Supplemental Material

Double exponential fits were made to the NMDA receptor current decay following application of 1, 10, and 50 μM memantine in the continuous presence of 10 μM NMDA + 10 μM glycine at -66 mV. For 1 and 10 μM memantine, the data used for Fig. 2 were fit; for 50 μM memantine, the data used for Fig. 4D (Trapping Protocol) were fit. For each current decay, 13 s of data were fit, starting at a time t_p (see Methods) after barrel movement. The results are shown in Supplemental Table 1. Interpretation of the fast component of block and its amplitude is difficult because: (1) The binding kinetics of channel blockers is complex, and in general more than 2 exponentials are expected even when there is only one blocker binding site; (2) Especially at higher memantine concentrations, a very fast component of block was largely complete before fitting was begun, and so neither the amplitude nor the time constant of the fastest component is reflected by the fitting results. Thus, only τ_s in Supplemental Table 1 is likely to be a reliable reflection of the time course of block onset.

Table S1. Time constants of current relaxations during onset of inhibition by memantine

[Mem] (μM)	τ_f (s)	A_f	τ_s (s)
1	0.25 ± 0.11	0.31	6.06 ± 1.11
10	0.25 ± 0.10	0.41	2.66 ± 0.37
50	0.27 ± 0.08	0.48	1.41 ± 0.08

τ_f is the faster and τ_s the slower time constant determined from double exponential fits to current relaxations. A_f is the fractional amplitude of the faster component. Number of cells for each measurement is 4.