Serotonin Reduces Polysynaptic Inhibition via 5-HT$_{1A}$ Receptors in the Superficial Entorhinal Cortex

DIETMAR SCHMITZ, 1 TENGIS GLOVELI, 1 RUTH M. EMPSON, 2 AND UWE HEINEMANN 1

1 Department of Neurophysiology, Institute of Physiology at the Charité, Humboldt University Berlin, 10117 Berlin, Germany; and 2 University Department of Pharmacology, Oxford University, Oxford OX1 3QT, United Kingdom

Serotonin reduces polysynaptic inhibition via 5-HT$_{1A}$ receptors in the superficial entorhinal cortex. J. Neurophysiol. 80: 1116–1121, 1998. The superficial cells of the entorhinal cortex (EC), main input to the hippocampus, receive a serotonergic input from the raphe nuclei and express 5-hydroxytryptamine creatine sulfate complex (5-HT) receptors at high density. With the use of intracellular recordings, we investigated the effects of serotonin on synaptic inhibition of layer II and III neurons of the EC. Serotonin reduced both polysynaptic fast and slow inhibitory postsynaptic potentials (IPSPs) in projection neurons of the superficial EC. Polysynaptic fast and slow IPSPs were depressed by serotonin in a dose-dependent manner (0.1–100 μM). Serotonin in a concentration of 1 μM reduced the amplitudes of polysynaptic fast and slow IPSPs by ~40 and 50%, respectively. To identify the subtype of the 5-HT$_{1A}$-receptor mediating the effects on polysynaptic IPSPs, we applied various 5-HT$_{1A}$-receptor agonists and antagonists. Although the serotonin agonists for the 5-HT$_{1B,2C,3}$ receptors were ineffective, the effects were mimicked by the 5-HT$_{1A}$-receptor agonists (8-OH-DPAT, 5-CT) and prevented by the 5-HT$_{1A}$-receptor antagonist NAN-190. To look at the direct effects of 5-HT on inhibitory interneurons, we elicited monosynaptic IPSPs in the absence of excitatory synaptic transmission. In contrast to the polysynaptic IPSPs, monosynaptic IPSPs were not significantly affected by serotonin. Recordings from putative inhibitory interneurons revealed that their excitatory postsynaptic potentials (EPSPs) were reversibly reduced by serotonin. We conclude that serotonin suppresses polysynaptic inhibition in projection neurons of layers II and III of the EC by depression of EPSPs on inhibitory interneurons via 5-HT$_{1A}$ receptors.

INTRODUCTION

The superficial cells of the entorhinal cortex (EC) form the two branches of the perforant path, the main input to the hippocampus (Steward and Scoville 1976). Layer II cells project to the dentate gyrus and CA3 region, whereas layer III cells project to CA1 and the subiculum (Steward and Scoville 1976). It has been reported that serotonergic fibers entering the EC and 5-HT receptors are expressed at high density in the superficial layers (Bobillier et al. 1975; Mengod et al. 1996; Pazos and Palacios 1985; Pazos et al. 1985). So far, there is only little known about the functional role of serotonin in the EC. However, changes in the serotonergic system are associated with characteristic lesions in the EC in Alzheimer’s and Korsakow’s disease (Beal et al. 1989; Crino et al. 1989; Langlais et al. 1987; Tejani-Butt et al. 1995).

We previously showed that serotonin can effectively decrease excitatory postsynaptic potentials (EPSPs) in principal cells in the EC (Schmitz et al. 1995a, 1997, 1998). However, it has been reported that most of the superficial EC neurons are under strong inhibitory control (Gloveli et al. 1997a–c; Jones 1993–1995). Moreover, the balance between synaptic excitation and inhibition seems to play a crucial role within this area for epileptogenesis (Heinemann 1987; Jones and Heinemann 1988) and ‘‘information transfer’’ to the hippocampus (Gloveli et al. 1997b; Jones 1993).

