The metabolic response to dietary proteins, age and hormonal factors includes marked changes in protein synthesis, especially in liver, muscle and intestine (1–5). Protein synthesis in the brain is also sensitive to the alteration of dietary amino acid composition in young rats (6, 7). Many investigators have reported that protein synthesis declined in specific tissues (e.g., liver or muscle) and in the whole body throughout development in mammals after weaning (8–10). We demonstrated that the rate of protein synthesis in the brain decreased with age in rats after weaning (11). In many investigations, not only age but also growth hormone (GH) deficiency has been shown to affect many functions related to the central nervous system in mammals (12). GH is well known as the anabolic hormone in protein metabolism. Several investigators have demonstrated that the protein synthesis in visceral organs, skeletal muscles and brains was increased by GH in rats (13, 14).

Ornithine is a kind of amino acid widely distributed in the liver of mammals and various foods such as Corbicula (Asian clam). Ornithine is also a urea cycle intermediate and the substrate of citrulline synthesis. Urea formation has been shown to be stimulated by adding ornithine to perfused liver (15, 16) and to isolated hepatocytes (17). Recently, ornithine has been attracting attention as a functional food for improvement of hepatic function and growth hormone release (18). In a previous study, we (19) reported that administration of ornithine to young rats increased the concentration of plasma GH and the rate of protein synthesis in the brain, and that a positive correlation existed between the rate of protein synthesis in the brain and the plasma concentration of GH. Ohsumi et al. (14) demonstrated that hypophysectomy has been shown to decrease the rate of protein synthesis in the brain regions of rats, whereas treatment with growth hormone reversed the effect of hypophysectomy. However, the role of ornithine treatment in maintaining the rate of protein synthesis...
remains unknown in hypophysectomized rats.

The purpose of our study was to determine whether the ornithine affects the rate of brain protein synthesis in hypophysectomized aged rats, and whether the regulation of brain protein synthesis was mediated through changes in the concentration of GH in rats treated with or without ornithine. In our previous report (7), a positive correlation between the rate of protein synthesis and the RNA activity was found in the brain when the quality or quantity of dietary protein was manipulated in young and aged rats. However, the reduction with age in protein synthesis in the brain was related to a fall in the RNA concentration (11). Three questions were considered in the present study: 1) whether the dietary addition of ornithine might increase the plasma concentration of GH in hypophysectomized aged rats, 2) whether the dietary addition of ornithine might affect brain protein synthesis in hypophysectomized aged rats, and 3) whether greater RNA concentration or RNA activity in hypophysectomized and sham-operated rats given ornithine resulted in a greater protein synthesis rate in the brain than those in rats fed the basal diet. Therefore, we examined the effects of ornithine treatment on the GH concentration in plasma and three indicators of protein synthesis in rat brains: its rate, RNA concentration and RNA activity in hypophysectomized and sham-operated rats. We have already reported that the plasma concentration depended on the level of dietary addition of ornithine, and the plasma concentration of GH was the highest in rats administrated 0.5% and 0.7% ornithine added to a 20% casein diet compared with control rats (19). Thus, in this study, we used a 20% casein diet and 20% casein + 0.7% ornithine diet as the experimental diet.

MATERIALS AND METHODS

Chemicals. L-Tyrosine decarboxylase, L-tycyl-l-alanine and B-phenylalanine were purchased from Sigma Chemical (St. Louis, MO, USA). L-[2,4-3H]Phenylalanine (2.2 TBq/mmol) was obtained from Moravek (Brea, CA, USA). L-Ornithine–HCl was obtained from KYOWA (2.2 TBq/mmol) was obtained from Moravek (Brea, CA, USA). L-Ornithine–HCl was obtained from KYOWA HAKKO BIO CO., LTD. (Tokyo, Japan). All other reagents were purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan).

Animals and diet. Hypophysectomized and sham-operated male 24-wk-old Wistar rats (Japan SLC, Inc., Hamamatsu, Japan) were housed at 24°C in a room with a 12-h light-dark cycle. The rats were transferred to the experimental diet after being fed the 20% casein diet for 10 d. The experimental diets contained 0% or 0.7% ornithine-HCl added to the 20% casein diet (Table 1). All animals were individually housed and given free access to food and water. The approval of Aichi University of Education Animal Care and Use Committee was given for our animal experiments.

