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# Monoamine modulation of the synaptic inhibition in the hippocampus

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**Abstract.** Changes in the strength of synaptic inhibition have profound effects on the functions of cortical neurones. Accumulating evidence suggests that inhibitory synaptic transmission may be the target of action of monoamines. In the hippocampal dentate gyrus, norepinephrine and serotonin (5-HT) have multiple direct and indirect actions on the presumed inhibitory hilar neurones. These effects are mediated through distinct mechanisms and signalled by different receptor subtypes. The predominant effects of norepinephrine are excitatory and are mediated by ß-adrenergic receptors. Accordingly, both the $GABA_A$- and $GABA_B$-receptor-mediated inhibition in granule cells is enhanced by activation of the ß-adrenergic receptor. 5-HT has more complex effects inhibiting a subpopulation of the hilar neurones and exciting other hilar cells. Study of the effects of 5-HT on inhibition in granule cells revealed that 5-HT enhanced Cl-IPSPs and blocked K-IPSPs. These results are in line with the suggestion that Cl- and K-IPSPs in granule cells are generated by two distinct populations of inhibitory neurones.

**Key words:** synaptic inhibition, norepinephrine, 5-HT, hilar neurones, dentate gyrus, hippocampus

Review

## INTRODUCTION

Normal functioning of the central nervous system requires the existence of a delicate balance between excitation and inhibition. Relatively small changes in the GABAergic neurotransmission can have striking effects on the functional state of nerve cells, resulting in profound alterations of neuronal excitability. Recordings from cortical neurones indicate the presence of spontaneous inhibitory potentials (IPSPs), mediated by $GABA_A$ receptors through an opening of $Cl^-$ channels (Alger and Nicoll 1980). Most of this activity stems from an action potential firing of inhibitory neurones (Miles and Wong 1987). The perpetual barrage of spontaneous GABAergic activity is likely to be a critical factor in regulation of the neuronal excitability and the target of action of several neuroactive compounds.

A growing body of evidence suggests that norepinephrine (NE) and serotonin (5-hydroxytryptamine; 5-HT) may modulate the inhibitory synaptic transmission in the hippocampus (Madison and Nicoll 1988, Doze et al. 1991, Ropert and Guy 1991, Bijak and Misgeld 1995). The hippocampus receives a prominent noradrenergic innervation from the locus coeruleus (Amaral and Sinnamon 1977, Moore and Bloom 1979). Noradrenergic axons form a fairly dense plexus within the hilus of the dentate gyrus (Blackstad et al. 1967, Oleskevich et al. 1989). It has been shown that in the hilus tyrosine hydroxylase-labelled terminals form synapses with GABA-labelled perikarya (Milner and Bacon 1989). The hippocampus is also a principal target of serotonergic afferents which stem from the midbrain raphe nuclei (Parent et al. 1981). Serotonin-containing fibres innervate extensively the stratum lacunosum moleculare of the CA1 and CA3 regions and the dentate hilus (Freund et al. 1990). GABAergic interneurones are the major postsynaptic target of raphe afferents in the rat dentate gyrus (Freund et al. 1990, Halasy et al. 1992).

This report reviews studies that investigated the effects of NE and 5-HT on the GABA-mediated inhibition in the dentate gyrus circuitry. The major

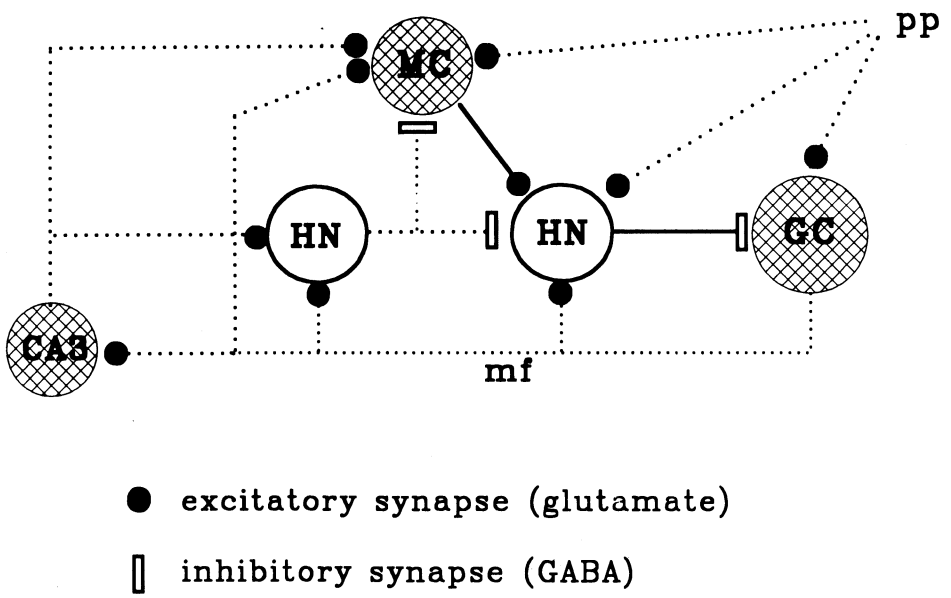


Fig. 1. Schematic diagram of the local circuitry in the rat hippocampal dentate gyrus. The input from the entorhinal cortex (perforant path, pp) activates synaptically granule cells (GC) and both inhibitory (HN) and excitatory (MC) interneurones in the dentate gyrus. The granule cell output - *via* mossy fibres (mf)- excites pyramidal cells (CA3). Mossy fibre collaterals also activate local circuit interneurones (HN and MC). Inhibitory interneurones synapse on granule cells and on local circuit interneurones (HN and MC). Excitatory mossy cells synapse on local inhibitory interneurones. The additional excitatory input is provided by CA3 cell axon collaterals. The dotted lines represent synaptic connections not considered in the present study. The hatched circles represent excitatory glutamatergic cells; open circles inhibitory GABAergic cells.

questions were: (1) how NE and 5-HT affect inhibitory interneurones in the hilus of the dentate gyrus; (2) how $GABA_A$- and $GABA_B$-receptor mediated IPSPs in the target neurones (granule cells) are affected by NE and 5-HT; (3) whether the action on interneurones can be correlated with the effects of NE and 5-HT on synaptic IPSPs in granule cells.

