# Kindling induces the long-lasting expression of a novel population of NMDA receptor in hippocampal region CA3

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## 摘要

## Abstract

Kindling refers to a phenomenon in which repeated application of initially subconvulsive electrical stimulations produces limbic and clonic motor seizures of progressively increasing severity. Once established, the increased excitability is lifelong. Enhanced function of synapses using the NMDA subtype of glutamate receptor could contribute to the expression of the increased excitability. We previously found that CA3 pyramidal cells of hippocampus of kindled animals exhibit a selective and long-lasting (1 month) increased sensitivity to NMDA-evoked depolarization. The goal of this study was to develop a molecular explanation of the enhanced sensitivity to NMDA. We used radioligand binding studies of membranes isolated from microdissected regions of hippocampus including fascia dentata, CA3, and CA1. We also used quantitative in situ hybridization with subtype-specific riboprobes or oligonucleotides to determine whether increased expression of one or more of the genes encoding NMDA receptors was present in hippocampal granule and pyramidal cells of kindled animals. When studied 28 d after the last evoked seizure, we found that kindling induced a 2.8-fold increase in the number of binding sites for the competitive NMDA receptor antagonist 3-[(+/-)-2-(carboxypiperazine-4-yl)][1,2-3H-]propyl-1-phosphonic acid (3H-CPP). This increase was confined to region CA3 within the hippocampus. Similar, though much smaller, changes were detected 24 hr after the last evoked seizure. Surprisingly, no changes in the binding of another competitive NMDA receptor antagonist, cis-4-(phosphonomethyl)-2-3H-piperidinecarboxylate (3H-CGS-19755), were detected at either time point in any hippocampal region. Transcript levels of the NMDA receptor genes NMDAR1, NR2A, NR2B, NR2C, and NR2D and a glutamate-binding protein (GBP) were not altered by kindling. These findings demonstrate that kindling induces the expression of an NMDA receptor that is novel in that it is recognized by 3H-CPP but not by 3H-CGS-19755. The molecular basis of this novel NMDA receptor is not determined by differential expression of mRNA transcripts of known NMDA receptor genes. The direction, time course, and location of the kindling-induced increase in 3H-CPP binding suggest that this novel

receptor may underlie the increased sensitivity of CA3 neurons to NMDA observed in kindled animals.