We therefore recorded from EC layers II and III projection and local circuit cells to clarify the effects and mechanisms by which serotonin affects inhibitory synaptic transmission in the superficial EC.

METHODS

Slice preparation

Horizontal slices containing the hippocampus, entorhinal, perirhinal, and temporal cortex were prepared from adult Wistar rats (180–250 g). In brief, the animals were deeply anesthetized with ether, decapitated, and the brain removed. Tissue blocks containing the temporal cortex and hippocampus were mounted on a Vibratome (Campden Instruments, Loughborough, UK) in a chamber filled with cold (~4°C) artificial cerebrospinal fluid (ACSF) containing (in mM) 124 NaCl, 26 NaHCO$_3$, 3 KCl, 1.25 NaH$_2$PO$_4$, 1.6 CaCl$_2$, 1.8 MgSO$_4$, and 10 glucose, saturated with 95% O$_2$–5% CO$_2$, pH 7.4. Horizontal slices were cut at 400-μm thickness and transferred to an interface chamber where they were maintained at 35°C and perfused with ACSF at a rate of 1.5–1.8 ml/min. The slices were allowed to rest for ~1 h after the preparation before recording.

Electrophysiological recordings

Intracellular electrodes were pulled from borosilicate glass (1.2 mm OD) and filled with 2 M K$^+$-acetate. Electrode resistance was 35–120 MΩ. Intracellular recordings were performed with a Neurodata IR 183 (Neurodata Instruments, New York, NY) or a SECIOL (NPI Instruments, Tamm, Germany) amplifier. Cells were impaled and then allowed to rest for 5–10 min before recording. Only cells with resting potentials more negative than ~50 mV were accepted. Resting membrane potentials of the cells were corrected after the recording by subtraction of the remaining tip potential after withdrawal of the pipette. Compound polysynaptic potentials were evoked by electrical stimulation (0.05-ms duration, 1–30 V) at 0.1–0.05 Hz via a bipolar insulated stimulation electrode placed in the lateral EC. The signals were filtered at 3 kHz, digitized at

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked ‘‘advertisement’’ in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

0022-3077/98 $5.00 Copyright © 1998 The American Physiological Society
Drugs and solutions

Bicuculline methiodide (5 μM) and 5-HT (0.1–100 μM) were both purchased from Sigma (Deisenhofen, Germany). (+)-2-Amino-5-phosphonopentanoic acid (APV; 30 μM), 1-(2-methoxyphenyl)-4-{[4-(2-phthalimido)butyl]piperazine hydrobromide (NAN-190; 50 μM), ±8-hydroxy-2-(di-n-propylamino) tetralin HBr (8-OH-DPAT; 10 μM), CGS-12066 maleate (10 μM), 2-methyl-5-hydroxytryptamine maleate (2-methyl-5-HT; 50 μM), α-methyl-5-hydroxytryptamine maleate (α-methyl-5-HT; 50 μM), 5-carboxamidotoxamine maleate (5-CT; 1 μM), and ritanserin (10 μM) were all from Research Biochemicals (Natick, MA). 1,2,3,4-Tetrahydro-6-nitro-2,3-dioxo-benzo[1]quinoxaline-7-sulfonamide (NBQX; 10 μM) was a gift from Novo Nordisk ( Bagsvaerd, Denmark), and CGP55845A (2 μM) was a gift from Ciba-Geigy (Basel, Switzerland).

Data analysis and statistics

Data were analyzed off-line with SIGAVG (CED, Cambridge, UK) or Wintida (HEKA, Lambrecht, Germany) software. Amplitudes of evoked synaptic potentials were measured from averaged (3–10) sweeps. Data are expressed as means ± SE. Because the mean data values are rounded to one number after the comma, the percentage change is in some occasions slightly different. Drug effects were analyzed with Student’s t-test (Sigmaplot, Jandel, USA) for paired data, and an error probability of P < 0.05 was regarded as significant.