A simplified scheme on Fig. 1 shows that multiple sites exist for the effects of NE and 5-HT on the GABA-mediated synaptic inhibition in the dentate gyrus circuitry. The activity of inhibitory interneurones (HN) may be affected directly by an action on their membrane potential and/or firing properties. Another site of modulation of the synaptic inhibition is the excitatory input to inhibitory neurones provided -among others- by mossy cells (MC). The other potential site of modulation are GABAergic terminals.

## INHIBITORY HILAR NEURONES

Studies of electrophysiological and pharmacological properties of hippocampal neurones have been concentrated on principal excitatory cells (pyramidal and granule cells). Inhibitory interneurones, which are the other major cell type in the hippocampus, have not been so well characterized, because it is difficult to obtain intracellular recordings from these sparsely distributed elements. Interneurones account for only 10-12% of the total cell population in the hippocampus proper (Olbrich and Braak 1985), but their axons ramify extensively in the pyramidal and granule cell layers (Buckmaster and Schwartzkroin 1995). In the hilar region, about 60% of the neurones stain for glutamate decarboxylase (GAD), a rate limiting enzyme of GABA synthesis (Ribak et al. 1978, Seress and Ribak 1983). These GABAergic neurones innervate granule cells and other interneurones in the hilus (Misgeld and Frotscher 1986, Halasy and Somogyi 1993) and are likely to be in part responsible for the barrage of inhibitory postsynaptic potentials recorded in granule cells (Müller and Misgeld 1990, Misgeld et al. 1992a).

Intracellular recordings from the hippocampal interneurones which were subsequently identified morphologically by intracellular staining as aspiny or sparcely spiny, revealed that interneurones had several distinctive electrophysiological characteristics such as, brief-duration action potentials with large fast after-hyperpolarizations (AHPs), outward rectification and little spike frequency adaptation (Schwartzkroin and Mathers 1978, Kawaguchi and Hama 1987, Buckmaster and Schwartzkroin 1995). A population of neurones impaled in the hilar region had similar properties (Fig. 2;

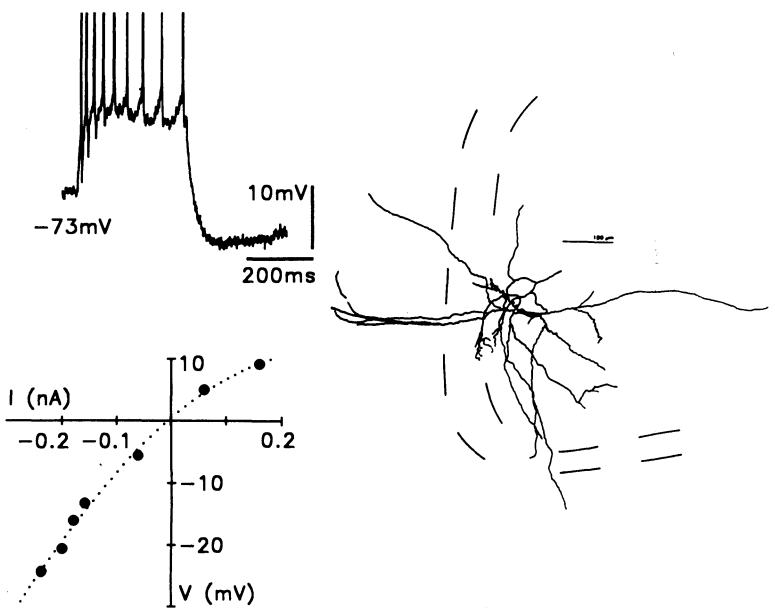


Fig. 2. Electrophysiological and morphological characteristics of the presumed inhibitory hilar neurones. A hilar neurone displaying little spike frequency adaptation (current pulse 0.4 nA) and a characteristic I/V curve. A camera lucida drawing of another hilar neurone exhibiting similar electrophysiological properties. The hilar neurone was stained intracellularly with horseradish peroxidase. The border of the granule cell layer is indicated by a broken line.

Misgeld and Frotscher 1986, Scharfman et al. 1990, Misgeld et al. 1992b). In those neurones, the action potentials elicited by current pulses had pronounced AHPs (10 mV) and little discharge frequency adaptation. The input resistance of the presumed inhibitory hilar neurones showed an outward rectification.

## EFFECTS OF NE ON THE PRESUMED INHIBITORY HILAR NEURONES

### Effects on the resting membrane potential

Most of the fast spiking hilar neurones showed no changes in membrane potential when NE (2-5 μM) was applied. In some neurones, NE induced either a hyperpolarization or a depolarization, but those effects were small, rarely exceeding 3 mV in amplitude. The depolarization induced by NE was accompanied by an increase in the input resistance and could be mimicked by the ß-adrenergic agonist isoproterenol (0.1-1 μM). The hyperpolarization could be mimicked by the $\alpha_1$-adrenergic agonist phenylephrine and by the $\alpha_2$-adrenergic agonist clonidine. Those effects were fairly similar to the described action of NE on hippocampal pyramidal neurones (Madison and Nicoll 1986).