Experimental design. Two experiments were conducted on four groups of rats. On day 1 of the experimental period, two groups were hypophysectomized and the other two groups were sham-operated controls, and fed the 20% casein diet for 10 d. In Experiment 1, the effect of dietary ornithine on the plasma concentration of GH in hypophysectomized rats was investigated in hypophysectomized rats.

Table 1. Composition (g/100 g of diet) of experimental diets.

| Ingredient               | 20% Casein | 20% Casein + 0.7% ornithine |
|--------------------------|------------|----------------------------|
| Casein                   | 20.0       | 20.0                       |
| Ornithine-HCl1           | 0          | 0.7                        |
| Cystine                  | 0.3        | 0.3                        |
| Cornstarch               | 43.3       | 42.9                       |
| Sucrose                  | 21.7       | 21.4                       |
| Corn oil                 | 5.0        | 5.0                        |
| AIN-93M mineral mix1     | 3.5        | 3.5                        |
| AIN-93JX vitamin mix1    | 1.0        | 1.0                        |
| Cellulose2               | 5.0        | 5.0                        |
| Choline chloride         | 0.2        | 0.2                        |

1 Supplied by KYOWA HAKKO BIO CO., LTD., Tokyo, Japan.
2 Supplied by Oriental Yeast Co., Ltd., Tokyo Japan.
3 Supplied by CLEA Japan, Inc., Tokyo, Japan (45).

Table 2. Effect of the addition of ornithine to a basal diet on plasma concentration of growth hormone in the hypophysectomized aged rats.1

|                  | Final body weight (g) | Plasma GH2 (μg/L) |
|------------------|-----------------------|-------------------|
| Control          | 364.4±4.5             | 10.9±1.1b         |
| Control+ornithine| 363.8±3.5             | 45.9±6.6a         |
| Hypophysectomy   | 256.8±8.3*            | 4.1±0.7*          |
| Hypophysectomy+ornithine | 257.2±3.8* | 4.0±0.4*          |

ANOVA

|                  | NS                     | p<0.05            |
|------------------|------------------------|-------------------|
| Ornithine        |                        | p<0.05            |
| Hypophysectomy   | p<0.01                |                   |
| Hypophysectomy×ornithine | NS                  | p<0.05            |

1 Values are means and SE, n=6. *Significantly different from corresponding value in rats of control group (p<0.05). The superscript letters indicate significantly differences of means (p<0.05) due to the type of ornithine treatment within the control or hypophysectomy groups.
2 Growth hormone.
and sham-operated control rats. In our previous experiment, the plasma concentration of GH rose very rapidly after ornithine treatment (19). Therefore, in the present study, the plasma concentration of GH was measured after only one 3-h feeding period of the test diet. After feeding on the 20% casein diet for 10 d (one 3-h feeding period per day; from 9:00–12:00), the rats were given the experimental diets for 1 d (only one 3 h period). After the 3 h feeding period, they were decapitated and the plasma was collected in glass tubes and stored at −80°C. The concentration of plasma GH was measured by the method of Elia (SPI bi, Massy, Cedex, France). In Experiment 2, the effect of dietary ornithine on the brain protein synthesis rates was investigated in hypophysectomized and sham-operated control rats. All rats of each group were divided into two groups and fed the experimental diets for 10 d ad libitum. The experimental diets contained 0% or 0.7% ornithine added to the 20% casein diet (Table 1). The fractional rates of protein synthesis in the brain and liver were measured by the method of Garlick et al. (20). The rats were decapitated between 1000 and 1200 h. Brain regions (21) and liver were quickly removed and frozen in liquid nitrogen. The concentrations of protein and RNA in brain and liver were measured according to the methods of Lowry et al. (22) with bovine serum albumin as a standard, and Flick and Munro (23), respectively.

