Supplementary Material

Alternative assessment of UP state amplitude

For the purpose of Figure 1, UP state amplitude was derived from frequency distributions of voltage values by using modes to describe the membrane potential more representative of UP and DOWN states as described in Tseng et al. (2001).

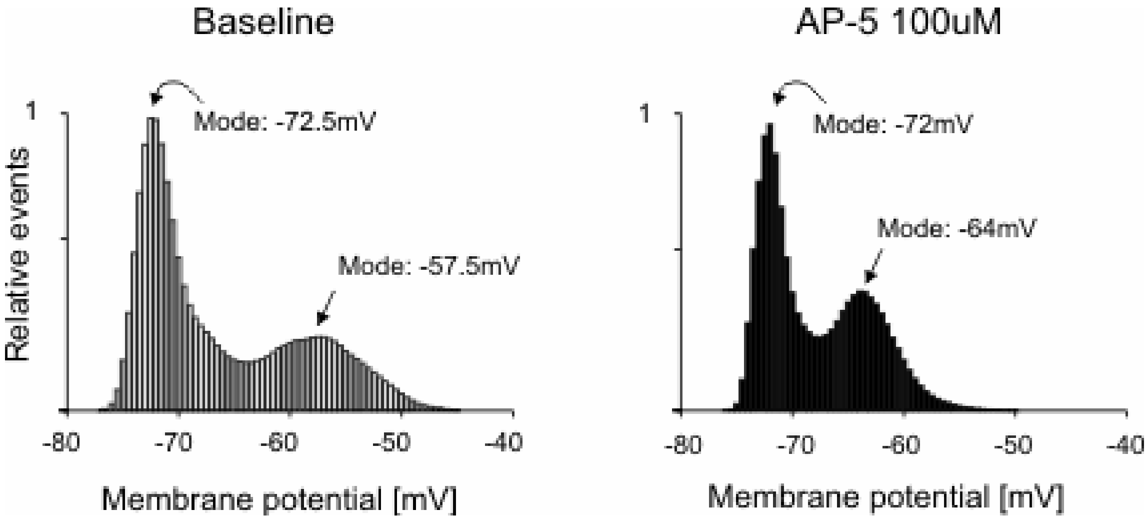


Figure S1. Frequency distributions of the membrane potential in the baseline condition and under AP-5 for a representative MSN. The DOWN and UP states membrane potentials are indicated with arrows.

Moreover, to dispel any concerns regarding the suitability of modes as representative of the UP and DOWN states, we measured UP and DOWN state membrane potentials in signal averages like those seen in Figure 1C. For the DOWN state we took the more negative average value, for the UP state the average voltage 100 ms after the transition. The results are as follows:

	baseline (mV)	**treatment (mV)**
naïve (n=9)	19.6 ± 1.5	18.2 ± 0.8
continuous aCSF (n=8)	14.4 ± 1.6	13.1 ± 1.8
AP-5 (n=9)	15.4 ± 0.8	11.3 ± 0.8 *

Data are mean ± SEM. *p<0.001 versus baseline, Tukey test after p=0.03 interaction in a two-way ANOVA with experimental group and treatment (repeated measure) as factors.

