

The effect of phosphatidylserine administration on cognition and symptoms of reactive attachment disorder - a randomized, double-blind, placebo-controlled clinical trial in adolescents

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Background

Reactive Attachment Disorder (RAD) occurs in 1% of the general population and is caused by a disregard for a child's emotional or physical needs, or a repeated change in caregivers. Children with RAD display persistent social and emotional disturbances resulting in underperforming at school. Phosphatidylserine (PS) is a naturally occurring phospholipid that is most concentrated in the brain and has unique regulatory and structural functions. Supplementation with PS beneficially influences numerous neurotransmitter systems such as acetylcholine, dopamine, serotonin and norepinephrine. PS improves the cognitive response to physical or mental stress, and has been shown to improve memory and cognition in healthy individuals. In addition, PS has previously been shown to improve symptoms of attention-deficit hyperactivity disorder (ADHD) and short-term auditory memory in children with ADHD.

Methods

We hypothesized that PS supplementation results in favorable changes in cognition and RAD symptoms in adolescents. **METHODS:** Thirty male and female adolescents (PS: n=14 (11 male, 3 female), 17.7±3.3 years; PLA n=16 (13 male, 3 female), 19.4±2.4 years) from Showa Gakuen school (Tokyo, Japan) ingested 200mg of PS (LIPAMINE-PS, Healthy Navi Co., Ltd., Japan) in form of a cocoa flavored chewable tablet or a matching placebo for two months in a randomized, double-blind, parallel design in accordance with the Basic Principles of the Declaration of Helsinki. Main outcome measures included: (i) RAD symptoms based on DSM-IV-TR; (ii) cognitive tests to evaluate memory, attention and concentration: short-term auditory memory

(Digit Spin Forward), working memory (Digit Span Backward), attention and working memory (Serial Subtraction Test: Serial Sevens), visual-motor integration skills (Beery-Buktenica Developmental Test), processing speed, mental flexibility and language skills. Subjects were randomized into groups based on their baseline working memory scores. Statistical analysis was performed using STATCEL 2 (Oms-Publishing, Saitama, Japan). A p-value of <0.05 was considered statistically significant.

Results

PS administration resulted in a statistically significant decrease in RAD symptoms (-65%) and an increases in sort-term auditory memory (+26%), working memory (+30%), calculus performance (+48%), Visual-Motor Integration (+32%), and processing speed (+32%), p<0.01, as well as language skills (+28%, p<0.05), compared to baseline, while the placebo group showed an improvement in processing speed (+24%, p<0.05).

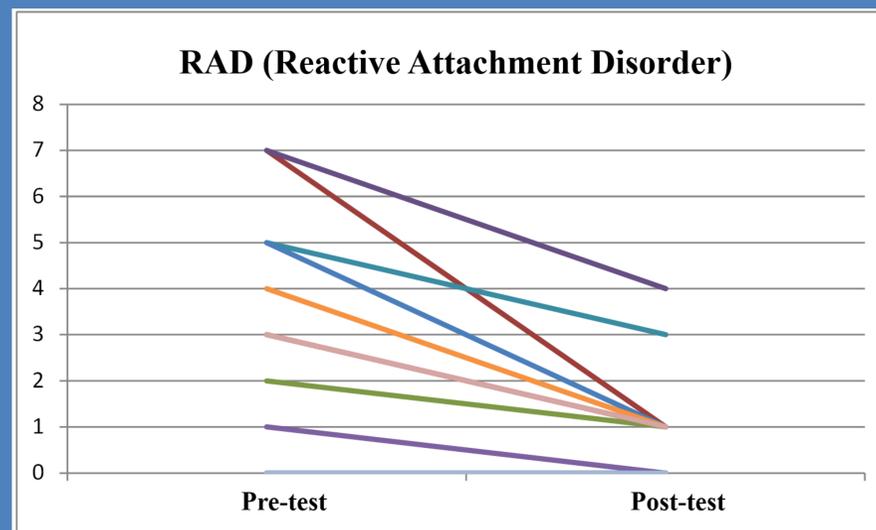


Figure 1. Individual Changes in RAD in the Phosphatidylserine group.

	Phosphatidylserine			Placebo		
	Baseline	Post	Δ	Baseline	Post	Δ
Reactive Attachment Disorder (RAD)						
RAD Symptoms (DSM-IV-TR)	2.6±2.6	0.9±1.2**	-65%	1.2±1.6	1.3±1.7	+8%
Cognition (memory, attention, concentration)						
Short-Term Auditory Memory (Digit Span Forward)	8.7±3.0	11.0±2.5**	+26%	8.0±3.7	8.3±3.3	+4%
Working Memory (Digit Span Backward)	6.4±3.9	8.3±3.5**	+30%	6.3±4.1	6.1±3.6	-3%
Serial Subtraction Test (Serial Sevens)	6.5±5.0	9.6±4.4**	+48%	7.6±6.4	4.4±4.7**	-29%
Visual-Motor Integration (Beery-Buktenica Test)	17.2±5.1	22.7±4.5**	+32%	16.5±5.6	17.2±5.8	+4%
Language Skills	3.9±2.9	5.0±3.2*	+28%	4.8±2.5	5.8±3.3	+21%
Processing Speed	30.8±12.4	40.8±12.8**	+32%	30.4±14.2	37.3±20.4*	+23%
Mental Flexibility	5.8±3.2	6.8±2.4	+17%	4.9±3.9	5.4±3.6	+10%

Data shown as mean±SD. Statistically significant different within group over time: * P<0.05, ** P<0.01.

Table 1. Mean scores at baseline and post-supplementation.

Conclusion

PS supplementation can be an important nutritional strategy to improve RAD symptoms and cognition in adolescents.

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References

- [1] Hardy LT: Attachment theory and reactive attachment disorder: theoretical perspectives and treatment implications. *J Child Adolesc Psychiatr Nurs* 2007, 20(1):27-39.
- [2] Glade MJ, Smith K: Phosphatidylserine and the human brain. *Nutrition* 2015, 31(6):781-6.
- [3] Hirayama S, Terasawa K, Rabeler R, Hirayama T, Inoue T, Tatsumi Y, Purpura M, Jäger R: The effect of phosphatidylserine administration on memory and symptoms of attention-deficit hyperactivity disorder: a randomised, double-blind, placebo-controlled clinical trial. *J Human Nutr Diet* 2014, Suppl 2:284-291.