**Fractional rate of protein synthesis in tissues.** Radioactive L-[2,4-3H]phenylalanine was combined with unlabeled phenylalanine to yield a dose of 1.85 MBq and a concentration of 150 mmol/L saline. Rats were injected with the radioisotope via the tail vein at a dose of 1 mL/100 g body weight. At 10 min after injection, rats were quickly decapitated. Specific radioactivities of [3H]phenylalanine in tissue samples were determined according to the method described in our previous report (24). Tissue samples were homogenized with 10 volumes of cold 0.2 mol/L perchloric acid and then centrifuged at 2,800 ×g for 15 min at 4°C. The supernatant was used for the measurements of specific radioactivity after adjusting the pH to 6.0–7.0 with saturated potassium citrate. The precipitate containing protein was washed three times with 5 mL of 0.2 mol/L perchloric acid, suspended in 10 mL of 0.3 mol/L NaOH and incubated at 37°C for 1 h. Protein-bound phenylalanine was obtained by precipitating the protein with 2 mL of 2 mol/L perchloric acid, washing the pellet with 5 mL of 0.2 mol/L perchloric acid twice and hydrolyzing the protein in 10 mL of 6 mol/L HCl for 24 h at 110°C. The HCl was evaporated to dryness, and the amino acids were dissolved in citrate buffer (pH 6.3). The determination of the specific radioactivity of [3H]phenylalanine involved its enzymatic conversion into phenethylamine, followed by a radioactivity count (Accuflex LSC 7400, Aloka Co., Tokyo, Japan) and fluorometric determination (F-3000, Hitachi Co., Tokyo, Japan). In a preliminary experiment, we determined whether the method of Garlick et al. (20) could be used to measure the rate of protein synthesis in the brain under this experimental condition. Specific radioactivities of free phenylalanine in the plasma, cere-

### Table 3. Effect of the addition of ornithine to a basal diet on body weight gain, and relative weights in liver and brain regions of hypophysectomized aged rats.1

| Group | Control | Hypophysectomy + ornithine | Hypophysectomy | p
|------|---------|---------------------------|----------------|------------------|
| Body weight gain (g/10 d) | 19.8 ± 1.2 | 19.4 ± 1.8 | 19.8 ± 0.5 | NS |
| Food intake (g/d) | 19.9 ± 0.7 | 19.4 ± 0.5 | 19.8 ± 0.5 | NS |
| Liver | 3.2 ± 0.06 | 3.2 ± 0.06 | 3.2 ± 0.06 | NS |
| Cerebral cortex | 0.093 ± 0.002 | 0.093 ± 0.002 | 0.093 ± 0.002 | NS |
| Hippocampus | 0.039 ± 0.002 | 0.040 ± 0.001 | 0.040 ± 0.001 | NS |
| Cerebellum | 0.114 ± 0.003 | 0.115 ± 0.002 | 0.115 ± 0.002 | NS |
| Hippocampus | 0.122 ± 0.003 | 0.123 ± 0.004 | 0.123 ± 0.004 | NS |
| Tissue protein (mg/g tissue) | 198 ± 0.0 | 199 ± 0.0 | 199 ± 0.0 | NS |
| Brain regions | 200 ± 0.0 | 200 ± 0.0 | 200 ± 0.0 | NS |

1Values are means and SE, n = 6. *Significantly different from corresponding value in rats of control group (p < 0.05). The superscript letters indicate significantly differences of means.
Table 4. Effect of the addition of ornithine to a basal diet on protein synthesis in liver and brain regions of hypophysectomized aged rats.1