### Effects on the slow afterhyperpolarization

Application of NE reduced the amplitude and duration of slow AHP following single action potentials or a train of action potentials. The slow AHP results from the activation of calcium-activated potassium conductance, and was shown to be reduced by NE in principal hippocampal neurones (Haas and Konnerth 1983, Madison and Nicoll 1986). To determine the receptor subtype involved in the NE-induced effect on the AHP in hilar neurones, specific noradrenergic receptor agonists were employed. The ß-noradrenergic agonist isoproterenol blocked the slow AHP (Fig. 3A), while the α-noradrenergic agonists phenylephrine and clonidine were ineffective. The ß-receptor antagonist propranolol markedly attenuated the NE-induced blockade of AHP. The above results indicate that, like in principal cells, NE reduces the AHP in the presumed inhibitory hilar neurones by activating the ß-noradrenergic receptor.

### Effects on the firing properties of hilar neurones

It was shown that NE altered the firing properties of hippocampal neurones by blocking their accommodation (Haas and Konnerth 1983, Madison and

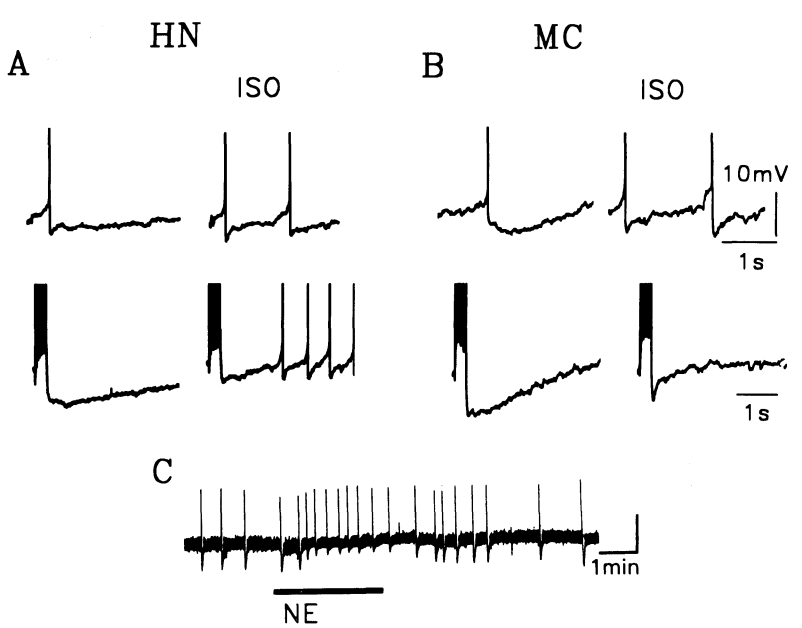


Fig. 3. The effect of isoproterenol (ISO, 1 μM) on afterhyperpolarization (AHP) in (A) a presumed inhibitory hilar neurone (resting membrane potential, RMP -61 mV) and (B) a mossy cell (RMP -63 mV). Isoproterenol reduced the slow AHP following a single action potential and a train of action potentials induced by injection of a depolarizing current pulse (0.5 nA, 400 ms) and increased the frequency of spontaneous discharges. C, the effect of norepinephrine (NE, 5 μM) on burst discharges recorded in a hilar neurone (RMP -70 mV) in the presence of picrotoxin and bicuculline (50 μM). NE was applied at the time indicated by the bar below the record.

Nicoll 1986). In contrast to other hippocampal neurones, fast spiking hilar neurones did not show spike frequency adaptation and NE did not change their firing induced by the depolarizing current pulse (Fig. 4A). However, due to the effect on the AHP, the spontaneous discharge activity of hilar neurones was enhanced in the presence of either NE or the ß-adrenergic receptor agonist isoproterenol (Fig. 3A). NE and isoproterenol also increased the frequency of burst discharges recorded in hilar neurones in the presence of $GABA_A$ receptor antagonists (Fig. 3C).

## EFFECTS OF NE ON THE SYNAPTIC EXCITATION OF INHIBITORY INTERNEURONES

Hilar neurones receive excitatory synapses from the perforant path, mossy fibres of granule cells, axons of mossy cells and also from axon collaterals of CA3 neurones (Fig. 1; Lübbers and Frotscher 1987, Müller and Misgeld 1991). It has been shown that the glutamatergic synaptic transmission plays a role in synchronization of inhibitory hilar neurones (Bijak and Misgeld 1993). Entorhinal neurones, which are the cells of origin for the perforant path - a main excitatory input to the dentate gyrus - are not contained in the slice preparation used in these studies. Mossy cells, granule cells and CA3 neurones are preserved in the transverse hippocampal slice (Fig. 1), hence, their excitatory input to inhibitory interneurones in the dentate gyrus may be affected by NE application.

