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NMDA receptor antagonists reduce medial, but not lateral, perforant path-evoked EPSPs in dentate gyrus of rat hippocampal slice

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Summary. NMDA receptor antagonists produced differential effects on medial and lateral perforant path-evoked excitatory postsynaptic potentials (EPSPs) recorded in the dentate gyrus molecular layer of hippocampal slices. D-(−)-2-amino-5-phosphonovaleric acid (D(−)APV) and 3-[(±)-2-carboxypiperazin-4-yl]-propyl-1-phosphonic acid (CPP) significantly reduced the peak amplitude and total area, but not the initial negative slope, of the medial perforant path-evoked EPSP. Neither antagonist affected any component of the lateral perforant path-evoked EPSP. In contrast, population spikes evoked by stimulation of either pathway were depressed.

Key words: Synaptic transmission – Excitatory amino acids – NMDA receptor antagonists – Hippocampal formation – Long-term potentiation – Rat

Introduction

Glutamate has been shown to be a transmitter in the perforant path (PP; White et al. 1977), which actually consists of two anatomically and functionally discrete subdivisions, the medial and lateral PPs (Hjorth-Simonsen 1972; Hjorth-Simonsen and Jeune 1972). The axons in the medial PP project to granule cell dendrites in the middle third of the molecular layer of the dentate gyrus, whereas the lateral PP projects to the outer third of the molecular layer (Steward 1976). It is not clear whether the N-methyl-D-aspartate (NMDA) subtype of glutamate receptor is involved in synaptic transmission from the PP to hippocampal dentate granule cells. Cotman et al. (1987) demonstrated that there is a high density of NMDA receptors in the molecular layer of the dentate. Inspection of their figures suggests that the maximal density of NMDA receptors is in the middle third of the molecular layer, which corresponds to the terminal field of the medial PP. Several electrophysiological studies have suggested that there is an NMDA receptor-mediated component of PP-evoked responses (Koerner and Cotman 1981; Burgard et al. 1989; Lambert and Jones 1989). However, other groups have reported that there is no NMDA receptor-mediated component of either the population spike (Coan et al. 1987) or the medial (Crunelli et al. 1982; Collingridge et al. 1984) or lateral (Collingridge et al. 1984; Mody et al. 1988) PP-evoked EPSP in physiological concentrations of extracellular magnesium. In only one (Collingridge et al. 1984) of the previous studies was a depth-profile for differential activation of lateral and medial PP presented. In view of the diversity of experimental methods employed and apparently contradictory results obtained in previous studies, it is important to determine the contribution of NMDA receptors to the medial and lateral PP EPSPs under defined conditions.

Both the medial and lateral pathways can show long-lasting modifications of synaptic activity. High-frequency stimulation of either pathway can induce long-term potentiation (LTP; McNaughton and Barnes 1977; Winson and Dahl 1986), one form of synaptic plasticity (Sarvey et al. 1989). Additionally, activation of β-adrenergic receptors can induce a long-lasting *potentiation* (LLP) of responses to medial PP stimulation with a concomitant long-lasting *depression* of responses to lateral PP stimulation (Dahl and Sarvey 1989).

Induction of LTP (Morris et al. 1986; Wigström et al. 1986; Errington et al. 1987) and β-adrenergic agonist-induced LLP (Burgard et al. 1989) in the dentate gyrus is blocked by the NMDA receptor antagonists D-(−)-2-amino-5-phosphonovaleric acid (D(−)APV) and 3-[(±)-2-carboxypiperazin-4-yl]-propyl-1-phosphonic acid (CPP).

In this paper, we show that the NMDA receptor antagonists D(−)APV and CPP reversibly depress a component of the subthreshold medial PP-evoked excitatory postsynaptic potential (EPSP). D(−)APV and CPP are without effect on lateral PP-evoked EPSPs. In contrast, population spikes elicited by stimulation of either pathway are depressed.