|                      | Control | Control+ornithine | Hypophysectomy | Hypophysectomy+ornithine | ANOVA          |
|----------------------|---------|-------------------|----------------|--------------------------|----------------|
|                      |         |                   |                |                          | Ornithine | Hypophysectomy | Hypophysectomy ×ornithine |
| **Protein synthesis, Ks (%/d)** |         |                   |                |                          | p<0.05    | p<0.01        | p<0.05                     |
| Liver                | 83.1±0.7b | 98.7±0.8a         | 61.2±1.5*      | 62.1±1.6*                | p<0.05    | p<0.01        | p<0.05                     |
| Cerebral cortex      | 19.0±0.4b | 22.8±0.7*         | 14.7±0.3*      | 15.0±0.2*                | p<0.05    | p<0.01        | p<0.05                     |
| Cerebellum           | 20.8±0.4b | 25.1±0.3*         | 16.8±0.3*      | 17.1±0.5*                | p<0.05    | p<0.01        | p<0.05                     |
| **Absolute protein synthesis (mg protein synthesized/(tissue·d))** |         |                   |                |                          | p<0.05    | p<0.01        | p<0.05                     |
| Liver                | 1,974±60b | 2,345±69a         | 947±75*        | 962±60*                  | p<0.05    | p<0.01        | p<0.05                     |
| Cerebral cortex      | 11.2±0.3b | 13.5±0.3*         | 7.1±0.2*       | 7.4±0.2*                 | p<0.05    | p<0.01        | p<0.05                     |
| Cerebellum           | 10.4±0.3b | 12.4±0.2*         | 6.6±0.2*       | 6.7±0.2*                 | p<0.05    | p<0.01        | p<0.05                     |
| Hippocampus2         | 20.6     | 24.3              | 17.5           | 17.9                     | p<0.05    | p<0.01        | p<0.05                     |
| **RNA/protein (mg RNA/g protein)** |         |                   |                |                          | NS        | p<0.01        | NS                         |
| Liver                | 36.1±0.3 | 36.2±0.3          | 32.5±0.2*      | 32.6±0.1*                | NS        | p<0.01        | NS                         |
| Cerebral cortex      | 15.6±0.2 | 15.6±0.2          | 13.2±0.3*      | 13.3±0.1*                | NS        | p<0.01        | NS                         |
| Cerebellum           | 15.3±0.2 | 15.3±0.2          | 13.2±0.2*      | 13.4±0.1*                | NS        | p<0.01        | NS                         |
| Hippocampus2         | 15.8     | 15.9              | 15.7           | 15.7                     | NS        | p<0.01        | NS                         |
| **RNA activity (g protein synthesized/(g RNA·d))** |         |                   |                |                          | p<0.05    | p<0.01        | p<0.05                     |
| Liver                | 23.1±0.4b | 27.3±0.2a         | 18.8±0.4*      | 19.0±0.5*                | p<0.05    | p<0.01        | p<0.05                     |
| Cerebral cortex      | 12.2±0.2b | 14.7±0.4*         | 11.2±0.1*      | 11.3±0.2*                | p<0.05    | p<0.01        | p<0.05                     |
| Cerebellum           | 13.7±0.4b | 16.4±0.3*         | 12.7±0.2*      | 12.8±0.4*                | p<0.05    | p<0.05        | p<0.05                     |
| Hippocampus2         | 13.3     | 15.9              | 11.1           | 11.2                     | p<0.05    | p<0.05        | p<0.05                     |

1Values are means and SE, n=6. *Significantly different from corresponding value in rats of control group (p<0.05). The superscript letters indicate significantly differences of means (p<0.05) due to the type of ornithine treatment within the control or hypophysectomy groups.
2Data were obtained by a single analysis of pooled samples from six rats.
Plasma concentration of growth hormone (Experiment 1)

In the sham-operated control groups, the plasma concentration of GH increased significantly with the 20% casein + 0.7% ornithine diet compared with the 20% casein diet alone (Table 4). However, when rats were hypophysectomized, the dietary ornithine did not affect the fractional or absolute rates of protein synthesis, or RNA activity in the liver or brain regions (Table 4). Correlations between the fractional rate of protein synthesis and RNA activity were significant in the liver (r = 0.971, p < 0.001), cerebral cortex (r = 0.951, p < 0.001) and cerebellum (r = 0.930, p < 0.001). Compared with control groups, lower RNA concentrations (mg RNA/g protein) of liver and brain regions were observed in each group of hypophysectomized rats treated with or without ornithine, which did not differ (Table 4). The fractional rate of protein synthesis was correlated to the RNA concentration in the liver (r = 0.797, p < 0.01), cerebral cortex (r = 0.776, p < 0.01) and cerebellum (r = 0.725, p < 0.01).

DISCUSSION

In older people, the deficiency of GH affects body composition and function. Treatment of adult GH-deficient patients with human GH is reported to improve the psychological well being and memory function (12, 26). In a previous study, we demonstrated that the protein synthesis in the brain regions of hypophysectomized aged rats was increased by GH treatment (14), and that the concentration of plasma GH and protein synthesis in the brains of young rats were also increased by ornithine treatment (19). However, little information is available on the effects of ornithine treatment on the rate of brain protein synthesis during growth hormone deficiency. We hypothesized that the rate of brain protein synthesis would not increase in hypophysectomized aged rats fed ornithine. Therefore, we determined whether the dietary addition of ornithine also increased the GH concentration in plasma of hypophysectomized and sham-operated control rats. The plasma concentration of GH was significantly higher in rats given ornithine (only one 3 h period) than that in control rats alone (Table 2). The treatment of ornithine may have regulated plasma concentration of GH in the present investigation.

