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Omega-3 fatty acid supplementation changes intracellular phospholipase A2 activity and membrane fatty acid profiles in individuals at ultra-high risk for psychosis.

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Abstract

The identification of an ultra-high risk (UHR) profile for psychosis and a greater understanding of its prodrome have led to increasing interest in early intervention to delay or prevent the onset of psychotic illness. In a randomized placebo-controlled trial, we have identified long-chain ω-3 (ω-3) polyunsaturated fatty acid (PUFA) supplementation as potentially useful, as it reduced the rate of transition to psychosis by 22.6% 1 year after baseline in a cohort of 81 young people at UHR of transition to psychosis. However, the mechanisms whereby the ω-3 PUFAs might be neuroprotective are incompletely understood. Here, we report on the effects of ω-3 PUFA supplementation on intracellular phospholipase A2 (inPLA(2)) activity, the main enzymes regulating phospholipid metabolism, as well as on peripheral membrane lipid profiles in the individuals who participated in this randomized placebo-controlled trial. Patients were studied cross-sectionally (n=80) and longitudinally (n=65) before and after a 12-week intervention with 1.2 g per day ω-3 PUFAs or placebo, followed by a 40-week observation period to establish the rates of transition to psychosis. We investigated inPLA(2) and erythrocyte membrane FAs in the treatment groups (ω-3 PUFAs vs placebo) and the outcome groups (psychotic vs non-psychotic). The levels of membrane ω-3 and ω-6 PUFAs and inPLA(2) were significantly related. Some of the significant associations (that is, long-chain ω-6 PUFAs, arachidonic acid) with inPLA(2) activity were in opposite directions in individuals who did (a positive correlation) and who did not (a negative correlation) transition to psychosis. Supplementation with ω-3 PUFA resulted in a significant decrease in inPLA(2) activity. We conclude that ω-3 PUFA supplementation may act by normalizing inPLA(2) activity and δ-6-desaturase-mediated metabolism of ω-3 and ω-6 PUFAs, suggesting their role in neuroprogression of psychosis.

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