

---

**SHORT PAPER****Subjective effects of glycine ingestion before bedtime on sleep quality**

Kentaro INAGAWA,<sup>1</sup> Takenori HIRAOKA,<sup>2</sup> Tohru KOHDA,<sup>2</sup> Wataru YAMADERA<sup>3</sup> and Michio TAKAHASHI<sup>1</sup>

<sup>1</sup>Research Institute for Health Fundamentals, Ajinomoto Co., Inc., Kawasaki, <sup>2</sup>Health Service Development Department, Ajinomoto Co., Inc., Tokyo, and <sup>3</sup>Department of Psychiatry, Jikei University School of Medicine, Tokyo, Japan

**Abstract**

The effects of glycine on sleep quality were examined in a randomized double-blinded cross-over trial. The volunteers, with complaints about the quality of their sleep, ingested either glycine (3 g) or placebo before bedtime, and their subjective feeling in the following morning was evaluated with the St. Mary's Hospital Sleep Questionnaire and Space-Aeromedicine Fatigue Checklist. The glycine ingestion significantly improved the following elements: "fatigue", "liveliness and peppiness", and "clear-headedness". These results suggest that glycine produced a good subjective feeling after awakening from sleep.

**Key words:** amino acid, glycine, subjective effect on sleep.

---

**INTRODUCTION**

Although less severe than psychiatric cases, it is disturbing that recently the number of individuals who are dissatisfied with their sleep quality has increased. While chemicals that may mildly improve sleep quality are usually favored by these individuals, sleeping tablets are often avoided as such drugs are believed to develop addiction and tolerance, and also cause rebound after the drug intervention is ended.

Glycine is one type of nonessential amino acids. Endogenous glycine plays an important role in the peripheral and central nervous system (CNS). In addition to its well-known role as an inhibitory neurotransmitter, it has been reported recently that glycine plays a role as an allosteric modulator for the N-methyl-D-

aspartate (NMDA) receptor.<sup>1</sup> It has been reported that orally administered glycine (Bioglycine; Konapharma, Pratteln, Switzerland) shows beneficial effects on memory and attention in healthy volunteers without the pharmacological effect on subjective mood observed in administration of a CNS stimulant.<sup>2</sup> Our preliminary observation of healthy volunteers has suggested that glycine improves sleep quality (unpublished data 2003).

In the present study, the effects of glycine ingestion (3 g) before bedtime were examined in a randomized double-blinded crossover trial. The sleep quality of participants who were administered with glycine or with a placebo was measured with the standardized questionnaires which assess subjective characteristics of sleep (St. Mary's Hospital [SMH] Sleep Questionnaire and Space-Aeromedicine [SAM] Fatigue Check list).

**METHODS**

Nineteen female volunteers (employees of Ajinomoto Co., Inc. age: 24–53 years, mean: 31.1 years) participated in the present study. The women experiencing

---

Correspondence: Dr Kentaro Inagawa, Research Institute for Health Fundamentals, Ajinomoto Co., Inc., 1-1 Suzukicho, Kawasaki-ku, Kasawaki-shi 210-8681, Japan. Email: kentaro\_inagawa@ajinomoto.com

Accepted for publication 9 August 2005.

menstruation during the study period were excluded. Substances that may affect sleep such as caffeine, vitamin B<sub>12</sub>, or alcohol were prohibited and the participants' lifestyle pattern was kept constant during the study period. The study protocol was a randomized double-blinded crossover trial. The study design based on our preliminary observation was as follows. The participants took flavored glycine (3 g) or flavored placebo within 1 h before bedtime from Monday to Thursday in a certain week, and after that there was a 3-day washout period between the following Friday and the following Sunday. From the following Monday to the following Thursday the participants resumed taking the other of the flavored test substances (3 g) that had not been taken in the previous administration period.

The effect of glycine on the subjective sleep quality was evaluated every morning in a study period for 4 days by using the SMH Sleep Questionnaire<sup>3,4</sup> and the SAM Fatigue Checklist.<sup>5</sup> The SMH Sleep Questionnaire refers to participants' sleep over the preceding 24 h and contains 14 items concerning sleep quality such as depth, awakening in the middle of the night, satisfaction, refreshed feeling upon awakening, difficulty in falling asleep and early awakening. For example, for item 10, "How clear-headed did you feel after getting up this morning?", the participant was instructed to select her response from 6 choices such as "1. Still very drowsy indeed, 2. Still moderately drowsy, 3. Still slightly drowsy, 4. Fairly clear-headed, 5. Alert", and "6 Very alert". The SAM Fatigue Checklist refers to participants' feeling upon awakening and consists of 10 questions such as "very lively?" and "extremely tired?". For example, for Question a, "very lively?", the participants had to rated their feeling on a 3-point Likert Scale such as "0. very lively; 1. lively; 2. not at all lively". The SAM Fatigue Checklist was translated into Japanese in the Department of Psychiatry, Jikei University School of Medicine, with the permission of the authors.<sup>6</sup>

The data obtained with each questionnaire were analyzed using Wilcoxon's signed rank test, and the statistical significance was defined as  $P < 0.05$ .

