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Effects of Panax ginseng-containing Tea on Cognitive Performance in Adolescence

—A Randomized, Double-blinded, Placebo-controlled Parallel Comparison Trial—

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ABSTRACT

Objectives The purpose of this present study was to investigated effect of ginseng-containing tea intake on cognitive performance.（UMIN000034367）

Methods Subjects was 40 volunteers, aged between 13 and 18 years, were randomly allocated to either the placebo group, in which subjects consumed placebo tea, or the ginseng group, in which subjects consumed the ginseng-containing tea. The cognitive performances measured by Benton Visual Retention Test（BVRT）, Uchida-Kraepelin psychodiagnostic test（UKT）and TK system Tanaka AB style intelligence test that before and after a 4 week.

Results There was a significant interaction over 4 weeks in BVRT score and between the ginseng group and the placebo group.

Conclusion These results suggest that Panax ginseng containing tea was beneficial in the visual cognitive performance improvement among adolescence.

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KEY WORDS　Panax ginseng, Adolescence, Cognitive performance

INTRODUCTION

The improvement of cognitive performance is an important topic for adolescence. One of cognitive performances; aspects of executive functioning, including response inhibition, working memory, and attentional, set shifting and planning.[1)] Among these, working memory has been shown to explain at least as much variance in academic achievement as intelligence, which is usually considered the most powerful predictor of academic success.[2-4)] The Ministry of Education, Culture, Sports, Science and Technology in Japan（2012）reports that the number of students with potential for developmental disorders（i.e. learning disability・attention deficit hyperactivity disorder・autism spectrum disorder）is about 6.5%.[5)] Gathercole and Alloway（2009）suggested that the having small working memory was uncomfortable and difficult to con-

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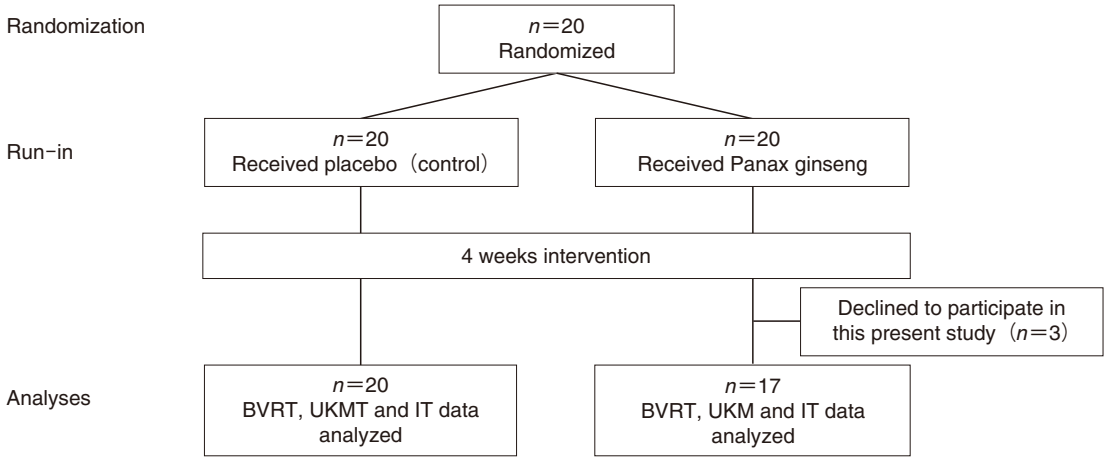

Fig. 1　Schematic of the flow of participants through the randomized double-blind, placebo-controlled trial investigating of Panax ginseng in the treatment of adolescence

BVRT, Benton Visual Retention Test; UKT, Uchida-Kraepelin psychodiagnostic test; IT, TK system Tanaka AB style intelligence test

duct learning activities complicatedly among adolescence.[6] Therefore, improving the working memory, which is one of cognitive performance, may make motivation for learning better.

