DHA Alters Raft-like Membrane Domains as Revealed by Solid State ^{2}H NMR Spectroscopy

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Dietary omega-3 polyunsaturated fatty acids (n-3 PUFAs), such as docosahexaenoic acid (DHA, 22:6), are correlated with the prevention of neurological and autoimmune disorders in humans. These fatty acids must be obtained from the diet, such as oil fish or fish oil supplements, as they cannot be generated within the human body. The origin of the health benefits at the molecular level is still under question. A membrane-mediated mechanism in which n-3 PUFAs are incorporated into phospholipids and modulate molecular organization is one possibility. Cellular membranes are inhomogeneous where structurally diverse lipids can exist in separate domains. Regions rich in sphingomyelin (SM) and cholesterol, commonly called lipid rafts, contain important signaling proteins. In a recent solid-state ^{2}H nuclear magnetic resonance (^{2}H NMR) study of a model membrane composed of 1-[$^2H_{31}$] palmitoyl-2-docosahexaenoyl-phosphatidylcholine (PDPC-d_{31}), a deuterated analog of a DHA-containing phospholipid, in mixtures with SM and cholesterol, we discovered that DHA could significantly enter raft-like domains. How DHA affects the molecular organization within the raft-like domains is addressed here by observing PSM-d_{31}, an analog of SM with a perdeuterated *N*-palmitoyl chain. The ^{2}H NMR spectra for PSM-d_{31}, in mixtures with PDPC and cholesterol, exhibit two spectral components, a larger more ordered component that we attribute to raft-like domains and a smaller less ordered component that we attribute to non-raft-like domains. On average, the order of PSM-d_{31} is reduced and, thus, disordering of PSM-d_{31} by PDPC is indicated. Our observations confirm that DHA can infiltrate rafts and affect molecular organization, which has implications for the signaling of raft and non-raft proteins. Furthermore, these results are consistent with in vivo studies showing that DHA infiltrates rafts.