Supporting Information

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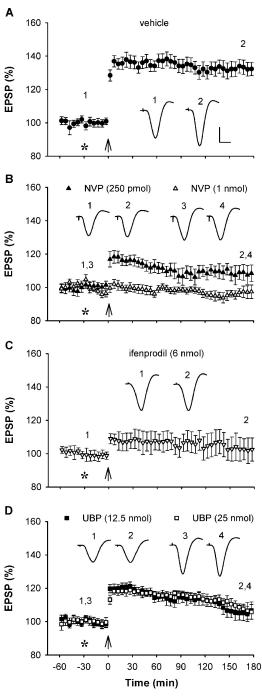


Fig. S1. Dose-dependence of the inhibition of LTP by NMDAR antagonists. (*A*) Application of conditioning high frequency stimulation (HFS, arrow) triggered robust LTP (132.2 \pm 3.4%, n=10, P<0.05 compared to pre-HFS baseline, paired t test) in animals that received an intracerebroventricular injection of vehicle (asterisk, 5 μ L). NVP-AAM077 (250 pmol or 1 nmol) (*B*), ifenprodil (6 nmol) (*C*), or UBP141 (12.5 nmol or 25 nmol) (*D*) inhibited LTP induction (108.0 \pm 4.6%, 97.3 \pm 3.3%, 102.1 \pm 7.1%, 105.6 \pm 3.9% and 106.1 \pm 3.9% pre-HFS mean baseline EPSP amplitude \pm SEM, respectively at 3 h post-HFS, n=4–5 per group; P<0.05 compared with vehicle-injected controls; one-way ANOVA followed by post hoc Tukey's test). Values are the mean percentage of pre-HFS baseline EPSP amplitude (\pm SEM). Insets show representative EPSP traces at the times indicated. Calibration bars: vertical, 2 mV; horizontal, 10 ms.

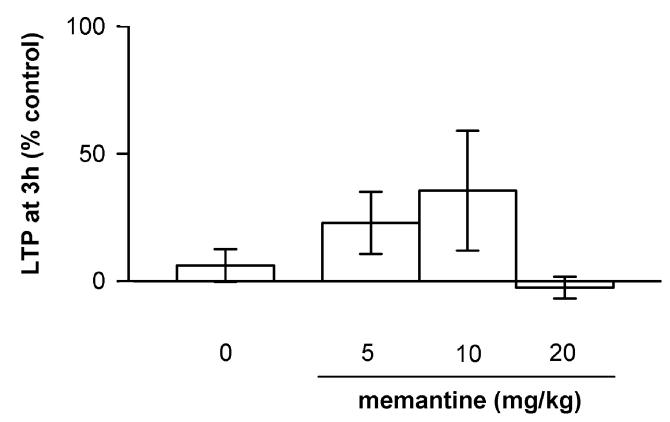


Fig. 52. Dose-dependence of the effects of memantine on the inhibition of LTP by $A\beta_{1-42}$. Systemic (i.p.) injection of memantine (5 mg/kg, n=3; 10 mg/kg, n=5, and 20 mg/kg, n=3) only partly prevented the $A\beta_{1-42}$ -mediated inhibition of LTP ($A\beta_{1-42}$ alone, n=5). LTP values are expressed as the mean % control magnitude of LTP ($A\beta_{1-42}$) the second control magnitude of LTP ($A\beta_{1-42}$).

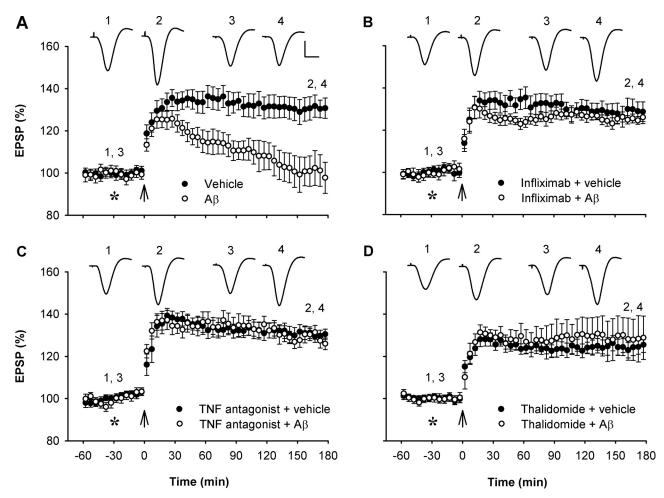


Fig. S3. TNFα-dependence of A $β_{1-42}$ -mediated inhibition of LTP (A) l.c.v. injection of soluble A $β_{1-42}$ (250 pmol, asterisk) inhibited LTP induced by high frequency stimulation (HFS, arrow) (n=5; P<0.05 compared with vehicle, n=8). (B) Coinjection of the TNFα antibody infliximab, at a dose (25 µg, i.c.v., asterisk) that did not affect LTP on its own (n=4), prevented the inhibition of LTP by A $β_{1-42}$ (n=5; P<0.05). (C) Similarly coinjection of a TNFα binding peptide antagonist, at a dose (2 nmol, i.c.v., asterisk) that did not affect LTP on its own (n=5), prevented the inhibition of LTP by A $β_{1-42}$ (n=5; P<0.05). (D) Moreover systemic pretreatment (R=0) with the TNFα production inhibitor thalidomide, using a dose (45 mg/kg i.p.) that did not affect LTP on its own (n=6), also prevented the inhibition of LTP by A $β_{1-42}$ (n=4; P<0.05). Values are the mean percentage of pre-HFS baseline EPSP amplitude (\pm SEM). Calibration bars for EPSP traces: vertical, 2 mV; horizontal, 10 ms.

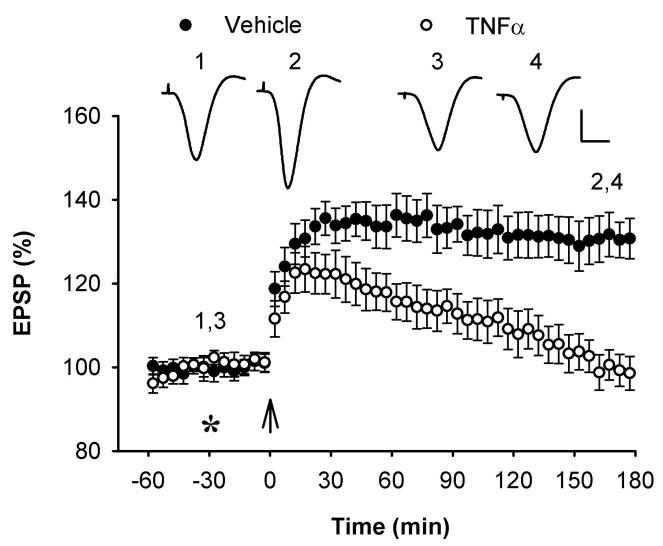


Fig. S4. TNF α -mediated inhibition of LTP. Intracerebroventricular injection of TNF α (asterisk, 1.5 pmol) inhibited high frequency stimulation (arrow) -induced LTP (n=5; P<0.05 compared with vehicle, n=8; P>0.05 compared with baseline. Values are the mean percentage of pre-HFS baseline EPSP amplitude (\pm SEM). Calibration bars for EPSP traces: vertical, 2 mV; horizontal, 10 ms.