Mossy cells, which represent the most abundant cell type in the hilus (Amaral 1978, Ribak et al. 1985) can be distinguished from other neurones in the hilar region by their morphological and electrophysiological properties. The cell body of mossy cells is multipolar, and somata as well as proximal dendrites are covered by thorny excrescences (Fig. 5). Electrophysiologically mossy cells could be distinguished from the presumed inhibitory hilar neurones by spike frequency adaptation, variable afterpotentials following single action potentials, and inward rectification (Fig. 5; Scharfman and

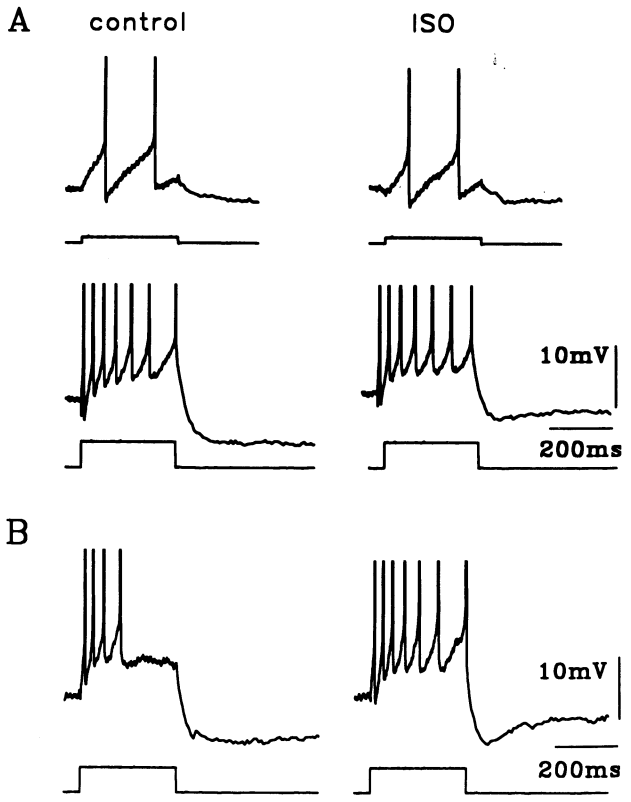


Fig. 4. The effect of isoproterenol (ISO, 1 µM) on the train of action potentials in (A) a presumed inhibitory hilar neurone (RMP -61 mV, current pulses 0.05 nA upper trace and 0.5 nA lower trace, 400 ms) and (B) a mossy cell (RMP -63 mV, current pulse 0.5 nA). In the hilar neurone, the number of action potentials induced by the current pulse was not changed by isoproterenol, as that cell type displayed no accommodation. In the mossy cell, isoproterenol removed accommodation of the discharge induced by the current pulse.

Schwartzkroin 1988, Misgeld et al. 1992b, Bijak and Misgeld 1995).

Like in the presumed inhibitory hilar neurones, NE (2-10 µM) had only small effect on the resting membrane potential but it strongly altered the firing properties of mossy cells. NE and isoproterenol reversibly reduced the amplitude and duration of slow AHP following single action potentials or a train of action potentials (Fig. 3B). Furthermore, activation of ß-adrenergic receptors decreased the discharge frequency accommodation (Fig. 4B). All the above-described effects could contribute to the observed increase in the frequency of spontaneous discharges of mossy cells. This, in turn, would result in en-

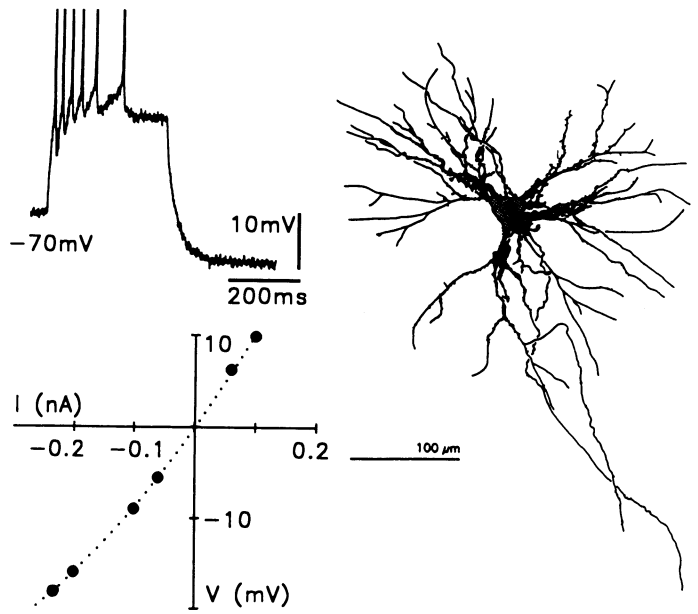


Fig. 5. Electrophysiological and morphological characteristics of mossy cells. A mossy cell displaying spike frequency adaptation (current pulse 0.4 nA), and a characteristic I/V curve. A camera lucida drawing of another mossy cell exhibiting similar electrophysiological properties. The cell was stained intracellularly with horseradish peroxidase.

hancement of the spontaneous excitatory postsynaptic potentials (EPSPs), recorded in the presumed inhibitory hilar neurones. In fact, NE and isoproterenol significantly enhanced the frequency of spontaneous EPSPs recorded in hilar neurones (Fig. 6).

The passive and active membrane properties of CA3 pyramidal neurones and granule cells were affected by NE and the ß-adrenergic agonist isoproterenol in a manner similar to that observed in mossy cells. However, the discharge rate was increased in CA3 neurones, but not in granule cells, due to the fact that in the latter cell type the resting membrane potential (around -80 mV) was far away from the spiking threshold.

## EFFECT OF NE ON INHIBITORY POSTSYNAPTIC POTENTIALS OF GRANULE CELLS

The inhibitory innervation of granule cells of the hippocampal dentate gyrus comes from at least five types of GABAergic neurones which specifically innervate the spatially segregated parts of granule cells (Halasy and Somogyi 1993). Part of those inhibitory neurones were found in the hilar region of the dentate gyrus (Misgeld et al. 1992a); therefore, the observed increase in discharge rate of hilar neurones induced by activation of ß-adrenergic receptors should be accompanied by an enhancement of the synaptic inhibition recorded in granule cells.

