Efficacy of Combined Use of Chlorella and Ascidian-derived Plasmalogen for Prevention of Dementia

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[Objectives]

The increase in dementia is a social problem not only in Japan but also worldwide. The world's number of people with dementia is estimated to be approximately 57 million in 2019. In Japan, the number of people with dementia aged 65 years or older is approximately 6 million as of 2020, and expected to increase to approximately 8 million in 2040. Efforts to prevent the spread of dementia are becoming more important. So, along with developing drugs, the development of preventive measures by using foods that can be taken daily or their ingredients are expected.

It has been reported that 65-70% of Japanese dementia patients have Alzheimer's dementia, and as one of the causes of this type of dementia, plasmalogen, which is a kind of phospholipid in the brain, is attracting attention. The human brain is a very lipid-rich tissue, and ethanolamine plasmalogen accounts for approximately 8% of the dry weight. Plasmalogen is a component of the cell membranes of nerve cells, and involved in information exchange, transmission, etc. in the brain. It is known that plasmalogen decreases in the brain of patients with Alzheimer's disease.

Ascidian, a chordate, is evolutionarily similar to vertebrate, and rich in plasmalogen which contains DHA (docosahexaenoic acid) abundantly found in the human brain. Ascidian-derived plasmalogen has been reported to inhibit apoptosis of neuroblasts, suppress aggregation of amyloid-β, and improve cognitive function. Chlorella is very rich in lutein, which is the main antioxidant component of human red blood cells, compared to other foods. A drinking test in middle-aged and elderly people has shown that chlorella intake may decrease peroxidized phospholipids in red blood cells (reducing the increase in senescent erythrocytes), improve oxygen supply to the brain tissue, and be useful in the prevention of dementia.

In this study, we examined the effects on cognitive functions of the combined use of ascidian-derived plasmalogen and chlorella, which are foods useful for the prevention of dementia.

[Methods]

The study was conducted by dividing 6-week-old male rats into 4 groups (5 animals/group): Control group (Con; salad oil + ordinary feed), Chlorella group (CHL; salad oil + chlorella mixed feed), Ascidian extract group (HRE; ascidian extract + ordinary feed), and Combination group (CHL+HRE; ascidian extract + chlorella mixed feed). Ascidian extract, containing ascidian-derived plasmalogen at a dose of 0.07 mg/day, was administered once daily for one week. Additionally, chlorella powder was fed as part of a combined feed containing 1% chlorella, at a dose of 200 mg/day, for one week. After the 1-week treatment, we measured the activation of the brain-derived neurotrophic factor (BDNF) signaling system (BDNF-TrkB-CREB signaling system)* in the hippocampus, which is involved in learning and memory.

[Results]

The expression amount of hippocampal BDNF showed no significant difference in the CHL and HRE groups compared to the Con group, but in the CHL+HRE group it showed a tendency toward increase ($p = 0.078$) with a significant increase compared to each single treatment group (Figure 1A). Furthermore, the activation of TrkB, which is a specific receptor of BDNF, significantly increased in the CHL+HRE group compared to the Con group (Figure 1B). The subsequent activation of CREB also significantly increased in the CHL+HRE group compared to the Con, CHL, and HRE groups (Figure 1C).

