



Green nut oil or DHA supplementation restored decreased distribution levels of DHA containing phosphatidylcholines in the brain of a mouse model of dementia

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博士（医学） Ariful Islam

論文題目

Green nut oil or DHA supplementation restored decreased distribution levels of DHA containing phosphatidylcholines in the brain of a mouse model of dementia

（グリーンナッツオイルまたは DHA の摂取は、認知症モデルマウス脳内の DHA 含有ホスファチジルコリン分布レベルの低下を回復させた）

論文の内容の要旨

[Introduction]

Dementia is one of the major global health problems mainly in elderly people. As the world's population is aging rapidly, dementia has become a concern throughout the world and it places substantial burden on patients having dementia. Previous studies reported decreased levels of DHA and DHA-containing phosphatidylcholines (DHA-PCs) in the dementia patients, which are required for the survival and functions of neuronal cells. Recently we have reported that supplementation of DHA and green nut oil (GNO); oil extracted from the seeds of *Plukenetia volubilis* seeds increase brain DHA and memory efficiency in senescence-accelerated mice prone 8 (SAMP8), model mice of dementia. We have conducted this study to reveal DHA-PC contents of SAMP8 mice brain compared to wild type (WT) mice, and the effects of DHA or GNO supplementation in DHA-PCs contents in SAMP8 mice brain for the first time.

[Materials and Methods]

Thirteen-week-old C57BL/6JJmsSlc and SAMP8 male mice were purchased from SLC Inc. (Japan) and Sankyo Labo Service Corporation, Inc. (Japan), respectively. All mice were reared at standard laboratory conditions. After first week of rearing period, brain samples were collected from WT and SAMP8 (n = 3) after cervical dislocation and stored at -80°C. Remaining SAMP8 mice were divided into three groups and, treated with corn oils (as control), GNO, and DHA for 14 weeks. After treatment, brain samples of all mice were collected after cervical dislocation and stored at -80°C. For desorption electrospray ionization mass spectrometry (DESI-MSI) analysis, 10 µm sagittal brain sections were prepared. For the confirmation of candidate ions, lipids were extracted following slightly modified Bligh and Dyer extraction method then subjected to liquid chromatography electrospray ionization tandem mass spectrometry (MS/MS) analysis using Synapt G2 Q-TOF mass spectrometer (Waters Corp., Manchester, UK) coupled to Acquity UPLC H-Class system (Waters, Milford, MA, USA). All experiments were performed according to the protocols of Animal Care and Use Committee of the Hamamatsu University School of Medicine (No. H29-084), and Showa Women's University Animal Research Committee (No. 17-04).

[Results]

DESI-MSI mass spectra were acquired from the sagittal brain sections of WT and SAMP8 mice in positive ion mode over 500-1000 m/z (mass/charge ratio) range to explore the changes of DHA-PCs distribution after GNO or DHA supplementation. Four candidate peaks corresponded to the molecular ions of DHA-PCs were noted from the mass spectra acquired from all mice with m/z 806.6, 834.6, 844.5, and 872.6. Molecular ions corresponded to those peaks were confirmed by MS/MS analysis. In this study, we observed significantly decreased distribution of the brain DHA-PCs, PC (16:0_22:6), and PC (18:0_22:6) in SAMP8 mice ($n = 3$) compared to WT mice ($n = 3$). The distribution of DHA-PCs decreased in several brain regions of SAMP8 mice including hippocampus, cerebellum, cerebral cortex, caudate putamen, and ventral striatum compared to WT mice. After 14 weeks of treatment with GNO ($n = 5$) or DHA ($n = 5$), notable accumulation of DHA-PCs in SAMP8 mice in several brain regions was observed including the hippocampus, cerebellum, cerebral cortex, caudate putamen, and ventral striatum compared to control mice ($n = 5$). These data indicate that GNO or DHA supplementation has the potentiality to ameliorate the decreased distribution of the brain DHA-PCs in dementia.

s a prevalent disease in elderly people affecting memory, thinking, behavior and the ability to perform routine activities. Previous studies have reported altered lipid metabolism and its association with progression on dementia. Our group had also reported decreased brain DHA-PCs in dementia patients. Recently we have reported that GNO or DHA supplementation can augment brain DHA and memory function in model mice of dementia (SAMP8). In this study, we have explored that, similar to human dementia patients, SAMP8 mice also have decreased brain DHA-PCs compared to WT mice. Moreover, dietary supplementation of DHA or GNO increased brain DHA-PCs in several regions of SAMP8 mice brain associated with memory and motor functions including hippocampus, cerebellum, cerebral cortex, caudate putamen, and ventral striatum.

[Conclusion]

In summary, we have explored that GNO or DHA supplementation can restore decreased brain DHA-PCs in SAMP8 mice; model mice of dementia. After GNO or DHA supplementation, increased accumulation of DHA-PCs in the hippocampus as well as in the cerebellum, cerebral cortex, caudate putamen, and ventral striatum were also noted in this study. DHA-PCs play crucial role in brain development and neuronal function. Recently, we have also reported that GNO or DHA supplementation could ameliorate decreased brain DHA and memory function in SAMP8 mice. Moreover, all these findings also revealed the possibility of GNO as a source of DHA alternative to

fish oil in the future.