RESULTS

We performed intracellular recordings from projection and local circuit neurons of layers II and III of the medial EC. We could identify different projection and local circuit-cells on the basis of the previously reported morphological and electrophysiological characteristics (Alonso and Klíck 1993; Gloveli et al. 1997a; Jones 1994).

Serotonin reduces IPSP independent of the effects on membrane properties

EPSP–polysynaptic inhibitory postsynaptic potential (IPSP) sequences in projection neurons of the superficial EC were evoked by electrical stimulation of the lateral EC. In a first series of experiments we tested serotonin in a concentration range of 0.1–100 μM on polysynaptic IPSPs. Both polysynaptic fast and slow IPSPs (fIPSPs and sIPSPs, respectively) were depressed by serotonin in a dose-dependent manner. At a concentration of 0.1 μM the polysynaptic fIPSP and sIPSPs were reduced from −3.0 ± 0.6 to 2.6 ± 0.3 mV (12% decrease; n = 4, P < 0.05) and −2.5 ± 0.5 to −2.1 ± 0.3 mV (17% decrease; n = 4, P < 0.05), respectively. At a concentration of 1 μM the fIPSPs were reduced from −2.7 ± 0.6 to −1.7 ± 0.5 mV (38% decrease; n = 13, P < 0.01) and the sIPSPs from −2.0 ± 0.5 to −1.0 ± 0.3 mV (52% decrease; n = 16, P < 0.01). After application of 10 μM, fIPSPs were depressed from −3.7 ± 0.2 to −1.4 ± 0.5 mV (62% decrease; n = 9, P < 0.01) and the sIPSPs from −2.5 ± 0.4 to −0.8 ± 0.2 mV (68% decrease; n = 10, P < 0.01). The highest concentration tested was 100 μM. At this concentration, serotonin reduced the fIPSP amplitude from −3.0 ± 0.9 to −0.8 ± 0.4 mV (74% decrease; n = 7, P < 0.01), whereas the sIPSPs were diminished from −3.4 ± 0.8 to −0.9 ± 0.4 mV (74% decrease; n = 6, P < 0.01; Fig. 1, A and B). We did observe in approximately one-third of the cells (6/20 neurons tested) that serotonin induced a small hyperpolarization (1–3 mV) that reversed at approximately −95 mV and was blocked by K+–channel blockers (not shown). However, in most cases (7/9 of the cells) the effects of serotonin on IPSPs were independent of any effects of 5-HT on intrinsic properties of the cell, suggesting that the effects of 5-HT on synaptic transmission were independent of the properties of the post-synaptic cell.

Effects of 5-HT–receptor agonists and antagonists on polysynaptic IPSPs

To identify the subtype of the 5-HT receptor mediating the depression of polysynaptic IPSPs, we applied various specific agonists: 8-OH-DPAT and 5-CT (both agonists on the 5-HT1A and 5-HT7 receptor), CGS-12066 (5-HT1D), α-methyl-5-HT (5-HT2C), and 2-methyl-5-HT (5-HT1C). However, only 8-OH-DPAT and 5-CT mimicked the effect of 5-HT on polysynaptic IPSPs (Fig. 2, A–C). 5-CT reduced the polysynaptic fIPSPs from −2.5 ± 0.5 to −1.0 ± 0.4 mV (62% decrease; n = 7, P < 0.01) and the polysynaptic sIPSPs from −2.4 ± 0.5 to −0.7 ± 0.2 mV (70% decrease; n = 7, P < 0.01). In seven cells 8-OH-DPAT reduced the polysynaptic fIPSPs from −4.0 ± 1.1 to −1.5 ± 0.7 mV (70% decrease; P < 0.01) and the sIPSPs from −3.0 ± 0.6 to −1.0 ± 0.4 mV (67% decrease; P < 0.01). In contrast, all other specific agonistic drugs (CGS-12066, α-methyl-5-HT, 2-methyl-5-HT) were ineffective to mimic the serotonin effect on polysynaptic IPSPs (not shown). This result suggests that 5-HT1A and/or 5-HT7 receptors are involved in the effect of serotonin. The 5-HT1A receptor is a recently identified 5-HT–receptor subtype (Lovenberg et al. 1993; Ruat et al. 1993) that has a closely related agonist profile as the 5-HT1A receptor. However, the 5-HT7 receptor antagonist ritanserin could not antagonize the effect of serotonin on polysynaptic IPSPs (n = 5, P = 0.3). On the other hand, the 5-HT1A–receptor antagonist NAN-190 antagonized the effect of serotonin on polysynaptic IPSPs (fIPSPs: −2.6 ± 0.5 to −2.5 ± 0.3 mV, n = 5, P = 0.7; sIPSPs: −2.1 ± 0.6 to −2.2 ± 1.0 mV, n = 5, P = 0.6). Thus the depression of the polysynaptic IPSPs appears to be mediated by 5-HT1A receptors.