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Material and methods

Transverse slices prepared from hippocampi of adult male rats (Sprague-Dawley, Taconic Farms; 150–200 g) were maintained at 35°C in a modified Andersen interface chamber. Previously described (Dahl and Sarvey 1989; Stanton and Sarvey 1987) techniques of electrical stimulation, electrophysiological recording, and tissue maintenance were employed. Artificial cerebrospinal fluid (ACSF) consisting of (mM): NaCl 125, $NaHCO_3$ 26, KCl 3, $CaCl_2$ 2.4, $NaHPO_4$ 1.2, $MgSO_4$ 1.3, and dextrose 10 was continuously bubbled with 95% O_2/5% CO_2.

Field potential recordings were made with glass micropipette electrodes filled with 2 M NaCl (resistance 5–15 MΩ). Monopolar stimulating electrodes (single 100 μm diameter Teflon-insulated stainless steel wires), with the return path provided by a silver chloride-coated silver wire in contact with the bath ACSF, were employed. Stimulus currents varied from slice to slice (50–150 μA), but were chosen to evoke EPSPs or population spikes less than 30% of their maximum amplitude to preclude current spread beyond the selected pathway. For EPSP evaluation, simultaneous bilevel (molecular and granule cell layers) recordings revealed that EPSPs were far below threshold to evoke population spikes. The frequency of stimulation was 0.2 Hz.

Standard procedures of response measurement were employed (Scharfman and Sarvey 1985; Stanton and Sarvey 1987). EPSPs were analyzed by measurement of the (1) maximum initial negative slope, (2) peak amplitude, and (3) total area of the response between the points of initial excursion from, and return to, baseline. Population spikes were measured by their (1) amplitude, (2) total area between the two positive peaks corresponding to the beginning and end of the spike (Scharfman and Sarvey 1985), and (3) latency to negative peak.

D(−)APV and CPP were obtained from Tocris Neuramin (Essex, UK). Both drugs were soluble in ACSF and applied by perfusion for 30 min. A concentration of 10 μM D(−)APV and 1 μM CPP was selected from the established efficacies of these drugs in blocking LTP and ß-adrenergic agonist-induced LLP (Burgard et al. 1989). Experiments were terminated after 30 min of wash in drug-free ACSF, at which time all effects had fully reversed to pretreatment values. Effects of D(−)APV and CPP were evaluated using the two-tailed Student's *t* distribution with the level of significance set at 0.05. Data are expressed as mean percent ±standard error of the mean (SEM) of pretreatment values.

The location of the medial and lateral PPs in the molecular layer of the hippocampal slice is shown in Fig. 1A and B. Representative recordings from three positions are illustrated in Fig. 1C. Note that, at the level of maximum negative medial PP-evoked EPSP in the mid-molecular layer, the lateral PP-evoked EPSP is positive (Winson and Dahl 1986; Dahl and Sarvey 1989). Similarly, the lateral PP EPSP shows a maximum negativity in the outer molecular layer where the medial PP-evoked EPSP is positive. The negative EPSPs correspond to the location of current sinks (i.e., flux of positive current into cellular elements) for lateral and medial PP terminal fields.

Results

EPSPs

Effects of D(−)APV on medial and lateral PP-evoked EPSPs are illustrated in Fig. 2A and B. Perfusion with D(−)APV (10 μM) for 30 min was without effect on the initial negative slope of the medial PP-evoked EPSPs [101 ±2.5% of pretreatment slope, n=6, Not Significant (N.S.)]. Thus, NMDA receptor activation does not appear to contribute to the initial component of the medial PP-evoked EPSP. However, a 30-min perfusion with D(−)APV depressed the peak amplitude (to 82±3.9%, n=6, $p<0.05$) and the total area (to 87±1.8%, n=6, $p<0.05$) of the EPSP. The D(−)APV-induced depression of medial PP-evoked EPSPs reversed to pretreatment values following a 30 min wash with drug-free ACSF (peak amplitude 103±0.03; area 102±0.01). Thus, the NMDA receptor antagonist D(−)APV produced a reversible depression of the peak amplitude and total area of the medial PP-evoked EPSP, but had no effect on its initial slope.