Spontaneous $GABA_A$ receptor-mediated IPSPs can be recorded in granule cells with KCl-filled electrodes. These IPSPs are mostly action potential--dependent events, since their frequency and amplitude are substantially reduced by TTX (Bijak and Misgeld 1995). NE and isoproterenol markedly increased the frequency of the Cl-IPSPs. The recording in the presence of excitatory amino acid receptor antagonists ensures that spontaneous IPSPs stem from the intrinsic activity of interneurones. Under such pharmacological conditions the

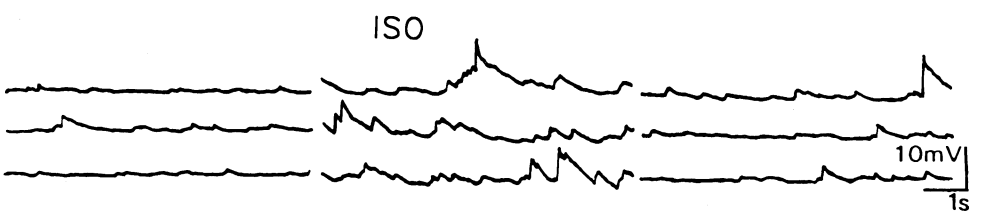


Fig. 6. The effect of isoproterenol (ISO, 0.1 µM) on spontaneous EPSPs recorded in a hilar neurone (RMP -70 mV) in the presence of picrotoxin and bicuculline (50 µM).

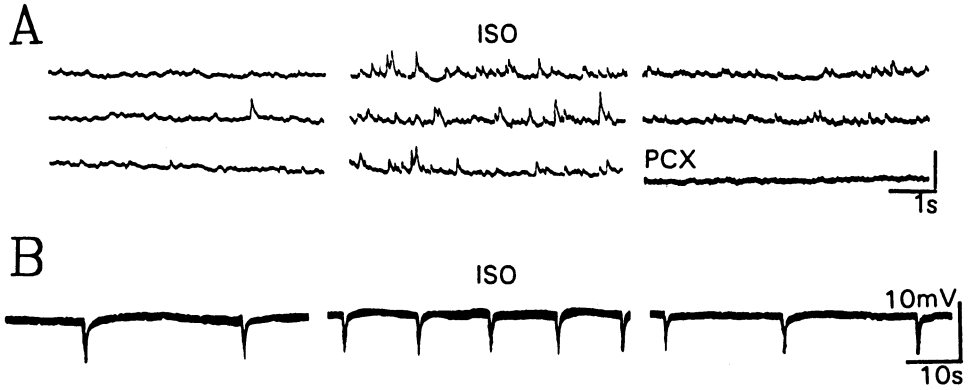


Fig. 7. The effect of isoproterenol (ISO, 0.1 μM) on spontaneous IPSPs recorded in a granule cell. A, a granule cell (RMP -80 mV) was recorded in the presence of CNQX (5 μM) with a KCl-filled electrode; Cl-IPSPs are seen as depolarizing events. Application of isoproterenol caused a marked increase in the frequency of spontaneous IPSPs; that effect was reversed upon washing isoproterenol off the bath. Addition of picrotoxin (PCX, 20 μM) blocked all the spontaneous IPSPs. B, in another granule cell (depolarized by current injection to -65 mV) the frequency of K-IPSPs recorded in the presence of picrotoxin and bicuculline (50 μM) was increased by isoproterenol.

frequency of monosynaptic spontaneous IPSPs was significantly increased by NE and isoproterenol (Fig. 7A).

NE and isoproterenol also enhanced the frequency of tetrodotoxin-resistant IPSPs indicating that the GABAergic transmission in the dentate gyrus is also enhanced by a direct effect of NE on the GABA release (Bijak and Misgeld 1995). Likewise, NE acting on ß-receptors augments the action potential-independent IPSPs in hippocampal pyramidal cells (Bijak et al. 1991) and in cerebellar neurones (Llano and Gerschenfeld 1993).

The stimulation-induced synaptic inhibition of hippocampal neurones consists of two separate components: an early IPSP, induced by a Cl-conductance increase and mediated by $GABA_A$ receptors, and a late IPSP, induced by a K-conductance increase and mediated by $GABA_B$ receptors (for rev. see Misgeld et al. 1995). The spontaneous,

