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Original Articles

Effect of Korean Red Ginseng on Cognitive Function and Quantitative EEG in Patients with Alzheimer's Disease: A Preliminary Study

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Abstract

Background: Korean red ginseng (KRG) has a nootropic effect. This study assessed the efficacy of KRG on cognitive function and quantitative electroencephalography (EEG) in patients with Alzheimer's disease (AD).
Methods: Fourteen patients with AD (mean age, 74.93 years; 11 women and 3 men) were recruited and treated with KRG (4.5 g per day) for 12 weeks. Cognitive function was assessed by the Korean Mini-Mental State Examination (K-MMSE) and the Frontal Assessment Battery (FAB). EEG performed before and after treatment were analyzed with quantitative spectral analysis.
Results: The FAB score improved significantly after 12 weeks of treatment. In the relative power spectrum analysis performed according to responsiveness, alpha power increased significantly in the right temporal area of the responders. The increments of relative alpha power in the right temporal, parietal, and occipital areas were significantly higher in the responders than the nonresponders.
Conclusions: This study indicates the efficacy of KRG on frontal lobe function in AD, related to increasing relative alpha power.

Introduction

Experimental and clinical data have indicated the efficacy of ginseng against Alzheimer's disease (AD).[1–4] Although the exact action mechanism of ginseng is unclear, cholinergic, anti-amyloidogenic, and neuroprotective effects have been suggested.[5–7]

Several studies showed positive efficacy of commercial anti-dementia drugs on quantitative electroencephalography (EEG) in patients with AD by decreasing slow activity and increasing fast activity.[8,9] Additionally, efficacies were revealed in frontal, parietal, and temporal areas, which were well known to be affected in AD.[9]

The aims of this study were to elucidate the effect of Korean red ginseng (KRG) on cognition and on quantitative EEG in AD.

Materials and Methods

Patients

Fourteen patients with AD were recruited at Seoul Medical Center. Their mean age (± standard deviation) was 74.93 ± 7.63 years, and 78.57% were women ($n = 11$). The National Institute of Neurological Disorders and Stroke–Alzheimer's Disease and Related Disorders Association criteria were used for the diagnosis of AD.[10] Patients were excluded if they had a history of psychiatric disorder, seizure disorder, or mental condition that would limit the completeness of the study and if they had cognitive impairment due to stroke, hypoxic brain injury, neoplasia, infection, and medications, such as antidepressants or psychoactive drugs.

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All the patients were treated with KRG (total powder capsule, 6-year-old root; KT&G Corporation, Daedeok District, Korea) at a dose of 4.5 g per day. Ginsenosides, which are composed of Rb1 (1.96%), Rb2 (2.18%), Rc (1.47%), Rd (0.72%), Re (1.11%), Rf (0.24%), Rg1 (0.49%), Rg2 (0.13%), Rg3 (0.12%), Rh1 (0.12%), and Rh2 (0.003%), are the active constituent of KRG and account for 8.54% of the herb.[3] Standard medical treatment was maintained during the study period. All patients provided written informed consent, and the institutional review board of Seoul Medical Center approved the study.

Neuropsychological tests

A supervised test technician administered the neuropsychological tests before and 12 weeks after treatment. Frontal lobe function was assessed by using the Frontal

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Assessment Battery (FAB).[11] The Korean Mini-Mental State Examination (K-MMSE) was used for global cognitive function assessment.[12]

Quantitative EEG

The quantitative EEG method has been described previously in articles on EEG and medial temporal lobe atrophy.[13] This method is described again here for reader convenience.

Digital EEG recordings (SynAmps2 Neuroscan system, Compumedics, Charlotte, NC) were obtained in the resting condition (eyes closed) after regular sleep. The EEG was recorded from 17 sites (F3, F4, F7, F8, Fz, T3, T4, T5, T6, C3, C4, Cz, P3, P4, Pz, O1, and O2) according to the international 10–20 system. The impedance of the electrode was kept below 5 kΩ at each electrode site. All EEGs were recorded with a sampling rate of 500 Hz/channel and filtered by using a 0.1–40-Hz bandpass filter. The neurologist analyzed the recorded EEG data in 20 epochs of 2 seconds without artifact or sleep waves. A digital fast Fourier transform–based power spectrum analysis computed the power density of EEG with range of 1–25 Hz ($1 \sim 4$ Hz, $4 \sim 8$ Hz, $8 \sim 12$ Hz, and $12 \sim 25$ Hz). For this study, relative power was chosen, which was expressed by the power in an EEG component band, in proportion to other bands.

