A review of human and animal studies assessing the effects of oral polysaccharides on cognitive function and mood

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BACKGROUND: Recent research on the consumption of Ambrotose® complex, a mixture of polysaccharides from aloe vera, Larch and various gums, has demonstrated improvements in cognitive function and mood in healthy adults. While the immunomodulatory functions of specific oral polysaccharides are fairly well-established (1), their ability to affect brain function is a relatively novel concept. A comprehensive collection of the available literature on this subject would be a useful tool for researchers interested in the cognitive and mood effects of dietary polysaccharides.

OBJECTIVE: To review clinical and animal studies demonstrating the use of orally administered plant-, fungal-, or lichen-derived polysaccharides for support of cognitive function and mood.

STUDY DESIGN: Randomized, double-blind, placebo-controlled studies of healthy humans and well-controlled animal studies were identified by conducting electronic searches on PubMed and Google Scholar. Reference lists of articles were also searched for additional relevant studies. Only articles published in English were included in this review.

OUTCOMES MEASURED: All studies measured outcomes of brain function, including, but not limited to, results from behavioral tasks of learning and memory and mood state questionnaires and recordings of brain electrical activity.

RESULTS: Five randomized clinical studies (Table 1) and seven animal studies (Table 2) were identified. In a compilation of four human studies, supplementation with Ambrotose® complex was shown to improve recall, recognition memory and mood in healthy middle-aged adults and enhance perception, working memory and brain wave frequencies associated with attention and arousal in healthy college students. Improvements in mood have also been observed in a study of healthy humans following consumption of beta-glucan. In two animal studies, oral administration of isolichenan, an alpha-glucan, resulted in improved learning and memory in rats with cognitive impairments, but not in healthy animals. Social withdrawal in a study of mice with sickness behavior was lessened with the addition of pectin to the diet. Four animal studies demonstrated enhancements of the electrophysiological correlate of learning and memory, long-term potentiation (LTP; see Figure 1) in the hippocampi of healthy rats *in vivo* following oral administration of glucans from various sources.

Table 1. Cognitive and mood effects of oral polysaccharides in healthy humans.

Polysaccharide(s) (product name)	Source(s)	Study design	Population	N	Dose/day	Duration	Cognitive tests performed	Significant effects	Reference
Mixed polysaccharide product (Ambrotose complex)	*Aloe barbadensis* [leaf gel], *Larix* sp. [bark], *Anogeissus latifolia* [bark], *Astragalus gummifer* [stem], *Oryza sativa* [seed], glucosamine HCl	Randomized, double-blind, placebo-controlled	Healthy middle-aged adults	109	3.6 g	12 weeks	Rey Auditory-Verbal Learning Test (RAVLT); Visual Pattern Span Recall; Visual Pattern Span Recognition; Reading Span; Computation Span; Stroop; Letter Cancellation; Digit Symbol Coding, Boxes test, Matrix Reasoning & Spot the Word [Weschler Adult Intelligence Scale III]; Profile of Mood State (POMS) questionnaire; Depression Anxiety and Stress Scale; Perceived Stress Scale-10	Better performance on immediate recall tasks [RAVLT trials 2 & 5] and recognition memory task [RAVLT Recognition]; lower depression-dejection and anger-hostility scores [POMS]	(2)
		Randomized, double-blind, placebo-controlled, crossover	Healthy college students	30	1 tablespoon (approx. 5 g) once	45 min	Same-Different visual discrimination; Standard Progressive Matrices; Stroop	Better performance on visual discrimination task [Same-Different]	(3)
			Healthy college students	32	1 tablespoon (approx. 5 g) once	45 min	Reading Span; Operation Span	Better performance on simple working memory task [Reading span, first session]	(3)
			Healthy male college students	20	1 tablespoon (approx. 5 g) once	30 min	EEG recordings during focus on a stationary visual target	Enhanced power in theta, alpha and beta brain wave frequencies associated with attention and arousal	(4)
β-1,3/1,6 glucan (Wellmune WGP®)	*Saccharomyces cerevisiae*	Randomized, double-blind, placebo-controlled	Healthy adult marathon runners	75	250 mg or 500 mg	4 weeks	POMS questionnaire	250 mg reduced tension and fatigue at 4 weeks and reduced confusion at 2 and 4 weeks; 500 mg reduced anger at 2 weeks, reduced fatigue, tension and confusion at 2 and 4 weeks and increased vigor at 2 and 4 weeks	(5)

Table 2. Behavioral and electrophysiological effects of oral polysaccharides in rodents.