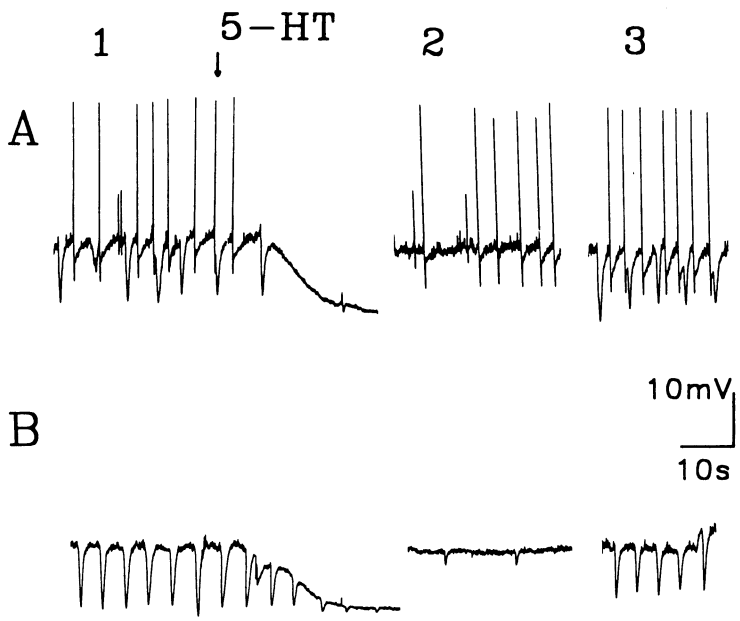


Fig. 8. The effect of 5-HT (5 μM) on giant IPSPs in a granule cell (RMP -80 mV; depolarized to -70 mV by current injection, recorded in the presence of CNQX 10 μM)). (A1) 4-AP induced giant IPSPs in the granule cell. Recording was obtained using a KCl-filled microelectrode to make Cl-IPSPs depolarizing and K-IPSPs hyperpolarizing. (A2) 5-HT hyperpolarized the cell and selectively blocked K-IPSPs. On washout (3) both Cl- and K-IPSPs were recorded. (B) In the presence of picrotoxin (50 μM) 4-AP induced only K-IPSPs. Those IPSPs were reversibly blocked by 5-HT. During the 5-HT-mediated hyperpolarization (A2 and B2), membrane potential was manually clamped back to predrug membrane potential to show that the effect was independent from membrane potential. 1, control; 2, during 5-HT application; 3, washout 8 min.

$GABA_B$ receptor- mediated, K-dependent IPSPs can be recorded in granule cells when inhibitory neurones are driven to burst discharges (Müller and Misgeld 1990, 1991, Misgeld et al. 1992b). Accordingly, in the presence of the $GABA_A$ receptor antagonist picrotoxin, K-IPSPs occur in some granule cells. The frequency of these K-IPSPs is increased by NE and isoproterenol (Fig. 7B).

## EFFECT OF 5-HT ON THE PRESUMED INHIBITORY HILAR NEURONES AND ON INHIBITION OF GRANULE CELLS

5-HT had two separate and distinct effects on the resting membrane potential of fast spiking hilar neurones: it induced either profound hyperpolarization, or slight depolarization in a small population of hilar neurones. The 5-HT-induced hyperpolarization was mediated by an increase in the K-conductance (Ghadimi et al. 1994) and it resembled the hyperpolarizing response to 5-HT, recorded in principal hippocampal cells (Andrade and Nicoll 1987). The depolarizing action of 5-HT could also be observed in pyramidal neurones, but only after blockade of $5\text{-HT}_{1A}$ receptors which mediate the hyperpolarizing response (Colino and Halliwell 1987).

5-HT increased the firing of hilar neurones which were not hyperpolarized by that agent. The activity of the hilar neurones that were hyperpolarized by 5-HT was inhibited. Similarly, the burst discharges induced by the convulsant 4-AP in hilar neurones were either enhanced or inhibited, depending on the degree of the cell hyperpolarization by 5-HT (Ghadimi et al. 1994).

4-AP induced giant Cl- and K-mediated IPSPs in granule cells (Müller and Misgeld 1991). 5-HT blocked the K-mediated IPSPs (Fig. 8); it either did not affect the Cl-dependent IPSPs (Fig. 8A) or increased their frequency (Ghadimi et al. 1994). Under normal pharmacological conditions the spontaneous Cl-IPSPs recorded in granule cells were also enhanced by 5-HT. The effect of 5-HT on hilar neurones and IPSPs in granule cells corroborated the assumption that different inhibitory cells generated Cl- and K-dependent IPSPs (Fig. 9; for rev. see Misgeld et al. 1995).

## DISCUSSION

The results presented above indicate that NE and 5-HT enhance the $GABA_A$ receptor-mediated synaptic inhibition in the dentate gyrus. While acting on the ß-adrenergic receptors of hilar neurones, NE increases their excitability by diminishing AHP and by producing a barrage of EPSPs and slight depolarization. The enhanced excitability of hilar neurones may contribute to the increased inhibition observed concurrently in granule cells. Although hilar neurones are a heterogenous cell group (Amaral 1978), the effects of NE are fairly uniform and, in many respects, comparable to those reported for pyramidal and granule cells (Haas and Konnerth 1983, Madison and Nicoll 1986, Haas and Rose 1987). Such a uniform action of NE on the hilar neurones is in line with the NE-induced enhancement of both $GABA_A$- and $GABA_B$-mediated inhibition. The effects of 5-HT suggest that neurones which mediate

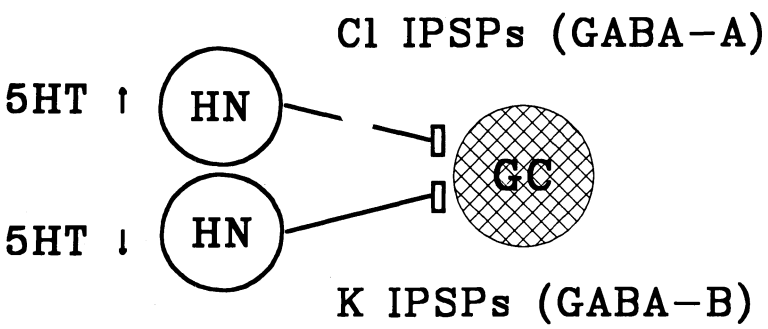


Fig. 9. Summary of the effects of 5-HT in the dentate network. Different hilar neurones generate $GABA_A$ and $GABA_B$-receptor mediated synaptic potentials in granule cells. 5-HT hyperpolarized and inhibited hilar neurones which generated $GABA_B$-receptor mediated inhibition. 5-HT either had no effect or excited hilar neurones which generated $GABA_A$-receptor mediated inhibition.

the $GABA_B$ receptor-dependent inhibition are inhibited, while at least part of the neurones that mediate the $GABA_A$ receptor-dependent inhibition are activated by 5-HT.

