

## Seizure and Epilepsy Models on Hippocampal Slices of Rats

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### - Abstract -

Hippocampal slice models can be a powerful tool to study the mechanism of partial epilepsy. Despite the loss of connection with the rest of the brain, in vitro hippocampal slice preparations allow detailed physiological and pharmacological studies, which would be impossible, in vivo. There are several methods to induce electrographic seizures on hippocampal slice models. Those are electrical pulse train stimulation, 0 Mg<sup>2+</sup> artificial cerebrospinal fluid and high concentration of extracellular K<sup>+</sup> on bath. Among them, the electrically triggered seizure may mimic the physiological communication between neuronal populations without any deterioration of normal physiologic and chemical status of the hippocampal slice models. Presumably, such communication from hyperexcitable areas to other neuronal populations is involved in the development of epilepsy. Electrographic seizures in hippocampal slice models occur in the network of neurons that are involved in epileptic seizures in the hippocampus in vivo. Because these models have many advantages and are very valuable to research of epileptogenesis on partial epilepsy, I would like to introduce the electrophysiological methods to induce electrographic seizure or epilepsy on hippocampal slice models briefly in this paper.

**Key Words :** Hippocampal slice models, Electrophysiological methods, Epileptogenesis

( )

가 1.

가

가 가

90

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1 2

mine 1mM, pH 7.3)<sup>2</sup>

1ml Gäwiler

가

36 5% CO<sub>2</sub>

, 2~3

1-2.

pentobarbital sodium(50mg/kg,

i.p.)

400 ~ 450µm

가

가

1.

가 가

가

가

<sup>3</sup>.

(14 ~ 21 )

1-3.

가

1-1.

(or-ganotypical hippocampal explant culture system)

가

가

6 ~ 8 Sprague-Dawley

가

가

가

(horizontal laminar flow hood)

<sup>3</sup>.

GBSS(Gey's balanced salt solution)

1-4.

. GBSS

Stoeling (tis-

가

sue slicer)

400 ~ 450µm

(porous membrane insert)

5 ~ 6

6

(six-well plate)

가

Gäwiler (50% BME, 25% HBSS, 25% , D-glucose 6.5mg/ml, gluta-

가

가

가 가  
가 가

ry postsynaptic potential; EPSP)  
가, 가  
(population spike; PS)가 EPSP  
CA1

PS 가 PS  
SA (artificial cerebrospinal fluid;  
aCSF) Ca<sup>2+</sup>  
NMDA D-APV(50μM) aCSF  
EPSP 가 PS 가  
AMPA

CNQX(20μM) EPSP  
4-6  
(epileptiform burst; EB)

10 ~ 200ms

EB

PS

EPSP  
(interictal spike; IS)

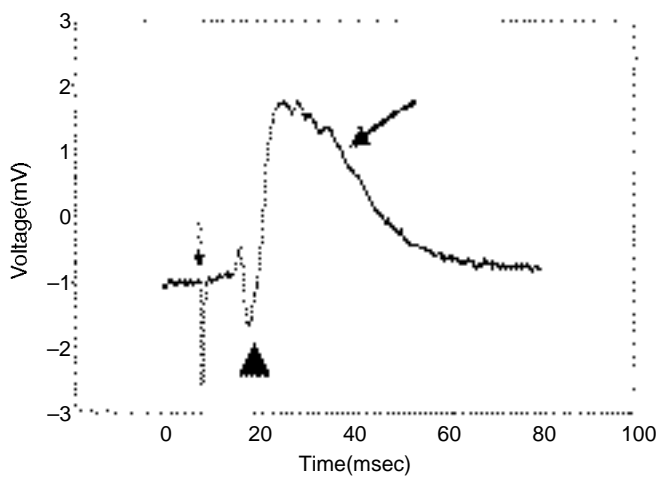
(Cornu Ammonis; CA) CA3

(synaptic activity; SA) CA1

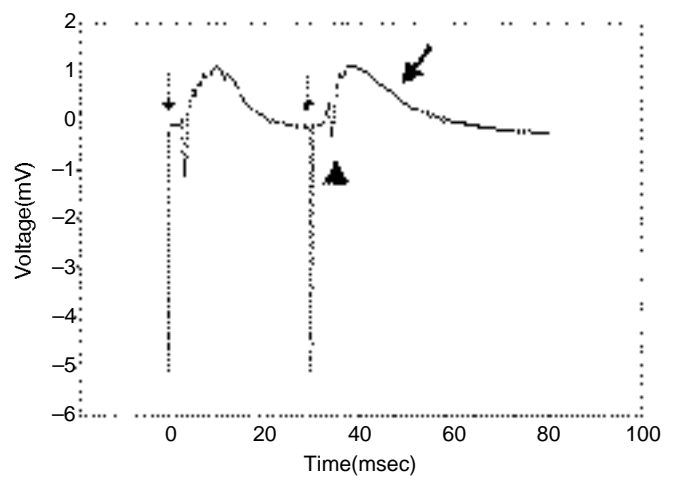
(Fig. 1).