In contrast, in the same slices, D(−)APV had no effect on the initial negative slope, (103±3.3%, n=6, N.S.), peak amplitude (105±4.0%, n=6, N.S.), or total area (100 ±1.1%, n=6, N.S.) of the lateral PP-evoked EPSPs. Thus, the depression of the peak amplitude and total area of the EPSP by D(−)APV is pathway-specific, that is, restricted to the medial PP-evoked EPSP.

Perfusion of slices with the NMDA receptor antagonist CPP (1 μM) produced pathway-specific effects on the medial PP-evoked EPSP, similar to D(−)APV (Fig. 2B). These were also completely reversed by 30 min wash with drug-free ACSF (peak amplitude 103±0.02; area 103 ±0.06)

Population spikes

While the effects of D(−)APV and CPP recorded in the molecular layer were specific to activation of the medial PP, population spikes recorded in the granule cell layer by activation of either pathway were reduced from pretreatment values (Fig. 2A and C). The amplitude of both medial and lateral PP-evoked population spikes after 30 min perfusion with D(−)APV were reduced to 51±6.3% (n=6, $p<0.05$) and 45±3.7% (n=6, $p<0.05$) of pretreatment, respectively. The total area of the medial and lateral PP-evoked population spikes was reduced to 53 ±7.2% (n=6, $p<0.05$) and 55±6.2% (n=6, $p<0.05$) of pretreatment values, respectively. Wash with drug-free ACSF for 30 min completely reversed the effect on amplitude (medial PP 102 ±0.04; lateral PP 104±0.03) and area (medial PP 98±0.02; lateral PP 104±0.05). The decrease in area of the population spike suggests that the decrease in amplitude is not simply due to decreased synchrony of firing of action potentials. Note that the depression of the lateral PP-evoked population spike was not significantly different from the depression of the medial PP-evoked population spike (Student's *t*-test).

CPP similarly reduced the amplitude and area of population spikes evoked by activation of either the medial or lateral PPs, which confirmed the results obtained with D(−)APV. These results are shown in Fig. 2C. Upon 30 min wash with drug-free ACSF, population spike amplitude (medial PP 98±0.05; lateral PP 103±0.07) and area (medial PP 102±0.04; lateral PP 101±0.03) returned to pretreatment values. Thus, the pathway-specific depression of the EPSP is not translated into a similarly specific depression of the population spike, as both the medial and lateral PP-evoked spikes are equally affected.

Although the population spike amplitude and area were reduced, there were no changes in latency of medial (100±2.6%, n=6, N.S.) or lateral PP-evoked population spikes (103±2.3%, n=6, N.S.) after a 30 min perfusion

