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A DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL STUDY ON THE EFFECT OF A STANDARDIZED GINSENG EXTRACT ON PSYCHOMOTOR PERFORMANCE IN HEALTHY VOLUNTEERS

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Summary

Various tests of psychomotor performance were carried out in a group of 16 healthy male volunteers given a standardized preparation of Korean ginseng (G 115; 100 mg twice a day for 12 weeks) and in a similar group given identical placebo capsules under double-blind conditions. A favourable effect of G 115 relative to baseline performance was observed in attention (cancellation test), processing (mental arithmetic, logical deduction), integrated sensory-motor function (choice reaction time) and auditory reaction time. However, end performance of the G 115 group was superior statistically to the placebo group only in mental arithmetic. No difference between G 115 and placebo was found in tests of pure motor function (tapping test), recognition (digit symbol substitution) and visual reaction time. No adverse effects were reported. It is concluded that G 115 may be superior to placebo in improving certain psychomotor functions in healthy subjects.

Introduction

The term "ginseng" is generally understood to mean the dried root of *Panax ginseng* C.A. Meyer, a perennial plant cultivated in the far East. Although preparations of ginseng have been used empirically in Chinese medicine for thousands of years (Hsu, 1976), a more scientific approach to its medical use has been made possible in the last two decades by identification of the active principles, the development of suitable techniques for their isolation and standardization and, finally, widespread laboratory and clinical evaluation of their specific pharmacologic properties. In particular, it has been possible to demonstrate that the biological activity of the crude extract of the dried root appears to be entirely accounted for by a unique class of tri-terpenoid glycosides known as ginsenosides (Iida et al., 1968).

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Pharmacological studies in animals have shown that ginseng or its active components prolong survival to physical or chemical stress (Brekhman and Dardymov, 1969) possibly by increasing adrenal responsiveness (Petkov and Staneva-Stoicheva, 1965), stimulate learning and memory (Brekhman and Dardymov, 1969), and enhance psychophysical performance and resistance to fatigue (Popov and Goldway, 1973; Takagi et al., 1974; Brekhman and Dardymov, 1969).

Among the various types of ginseng, Korean ginseng appears to be particularly rich in ginsenosides. A preparation of Korean ginseng containing a standardized concentration of ginsenosides has proved particularly effective in a number of clinical (Forgo et al., 1981; Forgo and Kirchdorfer, 1981; Quiroga and Imbriano, 1979; Dörling et al., 1980) and pharmacological (Petkov, 1978) studies. This preparation, known as G 115 and marketed under the name of Ginsana in a number of countries, is widely used for the treatment of a variety of conditions such as the reduced psycho-physical performance of the elderly and general fatigue states, particularly when associated with stressful life situations. In the light of the evidence reviewed above, it was of interest to set up a double-blind placebo-controlled study aimed at evaluating the effect of G 115 on some objective and subjective measures of psychomotor performance in healthy volunteers.

Methods

Subjects and protocol

Thirty-two male volunteers aged 20—24 years were studied. All subjects were students at a local University College and were in good physical condition as assessed by a medical examination and conventional laboratory tests. Subjects were randomly divided into two groups of equal size homogeneous for age and body weight (Table 1). Under double-blind conditions, one group was treated with G 115* (one capsule twice a day, taken at 0800 h and 1300 h, corresponding to a total daily dose of 200 mg of G 115) and the other with identical lactose-containing placebo capsules. Both treatments were carried out simultaneously and lasted for 12 weeks. All subjects were kept under medical supervision throughout the study. Laboratory tests and psychometric assessments were carried out before treatment and during the last week of treatment.

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*G 115 is the registered trademark of a ginseng extract containing all 13 ginsenosides from Korean Panax Ginseng. This extract, standardized by using HPLC and FDMS analyses, is marketed as GINSANA (GPL Ginsana Products Lugano SA, Lugano/Switzerland). For this study, GINSANA® capsules containing 100 mg of G 115 per capsule were used and the placebo capsules were visually indistinguishable from this product.

TABLE 1

AGE AND BODY WEIGHT OF THE MALE SUBJECTS INCLUDED IN THE STUDY

Subject	Age (years)	Body weight (kg)
1	20	77
2	20	75
3	22	76
4	23	75
5	20	57
6	21	79
7	24	52
8	20	71
9	24	70
10	24	69
11	23	56
12	22	78
13	21	68
14	22	72
15	20	73
16	24	64
Mean ± S.D.	21.9 ± 1.6	69.5 ± 8.4
17	23	55
18	21	71
19	20	76
20	24	55
21	22	72
22	20	82
23	21	60
24	24	71
25	23	80
26	23	55
27	20	76
28	20	79
29	21	64
30	23	82
31	22	60
32	20	76
Mean ± S.D.	21.7 ± 1.6	69.6 ± 10.0

Psychomotor assessment

Prior to the study, each subject was familiarized with the assessment techniques. All tests were carried out in a quiet environment at the same time of the day for each subject. Subjects were asked to refrain from drinking caffeine or alcoholic beverages on the assessment days. Methods of evaluation included the following.