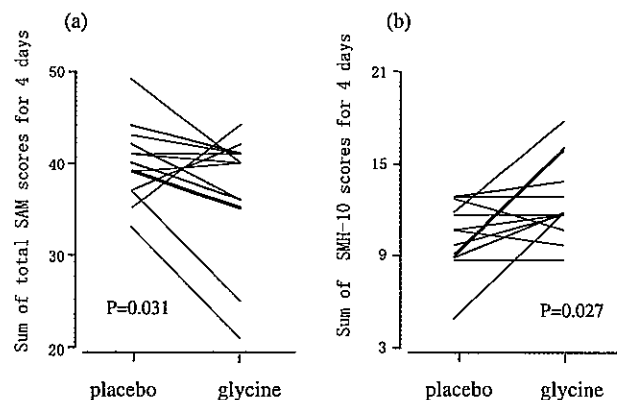
The study protocol was approved by the Institutional Review Board of Ajinomoto Co., Inc. All the participants enrolled in this study provided their written informed consent after receiving explanation on the study procedure and the potential risks of the study. After obtaining the written informed consent, the Pittsburgh Sleep Quality Index<sup>7,8</sup> concerning participants' sleep over the past month and a lifestyle checklist (a questionnaire concerning lifestyle and sleep characteristics such as

sleep satisfaction) were used to obtain the background information on sleep characteristics of the participants.

## RESULTS

In the present study, a total of 19 participants originally enrolled and 4 of them dropped out during the study. The efficacy evaluation by the 15 participants (age: 24–53 years, mean: 31.1 years) who completed the study satisfactorily was obtained. The life-style questionnaire indicated that each participant had dissatisfaction with sleep. They also scored 6 or more on the Pittsburgh Sleep Quality Index (the higher the score, the less the individual is satisfied with their sleep). These results indicated that the participants who took part in the present study had some sleep problems beforehand. No serious adverse events of the study protocol, including glycine and placebo intake, were observed during the study period.

Glycine had a significant effect ( $P = 0.031$ ) on total scores (the sum of scores for 10 items) of the SAM Fatigue Checklist (Fig. 1a). Looking at individual items, a significant effect of glycine was observed in Item a "very lively" ( $P = 0.008$ ) and also in Item e "extremely peppy" ( $P = 0.031$ ). For Item h "very refreshed", a tendency toward improvement ( $P = 0.065$ ) was observed. In the responses of the outcome of the SMH Sleep Questionnaire, a significant effect of glycine was observed only in Question 10 "How clear-headed did you feel after getting up this morning?" ( $P = 0.027$ , Fig. 1b). There were no significant differences in the sleep time



**Figure 1** The subjective effects of glycine on sleep evaluated with (a) the SAM Fatigue Checklist and (b) the SMH Sleep Questionnaire Item 10. Each line shows change in the sum of scores taken from the 4-day study period in each participant.

and sleep latency computed, based on replies to SMH questions between glycine administration and placebo administration.

## DISCUSSION

The present observation indicates that glycine significantly alleviates the feeling of fatigue upon getting up in the morning as measured in the SAM Fatigue Checklist. It also exerted a positive effect on clear-headedness in the morning judging from the scores for the item in the SMH Sleep Questionnaire, "How clear-headed did you feel after getting up this morning?". Other than fatigue and clear-headedness, no aspects (depth, awaking in the middle of the night, satisfaction, difficulty in falling asleep, etc.) were improved by glycine ingestion. These observations suggest that glycine ingested at night produces subjective sleep effects such as decreased fatigue, increased liveliness, peppiness and clear-headedness after getting up the next morning.

Furthermore, glycine has been ingested as a component of foodstuff for a long time, and the safety of glycine is considered higher than that of sleeping drugs. No serious side-effects were noted when up to 30 g/day of glycine was given in humans.<sup>9</sup>

These results suggest that the safety of glycine is relatively high and that oral glycine administration produces good subjective feeling after awakening from sleep in humans who are dissatisfied with their sleep quality.

## REFERENCES

- 1 Cooper JR, Bloom FE, Roth RH. Amino acid transmitters. In: Cooper JR, Bloom FE and Roth RH, eds. *The Biochemical Basis of Neuropharmacology*, 8th edn. Oxford University Press: Oxford, 2003; 105–50.
- 2 File SE, Fluck E, Fernandes C. Beneficial effects of glycine (Bioglycine<sup>®</sup>) on memory and attention in young and middle-aged adults. *J. Clin. Psychopharmacol.* 1999; **19**: 506–12.
- 3 Ellis BW, Johns MW, Lancaster R, Raptopoulos P, Angelopoulos N, Priest RG. The St. Mary's hospital sleep questionnaire: a study of reliability. *Sleep* 1981; **4**: 93–7.
- 4 Uchiyama M, Ohta K, Okawa M. Evaluation standards of sleep and sleep disorder. In: Matsushita M, ed. *Encyclopedia of Clinical Psychiatry, Vol. 13, Sleep Disorder*. Nakayama Shoten: Tokyo, 1999; 489–98 (in Japanese).
- 5 Harris DA, Pegram GV, Hartman BO. Performance and fatigue in experimental double-crew transport missions. *Aerospace Med.* 1971; **42**: 980–6.
- 6 Yamadera W. Psychophysical and psychological consequences after surgical treatment of obstructive sleep apnea syndrome. *Psychiatr. Neurol. Jap* 1994; **96**: 903–32 (in Japanese).
- 7 Buysse DJ, Reynolds CF III, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatr. Res.* 1989; **29**: 193–213.
- 8 Doi Y, Minowa M, Uchiyama M, Okawa M. Development of the Pittsburgh Sleep Quality Index Japanese version. *Jap. J. Psychiatr. Treat.* 1998; **13**: 755–68 (in Japanese).
- 9 Garlick PJ. The nature of human hazards associated with excessive intake of amino acids. *J. Nutr* 2004; **134**: 1633S–9S.