Supplementary table 1. Specificity of NMDAR antagonists

Drug	Target, IC_{50}
Ketamine $C_{13}H_{16}ClNO$, M_r = 237.7 g/M Plasma concentration: ~1μM (274 ng/ml) Ki (vs [^{3}H]MK-801) 1-2.5 μM (1)	***ACh receptors*** nicotinic acetylcholine receptor 15 μM m1 muscarininc acetylcholine receptor 6.5 μM (2) ***NMDA receptors*** neuronal NMDA receptors, phencyclidine binding site 10-15 μM classical 40 μM (3) NR1-NR3: 100 μM - 7-9% of current blocked (4) GABA receptor - stimulation ***Opioid receptors*** μ-opioid receptor (5) IC_{50} 27 μM(5) ***Serotonin receptors*** 5-HT_3 receptor 3-30 μM (6) ***Ion channels*** Ca^{2+}-sensitive (BK) K^+ channels: 0.77 -1.66 μM(7) 20±5 μM (cell line) (8) voltage-activated K^+ channels (6) hyperpolarization-activated cyclic nucleotide-gated cation channel HCN1 channels, 4-8 μM (9) L-type Ca^{2+} channels 33 μM (6) Pentameric ligand-gated ion channels (pLGICs) in bacteria, 58 μM (10)
Memantine $C_{12}H_{21}N \cdot HCl$ M_r= 215.76	***ACh receptors*** α4β2 neuronal nicotinic receptors IC_{50} 6.6-11.3 μM

g/M Daily dose: 10-20 mg, Plasma concentrations in rat 1 µM (11) and in humans 1 µM (12). Ki (vs ^{3}H-MK-801) 0.4-0.7 µM (1)	(12, 13) α7 nicotinic receptors 0.33-1.68 µM (12, 14) ***Dopamine D2 receptor*** Kd (vs ^{3}H-domperidone) ~ 1 µM (15) ***NMDA receptors*** Currents: 11.6±0.53µM (16); Memantine in NMDARs expressed in oocytes: NR1/NR2A: 0.9 µM, NR1/NR2B 0.4µM; NR1/NR2C: 0.3 µM, NR1/NR2D: 0.3 µM (-70 mV, Mg-free) ; and 10.3, 10.9, 2.0, 1.9 µM (at -30 mV in the presence of 1 mM Mg^{2+}) (17) Average IC_{50} ~ 1 µM at -60 mV (18) <u>Does not inhibit NR1/NR3 receptors! (19)</u> IC_{50} in striatum and hippocampus 1-3 µM ***Serotonin receptors*** 5-HT3 receptors IC_{50} similar to those for NMDARs (around 1 µM) (20) ***GABA receptors*** **<u>No effects</u>** (17)
Eliprodil (SL-82.0715) $C_{20}H_{23}ClFNO$, Mr= 347.85 g/M Daily dose 2.5-10-20 mg (21)	***Opiate Sigma-Receptor*** IC_{50} 29 nM (21, 24) ***NMDA receptors*** IC_{50} for Ca^{2+} uptake by rat cerebellar granule 2 µM (25) Two binding sites in spinal cord:

Plasma concentration in humans 2.9 µM (22) Ki (vs ^{3}H-MK-801) high and low affinity sites ~7 and 100 µM (23)	IC_{50}(high) 3.6 µM and IC_{50}(low) 102 µM single type in cortex and mid-brain 7-12 µM (23). Eliprodil/^{3}H-ifenprodil replacement studies: IC_{50} 0.13 µM (26) ***Ion channels*** R- and L-type Ca^{2+} channels are **<u>insensitive</u>** to eliprodil (27)
MK-801 (dizocilpine) $C_{16}H_{15}N$, Mr=221.297 g/M Daily dose - 47 nM - protective concentration in rat plasma (28) Ki (vs ^{3}H-MK-801) 2-14 nM Kd 5-26 nM (1)	***ACh receptors*** IC_{50} for Ca^{2+} fluxes in neurons 21 ± 2 µM IC_{50} for binding of radiolabeled antagonist 1.9 µM (29) ***Serotonin receptors*** **<u>No information</u>** available ***GABA receptors*** **<u>No effect</u>** on the GABA-R mediated currents(30) ***NMDA receptors*** IC_{50} 13-38 nM NR1/NR3 heterotetramer : 10 µM - no effect Currents: 0.13 + 0.02 µM. (16) Bi-phasic inhibition of Ca^{2+} uptake into cerebellar granule cells: IC_{50}(1) 5 nM and IC_{50}(2) 3 µM (25). ***Ion channels*** (+)-MK801 may be a strong I(Na) and I(to) blocker with some I(Ca) blocking activity , but the outward current through K(1) channels was unaffected and

	only slightly reduced the amplitude of L-type calcium channels (31)

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