Ginseng is generally taken to refer to the dried root of several species in the plant genus Panax（Araliaceae）. The most widely used family member is Panax ginseng, which is indigenous to the Far East（most notably Korea）.[7] It was first cultivated around 11 BC and has a medical history（as a wild herb）stretching back more than 5000 years.[8] The traditional use of ginseng is as a ‘panacea’ or treatment. In the US, it has previously been reported to be the most popular self- administered psychoactive herbal product[9] with many consumers taking it to aid ‘memory loss’ and ‘absent-mindedness’.[10] Regarding the memory function, ginseng can attenuate learning deficits in the damaged or aging brains in rodent models,[10,11] facilitate the generation of long-term potentiation[12] and increase hippocampal synaptic densities.[13] In human studies, It has been reported the improvement of cognitive performances in healthy subjects by ginseng.[13,14] Therefore, it seems to be possible that Panax ginseng-containing have the similar effect among adolescence. The purpose of this present study was to investigate the effect of ginseng-containing tea intake over 4 weeks on cognitive performance of adolescence.

SUBJECTS AND METHODS

1　Study design

The study employed a randomized, double-blind, placebo-controlled, parallel comparison design. Subjects were randomly assigned to cohorts receiving either ginseng or placebo（**Fig. 1**）. Each group was required to consume one apparently identical package, containing placebo or a total 510 mg panax ginseng extract. The panax ginseng extract was ONG-90HN（ONGANE JAPAN CO. LTD.）.

2　Subjects

Forty subjects aged 13 to 18 years old were recruited. Volunteers completed an initial health screening questionnaire which excluded subjects with some medical conditions（e.g. diabetes, glycaemia, psychiatric disorders, epilepsy and gastrointestinal disorders）. All subjects were in good health, not taking any drugs or medications, without food allergies and nonsmokers. Subjects were advised to refrain from taking any vitamins, other herbal supplements and over the counter medicines for the whole period of study. The written informed consents were obtained from all subjects and their parents before the enrollment of this present study. The study was carried out in accordance with the principals of the Declaration of Helsinki and Ethical Guideline for Medical and Health Research Involving Human Subjects, this present study was also registered at the institutional review board of Kinki University（approval number 201702）and UMIN

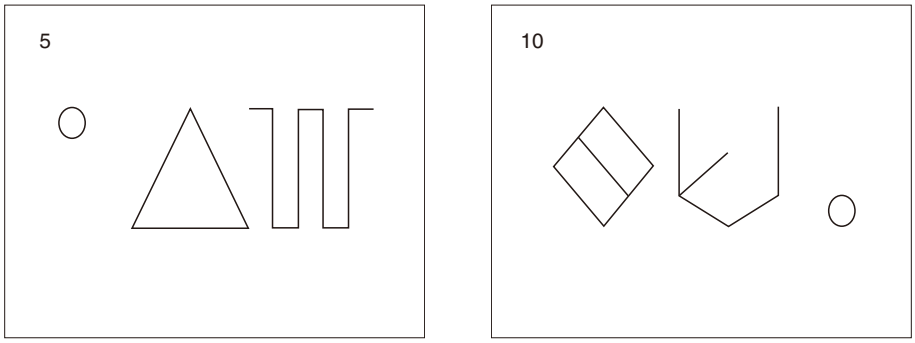

Fig. 2　Examples Benton Visual Retention Test

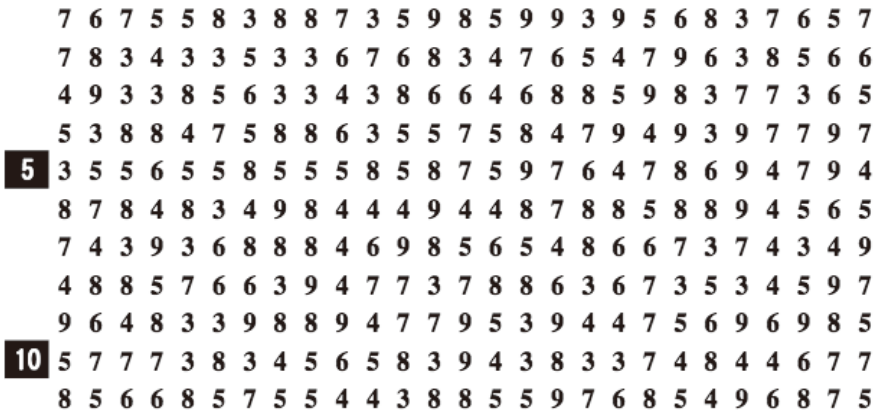

Fig. 3　Examples Uchida–Kraepelin psychodiagnostic test

Clinical Trial Registry（UMIN000034367）.

