Supplementary Material

Amino acid measurements

Plasma (20 μL) was homogenized in 180-μL HPLC-grade methanol on ice. The homogenates were centrifuged at 3,000 × *g* for 6 min at 4°C, and 20-μL supernatant was evaporated to dryness at 40°C. Next, 20-μL HPLC-grade H_2O, 20-μL 0.1 M borate buffer (pH 8.0), and 60-μL 50 mM 4-fluoro-7-nitro-2,1,3-benzoxadiazole (NBD-F; Tokyo Kasei Kogyo Co., Ltd., Tokyo, Japan) in HPLC-grade CH_3CN were added to the residue. The reaction mixture was then heated at 60°C for 2 min and immediately supplemented with 100-μL H_2O/CH_3CN (90/10) containing 0.1% trifluoroacetic acid to stop the reaction.

A 20-μL aliquot of the resultant solution was injected into the HPLC system. A reversed-phase octadecylsilane (ODS) column (TSKgel ODS-80Ts; Tosoh Corporation, Tokyo, Japan) was used to separate and quantify total (D- and L-) serine, and the gradient elution of the mobile phase was maintained at a constant flow rate of 0.8 mL/min. Mobile phase 1a consisted of H_2O/CH_3CN (90/10) containing 0.1% TFA; and phases 1b and 1c, of H_2O/CH_3CN (10/90) containing 0.1% TFA and CH_3CN, respectively. The time program for gradient elution was as follows: 0–25 min 1a:1b:1c = 92:8:0, 25–25.1 min linear gradient from 8% 1b to 100% 1b, 25.1–35 min 1a:1b:1c =

0:100:0, 35–35.1 min linear gradient from 8% 1b to 100% 1c, 35.1–40 min 1a:1b:1c = 0:0:100, and 40.1–60 min 1a:1b:1c = 92:8:0. The chiral column used for the separation and quantification of D- and L-serine with NBD-F comprised two Sumichiral OA-2500 columns (Sumika Chemical Analysis Service Ltd., Osaka, Japan) that were connected in tandem. The mobile phase was 15 mM citric acid in MeOH. The flow rate was isocratically pumped at 1.0 mL/min. The column temperature of all columns was maintained at 35°C. Fluorescence detection was performed at 530 nm with an excitation wavelength at 470 nm.

For determination of glutamate, glutamine, and glycine, a reversed-phase ODS column (TSKgel ODS-80Ts, Tosoh Corporation, Tokyo, Japan) was used. The gradient elution of the mobile phase was kept at a constant flow rate of 0.8 mL/min. The time program for gradient elution was as follows: 0–50.5 min, 1a:1b:1c = 95:5:0; 50.5–55.5 min, 1a:1b:1c = 0:100:0; and 55.5–57 min, 1a:1b:1c = 0:0:100. The temperature of all columns was maintained at 35°C. Fluorescence detection was performed at 530 nm with an excitation wavelength of 470 nm.