Statistical analysis

Quantitative EEG data were analyzed by using SPSS software, version 11.5 (IBM, Chicago, IL). The required two-tailed level of significance for all tests was set at 0.05. Statistical analyses were performed by using the Wilcoxon rank-sum and Mann–Whitney U test.

Results

Neuropsychological tests

The baseline characteristics and neuropsychological test scores of the participants are presented in Table 1. Significant improvement in the FAB score between baseline and 12 weeks of follow-up (9.07 ± 3.38 vs. 10.5 ± 3.94, respectively; $p = 0.01$) was evident, whereas the K-MMSE showed no significant differences (19.93 ± 4.80 vs. 18.79 ± 5.75; $p = 0.142$). No significant adverse events were reported among the patients throughout the study period.

To clarify the effect of KRG on the change in quantitative EEG, the patients were classified as responders (increments of FAB score) and nonresponders (no changes or decrements of FAB score) based on the FAB score change (Table 1). The differences in sex, mean age, mean year of education, baseline K-MMSE score, and baseline FAB score between the groups were not significant ($p = 0.258$, 1.000, 0.260, 0.606, and 0.797, respectively). The improvement of FAB in responders was clearly significant (9.44 ± 3.75 vs. 11.78 ± 3.87; $p = 0.007$). However, there was also no significant decline of K-MMSE in either group ($p = 0.932$ in responders and $p = 0.074$ in nonresponders) or in FAB among nonresponders ($p = 0.317$).

Quantitative EEG

Baseline quantitative EEG data did not significantly differ between responders and nonresponders for relative delta, theta, alpha, and beta waves at all sites. In the spectral analysis of the responders, relative alpha power increased significantly in the right temporal (T6) area (Table 2). In addition, relative theta power in the left parietal (P3) area increased and relative beta power in the right central (C4) area decreased significantly. However, relative delta power did not show any significant changes. In the spectral analysis of the nonresponders, relative delta power in the right occipital (O2) and relative theta power in multiple areas (O1, P3, C3, F3, O2, P4, C4, T4, F8, Pz, Cz, and Fz) increased significantly (Table 2). In addition, relative alpha power in multiple areas (C3, F3, P4, T6, C4, Pz, and Cz) decreased significantly. However, relative beta power showed no significant changes at follow-ups.

Comparison of the changes in relative power of two groups showed significant differences in the right hemisphere (O2, P4, T6) (Table 3). There were favorable results in responders compared with nonresponders, especially in the right temporal area (T6, 5.58 ± 7.64 vs -9.05 ± 8.19; $p = 0.004$). However, the changes in other waves showed no significant differences between two groups.

Discussion

This study evaluated the efficacy of KRG on cognitive function and the related quantitative EEG changes in patients with AD. KRG improved frontal lobe function, which was related to increasing relative alpha power.

Despite significant increment in FAB score in responders, the relative alpha power did not increase in the frontal areas; rather, it increased only in the temporal area (T6). A

Table 1. Baseline Patient Characteristics

	Total		*Responders*		*Nonresponders*	
Variable	*Baseline*	*Follow-up*	*Baseline*	*Follow-up*	*Baseline*	*Follow-up*
Men/women (*n/n*)	3/11		3/6		0/5	
Age (year)	74.93 ± 7.63		74.67 ± 6.38		75.4 ± 10.36	
Education (year)	6.08 ± 4.03		7.11 ± 3.86		3.75 ± 3.84	
K-MMSE score	19.93 ± 4.80	18.79 ± 5.75	20.56 ± 5.50	20.33 ± 6.04	18.8 ± 3.42	16 ± 4.42
FAB score	**9.07 ± 3.38**	**10.5 ± 3.94***	**9.44 ± 3.75**	**11.78 ± 3.87****	8.4 ± 2.88	8.2 ± 3.19

Values are presented as mean ± standard deviation.
Values in boldface indicate that statistically significant difference exists.
*$p < 0.05$ vs. baseline.
**$p < 0.01$ vs. baseline.
K-MMSE, Korean Mini-Mental Status Examination; FAB, Frontal Assessment Battery.