3　Benton Visual Retention Test（BVRT）[15]

The BVRT consists of 10 cards, each consisting of one or more simple geometric designs（**Fig. 2**）. The card was exposed for 10 s, and the subjects must draw immediately after its removal what he/she saw. The test requires spatial conceptualization, immediate recall, and vasomotor reproduction.

4　Uchida–Kraepelin psychodiagnostic test（UKT）[16]

The test material consisted of a 17×45 grid of figures（765 figures from 3 to 9, printed at random in 17 rows）（**Fig. 3**）. The subjects were asked to add adjacent figures horizontally and write a one-digit answer for as many figure-pairs as possible, as accurately as possible, in a 10 minutes period. When a cue was given, the subjects starts calculating. The subjects add the two figures at the left end of the first row and writes down the one-digit answer in pencil between the two figures. Performance on the arithmetic task（amount completed including errors for minutes）were obtained.

5　Intelligence test[17]

An intelligence test was assessed by “TK system Tanaka AB style intelligence test” which is Japanese version only. The test that can comprehensively measure intelligence by using a verbal expression（A expression）and a non-verbal expression（B expression）together. This examination consisting of a six item（to see below A, Mathematical reasoning; B, Numeric one-character collation replacement; C, Linguistic relationship understanding; D, Spatial composition reasoning; E, Rotational figure discrimination; F, Mathematical ability）and consists of a wide range of question ranging from easy question to difficult question. Also, since the question array is spiral system, it is an inspection with less measurement error. This test was carried out for 25 minutes. The grading of each item was raw score that was carried out based on the guidance. Then, the intelligence score was multiplied each raw data by the conversion rate. Finally, the intelligence standard score evaluates intelligence score adjusted with age.

6　Statistics

Data are expressed as means±standard deviation. Dif-

Table 1　Characteristics of participants

	Placebo (*n*=20)	Ginseng (*n*=17)	*P*-value
Male, *n*（%）	4（20）	3（17.6）	0.86
Age, y	15.6±1.8	16.0±1.8	0.42
Intake rate, %	91.3±12.5	94.7±6.8	0.31