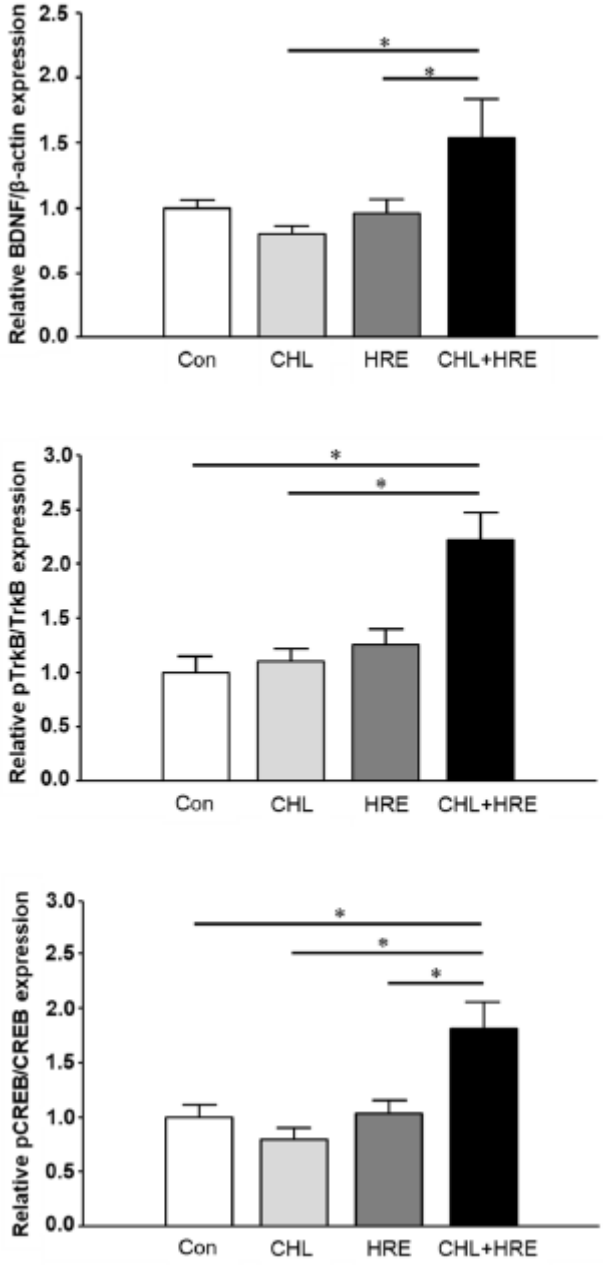

Figure 1. Effects of chlorella, ascidian extract, and their combination on the hippocampal BDNF signaling system

Hippocampal BDNF expression, TrkB activation, and CREB activation were measured by Western blotting. The BDNF expression, TrkB activation, and CREB activation were expressed as ratios compared to the control group (Con). The graph shows mean ± standard error (5 animals/group); *$p < 0.05$ was considered significant.

Con, control group; CHL, chlorella group (chlorella powder 200 mg/day was administered); HRE, ascidian extract group (ascidian-derived plasmalogen 0.07 mg/day was administered); CHL+HRE, combination group (chlorella powder 200 mg/day + ascidian-derived plasmalogen 0.07 mg/day was administered).

This study confirmed that the BDNF-TrkB-CREB signaling system is activated by the combination of chlorella and ascidian-derived plasmalogen, despite the relatively short duration of one week, at doses that have not been shown to be effective in each single treatment. The combination of chlorella and ascidian-derived plasmalogen promotes the activation of the BDNF signaling system, and it is expected that these ingredients improve cognitive function by different mechanisms. Therefore, it was suggested that the combination of both ingredients may exert a synergistic preventive effect on dementia.

*Explanation of the term
Brain-derived neurotrophic factor (BDNF) is a neurotrophic factor (neurotrophin), which plays an important role in learning and memory. The most influential mechanism where BDNF has an effect on the generation, growth, and repair of nerve cells is the pathway binding to tropomyosin receptor kinase B (TrkB), a specific receptor on the cell surface, to operate via cAMP response element-binding protein (CREB), a transcription factor (BDNF-TrkB-CREB signaling system) (see the figure below). It is known that the expression level of BDNF is low in the brain of Alzheimer's disease patients. So, it is considered useful to investigate the expression levels of BDNF, TrkB and CREB as the criteria to evaluate the progression of Alzheimer's disease.

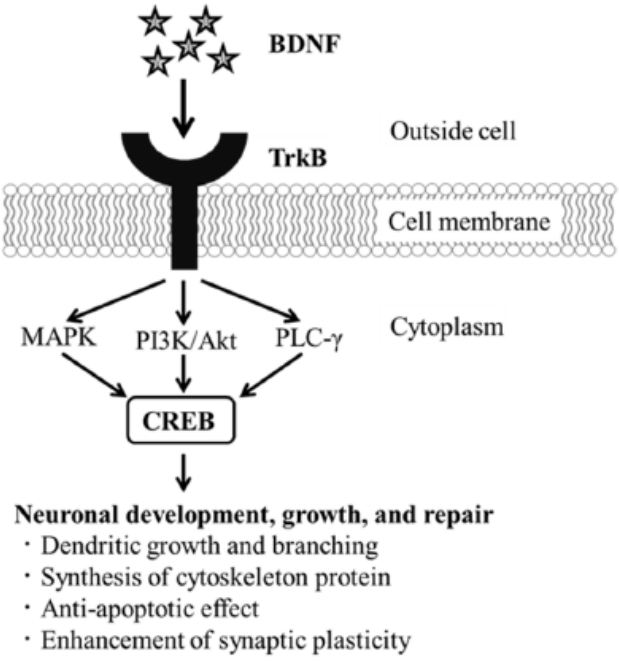

Figure. Generation, growth, preservation, and repair of nerve cells by the BDNF signaling system
BDNF, brain-derived neurotrophic factor; TrkB, tropomyosin receptor kinase B; CREB, cyclic AMP response element-binding protein; MAPK, mitogen-activated protein kinase; PI3K/Akt, phosphatidylinositol 3-kinase/protein kinase B; PLC-γ, phospholipase C-γ

Details

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