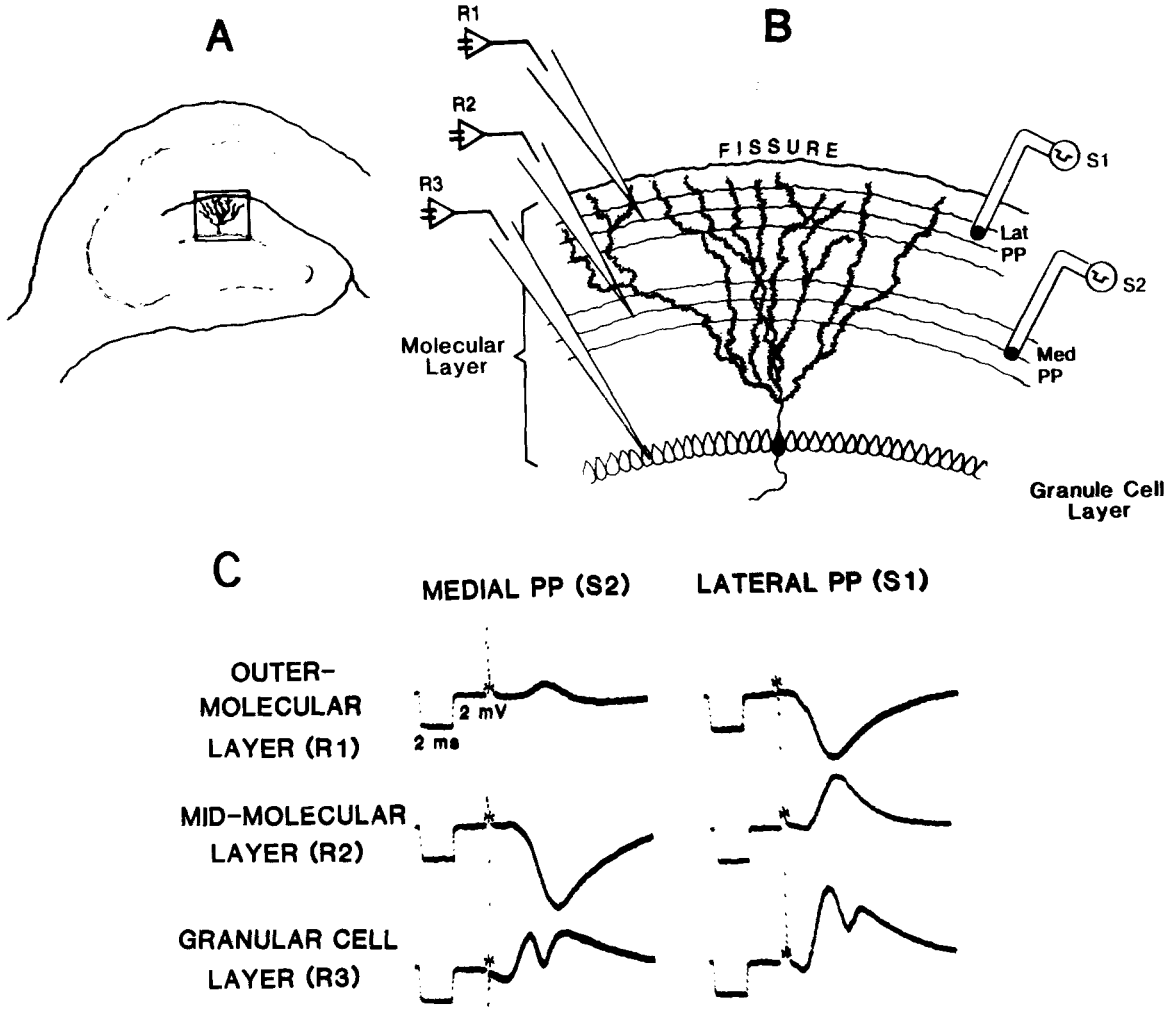

Fig. 1. **A** Scheme of a hippocampal slice. **B** Detail of the dentate gyrus, showing a granule cell and medial and lateral PPs in the molecular layer. The distance between the hippocampal fissure and granule cell layer is approximately 300 μm. Stimulating electrodes were positioned in the outer- (S1) and mid-molecular (S2) layers to activate the lateral or medial PPs, respectively. Recording electrodes were placed in the outer- (R1), mid-molecular (R2), and/or the granule cell layers (R3) to record EPSPs (R1 and R2) or population spikes (R3) in response to discrete stimulation of the separate pathways. **C** Responses recorded at three locations (R1, R2, R3) in the molecular-granule cell layers to discrete activation of the medial or lateral PPs. Stimulation (80 μs, 100 μA) of the medial PP evokes a negative EPSP in the mid-molecular layer (R2, Fig. 1B). The lateral PP-evoked response is positive at this recording position. Stimulation (60 μs, 100 μA) of the lateral PP evokes a negative EPSP in the outer-molecular layer (R1, Fig. 1B), where the medial PP-evoked EPSP is reversed. In the granule cell layer (R3, Fig. 1B) in a different slice, EPSPs elicited by stimulation of either pathway (medial: 80 μs, 100 μA; lateral: 80 μs, 100 μA) are positive, and population spikes are negative. The asterisk indicates the stimulus artifact

with D(−)APV (Fig. 2A and C). Population spike latencies were also unaffected by CPP (Fig. 2C). The lack of effect on the latency of either population spike provides evidence for a dissociation of the population spike from the NMDA receptor antagonist-sensitive component of the medial PP-evoked EPSP. Moreover, the difference between the latencies between medial and lateral PP-evoked population spikes was not significantly changed by D(−)APV exposure. This further indicates that stimulus isolation of the pathways was obtained (Abraham and McNaughton 1984).