Mean±SD

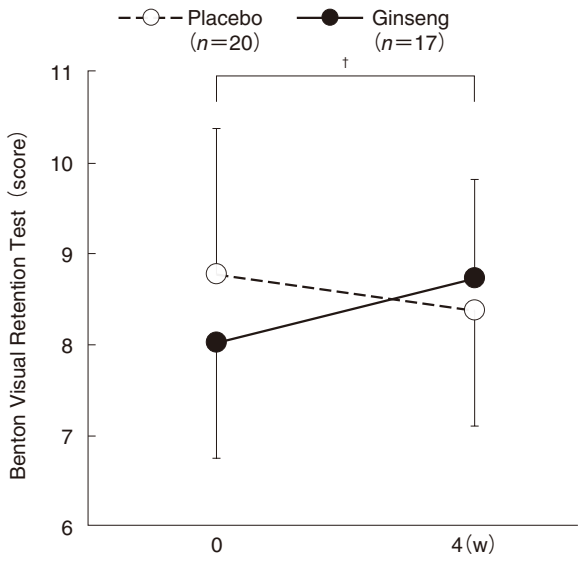

Fig. 4　Changes of cognitive performance test by Benton Visual Retention Test

Mean±SD
†$P<0.1$

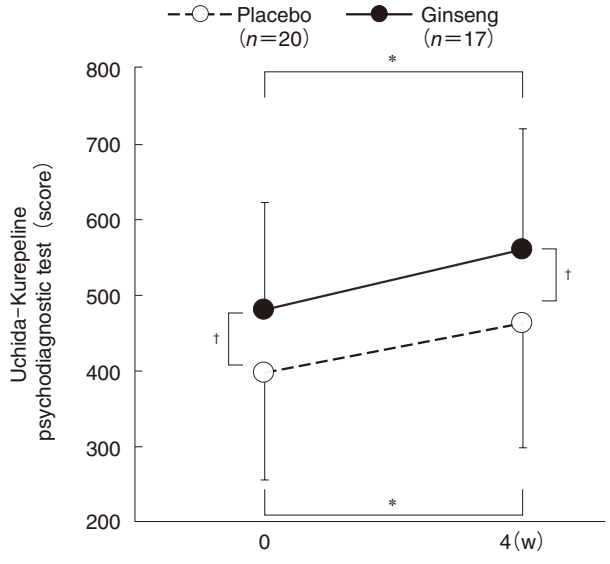

Fig. 5　Changes of Cognitive performance test by Uchida-Kraepelin psychodiagnostic test

Mean±SD
*$P<0.05$, †$P<0.1$

ferences of change in each cognitive performance score between the ginseng group and the placebo group were analyzed by independent t test. The comparison of pre and post intervention in BVRT score, UKT score and intelligence test scores were analyzed by paired *t*-test. The group comparison method, regarding individual evaluation average and comparison between before and after treatment for all outcomes, was analyzed by repeated ANOVA following Bonferroni post hoc test. Multiplicity according to various components of the intelligence test was not adjusted. The probability level of $P<0.05$ was set for statistical significance and $P<0.1$ was tendency. The Statistical analyses were performed using SPSS for Windows（version 23.0; SPSS Inc., Chicago, IL, USA）.

RESULTS

1　Subjects

Forty subjects were included and were randomly assigned to the ginseng group（*n*=20: male 4, female 16, mean age 16.0±1.7）or to placebo group（*n*=20: male 4, female 16, mean age 15.6±1.7）. At 4 weeks, 37 subjects（the ginseng group=17, placebo group=20）were reevaluated and included in the efficacy analysis（**Table 1**）. No significant different between the ginseng group and the placebo group were found in baseline characteristics including age, sex, BVRT and UKT. Three of the 40 subjects that were incorporated were excluded from the ginseng group due to withdrawal. Thus, thirty-seven subjects were analyzed. The intake rates calculated using the intake days were 91.3%（*n*=20）in the placebo group and 94.7%（*n*=17）in the ginseng group. There was no significant difference in intake rate.

2　Benton visual retention test（BVRT）

The BVRT score was found a significant interaction（$P=0.049$）. In the ginseng group, there was a tendency towards significant increase in the BVRT score（$P=0.085$）（**Fig. 4**）. While there was no significant difference between pre and post intervention in placebo group. There was no significant difference in comparison between placebo group and the ginseng group.

3　Uchida-Kraepelin psychodiagnostic test（UKT）

Significant increases of the UKT score were found in both the ginseng group and the placebo group（both groups: $P<0.05$）（**Fig. 5**）. No significant interaction

Table 2　TK system Tanaka AB style intelligence test

		Placebo (n=20)	Ginseng (n=17)	P-value
A : Mathematical reasoning	0 w	18.0±8.1	18.8±6.7	0.74
	4 w	22.8±12.0	26.0±10.1*	0.39
	Δ4 w	4.8±6.7	7.2±4.8	0.23
B : Numeric one-character collation replacement	0 w	11.3±3.6	11.3±2.8	0.10
	4 w	14.5±4.0*	14.3±3.9*	0.88
	Δ4 w	3.2±2.5	1.7±3.0	0.78
C : Linguistic relationship understanding	0 w	8.3±2.3	6.0±2.7	0.01
	4 w	9.4±2.4	8.7±2.8*	0.42
	Δ4 w	1.15±1.8	3.1±2.7	0.06
D : Spatial composition reasoning	0 w	8.0±2.2	8.2±1.9	0.74
	4 w	9.2±2.3†	9.5±2.3*	0.72
	Δ4 w	1.25±1.8	1.4±1.3	0.94
E : Rotational figure discrimination	0 w	20.7±11.1	21.9±9.3	0.71
	4 w	30.1±11.8*	30.8±12.4*	0.87
	Δ4 w	9.4±11.0	8.2±8.8	0.86
F : Mathematical ability	0 w	3.9±1.7	4.0±1.4	0.77
	4 w	4.5±2.2	5.0±1.9*	0.47
	Δ4 w	0.65±1.7	1.5±1.0	0.52
Intelligence score（IS）	0 w	118.5±33.4	114.5±30.0	0.71
	4 w	145.7±39.3*	149.6±43.1*	0.78
	Δ4 w	27.25±20.2	16.1±35.1	0.21
Intelligence standard score（ISS）	0 w	50.9±11.3	48.4±10.9	0.50
	4 w	59.9±13.4*	59.5±11.7*	0.93
	Δ4 w	9.05±6.8	4.6±11.2	0.28

