European Journal of Pharmacology, 154 (1988) 221–222
Elsevier

EJP 0150R

Rapid communication

D-Aminophosphonovaleric acid-sensitive spontaneous giant EPSPs in immature rat hippocampal neurones

R. Corradetti, J.L. Gaïarsa and Y. Ben-Ari *

INSERM U-029, Hopital de Port-Royal, 123 Boulevard de Port-Royal, 75014 Paris, Cédex 14, France

Received 8 August 1988, accepted 8 August 1988

N-Methyl-D-aspartate (NMDA)-receptor activation in both hippocampus and visual cortex of adult animals is involved in long-term changes in synaptic transmission. These synaptic modifications are thought to be triggered by calcium fluxes through the NMDA-activated channel. Recent experiments also suggest that NMDA-receptor activation plays a crucial role during critical periods of development (Kleinschmidt et al., 1987; Tsumoto et al., 1987).

We now report the presence of spontaneous, recurrent, network-driven giant EPSPs which were blocked by the selective NMDA-receptor antagonists, D-aminophosphonovaleric acid (D-APV) and (±)-3-(2-carboxypiperazin-4-yl)-propyl-1-phosphonic acid (CPP), in the CA3 region of hippocampal slices taken from rats 0-14 days old.

Fully submerged transverse hippocampal slices (500-600 μm) were superfused at 35°C, with oxygenated artificial cerebrospinal fluid of the following composition (mM): NaCl 126, KCl 3.5, $CaCl_2$ 2, $MgCl_2$ 1.3; NaH_2PO_4 1.4, $NaHCO_3$ 25 and glucose 11 (Gho et al., 1986). Intracellular recordings were made from CA3 pyramidal cells by means of KCl-filled electrodes (3 M, 40-60 MΩ). The potentials, amplified, were displayed on a computer-driven chart recorder.

Spontaneous, recurrent bursts were observed in 46 out of 58 cells (79%) during the first post-natal week (fig. 1A,B). These bursts consisted of depolarizations, 300-1200 ms in duration, which reached the threshold for spike discharge (fig. 1C), followed by a hyperpolarization. These spontaneous bursts gradually disappeared during the second post-natal week. The bursts appeared to be synaptically driven since: (i) their amplitude but not their frequency was changed by membrane hyperpolarization; (ii) they were blocked by tetrodotoxin (1 μM, n = 3, not shown); (iii) concomitant negative field potentials were recorded with extracellular microelectrodes, indicating synaptic activity in a large population of cells (n = 7, not shown). The activation of NMDA receptors was involved in burst generation, since NMDA-receptor antagonists and NMDA-channel blockers markedly reduced the frequency or completely

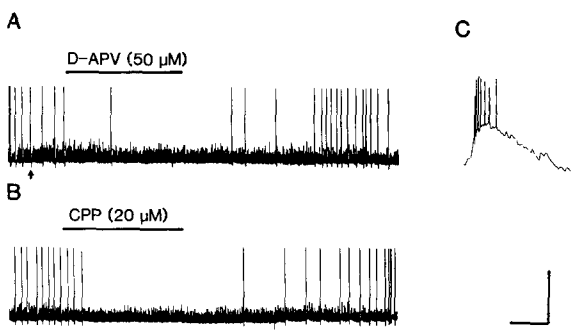

Fig 1 NMDA-receptor antagonists blocked spontaneous bursts in a 6-day-old rat. Bath application of D-APV (A) or CPP (B) for the time indicated by solid bars completely blocked the spontaneous bursts (upward deflections) A and B were from the same cell membrane potential, −79 mV The arrow in A indicates a burst which is displayed at a faster sweep in C Calibration bars 40 mV, 1 min (A,B), 50 mV, 150 ms (C)

* To whom all correspondence should be addressed

blocked the bursts. D-APV (50 μM, n = 19, fig 1A) fully blocked the bursts in 8 out of 19 cells, strongly reduced the frequency in 9 out of 19 cells, and was inactive in 2 cells. CPP (20 μM, n = 13, fig. 1B) completely blocked the bursts in 5 out of 13 cells, markedly reduced the frequency in 6 out of 13 and was inactive in 2 cells. The NMDA-channel blockers, ketamine (20 μM, n = 4) or phencyclidine (1 μM, n = 3) also blocked the spontaneous bursts (not shown). Since these bursts are network-driven other receptors could also contribute to burst generation, accounting for the incomplete blockade by NMDA-receptor antagonists.

The principal, novel finding of the present study is that spontaneous, recurrent, giant EPSPs were observed in the CA3 region during the first week of post-natal life and disappeared during the second week. That NMDA-receptors are involved in the generation of these bursts is consistent with quantitative autoradiographic data which show a marked (70%) reduction of NMDA-binding sites in the CA3 region after the first post-natal week (Dr. E. Tremblay, personal communication). Although the functional significance of these bursts remains to be determined, they may be important in the synaptogenesis occurring during this critical period.

Acknowledgements

We thank Dr R Neuman for his helpful comments R C is the recipient of an E M B O. fellowship

References

Gho, M., A E King, Y. Ben-Ari and E Cherubini, 1986, Kainate reduces two voltage-dependent potassium conductances in rat hippocampal neurons in vitro, Brain Res 385, 411

Kleinschmidt, A., M F Bear and W Singer, 1987, Blockade of 'NMDA' receptors disrupts experience-dependent plasticity of kitten striate cortex, Science 238, 355

Tsumoto, T., K. Hagihara, H. Sato and Y Hata, 1987, NMDA receptors in the visual cortex of young kittens are more effective than those of adult cats, Nature (London) 327, 513