Figure S1. Levels of phospho-active forms of ERK1/2 and Akt in rat brain (cortex) tissues at different time intervals (0 – 240 min) after administration of either (R,S)-ketamine, (R,S)-norketamine or (2S,6S)-hydroxynorketamine. Representative immunoblots are found in Figure 3. Scatter plots illustrating the relative levels of phosphorylated and total forms of ERK1/2 and Akt in response to (R,S)-ketamine, (R,S)-norketamine and (2S,6S)-hydroxynorketamine are shown (n= 3 independent experiments). **, P< 0.01 (ANOVA) compared with controls.
Figure S2. Expression of monomeric serine racemase (m-SR) protein in PC-12 cells after 36 h incubation with different concentrations of (R,S)-ketamine (0 – 10 µM) (A), (R,S)-norketamine (0 – 1 µM) (B), and (2S,6S)-hydroxynorketamine (0 – 0.1 µM) (C); where figure A(a), B(a), C(a) present Western blot analysis with anti-serine racemase antibody, and A(b), B(b), C(b) represent relative levels of m-SR after quantification and normalization with β-actin. Scatter plots illustrating the relative levels of m-SR in response to (R,S)-ketamine (Ket), (R,S)-norketamine (NK) and (2S,6S)-hydroxynorketamine (HNK) after quantification and normalization with β-actin are shown (n= 3 independent experiments). * indicates p<0.05 and ** indicates p<0.01 (ANOVA) compared with the control.
Figure S3. Effect of (R,S)-ketamine on the levels of phospho-active forms of mTOR, Akt, ERK1/2, p70S6K and 4E-BP1 in PC-12 cells. A, Cells were treated with different concentrations of (R,S)-ketamine (0 – 10 µM) for 1 h and processed for Western blot analysis. Representative immunoblots are presented. Scatter plots illustrating the relative ratio of phosphorylated versus total forms of mTOR (B), Akt (C), ERK1/2 (D), p70S6K (E), and 4E-BP1 (F) in response to (R,S)-ketamine are shown (n = 3 independent experiments). * indicates p<0.05 and ** indicates p<0.01 (ANOVA) compared with the control.
Figure S4. Effect of (R,S)-norketamine on the levels of phospho-active forms of mTOR, Akt, ERK1/2, p70S6K and 4E-BP1 in PC-12 cells. A, Cells were treated with different concentrations of (R,S)-norketamine (0 – 1 µM) for 1 h and processed for Western blot analysis. Representative immunoblots are presented. Scatter plots illustrating the relative ratio of phosphorylated versus total forms of mTOR (B), Akt (C), ERK1/2 (D), p70S6K (E), and 4E-BP1 (F) in response to (R,S)-norketamine are shown (n = 3 independent experiments). * indicates p<0.05 and ** indicates p<0.01 (ANOVA) compared with the control.
Figure S5. Effect of (2S,6S)-hydroxynorketamine on the levels of phospho-active forms of mTOR, Akt, ERK1/2, p70S6K and 4E-BP1 in PC-12 cells. A, Cells were treated with different concentrations of (2S,6S)-hydroxynorketamine (0 – 0.1 µM) for 1 h and processed for Western blot analysis. Representative immunoblots are presented. Scatter plots illustrating the relative ratio of phosphorylated versus total forms of mTOR (B), Akt (C), ERK1/2 (D), p70S6K (E), and 4E-BP1 (F) in response to (2S,6S)-hydroxynorketamine are shown (n = 3 independent experiments). * indicates p<0.05 and ** indicates p<0.01 (ANOVA) compared with the control.