MED64-Quad II System Accelerates the Studies of the Roles of NMDA Receptor in Synaptic Plasticity and Epileptogenesis in Acute Mouse Hippocampal Slice

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Results

1. NMDA receptor-dependent LTP on MED64-Quad II

A LTP on Quad II

B 30uM MK-801 blocks LTP

C 50uM D-APV completely blocks LTP

3. MK-801 Pretreatment Completely Blocked NMDA depressant effect on fEPSPs


4. MK-801 Co-application with NMDA Did not Abolish NMDA Initial Depression, but Blocked late NMDA depression

A Sample of fEPSP traces. B Sample time course of fEPSP slope and amplitude normalized to control. Open bar indicates MK-801 50uM bath application. Filled bar indicates NMDA 30uM bath application. MK-801 did not abolish NMDA initial depression, but late depression. N = 7. Inset: micrograph.

5. NMDA Depression Was Independent of GABA_A Receptor Block


6. NMDA Increased Spike Frequency and Induced Synchronized Burst

A Spike frequency increased graded increase of concentration of NMDA with apparent synchronized burst at 30µM in a slice. The sensitivity to NMDA exposure to start burst varied among slices. The burst started at NMDA concentration 3µM and spike abolishment to 30µM NMDA. B. An example of a recording of one hippocampal slice to show the synchronized burst (spikes dispersions) in all 16 electrodes during bath perfusion of 30µM NMDA using software MatLab. C. An example of the raw traces of spontaneous spikes with bursts together, during NMDA 30µM bath. The reversible effect NMDA 10µM to increase the spontaneous spikes with bursts was seen in 6 out of 6 tested slices.

NMDA induced the synchronized burst which was attenuated by APV

B Normal ACSF

C NMDA 10µM

D NMDA 10µM + APV 50µM

E Comparison of number of synchronized burst among 3 groups (P<0.01, N = 7).

7. 8. Simplified Schematic Diagram of Involvement of Synaptic, Presynaptic, Extrasynaptic NMDA Receptors, and GABA_A Receptor in NMDA-induced EPSP Depression

A Schematic diagram of the MED64-Quad II system. The system consists of a MED64-Quad II platform and a MedLab High-Throughput Electronic Microscopy (MedLab HT-EM) system. The MED64-Quad II platform is used for simultaneous recording of up to 16 electrodes, while the MedLab HT-EM system is used for high-resolution imaging. B. A schematic diagram of the recording setup. The setup consists of a MED64-Quad II platform connected to a MedLab HT-EM system. The MED64-Quad II platform is used for simultaneous recording of up to 16 electrodes, while the MedLab HT-EM system is used for high-resolution imaging.

Conclusions

1. NMDA bath application caused excitotoxicity by shunting down synaptic transmission, which is independent of GABA_A receptor block. These effects can be blocked or diminished by NMDA receptor antagonist APV and channel blocker MK-801. NMDA increased spontaneous spikes and induced synchronized bursts can be a useful model for epileptic study. The results indicate that NMDA is essential for LTP, synaptic plasticity, and epileptic study model or studies on other disease models.

2. A high sensitive MED64-Quad II system not only increases throughput by simultaneous recording on 4 hippocampal slices in one experiment, but also is a useful tool for mechanistic study with increased productivity. Thus, MED64-Quad II system is a useful tool for LTP study, and epileptic study model or studies on other disease models.