PROTECTIVE EFFECT OF GREEN TEA CATECHINS AGAINST AMYLOID β-INDUCED MEMORY IMPAIRMENT INVOLVES INHIBITION OF BRAIN OXIDATIVE STRESS IN ALZHEIMER'S DISEASE MODEL RATS

Abdul M.Haque[1], Michio Hashimoto[1], Masanori Katakura[1], Yukihiko Hara[2] and Osamu Shido[1]

[1]Department of Environmental Physiology, Shimane University Faculty of Medicine, Izumo, shimane 693-8501, Japan. [2]Mitsui Norin Co., Ltd, Shinjuku-ku, Tokyo 160-8381, Japan.

Summary

We reported that the green tea catechins exert antioxidative action in brain and improve spatial cognitive learning ability in young rats. In this study, we investigated whether administration of green tea catechins, Polyphenon E (PE: EGCG 63%; EC 11%; EGC 6%; ECG 6%) prevents oxidative stress as well as behavioral changes in animal model of Alzheimer's disease, rats infused with $A\beta_{1-40}$ into the cerebral ventricle. When measuring the learning ability using an eight–arm radial maze, long-term administration of PE (0.5%, w/v) prevented $A\beta_{1-40}$-induced spatial cognition learning impairment with a concomitant reduction of lipid peroxide and reactive oxygen species levels in brain tissues. We proposed that green tea catechins may facilitate antioxidant defense in brain and prevent $A\beta_{1-40}$-induced cognitive impairment in Alzheimer's disease model rats.

Key Words: Green tea, Antioxidant, Alzheimer's disease , Memory learning

Introduction

An increase in antioxidative defense in the hippocampus prevents (1) and/or ameliorates (2) learning impairment in an animal model of Alzheimer's disease (AD), rats infused with $A\beta_{1-40}$ into the cerebral ventricle. Recently we reported that long-term administration of green tea catechins improves spatial cognitive learning ability in rats (3). In this study, we investigated the effects of green tea catechins on Aβ-induced oxidative stress and cognitive impairment in AD-model rats.

Materials and Methods

Five-weeks-old male Wistar rats were orally administered green tea catechins (Polyphenon E, PE; Mitsui Norin Co., Ltd.) mixed with water (5 g/L PE) or water alone for 26 weeks. Twenty-weeks after PE administration, $A\beta_{1-40}$ or vehicle was infused into the cerebral ventricle using a mini osmotic pump and rats were subsequently sub-divided into Vehicle, Aβ, PE+Vehicle and PE+Aβ groups. Learning-related behavioral changes were assessed by an eight-arm radial maze (Toyo Sangyo Co.,) as described previously (4). After behavioral test, cerebral cortex and hippocampus were separated as described previously (1). LPO concentrations were determined by the thiobarbituric acid-reactive

substances (TBARS) assay (5). Reactive oxygen species levels (ROS) were determined as described previously (1). Protein concentrations were estimated by the method of Lowry et. al., (6). Behavioral data were tested by two-way (group and block) randomized block factorial ANOVA. All other parameters were analyzed by one-way ANOVA followed by Fisher's PLSD with post-hoc comparisons.

Results and Discussion

The effect of PE administration on reference and working memory-related learning ability in the Vehicle and $A\beta_{1-40}$-infused AD model rats is expressed as the mean number of RME and WME for each group, with the data averaged over blocks of six trials. Randomized two-factor (block and group) ANOVA revealed significant main effects of both blocks of trials [$F(4,308) = 14.66$, $P < 0.0001$] and groups [$F(3,231) = 26.87$, $P < 0.0001$] on the number of RMEs and WMEs [blocks ($F(4,308) = 41.23$, $P < 0.0001$, and groups: $F(3,231) = 32.13$, $P < 0.0001$]. The TBARS and ROS concentrations in hippocampus were significantly higher in the Aβ. group than those of the Vehicle, PE+Vehicle and/or PE+Aβ groups ($P < 0.0001$). In cerebral cortex, PE administration significantly suppressed Aβ-induced increase ROS levels to the levels of Vehicle and/or PE rats.

We assume that the lower LPO and ROS concentrations, combined with the higher acquisition of memory performance, are likely to be the effect of PE that prevents Aβ-induced oxidative stress at neuronal level. This is because; EGCG has been shown to prevent Aβ-induced ROS production and neuronal cell death in vitro (7). Moreover, aging increases oxidative stress which leads to cognitive decline (8). We thus suggest that, long-term administration of green tea catechins might prevent Aβ-induced cognitive impairment by increasing antioxidative defense in brain.

References

1. Hashimoto M., Hossain S., Shimada T., Sugioka K., Yamasaki H., Fujii Y., Ishibashi Y., Oka JI., Shido O., J Neurochem. 81(2002) 1084-1091.
2. Hashimoto M., Tanabe Y., Fujii Y., Kikuta T., Shibata H., Shido O., J Nutr. 135 (2005) 549-455.
3. Haque AM., Hashimoto M., Katakura M., Tanabe Y., Hara Y., Shido O., J Nutr. 136 (2006) 1043-1047.
4. Gamoh S., Hashimoto M., Sugioka K., Hossain MS., Hata N., Misawa Y., Masumura S., Neuroscience 93 (1999) 237-241.
5. Ohkawa H., Ohishi N., Yagi K., Anal Biochem. 95 (1979) 351-358.
6. Lowry OH., Rosebrough N.., Farr AL.., Randall RJ., J Biol Chem. 193 (1951) 265-275.
7. Choi YT., Jung CH., Lee SR., Bae JH., Baek WK., Suh MH., Park J., Park CW., Suh SI., Life Sci. 70 (2001) 603-614.
8. Liu R., Liu IY., Bi X., Thompson RF., Doctrow SR., Malfroy B., Baudry M., Proc Natl Acad Sci. USA 100 (2003):8526-8531.