Discussion

The present study indicates that there is an NMDA receptor antagonist-sensitive component of synaptic transmission from the medial PP, but not the lateral PP. Both D(−)APV and CPP, in concentrations known to block ß-adrenergic LLP and LTP induction (Burgard et al. 1989), reduced the peak amplitude and total area of medial PP-evoked EPSPs, but had no effect on lateral PP-evoked EPSPs. These antagonists did not affect the initial negative-going component of either the medial or the lateral PP-evoked EPSP. These results suggest that the initial phase of the medial PP-evoked EPSP does not contain an NMDA receptor-mediated component; this is in agreement with previous findings (Burgard et al. 1989). However, NMDA receptor activation becomes apparent as the EPSP reaches its maximum amplitude. Further support for this idea is found in the decrease in EPSP area produced by the NMDA receptor antagonists. Slow EPSPs mediated by NMDA receptors have also been

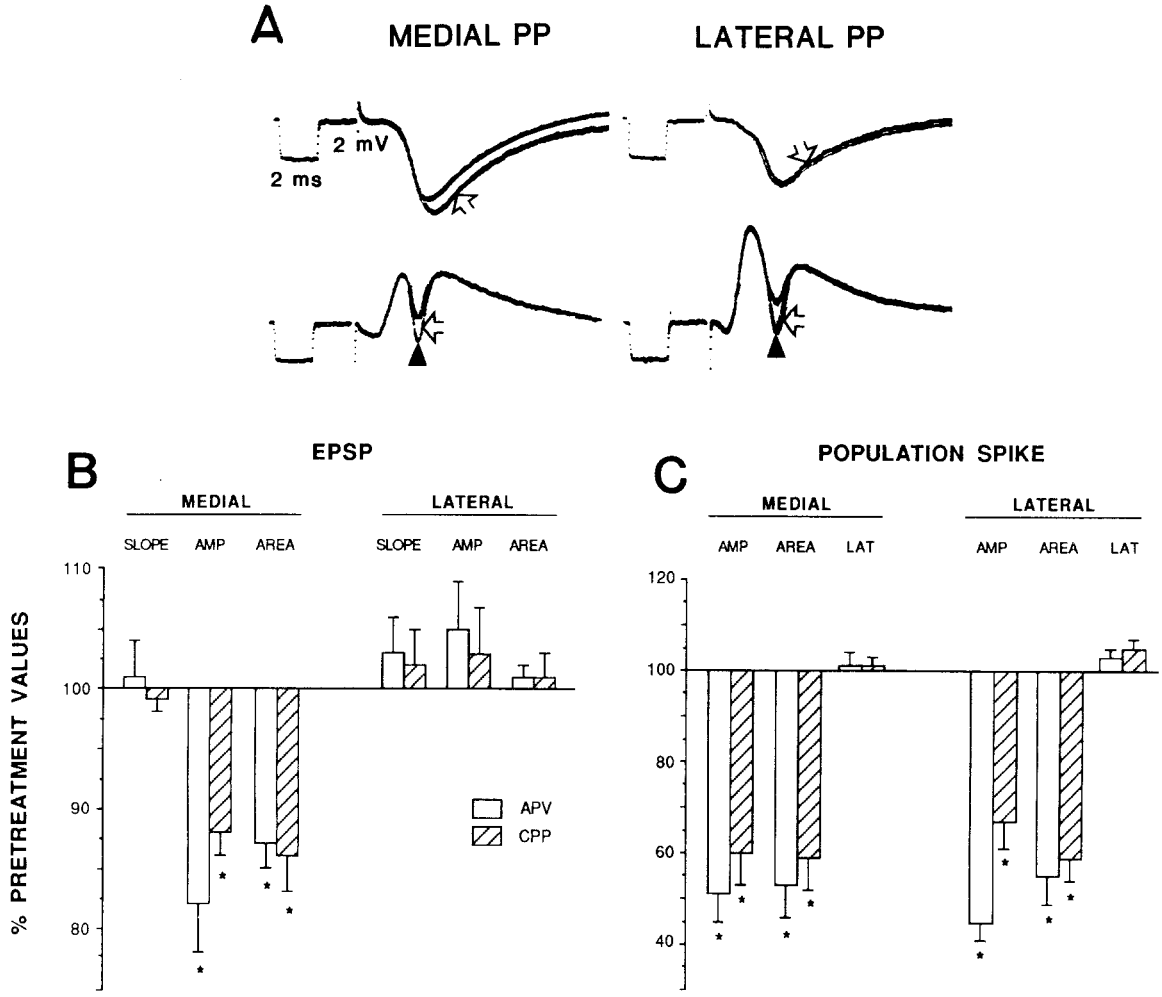

Fig. 2. **A** Effects of 10 μM D(−)APV on medial and lateral PP-evoked responses. The EPSPs (upper row) were recorded in the mid-molecular layer and outer-molecular layer of one slice; population spikes (lower row) were recorded in the granule cell layer of a second slice. Each trace is the digitized average of four responses. Medial PP stimulation was 50 μs, 80 μA for the EPSP and 70 μs, 80 μA for the population spike; lateral PP stimulation was 50 μs, 60 μA for the EPSP and 70 μs, 80 μA for the population spike. The open arrow indicates pre-treatment responses. The solid arrow indicates the peak of the population spike. **B**, **C** Histograms showing means and SEMs of response parameters before and during exposure to 10 μM D(−)APV or 1 μM CPP on medial and lateral PP-evoked (**B**) EPSPs (D(−)APV n=6; CPP n=4) and (**C**) population spikes (D(−)APV n=6; CPP n=3). Measurements during exposure to drugs are expressed as percent of pretreatment values. The asterisk indicates that the difference from pretreatment values is significant ($p<0.05$)