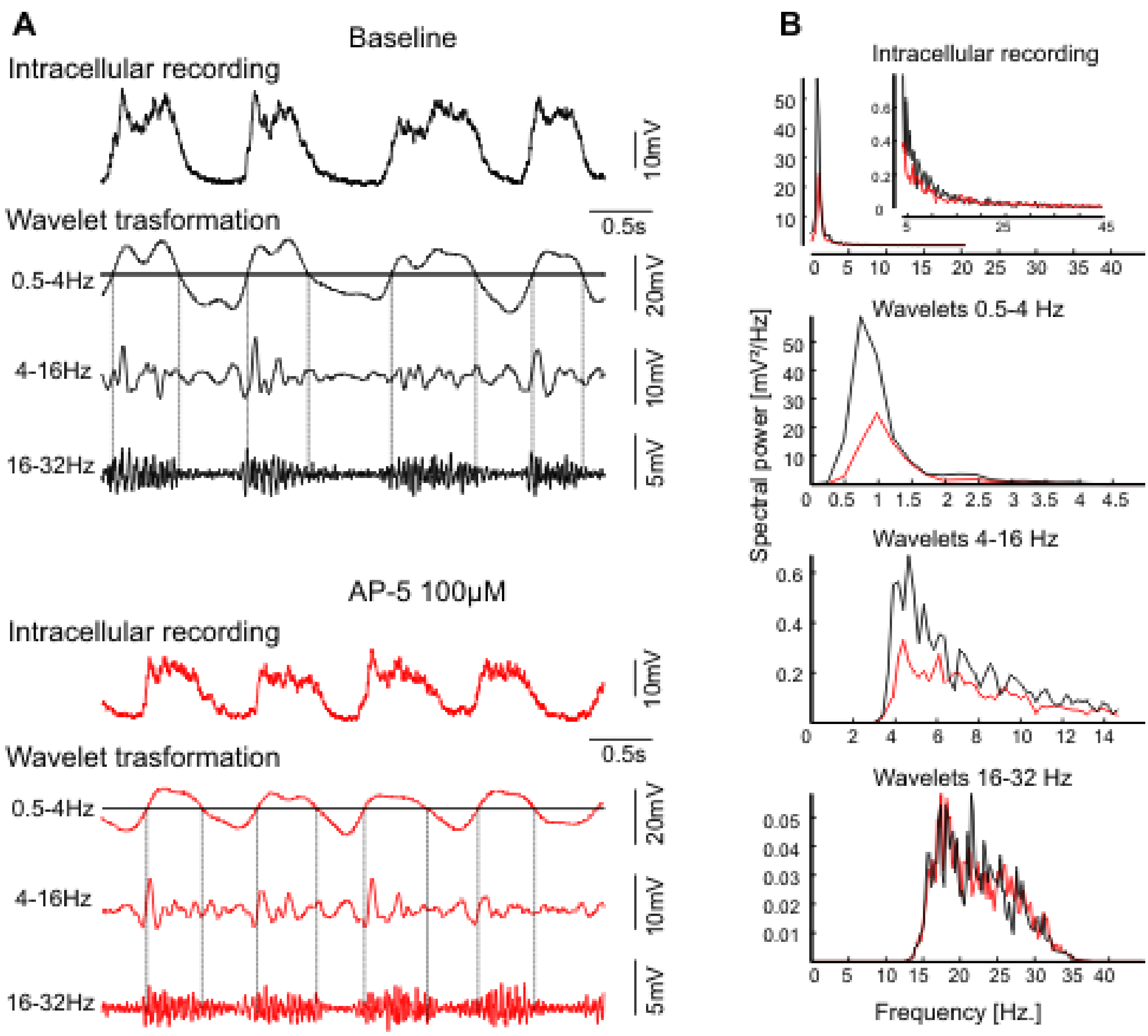
Thus, although this analysis yields higher UP state amplitudes, the outcome of the ANOVA confirms an effect of AP-5 on UP state amplitude.

Effect of AP-5 on high frequency components of the UP state

Fast modulations shape the membrane potential during the UP state. To examine the effect of NMDAR antagonism on these modulations we separated the fast components of the UP state from the prevailing low frequencies corresponding to transitions between UP and DOWN states. This was performed by using a discrete wavelet transformation performed by a finite impulse response digital filter approximation of the Meyer wavelet function (MatLab, The MathWorks, Inc., Natick, MA, USA) as described in Kasanetz et al. (2006, 2008). The procedure works like a band-pass filter that allows obtaining a family of waveforms retaining different frequency components of the original signal (see Figure 2S below). The waveforms used in the present study contained frequency information in the following bands: 0.5-4 Hz, 4-16 Hz and 16-32 Hz (as assessed from power spectra), where the 0.5-4 Hz band closely matched the time course of UP and DOWN states. Statistical analysis of the low frequency band demonstrated that AP-5 reduces its power ($p<0.001$, Tukey test versus baseline after $p=0.003$ interaction in a two-way ANOVA with experimental group and treatment as between and within group factors).

In this low frequency waveform we detected the transitions between UP and DOWN states as crossings of half wave amplitude (*gray line*) with a positive (DOWN to UP state) or negative (UP to DOWN state) slope (Kasanetz et al., 2006, 2008). This allowed isolating the plateau depolarization and computing the power of its high frequencies per UP state (as root mean squares) while avoiding contamination by DOWN states (which are very poor in fast modulations and are far from the membrane potential at which the NMDAR could have an effect). We performed separate two-way ANOVAs for each band to assess AP-5 effects, with experimental group and treatment (within group) as factors. The ANOVA showed no effect of AP-5 on frequencies between 16-32 Hz. For the 4-16 Hz band, the ANOVA revealed a significant effect of treatment ($p<0.001$), without significant interaction ($p=0.196$), possibly owing to a small effect of AP-5 at these frequencies ($p<0.01$, Tukey Test). The results are summarized in Figure 1G in the manuscript.

Figure 2S (next page). A. Wavelet decomposition of the membrane potential of a representative MSN recorded in the baseline condition (*black*) and under AP-5 (*red*). **B.** Auto-spectra of the signals and waveforms obtained after wavelet decomposition. More than 95% of the spectral power (mV^2/Hz) is concentrated in frequencies below 32 Hz. The vertical gray lines indicate transitions between UP and DOWN states, as detected in the 0.5-4 Hz frequency band.


A
Baseline
Intracellular recording
10mV
0.5s
Wavelet trasformation
0.5-4Hz
20mV
4-16Hz
10mV
16-32Hz
5mV
AP-5 100µM
Intracellular recording
10mV
0.5s
Wavelet trasformation
0.5-4Hz
20mV
4-16Hz
10mV
16-32Hz
5mV
B
Intracellular recording
Wavelets 0.5-4 Hz
Spectral power [mV²/Hz]
Wavelets 4-16 Hz
Wavelets 16-32 Hz
Frequency [Hz.]