**Supplementary materials and methods**

*Phospholipids*

Phospholipid kit (Olbracht Serdary Research Laboratories) contains bovine liver lysophosphatidylcholine (LPC) containing primary C18:0, egg yolk LPE containing primary C16:0 and C18:0, soybean phosphatidylinositol (PI) containing primary C16:0 and C18:2, bovine heart sphingomyelin (SM) containing primary C16:0, C18:0, and C18:1, porcine brain phosphatidylserine (PS) containing primary C18:0 and C18:1, bovine liver phosphatidylcholine (PC) containing primary C18:0 and C18:1, egg yolk phosphatidylethanolamine (PE) containing primary C16:0, C18:0, C18:1, and C18:2, bovine heart cardiolipin (CL) containing primary C18:2, phosphatidic acid (PA) from egg yolk PC containing primary C16:0 and C18:1 , and porcine brain cerebrosides (CB) containing primary C22:0 and C24:0.

*Antibodies*

The following commercially available antibodies were used: rabbit anti-MAP2 (1:1000; Sigma-Aldrich), goat anti-tau (1:1000; Santa Cruz Biotechnology), mouse anti-NeuN (1:500; Merk Millipore) antibodies, donkey Alexa Fluor 488-conjugated anti-goat IgG (1:500; Thermo Fisher Scientific), donkey Alexa Fluor 555-conjugated anti-rabbit IgG (1:500; Thermo Fisher Scientific), mouse anti-Tuj1 (neuron-specific class III β-tubulin, 1:5000; BioLegend), donkey Alexa Fluor 488-conjugated anti-mouse IgG (1:500; Thermo Fisher Scientific), mouse anti-phospho-p44/42 MAPK/ERK1/2 (Thr202/Tyr204) (E10, 1:2000; Cell Signaling Technology), and rabbit anti-p44/42 MAPK (ERK 1/2) antibodies (1:1000; Cell Signaling Technology).

*Immunocytochemical analysis*

At DIV3, phospholipid was applied to the medium at concentration of 0.1, 1, or 10 μM. Phospholipids were applied to the medium at DIV3. The cultures were fixed with 4% paraformaldehyde/4% sucrose at DIV14. The fixed cells were incubated with PBS buffer containing 0.25% Triton X-100 for 5 min and immunostained with rabbit anti-MAP2, goat anti-tau, and mouse anti-NeuN antibodies, followed by incubation with species specific Alexa Fluor 488-, 555-, and 647-conjigated antibodies. For analysis of the time course of neurite outgrowth, 1 μM 16:0 LPE (Avanti) or 18:0 LPE (Avanti) was applied to the culture medium at DIV0. The cultures were fixed at DIV0, 1, or 3. The fixed cells were immunostained with mouse anti-Tuj1 antibody, followed by incubation with donkey Alexa Fluor 488-conjugated anti-mouse IgG antibody. For inhibitor experiments, the cultures were treated with inhibitors in the presence or absence of 1 μM 16:0 LPE or 18:0 LPE at DIV0 and fixed at DIV3. The fixed cells were immnostained with anti-Tuj1 antibody as described above. The inhibitors used were as followed: Gi/Go inhibitor PTX (10 ng/ml; Wako Pure Chemical Industries), Gq/11 inhibitor YM-254890 (0.5 μM; Wako Pure Chemical Industrie), PLC inhibitor U73122 (0.5 μM; CAYMAN CHEMICAL), MEK/ERK inhibitor U0126 (5 μM; CAYMAN CHEMICAL), PKC inhibitor Sotrastaurin (10 μM; CAYMAN CHEMICAL), and PKC inhibitor Go6983 (1 μM; CAYMAN CHEMICAL).

*Image acquisition and quantification*

Images of culture experiments were taken with a confocal laser-scanning microscope (TCS SP8; Leica Microsystems) using HC PL APO CS2 20×/0.75 NA multiple immersion lens (Leica Microsystems) or HC PL APO CS 10×/0.40 NA multiple immersion lens (Leica Microsystems) under constant conditions in terms of laser power, pinhole size, gain, z-steps, and zoom setting throughout the experiments. All quantitative measurements were performed with ImageJ 1.52a software. For the quantification of MAP2 and tau staining areas, z-series of optical sections were projected by the brightest point method. MAP2 and tau staining areas were defined as area in which staining signal intensites were 2 and 3 times stronger than those of background signals on the same field, respectively. For analysis of the time course of neurite outgrowth, z-series of optical sections were projected by the brightest point method. Neurite of cortical neurons was identifed by Tuj1 signals, and the length of the longest neurite, the number of neurites emerging from the soma, and the numbers of branches per longest neurite were measured.

*Western blot analysis*

Primary cortical neuron cultures were prepared as described above and plated on the 24-well dish at a density of 5.0 × 105 cells /well. One to 100 μM 16:0 LPE or 18:0 LPE was applied to the culture medium at DIV7. For inhibitor experiment, the cultures were incubated with 100 μM 16:0 LPE or 18:0 LPE, with or without 5 μM U0126. After 10 min incubation, the cultures were solubilized with SDS sample buffer containing 2% SDS, 50 mM-Tris-HCI, pH6.8, 10% glycerol, 100 mM dithiothreitol, phosphatase inhibitor cocktail (Nakarai Tesque), and 0.025% Bromophenol Blue, followed by boiling at 95℃ for 10 min. For inhibition of MAPK, 5 μM MEK/ERK inhibitor U0126 was applied to the cell culture medium 30 min before treatment with LPEs. The cell lysates were separated by SDS-polyacrylamide gel electrophoresis and transferred to PVDF membrane. After blocking with PVDF Blocking Reagent for Can Get Signal (TOYOBO), the membranes were incubated with mouse anti-phospho-MAPK/ERK1/2 (Thr202/Tyr204) antibody, followed by incubation with horseradish-peroxidase-conjugated secondary antibody. After stripping, the membranes were probed with rabbit anti p44/42 MAPK antibody, followed by incubation with horseradish-peroxidase-conjugated secondary antibody. Can Get Signal Immunoreaction Enhancer Solution (TOYOBO) was used for dilution of antibodies. The proteins were visualized by ECL Select Western Blotting Detection System (GE Healthcare) and detected by Las-4000 mini luminescent imaging analyzer (GE Healthcare). The quantification analysis was performed using ImageQuant TL image analysis software (GE Healthcare). Intensities of phosphorylated ERK1/2 signals were normalized with those of ERK1/2 signals.