(excitato

30msec 가  
(paired shocks) Schaffer (Schaffer  
collaterals) CA1



**Figure 1.** Electrically evoked synaptic activity in CA1 area of organotypical hippocampal explant culture of rat. When stratum radiatum of CA3 area is stimulated with single electrical shock stimulation(300μA ~ 1mA, 0.1msec), a characteristic synaptic response is recorded in stratum pyramidale of CA1 area. Typical pattern of positive field EPSP(large arrow) and superimposed negative sharp population spike(arrowhead) is shown after stimulation artifact(small arrow).



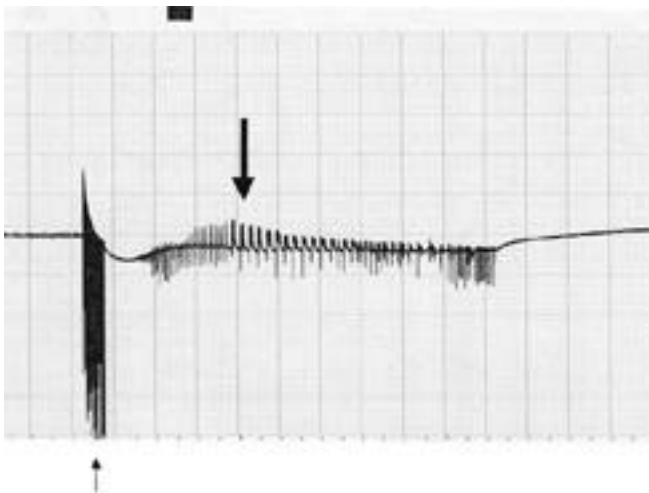
**Figure 2.** Paired pulse inhibition in organotypical hippocampal explant culture of rat. When paired electrical shocks(300μA ~ 1mA, 0.1msec)(small arrows) separated by 30msec is delivered to the Schaffer collaterals, pattern of paired pulse inhibition is observed in stratum pyramidale of CA1 area. The response of CA1 pyramidal neurons of second stimulation including both of population spike(arrowhead) and field EPSP(large arrow) is markedly attenuated compared with the response of first stimulation.

SA  
(paired pulse inhibition; PPI)  
(Fig. 2). PPI GABA

GABA  
PPI  
가  
가  
SA가  
가  
PPI가  
SA가  
(paired pulse facilitation)  
가

가  
(electrographic seizure;  
가  
(afterdischarge; AD) EGS  
<sup>3</sup>(Fig. 3).

EB CA3 , EGS  
CA3 EB  
EB EGS  
가 EB  
EGS EB가  
CA3 CA1  
가 EB가  
CA3 EB가



**Figure 3.** Electrically triggered seizure induced in CA1 area of organotypical hippocampal explant culture of rat. A pulse train stimulation(60Hz, 0.1 msec rectangular pulses, for 1sec)(small arrow) on the Schaffer collaterals reliably induce electrographic seizure(afterdischarge)(large arrow) in stratum pyramidale of CA1 area. Electrographic seizure is shown at 2sec after the pulse train stimulation and persisted for 16sec. Black bar on the upper border of this figure means 1sec duration and one large segment of y axis of the graph is 2mV.

3.

3-1.

EB  
EGS  
stimulation; PTS) 가 AD EGS (pulse train  
CA3 Schaffer

CA1, 2M NaCl, CA3  
 (submersion chamber)  
 aCSF((mM); NaCl 120, KCl 3.5, NaH<sub>2</sub>PO<sub>4</sub> 1.23, NaHCO<sub>3</sub> 25, CaCl<sub>2</sub> 1.8-2.0, MgSO<sub>4</sub> 0.6-1.2, Glucose 10), pH  
 aCSF 95%/5% O<sub>2</sub>/CO<sub>2</sub>  
 AD  
 0.1msec, 300 μA ~ 1mA

Schaffer, 2, EGS가  
 PTS(0.1msec, 60Hz) 1, 5~10  
 가  
 3-2.

