Requirement of dendritic calcium spikes for induction of spike-timing dependent synaptic plasticity

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Supplementary Material

Quantification of MK801 block

Repetitive stimulation of pharmacologically isolated NMDA EPSPs in the presence of low concentrations of MK801 (5 μM) caused a reduction in NMDA EPSP amplitude that could be fit with a single exponential function (Supplementary Fig. 1A). These data suggest that under our recordings conditions we are sampling synapses with a similar average release probability. Under these conditions, the fraction of NMDAR channels blocked by MK801 on any trial will be in proportion to the number of NMDAR channels open during an EPSP. As MK801 block is irreversible, with every trial the number of available NMDAR channels will be reduced by a constant fraction depending on the rate of MK801 block, β. Assuming an initial EPSP amplitude A_0, after the first trial the EPSP amplitude will be $A_0 \bullet (1 - \beta)$. After the second trial the EPSP amplitude will be $A_0 \bullet (1 - \beta) \bullet (1 - \beta)$, after the third trial it will be $A_0 . (1 - \beta) \bullet (1 - \beta) \bullet (1 - \beta)$, and so on. Hence, the EPSP amplitude A after n trials is given by:

$$A(n) = A_0 \cdot (1 - \beta)^n$$

By normalising EPSP amplitude to control before MK801 block A_0 becomes 1 and can be neglected. This relationship is exponential with a time constant dependent on the rate of block by MK801, β (Supplementary Fig. 1B). In principle, fitting an exponential to the EPSP decay in MK801 can be used to determine the rate of MK801 block β. In practice, however, this is only possible when EPSPs are evoked alone since the EPSP amplitude is masked by APs during pairing. Alternatively, the rate of MK801 block can be calculated from the reduction in EPSP amplitude after n trails by rearranging the relationship above to give:

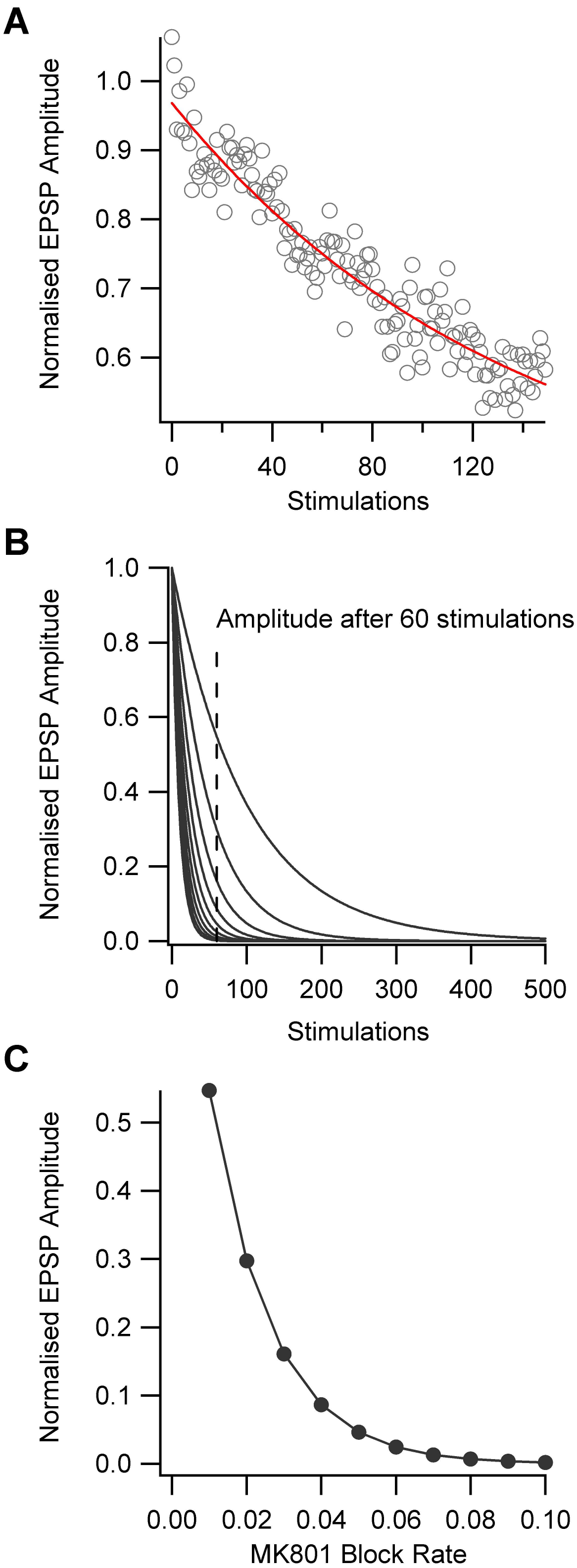
$$\beta = 1 - \sqrt[n]{A(n)}$$

This relationship indicates that NMDA EPSP amplitude after n trials in MK801 is related to the rate of MK801 block, β, in an exponential manner (Supplementary Fig. 1C). The ratio of the MK801 block during pairing EPSPs with APs ($\beta_{pairing}$) to that during EPSPs alone (β_{EPSP}) gives an estimate of how effective APs are at activating NMDARs. Given the equation above, the relative activation of synaptic NMDA receptor by APs compared to control, δ is:

$$\delta = \frac{\beta_{Pairing}}{\beta_{EPSP}} = \frac{1 - \sqrt[n]{A_{Pairing}(n)}}{1 - \sqrt[n]{A_{EPSP}(n)}}$$

with $A_{Pairing}(n)$ being the EPSP amplitude after n pairings of EPSPs and APs and $A_{EPSP}(n)$ being the EPSP amplitude after n stimulations of EPSPs alone. In our experiments n was 60.

Supplementary Fig. 1. Quantification of MK801 block. **A)** Plot of NMDA EPSP amplitude (grey circles) versus stimulation number in the presence of MK801 (5 μM). EPSP amplitude is normalized to control. Data has been fitted with a single exponential (red). **B)** Plots of NMDA EPSP amplitude versus stimulation number in a model of activity-dependent MK801 block of NMDA receptors showing different exponential reductions in EPSP amplitude in models with different rates of MK801 block, β (from 0.1 to 0.01 as indicated). **C)** Plot of NMDA EPSP amplitude after 60 stimulations versus the MK801 block rate, β, in the model. Data has been fitted with a single exponential (red).


A
Normalised EPSP Amplitude
1.0
0.9
0.8
0.7
0.6
0
40
80
120
Stimulations
B
Normalised EPSP Amplitude
1.0
0.8
0.6
0.4
0.2
0.0
Amplitude after 60 stimulations
0
100
200
300
400
500
Stimulations
C
Normalised EPSP Amplitude
0.5
0.4
0.3
0.2
0.1
0.0
0.00
0.02
0.04
0.06
0.08
0.10
MK801 Block Rate