

# EVALUATION OF THE EFFECTS OF NEPTUNE KRILL OIL ON ADULT ATTENTION DEFICIT AND HYPERACTIVITY DISORDER

LESLIE ROUDER, LCSW<sup>1</sup>

<sup>1</sup>DISABILITY SERVICES, BARRY UNIVERSITY, MIAMI, FLORIDA

## ABSTRACT

### OBJECTIVES

a) To evaluate the effectiveness of Neptune Krill Oil (NKO<sup>®</sup>) in the treatment of adult attention deficit and hyperactivity disorder (ADHD); b) To assess the safeness of long time usage of NKO<sup>®</sup> in adult population

### METHODS

A prospective phase I, open label, study. 30 patients with a mean (SD) age of 23 (1.2) years, having a diagnostic of ADHD for an average of 7 years, free of acute and chronic physical diseases were recruited. The treatment consisted of administration of NKO<sup>®</sup> as softgels (500 mg) once a day medication. The follow up consisted of two evaluations at 12 weeks and at 24 weeks. The patients were tested and retested in all the three Barkley Executive Brain functions: Executive, Behavioral Inhibition and Self Control.

### RESULTS

After completing the treatment, patients showed a statistically significant improvement in all three Barkley's Executive Function scores. NKO<sup>®</sup> was able to improve major brain executive functions after 24 weeks of treatment (60.2% for Concentration, 48.8% for Focus and 47.8 % for Planning skills).

### CONCLUSIONS

NKO<sup>®</sup> may be considered a safe, toxic free treatment able to improve brain executive function for adults having ADHD. This may act to reduce the need for stimulant medication, reducing treatment costs and improving the life quality of patients.

## INTRODUCTION

Attention Deficit and Hyperactivity Disorder (ADHD) was initially described as one of the most chronic conditions of childhood; recently it became clear that the disease manifests syndromic continuity, affecting adults as well. ADHD diagnostic and treatment are well coded: diagnostic is based on DSM-IV and treatment usually implies both pharmacologic and behavioral therapies. Stimulant drugs are the cornerstone of the pharmacologic treatment: drugs are prescribed over long periods of time fact that increases the risk of cumulative toxicity. Over-prescription and long term treatment cost are other concerns associated with classic pharmacologic treatments.

Dietary intake of polyunsaturated fatty acids (PUFA) from different marine natural sources has been positively associated with metabolic, chronic inflammatory and neuro-psychiatric improvement of conditions. Previously published research stated that natural extracts rich in PUFA can reduce the medication dose, improve quality of life and reduce treatment costs related with child and adult ADHD<sup>2</sup>.

Lipids are important constituents of brain, between 50 to 60% of adult brain being composed of lipids; 35% of them are phospholipids having different combinations of PUFA<sup>3</sup>. Both myelin sheath and the neuronal cell membrane have a high concentration of long chains PUFA. Commercially known as omega-3 acids, PUFA are combinations of eicosapentaenoic (EPA 20:5 n-3), docosapentaenoic (DPA 22:5 n-3) and docosahexaenoic (DHA 22:6 n-3) fatty acids frequently esterified with lyso-phosphatidylcholine.

PUFA role in human well being and health was intensely researched in the last years. It has already been proven that EPA is a physiologic competitor of arachidonic acid, influencing the formation of prostaglandin and leukotrienes. DHA accumulates in the brain during the prenatal cortical expansion. It was also shown that experimental DHA deficiency is responsible for neuronal growth deficits, serotonin and mesocorticolimbic dopamine secretion deficits. In animals, PUFA deficits in different neurodevelopment stages were connected with different anatomic regions reversible dysfunction: neonatal rats - striatum dysfunctions, adult rats - frontal dysfunctions and aged rats -

cortical and cerebellum dysfunctions<sup>4,5</sup>. In humans, the prenatal DHA deficiency is considered as one of the preventable neuron-developmental risk factors of future major psychopathology<sup>6</sup>. Beside neuronal growth and maturation, DHA acts on the prevention of neuronal apoptosis<sup>7</sup>, neuronal hormonal secretion<sup>8</sup>, ion channel regulation and dopamine - serotonin secretion<sup>9</sup>.

A possible association between the physiologic pool of long PUFA changes and behavioral alterations was investigated experimentally<sup>10,11,12</sup>. Clinical observations proved that in the blood of some psychiatric patients, the level of PUFA is also reduced<sup>13</sup>. A possible association between essential fatty acids (EFA), PUFA dynamics and specific psychiatric plurifactorial pathology was also described in schizophrenia<sup>14</sup>, bipolar disorder<sup>15</sup> and possible for chronic pain<sup>16</sup>.