가, 가, 가  
 EB, EGS  
 GABA가, GABA  
 가

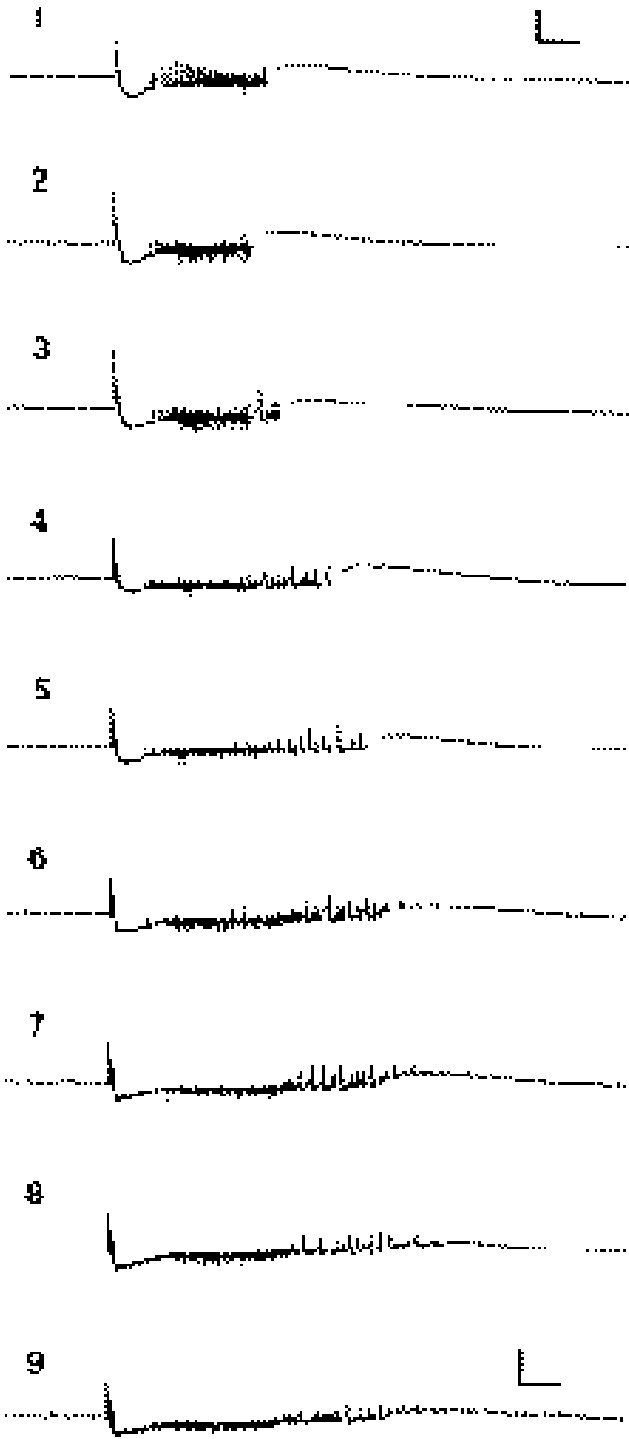
3-3.  
 Stasheff 1, 150~200g, 가  
 Sprague-Dawley 5, PTS, CA3

PTS, CA3, 가  
 , PTS, AD, (single stimulation)  
 EB, EB가, AD  
 EGS, EB, IS, CA3  
 PTS, (long term potentiation), 가  
 kindling, EB, EGS, IS

PTS, kindling  
 Kindling, PTS, EGS  
 가, EGS

EGS, 2, <sup>12</sup>(Fig. 4).  
 PTS, 가, D-APV, aCSF, D-  
 EGS, APV, PTS, 가, D-APV  
 EGS가, EGS, EGS, <sup>12</sup>, EGS  
 EGS가, <sup>13</sup>, EGS, PTS

PTS, EGS, aCSF, EGS, IS  
 가, EGS  
 3, 4. Mg<sup>2+</sup>, aCSF, NMDA



**Figure 4.** Stimulus-train induces the progressive development of electrographic seizures in organotypical hippocampal explant culture of rat. A 1 sec train of 60Hz 500μA rectangular pulses(0.1msec) is delivered at 10min intervals to the Schaffer collaterals. There is progressive lengthening of evoked afterdischarge duration. This culture was 14days in vitro. Calibration bars = 5sec, 2mV.(From Shin et al, 1992)

channels aCSF Mg<sup>2+</sup>, NMDA . 0 Mg<sup>2+</sup> aCSF

15,16 EGS가 aCSF D-APV 가

5. K<sup>+</sup> ([K<sup>+</sup>]o)

aCSF [K<sup>+</sup>]p 3.5mM [Ca<sup>2+</sup>]p [Mg<sup>2+</sup>]p 7~8.5mM [K<sup>+</sup>]p CA3b CA3c EB CA1

CA3 EGS EB CA1 D-APV 가 EGS NMDA CA3 EB

EGS , 0 Mg<sup>2+</sup> PTS [K<sup>+</sup>]p aCSF aCSF Mg<sup>2+</sup> EGS [K<sup>+</sup>]p

EGS PTS 가 kindling 가 가

가 NMDA 가 Mg<sup>2+</sup> NMDA

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