In the brain regions, ornithine supplementation to the basal diet elevated the fractional and absolute rates of protein synthesis in the control rats. Hypophysectomized rats had reduced the rates of protein synthesis in the brain regions and the plasma concentration of GH, but the dietary addition of ornithine did not reverse the effect of hypophysectomy (Table 4). The regulation in brain protein synthesis is mediated through changes in the body GH concentration when the dietary ornithine is manipulated. Recently, the possibility that ornithine itself may pass the blood-brain barrier through the cationic amino acid transporter is supported by several studies (27). In the future studies, the detailed mechanism by which the dietary ornithine induces the elevation of plasma GH concentration will be investigated.

In weaned rats, a reduction with age in protein synthesis in the brain and skeletal muscle was related to a fall in RNA concentration (10, 11). However, a positive

RESULTS

Plasma concentration of growth hormone (Experiment 1)

In the sham-operated control groups, the plasma concentration of GH increased significantly with the 20% casein + 0.7% ornithine compared with the 20% casein diet alone. The hypophysectomy caused a decrease in the plasma concentration of GH in each group treated with or without ornithine, which did not differ (Table 2). The fractional and absolute rates of protein synthesis in tissues (Experiment 2)

The hypophysectomized rats with or without ornithine treatment gained less body weight than the control or control plus ornithine groups, which did not differ (Table 3). The two control groups consumed more food than did either group of hypophysectomized rats treated with or without ornithine, which did not differ. The relative weights of the various brain regions and liver did not differ among the experimental groups. The fractional (Ks) and absolute rates of protein synthesis in the liver and some brain regions, such as cerebral cortex and cerebellum, increased significantly with the 20% casein + 0.7% ornithine diet compared with the 20% casein diet in the control groups (Table 4). In pooled samples of hippocampus, this rate tended to be higher in the ornithine-treated rats. In the control groups, the RNA activity [g protein synthesized/(g of RNA·d)] in the liver and brain regions increased significantly with the 20% casein + 0.7% ornithine diet compared with the 20% casein diet alone (Table 4). However, when rats were hypophysectomized, the dietary ornithine did not affect the fractional or absolute rates of protein synthesis, or RNA activity in the liver or brain regions (Table 4). Correlations between the fractional rate of protein synthesis and RNA activity were significant in the liver (r = 0.971, p < 0.001), cerebral cortex (r = 0.951, p < 0.001) and cerebellum (r = 0.930, p < 0.001). Compared with control groups, lower RNA concentrations (mg RNA/g protein) of liver and brain regions were observed in each group of hypophysectomized rats treated with or without ornithine, which did not differ (Table 4). The fractional rate of protein synthesis was correlated to the RNA concentration in the liver (r = 0.797, p < 0.01), cerebral cortex (r = 0.776, p < 0.01) and cerebellum (r = 0.725, p < 0.01).
correlation between the rate of protein synthesis and RNA activity was found in the brain of aged rats when the quantity and quality of dietary protein were manipulated (24, 28). Hormonal treatment such as GH also appeared to elevate the rate of protein synthesis and RNA activity in the brain (14). In the brain regions of rats of the present study, RNA activity, rather than RNA concentration, in the group fed the 20% casein + ornithine diet group was higher than in the control group fed the 20% casein diet alone (Table 4). The higher RNA activity in control rats fed the 20% casein + ornithine diet may have increased the rate of brain protein synthesis in this group. The dietary addition of ornithine failed to affect not only the rates of protein synthesis but also the RNA activity in the brain regions of the hypophysectomized groups.

The RNA activity is calculated by dividing the fractional rate of protein synthesis by the RNA/protein ratio, and reflects the protein contents synthesized per unit RNA in each tissue. Many studies suggested that the RNA activity represents the changes in the translational phase of protein synthesis (29). Little information on the mechanism by which the dietary ornithine affects RNA activity in the brain of aged rats is available. In previous studies, we reported that the aggregation of polyribosomes in the brain of aged rats decreased with a decrease in dietary protein, and that there was a correlation between the polysome profile and RNA activity (7, 30). In liver, muscle and brain the stimulation of protein synthesis caused by amino acids and hormonal factors are reported to be mediated by the increase in the initiation of mRNA translation (31–33). We reported that the ingestion of a higher quality and quantity of dietary protein enhanced brain protein synthesis through the activation of the binding of mRNA to the 40S ribosomal subunit (34). Of the many steps in the initiation process, eukaryotic initiation factor (eIF) 4E and phosphorylation of ribosomal protein S6 appear to be particularly important in the physiological regulation (35, 36). Anthony et al. (32, 36) and Yoshizawa et al. (35) demonstrated that the oral administration of leucine stimulated the rates of protein synthesis in liver and skeletal muscle concomitant with increased phosphorylation of 4E-BP1 and S6K1. Kato (13) suggested that GH might stimulate the translational phase of tissue protein synthesis. Measurement of the initiation factors of mRNA translation in the brain should be included in further studies for the effect of the addition of ornithine to the basal diet on protein synthesis in hypophysectomized and control aged rats.