One major source of PUFA is Fish oil (FO). Epidemiological studies have suggested that high fish oil consumption is inversely related with cognitive impairment and decline<sup>17,18,19</sup>. Fish oil consumption may have several disadvantages: a low concentration of PUFA per unit fact that impose the administration of large doses of FO in order to have a distinct clinical effect, a very low concentration of phospholipids (phosphatidylcholine) fact that reduce the Blood Brain Barrier (BBB) penetration and a high possible level of industrial pollutants like methylmercury, dioxins and polychlorinated biphenyls mainly in fish harvested from fishing farms<sup>20,21,22</sup>.

NKO<sup>®</sup> is natural marine biomass oil extracted from Antarctic Krill (*Euphausia Superba*) - zooplankton that habits only in a very specific area of Antarctic Ocean. It is rich in phosphatidylcholine, DHA and EPA, astaxanthin and vitamins. The molecular profile of NKO<sup>®</sup> is different from the profile of other omega 3 acids extracted from FO or other sources: both the omega 3 to omega 6 PUFA ratio (15 to 1) and the EPA / DHA ratio (1.6:1) are specific. The presence of PC which esterifies the two PUFA is of great clinical interests because it facilitates intestinal absorption, blood movement and BBB passage, allowing a rapid passage and high concentration in target tissues (brain and blood cells).

## MATERIALS AND METHODS

### PATIENTS

30 patients having a mean age of 23 years (SD of 1.2 years) were enrolled into the trial. All of the 30 patients enrolled were known as having ADHD for many years (mean 7 years and a SD of 3 years). The patients were tested and retested in all the three Barkley Executive Brain functions: Executive, Behavioral Inhibition and Self Control.

### STUDY DESIGN

The study was designed as a prospective phase I, open label, study. The study protocol was reviewed and approved by the Barry University - Miami Shores, Florida, USA Internal Review Board. The study was performed both in Florida and Montreal and was sponsored by Neptune Technologies and Bioresources and by the International Association of Attention Deficit Hyperactivity Disorder.

### OUTCOME MEASURES

The efficacy of NKO<sup>®</sup> on brain executive functions in adults having ADHD was investigated using a derivative of Barkley executive function scale (BEFS). The central issue of the method was to consider the brain executive functions control as a resultant of:

- Verbal and nonverbal memory,
- Self regulation of affects motivation and arousal,
- Reconstruction of behavior.

We developed a questionnaire which focused on three scales of evaluation, each of them having different number of items (questionnaire that was used from test to re-test sessions):

1. Behavior having 18 parameters and being concerned mainly with the executive functions connected with productive activities as attention to details, talkativeness, organizational capacities, distraction, follow instructions, restlessness, listening capacity, forgetfulness, sustained attention, pure hyperactivity.
2. Daily functional capacity having 10 parameters, concerned with social, educational, community and recreational activities (interest in create and maintain personal/social interactions, educational and community activities, acceptance of responsibilities, ability to perform tasks as driving, etc)
3. Social behavior having 8 parameters and being related with disruptive behavior, anger and impulsivity control (accepting and obeying rules, tempering anger, response inhibition, general and social angeriness, vindictive activities and behaviors)

The patients were investigated at baseline, at 12 weeks and after 24 weeks of treatment with NKO<sup>®</sup>.

## RESULTS

### Cognitive Function

#### Significant Impact On Adult ADHD

After 3 & 6 Months



Orange pill : NKO<sup>®</sup> 500 mg/day After 3 Months

Blue pill : NKO<sup>®</sup> 500 mg/day After 6 Months

## CONCLUSION

NKO<sup>®</sup> can be considered a safe, and effective treatment able to improve brain executive function for adults having ADHD. NKO<sup>®</sup> diminishes the need for stimulant medication, decreases treatment costs and improves the quality of patients. Further research is needed in order to better understand dosage and long term effects of the treatment in different physical and psychological conditions of adults and children.