Table 2. Changes in Quantitative Electroencephalographic Data for 12 Weeks in Responders and Nonresponders

	Delta		*Theta*		*Alpha*		*Beta*	
Variable	*Baseline*	*Follow-up*	*Baseline*	*Follow-up*	*Baseline*	*Follow-up*	*Baseline*	*Follow-up*
Responders								
O1	15.63 ± 7.99	19.81 ± 8.33	16.96 ± 10.68	19.40 ± 8.29	26.20 ± 14.20	31.43 ± 10.08	23.83 ± 7.53	19.57 ± 7.20
T5	16.59 ± 6.57	22.27 ± 10.12	19.25 ± 13.83	21.27 ± 12.07	27.25 ± 9.23	30.33 ± 13.00	23.89 ± 11.01	18.31 ± 9.18
P3	17.40 ± 6.71	18.67 ± 7.81	**17.34 ± 8.85**	**21.44 ± 8.51****	30.47 ± 10.39	32.78 ± 11.51	25.15 ± 9.95	21.46 ± 9.80
C3	19.70 ± 7.65	21.91 ± 8.13	16.77 ± 7.93	20.64 ± 8.61	28.08 ± 9.03	29.45 ± 8.82	25.31 ± 9.34	21.51 ± 9.44
T3	24.50 ± 8.49	26.68 ± 12.34	19.14 ± 12.88	21.32 ± 12.75	23.56 ± 7.43	25.23 ± 7.98	20.41 ± 6.95	17.75 ± 9.33
F3	26.30 ± 11.52	25.92 ± 11.38	18.09 ± 9.62	22.81 ± 10.01	24.27 ± 8.27	25.51 ± 7.46	21.50 ± 7.07	19.52 ± 9.22
F7	30.99 ± 12.24	32.27 ± 12.56	17.94 ± 11.19	21.23 ± 11.44	21.19 ± 6.30	22.28 ± 7.44	19.25 ± 6.17	16.90 ± 8.64
O2	16.89 ± 8.73	20.75 ± 6.24	18.66 ± 14.76	20.90 ± 7.56	23.65 ± 12.00	29.72 ± 12.51	24.02 ± 8.79	19.19 ± 6.34
P4	17.81 ± 7.80	18.87 ± 6.65	19.31 ± 14.91	22.28 ± 9.50	29.03 ± 10.88	31.37 ± 11.76	24.09 ± 9.39	21.66 ± 9.89
T6	18.36 ± 10.25	19.45 ± 6.89	20.34 ± 17.89	21.81 ± 10.58	**25.90 ± 10.79**	**31.47 ± 10.29***	22.79 ± 11.35	19.56 ± 8.29
C4	18.15 ± 6.98	22.45 ± 7.14	18.75 ± 13.35	20.15 ± 8.55	27.94 ± 10.00	29.19 ± 6.71	**24.79 ± 9.69**	**21.65 ± 10.67***
T4	25.65 ± 14.50	28.42 ± 13.48	18.48 ± 16.88	20.80 ± 13.52	20.01 ± 8.72	23.48 ± 5.23	21.47 ± 10.69	19.38 ± 10.96
F4	26.06 ± 11.55	25.60 ± 11.02	18.97 ± 11.05	22.43 ± 9.70	23.69 ± 7.88	25.40 ± 6.27	21.48 ± 8.60	19.77 ± 10.17
F8	32.47 ± 17.69	31.53 ± 12.49	18.09 ± 14.22	20.41 ± 10.98	19.26 ± 7.14	22.88 ± 5.97	18.62 ± 8.32	17.94 ± 9.46
Pz	18.68 ± 10.45	19.29 ± 7.01	18.68 ± 12.25	23.80 ± 10.02	30.94 ± 11.34	31.50 ± 10.49	22.80 ± 8.72	19.94 ± 9.15
Cz	20.04 ± 8.39	22.53 ± 9.76	18.43 ± 10.62	21.47 ± 10.50	28.03 ± 9.14	29.16 ± 9.76	23.53 ± 7.95	20.03 ± 8.77
Fz	25.74 ± 13.40	29.09 ± 19.30	19.47 ± 11.03	23.10 ± 11.45	24.39 ± 8.39	24.35 ± 9.41	20.99 ± 7.95	17.82 ± 10.11
Nonresponders								