Effects of serotonin on monosynaptic IPSPs

To look at the direct effects of 5-HT on inhibitory interneurons, we elicited monosynaptic IPSPs in the absence of excitatory synaptic potentials by local stimulation in the presence of NBQX and APV (Fig. 3). Under these conditions, a fIPSP or a sIPSP sequence could be recorded. The fIPSP and sIPSPs were pharmacologically identified as γ-aminobutyric acid-A (GABA_A) and GABA_A receptor-mediated events by their sensitivity to bicuculline and CGP55845A (n = 4 for each). However, serotonin (10 μM) had no significant effect on monosynaptic IPSPs in the
EC (5 ± 7% decrease in monosynaptic fIPSPs; n = 15, P = 0.3). In detail, we observed small reductions in fIPSPs in 6 of 15 cells (12 ± 8% reduction). Six cells of these 15 cells did not respond to 5-HT at all, and the remaining 3 cells responded even with a small increase (10 ± 8%). In the presence of NBQX and APV, sIPSPs were very small (see Fig. 3) or nonexistent. When present they were not consistent and only marginally affected by serotonin. However, occasionally, a relatively strong reduction of the monosynaptic sIPSPs was seen, but these studies were the exception rather than the rule, and the variability of the effects precluded any closer examination.

Serotonin decreases EPSPs in local circuit neurons

Local circuit neurons can be distinguished from projection cells by a number of morphological and electrophysiological criteria (Gloveli et al. 1997a; Jones and Buhl 1993). During the experiments, seven cells showed such properties; they had faster action potentials with a sharp onset of the spike-afterhyperpolarization or/and fired with higher frequencies and with less accommodation and often triggered doublets of action potentials on the top of synchronically evoked EPSPs (see Fig. 4, A–C). Despite some variation in the expression of each of these properties, we classified the neurons as local circuit neurons (Gloveli et al. 1997a; Jones and Buhl 1993). Because of the consistent effects of serotonin onto these cells, data were pooled for analysis. We evoked excitatory postsynaptic potentials in these neurons by electrical stimulation of the lateral EC. Serotonin (10 μM) reversibly reduced the amplitude of synchronically evoked EPSPs by 59 ± 11% (P < 0.05, n = 7, see Fig. 4D). In two of such cells the specific 5-HT1A-receptor agonist 8-OH-DPAT reduced the EPSP amplitudes by 42 and 49%, respectively.

Discussion

Our data show that serotonin induces changes of synaptic inhibition of EC layer II and III cells. Because these neurons of the EC form the main input to the hippocampus proper (Steward and Scoville 1976), the modulation by serotonin will markedly alter the information flow to the hippocampus.