## REFERENCES

1. Seidman LJ, Valera EM, Bush G., Brain function and structure in adults with attention-deficit/hyperactivity disorder. *Psychiatr Clin North Am.* 2004 Jun;27(2):323-47
2. Schachter HM, Kourad K, Merali Z, Lumb A, Tran K, Miguez M. Effects of omega-3 fatty acids on mental health. *Evid Rep Technol Assess (Summ).* 2005 Jul;116(1):1-11.
3. Schacheter et al, op cit
4. Xiao Y, Huang Y, Chen ZY. Distribution, depletion and recovery of docosahexaenoic acid are region-specific in rat brain. *Br J Nutr.* 2005 Oct;94(4):544-50
5. Kodas E, Vancassel S, Lejeune B, Guilloteau D, Chalou S. Reversibility of n-3 fatty acid deficiency-induced changes in dopaminergic neurotransmission in rats: critical role of developmental stage. *J Lipid Res.* 2002 Aug;43(8):1209-19.
6. McNamara RK, Carlson SE. Role of omega-3 fatty acids in brain development and function: potential implications for the pathogenesis and prevention of psychopathology. *Prostaglandins Leukot Essent Fatty Acids.* 2006 Oct;Nov;75(4-5):329-49.
7. Akbar M, Calderon F, Wen Z, Kim HY. Docosahexaenoic acid: a positive modulator of Akt signaling in neuronal survival. *Proc Natl Acad Sci U S A.* 2005 Aug 2;102(31):10858-63.
8. Machova E, Novakova J, Lisa V, Dolezal V. Docosahexaenoic acid supports cell growth and expression of choline acetyltransferase and muscarinic receptors in NG108-15 cell line. *J Mol Neurosci.* 2006;30(1-2):25-6
9. Young G, Conquer J. Omega-3 fatty acids and neuron-psychiatric disorders. *Reproduction, Nutrition, Development.* 2005; 45(1):1-28
10. Ozias MK, Carlson SE, Levant B. Maternal parity and diet (n-3) polyunsaturated fatty acid concentration influence accretion of brain phospholipid docosahexaenoic acid in developing rats. *J Nutr.* 2007 Jan;137(1):125-9
11. Fedorova I, Salem N Jr. Omega-3 fatty acids and rodent behavior. *Prostaglandins Leukot Essent Fatty Acids.* 2006 Oct;Nov;75(4-5):271-89.
12. Levant B, Ozias MK, Jones KA, Carlson SE. Differential effects of modulation of docosahexaenoic acid content during development in specific regions of rat brain. *Lipids.* 2006 May;41(5):407-14.
13. Young G, Conquer J. Omega-3 fatty acids and neuropsychiatric disorders. *Reprod Nutr Dev.* 2005 Jan-Feb;45(1):1-28. Review
14. Ohara K. The n-3 polyunsaturated fatty acid/dopamine hypothesis of schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry.* 2006 Dec 19
15. Holtzheimer PE 3rd, Nemeroff CB. Emerging treatments for depression. *Expert Opin Pharmacother.* 2006 Dec;7(17):2323-39. Review
16. Steenland HW, Ko SW, Wu LJ, Zhuo M. Hot receptors in the brain. *Mol Pain.* 2006 Nov 8;2:34. Review
17. Grant WB. Diet and the risk of dementia: does fat matters? The Rotterdam study. *Neurology.* 2003 60: 2020-2021
18. Kalmijn S., van Bortel MPJ, Ocke M, Dietary intake of fatty acids and fish in relation to cognitive performance at middle age. *Neurology* 2004 52 275-280
19. Morris MC, Evans DA, Bienias JL, Tangney CC, Bennett DA, Consumption of fish and n-3 fatty acids and the risk of incident Alzheimer disease *Arch Neurol* 2003 60: 940-946
20. Sioen I, Van Camp J, Verdonck F, Vanhacker F, Verbeke W, De Henauw S. Nutritional-toxicological conflict of fish consumption: a tool for combined intake assessment. *Commun Agric Appl Biol Sci.* 2006;71(1):263-6
21. Mozaffarian D, Rimm EB. Fish intake, contaminants, and human health: evaluating the risks and the benefits. *JAMA.* 2006 Oct 18;296(15):1885-99.
22. Bethune C, Seierstad SL, Seljeflot I, Johansen O, Arnesen H, Meltzer HM, Rosenlund G, Froyland L, Lundbye AK. Dietary intake of differently fed salmon: a preliminary study on contaminants. *Eur J Clin Invest.* 2006 Mar;36(3):193-201

THIS STUDY'S MANUSCRIPT IS IN PREPARATION  
THIS POSTER WAS DESIGNED BY NEUROPHOTOGRAPHY AT THE MONTREAL NEUROLOGICAL HOSPITAL AND INSTITUTE