O1	11.95 ± 6.47	15.93 ± 6.69	**14.95 ± 6.24**	**19.86 ± 8.85***	41.91 ± 19.53	35.80 ± 23.45	19.30 ± 8.59	18.05 ± 7.68
T5	14.70 ± 4.80	13.25 ± 5.79	19.94 ± 6.11	21.87 ± 8.73	35.88 ± 13.64	33.44 ± 21.59	21.23 ± 9.57	21.07 ± 10.13
P3	13.44 ± 4.48	15.72 ± 5.28	**17.89 ± 7.35**	**21.88 ± 7.77***	36.79 ± 14.88	32.16 ± 16.47	24.94 ± 8.08	22.35 ± 6.76
C3	13.90 ± 6.51	15.18 ± 6.26	**15.37 ± 7.13**	**20.14 ± 7.84***	**38.31 ± 19.45**	**33.80 ± 19.33***	24.39 ± 8.34	21.56 ± 6.43
T3	20.87 ± 15.91	14.21 ± 5.64	14.09 ± 4.29	17.93 ± 5.83	34.80 ± 21.06	29.49 ± 18.70	20.27 ± 9.16	24.16 ± 8.68
F3	15.19 ± 7.14	14.55 ± 5.33	**16.13 ± 7.55**	**21.35 ± 9.32***	**38.36 ± 20.28**	**35.00 ± 19.85***	21.56 ± 8.12	18.99 ± 6.50
F7	21.23 ± 13.13	17.02 ± 6.71	13.53 ± 5.59	18.89 ± 8.51	36.23 ± 21.75	33.36 ± 20.93	19.90 ± 7.29	19.96 ± 6.95
O2	**11.90 ± 6.88**	**15.55 ± 5.15***	**13.93 ± 6.59**	**20.26 ± 7.16***	43.62 ± 23.91	35.91 ± 18.30	18.82 ± 9.12	18.92 ± 7.18
P4	13.09 ± 6.59	15.76 ± 5.98	**16.61 ± 8.68**	**22.00 ± 8.60***	**41.04 ± 19.79**	**33.92 ± 17.75***	22.28 ± 8.91	20.91 ± 6.19
T6	12.79 ± 8.32	14.19 ± 6.09	15.75 ± 9.35	21.63 ± 8.93	**45.56 ± 24.41**	**36.51 ± 21.02***	17.78 ± 10.54	18.88 ± 9.13
C4	13.79 ± 6.33	14.11 ± 5.82	**16.58 ± 8.85**	**22.33 ± 9.23***	**37.65 ± 19.89**	**34.65 ± 19.88***	23.93 ± 8.88	20.76 ± 6.52
T4	16.72 ± 7.45	17.45 ± 5.96	**15.95 ± 7.45**	**22.04 ± 9.44***	36.27 ± 19.99	33.26 ± 19.03	20.38 ± 9.52	18.51 ± 7.57
F4	15.51 ± 6.99	15.94 ± 5.84	16.81 ± 8.70	22.18 ± 9.44	37.29 ± 20.33	34.75 ± 20.40	21.43 ± 8.32	17.82 ± 5.23
F8	20.43 ± 9.42	18.61 ± 8.06	**14.69 ± 7.14**	**20.84 ± 9.49***	33.62 ± 20.80	32.82 ± 20.01	20.47 ± 7.40	18.52 ± 4.93
Pz	14.63 ± 6.10	16.77 ± 6.80	**17.40 ± 8.39**	**22.46 ± 8.32***	**39.19 ± 17.43**	**34.07 ± 18.19***	22.25 ± 7.78	19.54 ± 5.64
Cz	15.00 ± 7.30	14.78 ± 5.58	**16.76 ± 7.64**	**22.58 ± 8.82***	**38.29 ± 19.93**	**35.02 ± 19.81***	22.32 ± 8.63	19.12 ± 6.72
Fz	15.51 ± 7.41	14.48 ± 4.98	**17.19 ± 8.29**	**22.88 ± 9.72***	39.01 ± 20.81	35.51 ± 20.02	20.01 ± 8.05	17.54 ± 5.94

Values are presented as mean ± standard deviation.
Values in boldface indicate that statistically significant difference exists.
*$p < 0.05$ vs. baseline.
**$p < 0.01$ vs. baseline.