Effects of serotonin on IPSPs in the EC

In our experiments polysynaptic fIPSP and sIPSPs were reduced by serotonin at low concentrations (~40 and 50% reduction at 1 μM for fIPSP and sIPSPs, respectively). A reduction of polysynaptic fIPSP (Schmitz et al. 1995b) and sIPSPs (Schmitz et al. 1995b; Segal 1990) was also reported for hippocampal area CA1. In area CA3 and in the dentate gyrus a modulation of GABAA responses by serotonin was reported (Ghadimi et al. 1994; Oleskevich and Lacaille 1992), and more recently a reduction of spontaneous GABAmediated IPSPs via 5-HT1A receptors was described in granule cells of the area dentata (Bijak and Misgeld 1997). Interestingly, activation of 5-HT1A receptors can reverse this effect (Bijak and Misgeld 1997). However, when IPSPs were pharmacologically isolated and monosynaptically isolated in the superficial EC they were much more resistant to serotonin and were only occasionally and then not often homogenously affected by serotonin. This lack of affection of monosynaptic GABA-mediated transmission in the EC was also described for the noradrenergic and dopaminergic system (Pralong and Jones 1993; Pralong and Magistretti 1995). This is in direct contrast to the hippocampus, where both the monosynaptic fIPSP and sIPSPs are reduced by serotonin via a presynaptic mechanism (Ghadimi et al. 1994;
5-HT REDuces POLysynAPTIC INHIBITION IN THE EC

FIG. 2. Effects of the 5-HT1A-receptor agonists 5-CT (1 μM) and 8-OH-DPAT (10 μM) on polysynaptic fIPSP and sIPSPs. A: both drugs, 5-CT and 8-OH-DPAT, strongly reduced polysynaptic fIPSPs in a layer II-stellate cell. B: polysynaptic sIPSPs in 2 different cells of layer III of the medial EC were suppressed by 5-CT (B1) and 8-OH-DPAT (B2). C: statistical diagrams pooled data from the effects of 5-CT and 8-OH-DPAT on polysynaptic fIPSP and sIPSPs. * Significant decreases in IPSP-amplitudes (see RESULTS). Control value is 100% in both diagrams.

Oleskevich and Lacaille 1992; Schmitz et al. 1995b; Segal 1990). Thus the suppression of polysynaptic fIPSP and sIPSPs in the EC is most likely caused by a reduced feed-forward or feed-back glutamate-mediated excitation of inhibitory interneurons. Indeed, this suggestion is supported by recordings from local circuit cells, presumably inhibitory interneurons, where the EPSPs were reversibly reduced by serotonin (see Fig. 4). Thus it is likely that the effects of 5-HT on polysynaptic IPSPs are mediated by a suppression of excitatory potentials at inhibitory interneurons. We recently showed that EPSPs in principal cells of the superficial EC are reduced by a presynaptic mechanism (Schmitz et al. 1998), and it is conceivable that this is the mechanism of EPSP reduction in putative interneurons as well.

The increase in total cell conductance induced by 5-HT is important for the interpretation of the depressant effects on synaptic responses because a general membrane conductance increase can reduce the amplitude of synaptic events (Ginsborg 1973). However, at least four arguments exclude such a postsynaptic shunting effect. First, only about one-third of neurons of the superficial medial EC were slightly hyperpolarized by serotonin, and in the other two-thirds of neurons we could observe a significant reduction in synaptic responses in the absence of any intrinsic conductance changes (e.g., Fig. 1A). Second, when increases in total cell conductance were seen, they were almost always outlived by the reduction of synaptic responses. Third, the concentration of serotonin necessary to affect synaptic potentials was lower than that which directly