The present paper shows that in order to understand the effect of monoamines on the neuronal network, their action on single elements of the network as well as on mutual interactions between these elements should be taken into account.

A number of *in vivo* studies have examined the effect of stimulation of NE and 5-HT centres on the spontaneous discharge of hippocampal neurones (Segal and Bloom 1974, 1976, Segal 1975, Curet and de Montigny 1988) and the principal conclusion from these reports is that the synaptically released NE and 5-HT inhibit neuronal firing. The inhibitory effects of NE *in vivo* are most frequently ascribed to the action of NE on a ß-adrenergic receptor (Segal and Bloom 1974, Bevan et al. 1977). In contrast, the ß-adrenoceptor activation *in vitro* mediates direct excitatory effects of NE on pyramidal and granule cells (Madison and Nicoll 1986, Haas and Rose 1987). Enhancement of the synaptic inhibition by NE *via* its action on a ß-adrenergic receptor may underlie the described *in vivo* noradrenergic inhibition of the hippocampal cell activity.

The hippocampus plays an important role in neuronal plasticity, learning and memory, as well as in seizure activity. In the hippocampus, dentate granule neurones act as a relay station: they receive the input from the entorhinal cortex *via* the perforant pathway and send the output to CA3 and CA1 neurones *via* a mossy fibre projection. Thus the activity of granule cells plays an important role in regulating the functional state of the hippocampal network. The studies of the dentate have clearly shown that the circuitry of the fascia dentata is quite complex, and that interactions between granule cells and other cell types may be crucial for regulation of the granule cell output. Therefore agents that modulate the synaptic inhibition in this area, such as NE or 5-HT, may be involved in regulation of the information transfer through the dentate gyrus.

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**REFERENCES**

Alger B.E., Nicoll R.A. (1980) Spontaneous inhibitory postsynaptic potentials in hippocampus: mechanism for tonic inhibition. Brain Res. 200: 195-200.

Amaral D.G. (1978) A Golgi study of cell types in the hilar region of the hippocampus in the rat. J. Comp. Neurol. 182: 851-914.

Amaral D.G., Sinnamon H.M. (1977) The locus coeruleus: neurobiology of a central noradrenergic nucleus. Prog. Neurobiol. 9: 147-196.

Andrade R., Nicoll R.A. (1987) Pharmacologically distinct actions of serotonin on single pyramidal neurones of the rat hippocampus recorded in vitro. J. Physiol. (Lond.) 394: 99-124.

Bevan P., Bradshaw C.M., Szabadi E. (1977) The pharmacology of adrenergic neuronal responses in the cerebral cortex: evidence for excitatory α- and inhibitory ß-receptors. Br. J. Pharmacol. 59: 635-641.

Bijak M., Misgeld U. (1993) Role of glutamatergic synaptic transmission in synchronized discharges of hilar neurons in guinea pig hippocampal slices. Neurosci. Lett. 163: 235-238.

Bijak M., Misgeld U. (1995) Adrenergic modulation of hilar neuron activity and granule cell inhibition in the guinea-pig hippocampal slice. Neuroscience 67: 541-550.

Bijak M., Misgeld U., Müller W. (1991) Interaction of noradrenergic and cholinergic agonists with ligands increasing K-conductance of guinea pig hippocampal neurons, in vitro. Eur. J. Neurosci. 3: 473-479.

Blackstad T.W., Fuxe K., and Hökfelt T. (1967) Noradrenaline nerve terminals in the hippocampal region of the rat and the guinea pig. Z. Zellforsch. 78: 463-473.

Buckmaster P.S., Schwartzkroin P.A. (1995) Interneurons and inhibition in the dentate gyrus of the rat in vivo. J. Neurosci. 15: 774-789.

Colino A., Halliwell J.V. (1987) Differential modulation of three separate K-conductances in hippocampal CA1 neurons by serotonin. Nature 328: 73-77.

Curet O., de Montigny C. (1988) Electrophysiological characterization of adrenoceptors in the rat dorsal hippocampus. II. Receptors mediating the effect of synaptically released norepinephrine. Brain Res. 475: 47-57.

Doze V.A., Cohen G.A., Madison D.V. (1991) Synaptic localization of adrenergic disinhibition in the rat hippocampus. Neuron 6: 889- 900.

Freund T.F., Gulyas A.I., Acsady L., Gorcs T., Tóth K. (1990) Serotonergic control of the hippocampus via local inhibitory interneurons. Proc. Natl. Acad. Sci. USA 87: 8501-8505.

Ghadimi B.M., Jarolimek W., Misgeld U. (1994) Effects of serotonin on hilar neurons and granule cell inhibition in the guinea pig hippocampal slice. Brain Res. 633: 27-32.

Haas H.L., Konnerth A. (1983) Histamine and noradrenaline decrease calcium-activated potassium conductance in hippocampal pyramidal cells. Nature 302: 432-434.

Haas H.L., Rose G. M. (1987) Noradrenaline blocks potassium conductance in rat dentate granule cells in vitro. Neurosci. Lett. 78: 171-174.

Halasy K., Miettinen R., Szabat E., Freund T.F. (1992) GABAergic interneurons are the major postsynaptic targets of median raphe afferents in the rat dentate gyrus. Eur. J. Neurosci. 4: 144-153.