Table 3. Comparison of Changes in Quantitative Electroencephalographic Data Between Responders and Nonresponders

	Delta		*Theta*		*Alpha*		*Beta*	
Variable	*Responders*	*Nonresponders*	*Responders*	*Nonresponders*	*Responders*	*Nonresponders*	*Responders*	*Nonresponders*
O1	4.18 ± 10.37	3.97 ± 7.23	2.45 ± 7.39	4.91 ± 3.96	5.23 ± 14.25	–6.11 ± 8.20	–4.26 ± 5.65	–1.24 ± 4.18
T5	5.68 ± 10.09	–1.46 ± 2.90	2.02 ± 4.31	1.92 ± 4.70	3.09 ± 8.20	–2.44 ± 14.79	–5.58 ± 7.35	–0.17 ± 6.66
P3	1.27 ± 10.44	2.27 ± 3.44	4.11 ± 2.21	3.99 ± 4.29	2.31 ± 11.09	–4.62 ± 3.37	–3.69 ± 4.38	–2.59 ± 2.89
C3	2.21 ± 10.09	1.28 ± 4.75	3.87 ± 4.47	4.77 ± 4.94	1.37 ± 10.65	–4.51 ± 2.75	–3.80 ± 4.89	–2.84 ± 3.07
T3	2.18 ± 13.83	–6.67 ± 11.99	2.19 ± 5.68	3.84 ± 4.75	1.67 ± 11.56	–5.31 ± 7.52	–2.66 ± 5.92	3.88 ± 5.35
F3	–0.38 ± 11.81	–0.64 ± 3.92	4.71 ± 6.49	5.23 ± 7.02	1.24 ± 11.77	–3.35 ± 2.06	–1.98 ± 4.88	–2.56 ± 4.13
F7	1.28 ± 11.59	–4.21 ± 8.09	3.30 ± 7.65	5.36 ± 6.43	1.09 ± 11.59	–2.87 ± 7.80	–2.35 ± 4.92	0.06 ± 3.80
O2	3.86 ± 9.45	3.65 ± 4.59	2.25 ± 9.37	6.33 ± 2.45	**6.07 ± 10.54**	**–7.72 ± 8.81***	–4.83 ± 6.67	0.10 ± 5.49
P4	1.06 ± 8.69	2.67 ± 3.30	2.96 ± 7.68	5.39 ± 3.92	**2.34 ± 8.76**	**–7.12 ± 4.83***	–2.43 ± 4.43	–1.37 ± 5.88
T6	1.09 ± 8.04	1.40 ± 2.30	1.46 ± 9.63	5.88 ± 4.02	**5.58 ± 7.64**	**–9.05 ± 8.19****	–3.23 ± 6.40	1.10 ± 6.29
C4	4.30 ± 9.41	0.32 ± 2.40	1.40 ± 8.44	5.75 ± 5.17	1.25 ± 10.14	–3.00 ± 2.20	–3.14 ± 3.71	–3.17 ± 4.13
T4	2.77 ± 15.49	0.74 ± 3.43	2.32 ± 6.93	6.09 ± 4.34	3.42 ± 8.02	–3.01 ± 8.44	–2.09 ± 5.34	–1.87 ± 4.10
F4	–0.45 ± 10.54	0.43 ± 4.34	3.46 ± 6.81	5.37 ± 6.63	1.72 ± 10.75	–2.54 ± 3.00	–1.71 ± 5.45	–3.60 ± 4.38
F8	–0.93 ± 20.87	–1.82 ± 7.61	2.31 ± 6.28	6.15 ± 5.91	3.63 ± 10.90	–0.81 ± 7.06	–0.68 ± 9.39	–1.95 ± 3.26
Pz	0.61 ± 13.24	2.14 ± 3.93	5.12 ± 6.36	5.06 ± 5.10	0.56 ± 11.50	–5.12 ± 2.16	–2.86 ± 4.92	–2.70 ± 5.51
Cz	2.48 ± 13.79	–0.22 ± 2.91	3.04 ± 6.95	5.82 ± 5.58	1.13 ± 14.01	–3.27 ± 1.45	–3.50 ± 5.25	–3.21 ± 4.28
Fz	3.35 ± 22.43	–1.03 ± 3.74	3.63 ± 6.82	5.68 ± 7.24	–0.04 ± 14.58	–3.50 ± 2.81	–3.17 ± 7.23	–2.46 ± 4.20

