr>
<tr>
<td>Randomized, double-blind, placebo-controlled, crossover</td>
<td>Healthy college students</td>
<td>30</td>
<td>1 tbsp (approx. 4 g)</td>
<td>45 min</td>
<td>Same-Different visual discrimination; Standard Progressive Matrices; Stroop</td>
<td>Better performance on visual discrimination task [Same-Different]</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>32</td>
<td>1 tbsp</td>
<td>45 min</td>
<td>Reading Span; Operation Span</td>
<td>Better performance on simple working memory task [Reading span, first session]</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Healthy male college students</td>
<td>20</td>
<td>1 tbsp</td>
<td>30 min</td>
<td>EEG recordings during focus on a stationary visual target</td>
<td>Enhanced power in theta, alpha and beta brain wave frequencies associated with attention and arousal</td>
<td>14</td>
</tr>
</tbody>
</table>
with probiotic supplementation\(^2\) and with enhanced learning and memory and elevated mood, particularly in the hippocampus.\(^3\) Specific cytokines are also known to be expressed in the brain. In particular, IL-1 and IL-6 are pro-inflammatory cytokines that have been shown to regulate learning and memory in healthy animals,\(^4,5\) while IL-1 \(\beta\), IL-6, and TNF-alpha are believed to play a pivotal role in “sickness behavior” – when inflammation leads to behavioral changes, including impaired cognitive function and anhedonia.\(^6\) These preliminary study results suggest that clinical improvements in brain function following Ambrotose product intake may be correlated with brain-specific changes in gene expression, particularly that of BDNF and IL-6 in areas of the brain important for regulating learning, memory, and mood behaviors.

CONCLUSIONS: In previous preclinical studies, Ambrotose complex and Advanced Ambrotose powder have been shown to exert prebiotic effects *in vitro*\(^7\) and modify serum glycosylation profiles in adults.\(^8,9\) The current study suggests that changes in the expression of genes in the brain associated with learning, memory and mood may contribute to the clinically-documented cognitive improvements reported for Ambrotose products. Additional research is needed to confirm these results and to better determine the mechanisms that underlie the cognitive benefits of Ambrotose products.

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REFERENCES