recorded in field CA1 hippocampal neurons (Collingridge et al. 1988; Kauer et al. 1988). NMDA receptor antagonists have been shown to depress synaptic transmission in field CA1 of the hippocampus (Hablitz and Langmoen 1986).

In agreement with our results, it has been shown that activation of the NMDA receptor does not contribute to the intracellularly recorded granule cell EPSP evoked by lateral PP stimulation (Mody et al. 1988). Koerner and Cotman (1981) determined that the potency of D,L-APV on EPSPs recorded in the mid-molecular layer was 12 times higher than on EPSPs recorded in the outer molecular layer, with the stimulating electrode placed in the outer molecular layer. Although we did not test higher concentrations of D(−)APV in order to avoid nonspecific effects, our findings are qualitatively similar to those of Koerner and Cotman (1981). Lambert and Jones (1989) state that there is an NMDA component of the PP-elicited EPSP.

In contrast to our findings and those of Burgard et al. (1989), Crunelli et al. (1982) reported that EPSPs evoked with a stimulating electrode in the medial PP were not affected by iontophoretically applied D,L-APV, although they did not show any data to support this. Also, D(−)APV has been reported to produce no effect on either the medial or lateral PP-evoked EPSPs (Collingridge et al. 1984) or population spikes (Coan et al. 1987). The disparity may result from differences in stimulating electrode placement, as the exact location within the PP was not mentioned in these latter papers. Although we cannot reconcile these studies with our own, we (1) demonstrated specific activation of only the medial or the lateral PP in each slice, (2) compared medial with lateral PP-evoked EPSPs in each slice, (3) compared the effects of the specific NMDA receptor antagonist CPP with those of D(−)APV, and (4) employed concentrations of these

antagonists that had been shown to be pharmacologically relevant in previous studies of LTP and ß-adrenergic LLP. We have previously shown that L(+)APV has no effect on medial PP-evoked responses (Burgard et al. 1989).