FIG. 3. Effects of serotonin on monosynaptic IPSPs. After the application of the glutamate-receptor antagonists NBQX and APV, all components of the PSPs were blocked (not shown; same cell as in Fig. 1; layer III-type 2 neuron) but we were able to evoke monosynaptic fIPSP and sIPSPs by a close stimulation position. In contrast to the polysynaptic IPSPs (see Fig. 1), the monosynaptic IPSPs were not affected by serotonin (10 μM).
altered membrane potential (not shown). Fourth, if serotonin would reduce the IPSP only by shunting it in the dendrites, one must expect that the monosynaptic IPSPs would be affected, too, but this was not the case. In addition, shunting of EPSPs in the dendrites of inhibitory interneurons seems to be also very unlikely because only one of the putative interneurons was slightly hyperpolarized by serotonin. We therefore conclude that the main effect of serotonin in the superficial layers of the EC is not caused by alterations of intrinsic neuronal properties but is specifically linked to a selective depression of synaptic potentials.

The 5-HT$_{1A,1B,2C,3}$ receptor subtypes show a high density of serotonin receptors in the EC (Pazos et al. 1985, 1990; Pazos and Palacios 1985). Therefore we tested the most commonly used selective agonists and antagonists of these receptor subtypes. The 5-HT$_{1A}$ receptor agonists 8-OH-DPAT and 5-CT could both mimic the effect of serotonin on polysynaptic IPSPs, whereas the specific agonists for 5-HT$_{1B,2C,3}$ receptors were ineffective. Because 8-OH-DPAT as well as 5-CT binds with high affinity to 5-HT$_{1A}$ and 5-HT$_7$ receptors and the limbic structures express significant levels of 5-HT$_7$ receptors (Lovenberg et al. 1993; Ruat et al. 1993), we tested both 5-HT$_{1A}$ and 5-HT$_7$ receptor antagonists. However, the effect of serotonin on polysynaptic IPSPs was only antagonized by the 5-HT$_{1A}$ receptor antagonist. These results suggest that activation of the 5-HT$_{1A}$ receptor is most likely responsible for the depression of polysynaptic IPSPs.

In summary, we conclude that serotonin suppresses polysynaptic inhibition in layers II and III of the EC via 5-HT$_{1A}$ receptors and depression of EPSPs on putative inhibitory interneurons. This modulatory action might affect the balance between excitation and inhibition within cortical networks and will alter the “information flow” from the EC to the hippocampus.

We thank Dr. A. Draguhn for helpful discussions and for reading the manuscript.

This work was supported by the Bundesministerium für Bildung und Forschung, a Royal Society Exchange Program Fellowship to R. M. Empson, and Deutsche Forschungsgemeinschaft Grant IN21/A1–1.

Address for reprints: D. Schmitz, Dept. of Neurophysiology, Institute of Physiology at the Charité, Humboldt University Berlin, Tucholskystr. 2, 10117 Berlin, Germany.

Received 4 March 1998; accepted in final form 20 May 1998.

REFERENCES

BEAL, M. F., MAZUREK, M. E., ELLISON, D. W., KOWAL, N. W., SOLOMON, P. R., 
AND PENDELBURY, W. W. Neurochemical characteristics of aluminum-
induced neurofibrillary degeneration in rabbits. *Neuroscience* 29: 

BIJAK, M. AND MISGELD, U. Effects of serotonin through serotonin 1A and 
serotonin 1D receptors on inhibition in the guinea-pig dentate gyrus in vitro. 

BORILLIER, D., PETETTE, E., SALVET, D., LIGIER, M., AND SEGUIN, S. 
Differential projections of the nucleus raphe dorsalis and nucleus raphe 

CRINO, P. B., VOGT, B. A., CHEN, J.-C., AND VOLCER, L. Neurotoxic effects 
of partially oxidized serotonin: tryptamine-4,5-dione. *Brain Res.* 504: 

Ghadimi B., M., JAROLIMEK, W., AND MISGELD, U. Effects of serotonin 
on hilar neurons and granule cell inhibition in the guinea pig hippocampal 

GINSBORG, B. L. Electrical changes in the membrane in junctional transmis-

GLOVELI, T., SCHMITZ, D., EMPSON, R. M., DUGLADZE, T., AND HEINEMANN, 
U. Morphological and electrophysiological characterisation of layer III 
cells of the medial entorhinal cortex of the rat. *Neuroscience* 77: 629– 
648, 1997a.

