Effect of green tea catechins on learning and memory in senescence-accelerated mice.

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Summary
The learning and memory function declines with aging. The effect of green tea catechins on learning and memory was investigated in senescence-accelerated mice (SAM).

Senescence-prone inbred strain, SAMP10, and senescence-resistant inbred strain, SAMR1, had free access to tap water containing green tea catechins (Polyphenon 70S) from 1-month-old to 6-, 9- and 12-month-old. These mice were carried out the passive avoidance test: An illuminated front chamber was connected to a dark chamber with grid floor. When a mouse entered the dark chamber from light one, it was given foot shock at 0.5 mA for 1 sec. The staying time in light chamber was recorded. And the retention of the passive avoidance response was also examined 1 month later.

The mean acquisition time for the passive avoidance was significantly longer in SAMP10 of 12-month-old mice than younger ones and same-aged SAMR1. However, aged SAMP10 mice incorporated catechins exhibited shorter time than control mice. The incorporation of green tea catechins seems to be effective for improvement of learning and memory function in aged mice.

Keywords
Green tea catechin, Aging, Senescence-accelerated mice (SAM), Learning, Memory

Introduction
The learning and memory function declines with aging. The decline is not a serious disease such as Alzheimer, however, variously affects on a quality of life. Age-related impairment of cognitive capacity has been linked to a number of deleterious morphologic and functional changes involving different parts of the brain. Oxidative damage has been considered as a likely cause of age-associated brain dysfunction because the brain is believed to be particularly vulnerable to oxidative stress. To prevent brain from oxidative molecular damage might be effective for keep up cognitive function. Catechins have been reported antioxidative and radical scavenging effects. Therefore, we investigated the influence of green tea catechins on learning and memory using senescence-accelerated mice (SAM).

SAM is senescence-prone inbred strain established by Takeda and his colleagues of Kyoto University. There are several senescence-prone inbred strains (SAMP) and resistant inbred strains (SAMR). Short life span and their own characteristic age-dependent pathology, such as senile amyloidosis, osteoporosis, cataract, and learning and memory deficits characterize SAMP strains. Among these strains, SAMP10 is characterized as a mouse model of spontaneous inherited brain atrophy with cognitive dysfunction by Shimada et al. In this study, SAMP10 mice treated with water containing green tea catechins from 1-month-old to 12-month-old. We report that green tea catechins affect on the function and morphology of SAMP10 brain.
Materials and Methods

Animals and water administration

Male and female SAMP10 and SAMR1 mice were bred under conventional conditions with constant temperature and humidity. They had free access to a normal diet (CE-2, Clea Co., Ltd.) and tap water containing 0.02% green tea catechins (Polyphenon 70S, Tokyo Food Techno Co., Ltd.) from 1-month-old to 6-, 9- and 12-month-old. Catechin water was freshly prepared every other day. Control mice were given normal diet and water. Polyphenon 70S contains about 70% of green tea catechins and 0% of caffeine. The green tea catechins consists of epigallocatechin gallate (EGCg) 31.7%, epigallocatechin (EGC) 15.7%, epicatechin gallate (ECg) 10.0%, epicatechin (EC) 8.5%, gallocatechin gallate (GCg) 4.5%, and catechin gallate (Cg) 1.0%.

Behavioral analyses

Acquisition test: Step-through passive avoidance task was carried out using SAMP10 and SAMR1 mice aged 5-, 8- and 11-month-old. The apparatus was composed of two components separated by a guillotine-type door, one of which was illuminated and was connected to the other, dark compartment through the door (Step Through Test System MST-01S, Muromachi Kikai). When a mouse was put in the light chamber, followed by the opening the door, it always entered the dark chamber because of its innate nocturnal habits. When the mouse entered the dark chamber, the door was closed and an electric foot-shock was delivered at 0.5 mA for 1 sec. The mouse was immediately removed from the dark chamber. One min later, the mouse was reintroduced to the light chamber. The mouse entering the dark chamber within 300 sec immediately received an identical electric shock after closing the door. Acquisition of the avoidance response was judged successful if the mouse remained in the light chamber for 300 sec. The trial was repeated until the mouse satisfied the acquisition criterion within 5 trials. The number of trials and the latency time in the light chamber was recorded.

Retention test: SAMP10 and SAMR1 mice carried out the acquisition test were used in the test. These mice were repeated the passive avoidance response (criterion of 300 sec) in the light chamber 24 h after the acquisition test described above. Retention of the passive avoidance response was examined one month after confirming the acquisition. The number of mice satisfied the acquisition criterion (300 sec) was examined.

Measurement of cerebral atrophy

After the passive avoidance test, SAMP10 and SAMR1 mice were sacrificed and their brains were removed immediately. The weights of the brains were compared between the aged mice drunk catechin water and control water.

Results

Acquisition test

The latency time in the light chamber within 5 trials was summed up and compared between SAMP10 and SAMR1 mice aged 5-, 8- and 11-month-old. They have drunk 5-6 ml water containing green tea catechins (GT-catechin) or control water (control) per day. In control SAMP10 mice, the latency time in the light chamber was significantly shorter in 12-month-old than younger SAMP10 and same-aged SAMR1 mice. That is, aged SAMP10 mice needed longer acquisition time for learning. In SAMP10 mice of GT-catechin, the time for learning was prolonged in 12-month-old mice but that was not significantly longer than same-aged SAMR1 mice were.
Retention test

The mice confirmed the acquisition test for 2 days were used to examine the retention ability 1-month later. The number of mice that could not remain in the light chamber for 300 sec was compared between 12-month-old SAMP10 and SAMR1 mice of GT-catechin and control. The failing ratio was clearly lower in SAMP10 mice incorporated green tea catechins than those of control. The ratio of SAMP10 of GT-catechin was similar to those of same-aged SAMR1 mice. The effect of catechins was not found in SAMR1 mice. Green tea catechins seem to be effective for improvement of learning and memory function in aged SAMP10 mice.

Cerebral atrophy in aged SAMP10

It has been reported that the cerebral atrophy was observed after 4-month-old in SAMP10 mice. We also observed a significant atrophy in 6-month-old SAMP10. The brain weights were significantly lighter in 12-month-old SAMP10 than same-aged SAMR1. However, the significant difference was not observed between 12-month-old SAMP10 and SAMR1 of GT-catechin. The atrophy seems to be suppressed in SAMP10 incorporated green tea catechins.

To investigate the effect of cerebral atrophy on learning function, the relationship between brain weight and time for acquisition was examined. In 12-month-old SAMP10 and SAMR1 mice, the rate of atrophy slightly related to the prolonged acquisition time.

Discussion

We observed that the incorporation of catechins for long term, of which concentration was as low as our drinking green tea, partly improved the morphologic and functional alterations of the brain in aged SAMP10. The cerebral atrophy was observed earlier than the cognitive dysfunction using step-through passive avoidance test in SAMP10. Some alterations bringing about atrophy might be caused in younger SAMP10 brain. And at least in mice aged 12-month-old, cerebral atrophy tended to be followed by lowered learning ability. The preventive effect of GT-catechin on aged brain is very interesting and important for keeping up the quality of longevous life. GT-catechin might prevent an oxidative damage in brain. It is need to study hard the mechanism and more effective condition.