Tapping test

In this test of motor performance, each subject had to sequentially finger tap two buttons placed 10 cm apart. The tapping rates during the two 30-s sessions of the test were measured and averaged.

Simple reaction time

Auditory and visual simple reaction times were determined by measuring the latency between 10 randomly spaced visual and acoustic stimuli, respectively, and the response (pressing a button). The means of 10 measurements with each stimulus were recorded in each of two sessions and the results of the two sessions were averaged.

Choice reaction time

In this test of sensory-motor performance, the subject sat in front of two buttons and had to respond to each of 10 different stimuli (either visual or acoustic, randomly arranged and spaced) by pressing the appropriate button. The average latency between stimulus and completion of the responses was recorded. The score was: mean reaction time/(10 − number of errors). The average of two sessions was taken as the final result.

Cancellation test

This test of attention was carried out by having each subject cross-out a one-digit number in a randomized sequence of digits. The number of correct digits cancelled during the 2 min of the test was recorded.

Digit symbol substitution test

Each subject was confronted with a list of 100 digits (1—9) taken from the Wechsler Adult Intelligence Scale (Wechsler, 1955). After being instructed about a specific association between each digit and a graphical symbol, the subject had 90 s to write below the 100 digits the corresponding symbols. The number of correct symbols written over a 90-s period was taken as the score.

Mental arithmetic

Each subject was asked to calculate mentally whether the sum of a randomized sequence of four two-digit numbers yielded an odd or an even number. The test was repeated 10 times and the average time to complete the task was recorded. The score was: number of correct responses/mean time.

Logical deduction

The subjects were asked to decide whether each of a series of logical deductions presented sequentially was true or not. The total number of right responses was recorded and the score was: number of correct responses/time.

Statistical analysis

For parameters showing a continuous distribution, within- and between-group comparisons were made by using the Student's *t*-test for paired and unpaired data, respectively. Data showing a non-continuous distribution were compared using Kendall's *S*-test (Armitage, 1971).

Results

All subjects completed the study. No adverse effects were reported and laboratory tests (full blood count, SGOT, SGPT, GGT, sodium, potassium, chloride, calcium, creatinine, BUN, bilirubin, alkaline phosphatase, urinalysis) remained within normal limits in all subjects. The results of psychomotor tests are summarized in Table 2.

Cancellation test

Baseline performance was similar in the two groups. Treatment with G 115 was associated with a statistically significant improvement of performance in this test while placebo had no effect. In spite of this, no significant difference between placebo and G 115 could be found at the completion of treatment.

Digit symbol substitution test

Baseline performance in this test was similar in both groups and improved to a similar but not significant extent with both treatments.

Mental arithmetic

No significant differences in baseline were found between the two groups. While no change was observed in the placebo group, a statistically significant improvement for the G 115 group was observed both versus baseline and the placebo group.

Tapping test

Neither treatment significantly affected performance in this test.

Simple reaction time

Neither treatment was found to affect visual reaction time significantly. Auditory reaction times decreased significantly after both treatments without any significant difference between the two treatments at the end of the study.

Choice reaction time

Prior to treatment, choice reaction time was significantly longer in the G 115 group. After treatment, choice reaction time showed minor changes in the placebo group and decreased significantly in the G 115 group. As a

TABLE 2

EFFECT OF G 115 AND PLACEBO ON OBJECTIVE PARAMETERS OF PSYCHOMOTOR FUNCTION

Test	Mean response ± S.D. (16 subjects)			
	Pre-treatment		Post-treatment	
	G 115	Placebo	G 115	Placebo
Cancellation test (No. of digits/2 min)	32 ± 9	31 ± 7	39 ± 4[a]	36 ± 7
Digit symbol substitution test (No. of symbols/90 s)	82 ± 11	82 ± 9	88 ± 11	89 ± 7
Mental arithmetic (correct responses/s)	0.49 ± 0.17	0.45 ± 0.12	0.61 ± 0.24[a,b]	0.45 ± 0.17
Tapping test (taps/30 s)	77 ± 17	76 ± 14	77 ± 11	84 ± 13
Visual reaction time (s)	0.20 ± 0.02	0.19 ± 0.01	0.20 ± 0.02	0.19 ± 0.03
Auditory reaction time (s)	0.21 ± 0.02	0.21 ± 0.02	0.19 ± 0.03[a]	0.19 ± 0.02[a]
Choice reaction time (s/10 − no. of errors)	0.068 ± 0.009[b]	0.056 ± 0.010	0.050 ± 0.006[a]	0.052 ± 0.005
Logical deduction (correct responses/s)	0.34 ± 0.07	0.32 ± 0.08	0.40 ± 0.10[a]	0.36 ± 0.11

[a] Significant difference from pre-treatment performance ($P < 0.05$ or better).
[b] Significant difference between the two experimental groups ($P < 0.05$ or better).

result, G 115 treatment was associated with levelling of the performance gap present between the two groups at the onset of the study.