Mean±SD
*P<0.05, †P<0.1 vs. 0 w

was found in UKT.

4　Intelligence test

Table 2 shows the results of Intelligence test at pre and post intervention. Changes in linguistic relationship understanding score was tendency towards difference in between the placebo group and the ginseng group（P=0.064）. However, there was a significant difference between the ginseng group and the placebo group in linguistic relationship understanding at the 0 week, and there was no significant difference in change of linguistic relationship understanding between the placebo group and the ginseng group after adjustment for the score at 0 w（*P change between the groups*=0.20）.

5　Adverse effects

No adverse events were reported during the 4 weeks intervention period.

DISCUSSION

This present study revealed an increase in BVRT score, which was used to assess the visuo-spatial domain of working memory,[18-21] when taking Panax ginseng-containing tea, as it showed that a significant interaction over 4 weeks in BVRT, was apparent between the ginseng group and the placebo group. In addition, a tendency towards significant increase of BVRT score was found only in the ginseng group. In changes of linguistic relationship understanding score of Intelligence test, a tendency towards significant difference between the placebo group and the ginseng group without adjustment for the score at 0 w was apparent. In the other several variables of Intelligence test, there were significant increases of in both the placebo group and the ginseng group, of which the causes were considered owing to the effect of time and learning effect.[22]

Several previous studies reported that improving cognitive performance by ingesting panax ginseng.[23-29] Despite growing evidence supporting the efficacy of Panax ginseng in modulating cognitive processes following a single dose,[26-28] few studies have directly investigated the cognitive and mood effects following more extended ginseng ingestion periods.[23-25,29] Scholey（2002, 2009）showed that the Panax ginseng was significantly improved cognitive performance at 6 h post-administration compared with placebo in healthy adults.[26,27] Scholey, et al.（2010）reported that Panax ginseng has most efficacious as a cognitive enhancer at 200-400 mg in young healthy

individuals.[27] Sorensen, et al.(1996)indicated that the effect of ginseng appears to be most marked in sick or elderly persons with lower levels of physical and mental functioning.[29] In this present study, the amount of Panax ginseng intake was 510 mg which is larger amount than it in previous study. The mean age of subjects in this present study, who were all adolescents, was also different from previous studies.[27,29] To the best of our knowledge, this is the first study to report an effect of ginseng among adolescents, and no adverse events with the 510 mg of ginseng intake.

Although few studies have shown the mechanism of the effect of ginseng on cognitive function, it has not clarified yet.[10,21,25,28,30] Kennedy, et al.(2003) suggested that these effects may be associated with ability of ginsenosides, which are one of components in ginseng, to modulate electroencephalograph activity through cholinergic neurotransmitter systems or the ability to increase cerebral blood flow hence intensify delivery of metabolic substrates to cerebral structures.[10] In addition, Smith, et al.(2014) reported that nitric oxide enhances endothelial function and modulates cerebral blood flow, efficient delivery of metabolic substrates to the active cortical sites could be one of the potential mechanisms underlying cognitive improvements exerted by ginseng species.[30] Following these reports in previous studies, the mechanism of the improvement of cognitive function in this present study may be explained by these pathways but have not been clear yet. A Japanese previous study showed the association between lower ability of visuo-spatial working memory and linguistic difficulty among Japanese pupils.[30] An increase of BVRT by taking Panax ginseng-containing tea may have a potential to improve the other ability. Further research is required to investigate the etiology of the effect of ginseng on cognitive function among young population.

CONCLUTION

To conclude, the effect of Panax ginseng-containing tea intake on cognitive performance among adolescence was revealed in this present study.

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