

## Suicide Risk Reduction and Omega-3 Highly Unsaturated Fatty Acids

CAPT Joseph R. Hibbeln M.D.,

*Laboratory of Membrane Biochemistry and Biophysics; Section of Nutritional Neuroscience  
NIAAA, NIH, Bethesda USA*

Deficiencies in omega-3 fatty acids may result in neurobiological abnormalities associated with increased risk of suicide, including hypofunction of the serotonergic system or dopaminergic neurotransmitter systems regulating reward and increased stress reactivity of the hypothalamic- pituitary-adrenal “stress” axis<sup>1</sup>. Deficiencies in omega-3 HUFAs cause serotonin levels to be reduced by nearly 50% in frontal cortex in animal studies<sup>2</sup>, and in human studies, lower levels of plasma DHA correlate to lower levels of CSF 5-HIAAA<sup>3</sup>. Epidemiologic data indicate that low fish consumption may be a risk factor, but certainly not a sole determinant for suicide mortality. Previously we examined 1,767 participants in northern Finland and found that frequent fish consumption (twice per week or more) significantly reduced the risk of reporting depressive symptoms (OR =0.63,  $p < 0.03$ ) and of reporting suicidal thinking (OR =0.57,  $p < 0.04$ ) after adjustment for confounding variables<sup>4</sup>.

Among 234 pregnant women enrolled in a prospective cohort study in Rio de Janeiro, Brazil, the prevalence of suicide risk was 19.6% and a major depressive episode was 17.0%, by MINI diagnostic interview<sup>5</sup>. In adjusted logistic regressions, a higher likelihood of suicide risk was observed among women with higher arachidonic acid levels [AA (20:4, n-6): OR=1.45, 95%CI 1.02-2.07] and adrenic acid levels [AdA (22:4, n-6): OR=1.43, 95%CI 1.01-2.04]. A higher likelihood of MDE was also observed among women with higher AA levels [OR=1.47, 95%CI 1.03-2.10] and AdA levels [OR=1.59, 95%CI 1.09-2.32]. Among patients hospitalized for severe mental illnesses low DHA status predicted greater risk of a new suicide attempt in a follow-up study of more than 800 days<sup>6</sup>. A case control study (n=1,600) among active duty US military, identified low DHA status was a significant risk factor for suicide death<sup>7</sup>.

Only one randomized controlled trial of omega-3 HUFAs in suicide or self-harm has been identified. Participants presenting to an emergency room with multiple episodes of deliberate self-harm (n=49) were randomized to placebo or 2 g/d of omega-3 HUFAs for 12 weeks and given no adjunctive psychotherapy. Supplementation reduced suicidal thinking by 45%, reduced depressive symptoms by 50%, reduced perceived stress by 30%, and increased

happiness by 33%<sup>8</sup>. BRAVO Study Design: In collaboration with the Medical College of South Carolina and Bernadette Marriott, Ph.D, we are conducting a double blind randomized placebo controlled study to assess reduction of risk of suicidal behaviors. 300 subjects will be randomized to either 3.3g/d of omega-3 HUFAs (with the EPA to DHA ratio of approximately 1:1), delivered in 3 fruit juice beverages/d (Smartfish®, Gaustadalléen 21,N-0349 Oslo, Norway); or 3 control fruit juice beverages/d containing macadamia nut oil for 6 months.

## References

1. Hibbeln J.R., Gow, R.V. The potential for military diets to reduce depression, suicide, and impulsive aggression: a review of current evidence for omega-3 and omega-6 Fatty acids, *Military medicine*, 179 (2014) 117-128
2. de la Presa Owens, S. and Innis, S.M., Docosaehaenoic and arachidonic acid prevent a decrease in dopaminergic and serotonergic neurotransmitters in frontal cortex caused by a linoleic and alpha-linolenic acid deficient diet in formula-fed piglets. *J Nutr*, 1999. 129: p. 2088-2093.
3. Hibbeln, J.R., Umhau, J.C., Linnoila, M., et al., A replication study of violent and nonviolent subjects: cerebrospinal fluid metabolites of serotonin and dopamine are predicted by plasma essential fatty acids. *Biol Psychiatry*, 1998. 44: p. 243-249.
4. Tanskanen, A., Hibbeln, J.R., Hintikka, J., et al., Fish consumption, depression, and suicidality in a general population. *Arch Gen Psychiatry*, 2001. 58(5): p. 512-3.
5. Vaz, J.S. Kac, G. Nardi, A.E. Hibbeln, J.R. Omega-6 fatty acids and greater likelihood of suicide risk and major depression in early pregnancy, *Journal of affective disorders*, 152-154 (2014) 76-
6. Sublette, M.E., Hibbeln, J.R., Galfalvy, H., et al., Omega-3 polyunsaturated essential fatty acid status as a predictor of future suicide risk. *Am J Psychiatry*, 2006. 163(6): p. 1100-2.
7. Lewis, M.D., Hibbeln, J.R., Johnson, J.E., et al., Suicide deaths of active-duty US military and omega-3 fatty-acid status: a case-control comparison. *J Clin Psychiatry*, 2011. 72(12): p. 1585-90.
8. Hallahan, B., Hibbeln, J.R., Davis, J.M., et al., Omega-3 fatty acid supplementation in patients with recurrent self-harm. Single-centre double-blind randomised controlled trial. *Br J Psychiatry*, 2007. 190: p. 118-22.