Halasy K., Somogyi P. (1993) Subdivisions in the multiple GABAergic innervation of granule cells in the dentate gyrus of the rat hippocampus. Eur. J. Neurosci. 5: 411-429.

Kawaguchi Y., Hama K. (1987) Two subtypes of non-pyramidal cells in rat hippocampal formation identified by intracellular recording and HRP injection. Brain Res. 411: 190-195.

Llano I., Gerschenfeld H.M. (1993) ß-Adrenergic enhancement of inhibitory synaptic activity in rat cerebellar stellate and purkinje cells. J. Physiol. (London) 468: 201-224.

Lübbers K., Frotscher M. (1987) Fine structure and synaptic connections of identified neurons in the rat fascia dentata. Anat. Embryol. 177: 1-14.

Madison D.V., Nicoll R.A. (1986) Actions of noradrenaline recorded intracellularly in rat hippocampal CA1 pyramidal neurones, in vitro. J. Physiol. (Lond.) 372: 221-244.

Madison D.V., Nicoll R.A. (1988) Norepinephrine decreases synaptic inhibition in the rat hippocampus. Brain Res. 442: 131-138.

Miles R., Wong R.K.S. (1987) Inhibitory control of local excitatory circuits in the guinea-pig hippocampus. J. Physiol. (Lond.) 388: 611-629.

Milner T. A., Bacon C. E. (1989) GABAergic neurons in the rat hippocampal formation: ultrastructure and synaptic relationships with catecholaminergic terminals. J. Neurosci 9: 3410-3427.

Misgeld U., Bijak M., Brunner H. (1992a) Granule cell inhibition and the activity of hilar neurons. In: The dentate gyrus and its role in seizures (Eds. C.E. Ribak, C.M. Gall and I. Mody). Epilepsy Res. Suppl. 7. Elsevier, Amsterdam, p. 113-118.

Misgeld U., Bijak M., Brunner H., Dembowsky K. (1992b) K-dependent inhibition in the dentate -$CA_3$ network of guinea pig hippocampal slices. J. Neurophysiol. 68: 1548-1557.

Misgeld U., Bijak M., Jarolimek W. (1995) A physiological role for $GABA_B$ receptors and the effects of baclofen in the mammalian central nervous system. Prog. Neurobiol. 46: 423-462.

Misgeld U., Frotscher M. (1986) Postsynaptic-GABAergic inhibition of non-pyramidal neurons in the guinea-pig hippocampus. Neuroscience 19: 193-206.

Moore R.Y., Bloom F.E. (1979) Central catecholamine neuron systems: anatomy and physiology of the norepinephrine and epinephrine systems. Ann. Rev. Neurosci. 2: 113-168.

Müller W., Misgeld U. (1990) Inhibitory role of dentate hilus neurons in guinea pig hippocampal slice. J. Neurophysiol. 64: 46- 56.

Müller W., Misgeld U. (1991) Picrotoxin- and 4-aminopyridine- induced activity in hilar neurons in the guinea pig hippocampal slice. J. Neurophysiol. 65: 141-147.

Olbrich H.-G., Braak H. (1985) Ratio of pyramidal cells versus non- pyramidal cells in sector CA1 of the human Ammon s horn. Anat. Embryol. 173: 105-110.

Oleskevich S., Descarries L., Lacaille J.-C. (1989) Quantified distribution of the noradrenaline innervation in the hippocampus of adult rat. J. Neurosci. 9: 3803-3815.

Parent A., Descarries L., Beaudet A. (1981) Organization of ascending serotonin neurons in the adult rat brain. A radioautographic study after intraventricular administration of [$^3$H]5-hydroxytryptamine. Neuroscience 6: 115-138.

Ribak C.E., Seress L., Amaral D.G. (1985) The development, ultrastructure and synaptic connections of the mossy cells of the dentate gyrus. J. Neurocytol. 14: 835-857.

Ribak C.E., Vaughn J.E., Saito K. (1978) Immunocytochemical localization of glutamic acid decarboxylase in neuronal somata following colchicine inhibition of axonal transport. Brain Res. 140: 315-332.

Ropert N., Guy N. (1991) Serotonin facilitates GABAergic transmission in the CA1 region of rat hippocampus in vitro. J. Physiol. (Lond.) 441: 121-136.

Scharfman H.E., Kunkel D.D., Schwartzkroin P.A. (1990) Synaptic connections of dentate granule cells and hilar neurons: results of paired intracellular recordings and intracellular horseradish peroxidase injections. Neuroscience 37: 693-707.

Scharfman H.E., Schwartzkroin P.A. (1988) Electrophysiology of morphologically identified mossy cells of the dentate hilus recorded in guinea pig hippocampal slices. J. Neurosci. 8: 3812-3821.

Schwartzkroin P.A., Mathers L.H. (1978) Physiological and morphological identification of a non-pyramidal hippocampal cell type. Brain Res. 157: 1-10.

Segal M. (1975) Physiological and pharmacological evidence for a serotonergic projection to the hippocampus. Brain Res. 94: 115- 131.

Segal M., Bloom F.E. (1974) The action of norepinephrine in the rat hippocampus. II. Activation of the input pathway. Brain Res. 72: 99-114.

Segal M., Bloom F.E. (1976) The action of norepinephrine in the rat hippocampus. III. Hippocampal cellular responses to locus coeruleus stimulation in the awake rat. Brain Res. 107: 499-511.

Seress L., Ribak C. E. (1983) GABAergic cells in the dentate gyrus appear to be local circuit and projection neurons. Exp. Brain Res. 50: 173-182.

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