Logical deduction

Baseline performance was similar in the two groups. Only G 115 was associated with a significant improvement in this test.

Discussion

The present study shows that under double-blind conditions G 115 appeared to be superior to placebo in enhancing certain aspects of psychomotor performance. Evidence for a favourable effect of G 115 was obtained in at least four independent and objective parameters. The improvement was in most cases detectable as a significant facilitation of performance over the baseline; however, in only one case did the difference of performance at the end of the study between G 115 and placebo group reach statistical significance. This may be explained by the considerable inter-subject variability and the trend towards improved performance in the control group. In no test was the placebo-treated group statistically superior to the G 115 group.

Close inspection of these results suggests that indices of attention (cancellation test) and processing (mental arithmetic) were among the parameters more clearly improved by treatment with G 115, while pure motor function (as reflected by the tapping test) was unaffected. The effect of the drug on choice reaction time, a parameter of integrated sensory-motor function, could not be established with certainty due to the difference in baseline values between the two groups.

These results are in line with two double-blind controlled studies recently performed in Switzerland (Forgo et al., 1981) and West Germany (Dörling et al., 1980) in a less homogeneous and generally older population. It is generally recognized in experimental and clinical studies that an improvement in psychomotor performance by pharmacological agents can be more easily induced when brain function is disturbed or impaired; therefore, the significant effect of G 115 in these young, intellectually-active volunteers appears remarkable. Further clinical studies on the efficacy of this product should be encouraged.

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References

Armitage, P. (1971). *Statistical Methods in Medical Research.* Blackwell Scientific Publications, Oxford, pp. 398—405.

Brekhman, I.I. and Dardymov, I.V. (1969) New substances of plant origin which increase non-specific resistance. *Annual Review of Pharmacology* 9, 419—430.

Dörling, E., Kirchdorfer, A.M. and Rückert, K.H. (1980) Haben Ginsenoside Einfluss auf das Leistungsvermörgen. *Notabene Medici* 10, 214—246

Forgo, I. and Kirchdorfer, A.M. (1981) On the question of influencing the performance of top sportsmen by means of biologically active substances. *Aerztliche Praxis* 33, 1784—1786.

Forgo, I., Kayasseh, L. and Staub, J.J. (1981) Einfluss eines standardisierten Ginseng-Extraktes auf das Allgemeinbefinden, die Reaktionsfähigkeit, Lungenfunktion und die gonadalen Hormone. *Medizinische Welt* 32, 751—756.

Hsu, S.V. (1976). The genus *Panax ginseng* in Chinese medicine. *Economic Botany* 30, 11—28.

Idia, Y., Tanaka, O. and Shibata, S. (1968) Studies on saponins of ginseng. The structure of ginsenoside Rgl. *Tetrahedron Letters* 52, 5449—5453.

Petkov, V. (1978) Effect of ginseng on the brain biogenic monoamines and 3',5'-AMP system. Experiments on rats. *Arzneimittel-Forschung (Drug Research)* 28, 388—393.

Petkov, V. and Staneva-Stoicheva, D. (1965) The effect of an extract of ginseng (*Panax ginseng*) on the function of the adrenal cortex. In: K. Chen and R. Mukerji (Eds.), *Pharmacology of Oriental Plants*, Pergamon Press, Oxford, pp. 39—50.

Popov, I.M. and Goldway, W.J. (1973) A review of the properties and clinical effects of ginseng. *American Journal of Chinese Medicine* 1, 263—270.

Quiroga, H.A. and Imbriano, A.E. (1979) Accion del extracto del *Panax ginseng* en las deficiencias cerebrovasculares. *Orientacion Médica* 28, 86—87.

Takagi, K., Saito, H. and Tsuchiya, M. (1974) Effect of *Panax ginseng* root on spontaneous movement and exercise in mice. *Japanese Journal of Pharmacology* 24, 41—48.

Wechsler, D. (1955) *A Manual for the Wechsler Adult Intelligence Scale.* Psychological Corporation, New York.