Population spikes elicited by activation of either the medial or lateral PP were depressed by D(−)APV and CPP. The decrease of lateral PP-evoked population spikes could not be predicted from the EPSP effects and suggests an additional site of NMDA receptor antagonist activity different from that affecting the EPSP. Indeed, current measurements from isolated CA1 neurons indicate that D(−)APV may enhance $GABA_A$ receptor-mediated inhibition in hippocampal neurons (Stelzer and Wong 1989). In our study, this may have produced an effect in the granule cell layer not specific to either pathway. Nevertheless, antidromic granule cell population spikes have been shown previously not to be affected by D(−)APV (Burgard et al. 1989). Thus, the drug effect does not appear to be directly on the action potential generating mechanism of the granule cells. Alternatively, it might be argued that, at the higher stimulus intensities required to elicit a population spike, depression of the lateral PP-evoked population spike could be explained by current spread to the medial PP. However, this is extremely unlikely, as the medial and lateral PP-evoked population spikes were depressed by about the same amount. Furthermore, the difference between the latencies was not changed by D(−)APV, as would be expected if the longer latency lateral PP response were contaminated by the shorter latency medial PP response (Abraham and McNaughton 1984).

Medial and lateral PP terminals differ anatomically (Hjorth-Simonsen 1972; Hjorth-Simonsen and Jeune 1972; Steward 1976) and in their response to pharmacological agents (Koerner and Cotman 1981; Lanthorn and Cotman 1981; Dahl and Sarvey 1989; Kahle and Cotman 1989). These differences also have physiological correlates (Wilson and Steward 1978; McNaughton 1980; Deadwyler et al. 1981; Abraham and McNaughton 1984). It is interesting that (1) D(−)APV and CPP specifically depress medial PP-evoked EPSPs, (2) ß-adrenergic agonist-induced LLP is limited to medial PP-evoked responses, and (3) D(−)APV and CPP block ß-adrenergic agonist-induced LLP. In contrast, LTP can be elicited in either the medial PP or the lateral PP (McNaughton and Barnes 1977; Abraham and Goddard 1983; Winson and Dahl 1986). However, LTP in the dentate gyrus is generally thought to require activation of the NMDA receptor subtype (Morris et al. 1986; Wigström et al. 1986; Errington et al. 1987). Perhaps the lateral PP is analogous to the granule cell mossy fiber projection to CA3 pyramidal cells; LTP of the mossy fiber response is not sensitive to D(−)APV, whereas LTP of CA3 associational fibers is blocked by this NMDA receptor antagonist (Harris and Cotman 1986). It remains to be seen whether LTP in the lateral PP-granule cell synapses can be prevented by NMDA receptor antagonists.

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References

Abraham WC, Goddard GV (1983) Asymmetric relationships between homosynaptic long-term potentiation and heterosynaptic long-term depression. Nature 305: 717–719

Abraham WC, McNaughton N (1984) Differences in synaptic transmission between medial and lateral components of the perforant path. Brain Res 303: 251–260

Burgard EC, Decker G, Sarvey JM (1989) NMDA receptor antagonists block norepinephrine-induced long-lasting potentiation and long-term potentiation in rat dentate gyrus. Brain Res 482: 351–355

Coan EJ, Newland CF, Collingridge GL (1987) Synaptic activation of NMDA receptors in medial and lateral perforant pathways in the absence of magnesium ions. Neurol Neurobiol 24: 353–356

Collingridge GL, Kehl SJ, McLennan H (1984) The action of some analogues of the excitatory amino acids in the dentate gyrus of the rat. Can J Physiol Pharmacol 62: 424–429

Collingridge, GL, Herron CE, Lester RAJ (1988) Synaptic activation of N-methyl-D-aspartate receptors in the Schaffer collateral-commissural pathway of rat hippocampus. J Physiol (Lond) 399: 283–300

Cotman CW, Monaghan DT, Ottersen OP, Storm-Mathisen J (1987) Anatomical organization of excitatory amino acid receptors and their pathways. Trends Neurosci 10: 273–280

Crunelli V, Forda S, Collingridge GL, Kelly JS (1982) Intracellular recorded synaptic antagonism in the rat dentate gyrus. Nature 300: 450–452

Dahl D, Sarvey JM (1989) Norepinephrine induces pathway-specific long-lasting potentiation and depression in the hippocampal dentate gyrus. Proc Natl Acad Sci USA 86: 4776–4780

Deadwyler SA, West MO, Robinson JH (1981) Entorhinal and septal inputs differentially control sensory-evoked responses in rat dentate gyrus. Science 211: 1181–1183