Values are presented as mean ± standard deviation.
Values in boldface indicate that statistically significant difference exists.
*$p < 0.05$ (responder vs. nonresponder).
**$p < 0.01$ (responder vs. nonresponder).

comparison of the changes in relative power with those in nonresponders showed that these were significantly increased in the posterior areas (temporal, parietal, and occipital areas). Frontal quantitative EEG could be insensitive to the antidementic treatment because of the limitations of the EEG in mild to moderate AD.[14] In a previous study, a spectral pattern of frontotemporal dementia did not significantly differ from that in controls except for a widespread increase of theta power, which could be the vulnerable point of frontal EEG evaluation.[15]

KRG displays clinical efficacy on general cognitive functions, including memory, in patients with AD and in healthy persons.[3,16] In animal studies, diverse ginsenosides, the active constituents of ginseng, have nootropic effects.[17] Ginsenosides Rg3 and Rg5/Rk1 enhanced psychomotor activity in a mouse model of amyloid β accumulation and displayed a neuroprotective effect involving the inhibition of the excitotoxic neuronal damage by glutamate or *N*-methyl-D-aspartate receptor.[18] Ginsenosides M1 improve memory disorder in a mouse model of AD by axonal extension activity in neuron degeneration and synaptic loss induced by amyloid β.[19] Although the follow-up period was too short to provide definite information in the current study, there were no significant decrements in K-MMSE score. In short, KRG had a positive effect on quantitative EEG at the temporal lobe in responders, which could enhance the memory function. Given that neuropsychological tests that assess frontal lobe functions, such as go-no-go, phonemic fluency, and Stroop test, were correlated with cortical atrophy of the temporoparietal region as well as the frontal lobe, the current results might show proper neurophysiologic responses.[20] Similarly, a poor result on a semantic fluency test was associated with cortical atrophy of the temporoparietal lobe in addition to the frontal lobe.[21] In line with these studies, without cortical involvement, subcortical pathology could cause the cognitive dysfunction.[22] If KRG affects the subcortical structures, the change in quantitative EEG could be limited.

It has been suggested that differences in the response to acetylcholinesterase inhibitors may be due to different functional features of the central neural systems.[23] Before treatment, posterior sources of delta, alpha 1, and alpha 2 frequencies were greater in amplitude in nonresponders compared with responders.[23] In the present study, however, baseline relative powers did not show significant differences in any frequency. Because ginseng has displayed diverse antidementic effects, factors other than an anti-acetylcholinesterase effect might affect the responsiveness. Another explanation is that a variety of outcomes could be produced according to the definition of treatment response in AD.[24] The response rate of antidementic drug varied from 26% to 63% in the same patient group in one study, depending on the definition of improvement used.

Limitations of the study include the small number of patients, relatively short duration, single follow-up during the study period, and lack of biomarkers. These could considerably weaken the power of statistical analysis to detect efficacy. Further studies are warranted to elucidate the neurophysiologic effect of KRG.

Conclusions

The efficacy of KRG for frontal lobe function in AD may be related to increasing relative alpha power.

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Author Disclosure Statement

No competing financial interests exist.