Polysaccharide(s)	Source(s)	Animals	Dose/day	Duration	Cognitive tests performed	Significant effects	Reference
α-glucan (isolichenan)	*Cetrariella islandica*	♂ Wistar rats receiving daily intracerebroventricular injections of β-amyloid peptide from Day -7 to Day 4	100 or 200 mg/kg per os (p.o.)	8 days	Morris water maze on Days 5–8	200 mg/kg reversed β-amyloid impaired spatial memory (decreased escape latency on Day 8); no effects on rats without β-amyloid peptide pretreatment	(6)
		5-week old ♂ Std-ddY mice treated with 30% ethanol p.o. 20 min before learning trial	100, 200 or 400 mg/kg p.o. once	30 min before learning trial	Passive avoidance step through and step down	All doses reversed the ethanol impaired fear memory acquisition (all doses increased step through latency and 400 mg/kg increased step down latency); no effects on mice without ethanol exposure	(6)
α-glucan (PC-2)	*Parmelia caperata*	Anesthetized 7-8-week old ♂ Wistar rats	125 or 250 mg/kg p.o. once	30 min before LTP induction (20 pulses at 60 Hz)	*In vivo* extracellular recordings in the dentate gyrus (DG) of the hippocampus	250 mg/kg enhanced the magnitude of LTP* for up to 40 min (measurements end at 1 hour)	(7)
α-glucan (PB-2)	*Flavoparmelia baltimorensis*	Anesthetized 5-6-week old ♂ Wistar rats	50, 100, or 200 mg/kg p.o. once	20 min before LTP induction (30 pulses at 60 Hz)	*In vivo* extracellular recordings in the DG of the hippocampus	100 and 200 mg/kg enhanced the magnitude of LTP* induction (measurements end at 1 hour)	(8)
β-glucan (Hoelen)	*Poria cocos* Wolf	Anesthetized 7-9-week old ♂ Wistar rats	125, 250 or 500 mg/kg p.o. once	30 min before LTP induction (20 pulses at 60 Hz)	*In vivo* extracellular recordings in the DG of the hippocampus	250 and 500 mg/kg enhanced the magnitude of LTP* for up to 25 min (measurements end at 1 hour)	(9)
β-1,3/1,6 glucan (lentinan)	*Lentinula edodes*	Anesthetized 7-8-week old ♂ Wistar rats	200 mg/kg p.o. once	30 min before LTP induction (20 pulses at 60 Hz)	*In vivo* extracellular recordings in the DG of the hippocampus	Enhanced the magnitude of LTP* induction (measurements end at 1 hour)	(10)
Pectin	Citrus [peel]	6–8 week old C56BL/6J mice injected intraperitoneally with 100 µg/kg lipopolysaccharide immediately before testing	10% pectin diet	Fed daily post-weaning @ 3 weeks old	Social exploratory behavior of a novel juvenile mouse	Faster recovery from LPS-induced social withdrawal compared to 5% cellulose diet	(11)

*See Figure 1 for explanation of hippocampal LTP

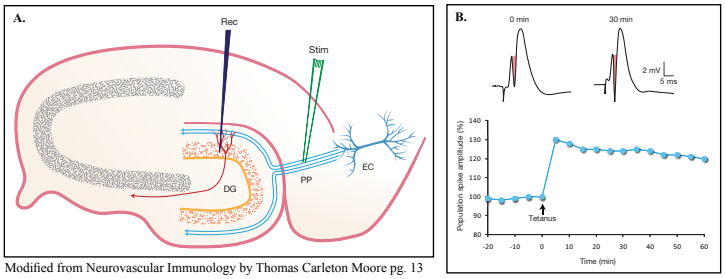

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Figure 1. Representative example of long-term potentiation (LTP) recorded from the rodent hippocampus. The hippocampus is an area of the brain that helps regulate learning and memory and contains one of only a few sites of adult neurogenesis (the generation of new neurons), the dentate gyrus (DG). Due to its organized neuronal circuitry, the hippocampus is commonly utilized to measure various types of synaptic transmission, including a form of synaptic plasticity called LTP. LTP takes place when presynaptic neurotransmitter release occurs repeatedly a few milliseconds before the postsynaptic neuron generates an action potential, rendering the postsynaptic neuron more sensitive to stimulation. Since its discovery in 1973, LTP has been widely studied as a possible cellular mechanism underlying learning and memory. A) Schematic of the general structure of the hippocampus and the placement of electrodes for recording one type of hippocampal LTP. Experimentally, LTP can be recorded from DG neurons when a series of short, high frequency stimuli (tetanus) is applied to the perforant path (PP), a cluster of axons projecting from the entorhinal cortex (EC). B) LTP illustration. The electrode placed in the DG begins by recording responses to single stimuli (baseline). Once a tetanus is applied to the PP through the stimulating electrode, a responding increase in population spike amplitude (reflecting a greater number of neurons firing) can then be seen in the DG neurons. This increase can last from hours to weeks, and possibly longer, depending on the stimulation and recording conditions.

CONCLUSIONS: This review presented research on a variety of polysaccharides that appear to have some influence on cognitive function and/or mood following oral administration in both human and animal studies. Currently, the most promising research in humans is on the mixed polysaccharide product Ambrotose complex, while animal studies appear to place an emphasis on glucans. Interestingly, effects occurred with both acute (<1 hour) and chronic (1–12 weeks) treatments, making it difficult for this review to hypothesize about the possible mechanisms of action underlying the observed changes in electrical activity along with memory behaviors and mood. Animal studies demonstrating the ability of glucans to acutely enhance LTP, the proposed cellular mechanism of learning and memory, implicate the hippocampus as one significant brain area of interest. Due to the differences in polysaccharides studied and outcomes measured, the literature is not yet sufficient to support broad generalizations about efficacy. Further research is warranted to help discern the range of effects of oral polysaccharides on brain function and behavior and to help elucidate the mechanisms behind which they may be occurring.

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