Errington, ML, Lynch, MA, Bliss, TVP (1987) Long-term potentiation in the dentate gyrus: induction and increased glutamate release are blocked by D(−) aminophosphonovalerate. Neurosci 20: 279–284

Hablitz JJ, Langmoen IA (1986) N-methyl-D-aspartate receptor antagonists reduce synaptic excitation in the hippocampus. J Neurosci 6: 102–106

Harris EW, Cotman CW (1986) Long-term potentiation of guinea pig mossy fiber responses is not blocked by N-methyl-D-aspartate antagonists. Neurosci Lett 70: 132–137

Hjorth-Simonsen A (1972) Projection of the lateral part of the entorhinal area to the hippocampus and fascia dentata. J Comp Neurol 146: 219–232

Hjorth-Simonsen A, Jeune B (1972) Origin and termination of the hippocampal perforant path in the rat studied by silver impregnation. J Comp Neurol 144: 215–232

Kahle JS, Cotman CW (1989) Carbachol depresses synaptic responses in the medial but not the lateral perforant path. Brain Res 482: 159–163

Kauer JA, Malenka, RC, Nicoll RA (1988) A persistent postsynaptic modification mediates long-term potentiation in the hippocampus. Neuron 1: 911–917

Koerner JF, Cotman CW (1981) Micromolar L-2-amino-4-phosphonobutyric acid selectively inhibits perforant pathway synapses from lateral entorhinal cortex. Brain Res 216: 192–198

Lambert JDC, Jones RSG (1989) Activation of N-methyl-D-aspartate receptors contributes to the EPSP at perforant path synapses in the rat dentate gyrus in vitro. Neurosci Lett 97: 323–328

Lanthorn TH, Cotman CW (1981) Baclofen selectively inhibits excitatory synaptic transmission in the hippocampus. Brain Res 225: 171–178

McNaughton BL, Barnes CA (1977) Physiological identification and analysis of dentate granule cell response to stimulation of the medial and lateral perforant pathways in the rat. J Comp Neurol 175: 439–454

McNaughton BL (1980) Evidence for two physiologically distinct perforant pathways to the fascia dentata. Brain Res 199: 1–19

Mody I, Stanton PK, Heinemann U (1988) Activation of N-methyl-D-aspartate receptors parallels changes in cellular and synaptic properties of dentate gyrus granule cells after kindling. J Neurophysiol 59: 1033–1054

Morris RGM, Anderson E, Lynch GS, Baudry M (1986) Selective impairment of learning and blockade of long-term potentiation by an N-methyl-D-aspartate receptor antagonist, AP5. Nature 319: 774–776

Sarvey JM, Burgard EC, Decker G (1989) Long-term potentiation: studies in the hippocampal slice. J Neurosci Meth 28: 109–124

Scharfman HE and Sarvey JM (1985) γ-Aminobutyrate sensitivity does not change during long-term potentiation in rat hippocampal slices. Neuroscience 15: 695–702

Stanton PK, Sarvey JM (1987) Norepinephrine regulates long-term potentiation of both the population spike and dendritic EPSP in hippocampal dentate gyrus. Brain Res Bull 18: 115–119

Stelzer A, Wong RKS (1989) $GABA_A$ responses in hippocampal neurons are potentiated by glutamate. Nature 337: 171–173

Steward O (1976) Topographic ogranization of the projections from the entorhinal area to the hippocampal formation in the rat. J Comp Neurol 167: 285–314

White WF, Nadler JV, Hamberger A, Cotman CW (1977) Glutamate as transmitter of hippocampal perforant path. Nature 270: 356–357

Wigström H, Gustafsson B, Huang Y-Y (1986) Mode of action of excitatory amino acid receptor antagonists on hippocampal long-lasting potentiation. Neuroscience 17: 1105–1115

Wilson RC, Steward O (1978) Polysynaptic activation of the dentate gyrus of the hippocampal formation: an olfactory input via the lateral entorhinal cortex. Exp Brain Res 33: 523–534

Winson J, Dahl D (1986) Long-term potentiation in the dentate gyrus: induction by asynchronous volleys in separate afferents. Science 234: 985–988