References

1. Quan Q, Wang J, Li X, Wang Y. Ginsenoside Rg1 decreases Aβ(1-42) level by upregulating PPARγ and IDE expression in the hippocampus of a rat model of Alzheimer's disease. PLos One 2013;8:e59155.
2. Fang F, Chen X, Huang T, et al. Multi-faced neuroprotective effects of Ginsenoside Rg1 in an Alzheimer mouse model. Biochim Biophys Acta 2012;1822:286–92.
3. Heo JH, Lee ST, Chu K, et al. An open-label trial of Korean red ginseng as an adjuvant treatment for cognitive impairment in patients with Alzheimer's disease. Eur J Neurol 2008;15:865–868.
4. Lee ST, Chu K, Sim JY, Heo JH, Kim M. Panax ginseng enhances cognitive performance in Alzheimer disease. Alzheimer Dis Assoc Disord 2008;22:222–226.
5. Kim J, Kim SH, Lee DS, et al. Effects of fermented ginseng on memory impairment and β-amyloid reduction in Alzheimer's disease experimental models. J Ginseng Res 2013; 37:100–107.
6. Lee MR, Yun BS, In OH, Sung CK. Comparative study of Korean white, red, and black ginseng extract on cholinesterase inhibitory activity and cholinergic function. J Ginseng Res 2011;35:421–428.
7. Liao B, Newmark H, Zhou R. Neuroprotective effects of ginseng total saponin and ginsenosides Rb1 and Rg1 on spinal cord neurons in vitro. Exp Neurol 2002;173:224–234.
8. Gianotti LR, Kunig G, Faber PL, et al. Rivastigmine effects on EEG spectra and three-dimensional LORETA functional imaging in Alzheimer's disease. Psychopharmacology 2008; 198:323–332.
9. Balkan S, Yaras N, Mihci E, et al. Effect of donepezil on EEG spectral analysis in Alzheimer's disease. Acta Neurol Belg 2003;103:164–169.
10. McKhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. Neurology 1984;34:939–944.
11. Kim TH, Huh YS, Choe JY, et al. Korean version of frontal assessment battery: psychometric properties and normative data. Dement Geriatr Cogn Disord 2010;29:363–370.
12. Kang YW, Na DL, Hahn SH. A validity study on the Korean Mini-Mental State Examination (K-MMSE) in dementia patients. J Korean Neurol Assoc 1997;15:300–307.
13. Lee SJ, Park MH, Park SS, Ahn JY, Heo JH. Quantitative EEG and medial temporal lobe atrophy in Alzheimer's dementia: preliminary study. Ann Indian Acad Neurol 2015; 18:10–14.
14. Rodriguez G, Vitali P, Canfora M, et al. Quantitative EEG and perfusional single photon emission computed tomography correlation during long-term donepezil therapy in Alzheimer's disease. Clin Neurophysiol 2004;115:39–49.
15. Caso F, Cursi M, Magnani G, et al. Quantitative EEG and LORETA: valuable tools in discerning FTD from AD? Neurobiol Aging 2012;33:2343–2356.

16. Yeo HB, Yoon HK, Lee HJ, et al. Effects of Korean red ginseng on cognitive and motor function: a double-blind, randomized, placebo-controlled trial. J Ginseng Res 2012; 36:190–197.
17. Heo JH, Kim M. The efficacy of ginseng on the cognitive function. J Ginseng Res 2009;33:161–164.
18. Bao HY, Zhang J, Yeo SJ, et al. Memory enhancing and neuroprotective effects of selected ginsenosides. Arch Pharm Res 2005;28:335–342.
19. Tohda C, Matsumoto N, Zou K, Meselhy MR, Komatsu K. Aβ(25-35)-induced memory impairment, axonal atrophy, and synaptic loss are ameliorated by M1, a metabolite of protopananxadiol-type saponins. Neuropsychopharmacology 2004;29:860–868.
20. Ahn HJ, Seo SW, Chin J, et al. The cortical neuroanatomy of neuropsychological deficits in mild cognitive impairment and Alzheimer's disease: a surface-based morphometric analysis. Neuropsychologia 2011;49:3931–3945.
21. Eastman JA, Hwang KS, Lazaris A, et al. Cortical thickness and semantic fluency in Alzheimer's disease and mild cognitive impairment. Am J Alzheimers Dis (Columbia) 2013;1: 81–92.
22. Roh JH, Lee JH. Recent updates on subcortical ischemic vascular dementia. J Stroke 2014;16:18–26.
23. Babiloni C, Cassetta E, Dal Forno G, et al.. Donepezil effects on sources of cortical rhythms in mild Alzheimer's disease: responders vs. non-responders. Neuroimage 2006;31:1650–1665.
24. Burns A, Yeates A, Akintade L, et al. Defining treatment response to donepezil in Alzheimer's disease: responder analysis of patient-level data from randomized, placebo-controlled studies. Drugs Aging 2008;25:707–714.

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