Recently, ornithine has been attracting attention as a functional food for the improvement of hepatic function and growth hormone release (18). The ingestion of ornithine resulted in higher rates of brain protein synthesis in sham-operated control rats, suggesting that brain function is affected. Recently several studies have shown that GH may affect many functions related to the central nervous system. Le Greves et al. (37) suggested that GH induced the gene expression of hippocampal N-methyl-D-aspartate receptor in rats, coinciding with improved learning and memory capabilities. As mentioned above, we demonstrated that hypophysectomy has reduced the rate of protein synthesis in the brain regions of rats, whereas treatment with GH reversed the effect of hypophysectomy, and that the changes in the brain protein synthesis likely depended on the body GH concentration (14). The GH-binding receptor has been identified in the brains of humans and rats (38). The possibility that GH itself may pass the blood-brain barrier is supported by several studies (39). Several investigators have reported that the protein synthesis in visceral organs and skeletal muscle was increased by GH in rats (13). On the other hand, circulating insulin-like growth factor-1 (IGF-1), an anabolic mediator of GH, has been also known to be transported across the blood brain-barrier and to be important in somatic growth but also in the regulation of brain function (40).

However, in the present study, we did not determine the effects of ornithine treatment on the gene expression of brain protein or the plasma concentration of IGF-1. In order to determine whether the regulation of brain protein synthesis was mediated through changes in the plasma GH when ornithine was added to the diet, it is also important to investigate the role of ornithine treatment on the transcriptional phase of brain protein synthesis in control or hypophysectomized rats. The effect of ornithine treatment on the mRNA concentrations in the brain and the plasma concentration of IGF-1 of aged rats is another question to consider in a further study.

The thyroid hormone is essential for normal growth in the brain (41). We (42) demonstrated that thyroid hormone treatment increased the rate of protein synthesis in the brain of young rats. As the thyroid stimulating hormone is secreted from the pituitary gland, the body concentration of thyroid hormone may be affected in the hypophysectomized rats. However, little documentation for the role of the thyroid hormone in maintaining brain protein synthesis is available in aged rats given dietary ornithine. Therefore, plasma concentration of thyroid hormone should be measured in a further examination of the mechanism by which the dietary addition of ornithine alters brain protein synthesis.

Ornithine is a urea cycle intermediate and is metabolized to citrulline or arginine by the urea cycle enzymes. Of note, several investigators reported that arginine treatment stimulated GH secretion in man (43). Citrul- line has been known to increase the muscle protein synthesis in aged rats (44). However, now the role of citrulline or arginine on the brain protein synthesis remains unknown. Therefore, unanswered questions include whether ornithine itself or a metabolite of ornithine, citrulline or arginine, mediates the effects of ornithine. The effects of dietary citrulline or arginine on brain protein synthesis should be determined in a future study.

In the present study, ornithine treatment also stimulated the fractional rates of protein synthesis and RNA activity in the liver of sham-operated control groups alone, and did not affect the indicators of protein synthesis in the liver of the hypophysectomized groups. The rates of protein synthesis of liver and skeletal mus-
ornithine ingestion also controls the body concentration of GH and the rate of brain protein synthesis in the sham-operated rats only, not in the hypophysectomized rats, and that the ornithine-induced increase in the concentration of GH is primarily responsible for changes in the brain protein synthesis. The RNA activity is at least partly related to the fractional rate of brain protein synthesis.

Acknowledgments
The authors are grateful to H. Kamiya, M. Toki and M. Nabeto for their valuable technical assistance. This study is supported in part by a grant from KYOWA HAKKO BIO CO., LTD.

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