GLOVELI, T., SCHMITZ, D., EMPSON, R. M., AND HEINEMANN, U. Frequency 
dependent information flow from the entorhinal cortex to the hippocam-

GLOVELI, T., SCHMITZ, D., AND HEINEMANN, U. Prolonged inhibitory poten-
tials in layer III projection cells of the rat medial entorhinal cortex induced 

HEINEMANN, U. Basic mechanisms of the epilepsies. In: *A Textbook of 
Clinical Neurophysiology*, edited by A. M. Halliday, S. R. Butler, and 

JONES, R.S.G. Frequency-dependent alterations in synaptic transmission in 

JONES, R.S.G. Entorhinal-hippocampal connections: a speculative view of 

JONES, R.S.G. Synaptic and intrinsic properties of neurons of origin of the 
perforant path in layer II of the rat entorhinal cortex in vitro. *Hippocam-

JONES, R.S.G. AND BOHL, E. H. Basket-like interneurones in layer II of the 
entorhinal cortex exhibit a powerful NMDA-mediated synaptic excitation. 

JONES, R.S.G. AND HEINEMANN, U. Synaptic and intrinsic responses of 
medial entorhinal cortical cells in normal and magnesium-free medium 

LANGLAIS, P. J., MAIR, R. G., ANDERSON, C. D., AND McEntee, W. J. 
Monoamines and metabolites in cortex and subcortical structures: normal 
regional distribution and the effects of thiamine deficiency in the rat. 

LOVENBERG, T. W., BARON, B. M., DE LEEUW, L., MILLER, J. D., PROSSER, 
R. A., REA, M. A., FOYE, P. E., RACKE, M., SLONE, A. L., SIEGEL, B. W., 
DANILESON, P. E., SUTCLIFFE, J. G., AND ERLANDER, M. G. A novel ade-
nylyl cyclase-activating serotonin receptor (5-HT7) implicated in the 

MENGOD, G., VILARÓ, M. T., RAURICH, A., LÓPEZ-GIMÉNEZ, J. F., CORTÉS, 
R., AND PALACIOS, J. M. 5-HT receptors in mammalian brain: receptor 
autoradiography and in situ hybridization studies of new ligands and 

OLESKIEVICH, S. AND LACAILLE, J.-C. Reduction of GABA-B inhibitory 
postsynaptic potentials by serotonin via pre- and postsynaptic mecha-
nisms in CA3 pyramidal cells of rat hippocampus in vitro. *Synapse* 12: 

PALACIOS, J. M., WAEBER, C., HOVER, D., AND MENGOD, G. Distribution of 

PRAVATI, A., CORTÉS, R., AND PALACIOS, J. M. Quantitative autoradiographic 
mapping of serotonin receptors in the rat brain. II. Serotonin-2 receptors. 

PRAVATI, A. AND PALACIOS, J. M. Quantitative autoradiographic mapping of 
serotonin receptors in the rat brain. I. Serotonin-1 receptors. *Brain Res.* 

PRAVATI, E. AND JONES, R.S.G. Interactions of dopamine with glutamate-
and GABA-mediated synaptic transmission in the rat entorhinal cortex 

SMITH, D., AND MAGISTRATTI, P. J. Noradrenaline increases K-conduc-
tance and reduces glutamatergic transmission in the mouse entorhinal 

RUAT, M., TRAFFFORT, E., LEURS, R., TARDIVEL-LACOMBE, J., DIAZ, J., 
ARRANG, J.-M., AND SCHWARTZ, J.-C. Molecular cloning, characteriza-
tion, and localization of a high-affinity serotonin receptor (5-HT7) acti-
1993.

SCHMITZ, D., EMPSON, R. M., GLOVELI, T., AND HEINEMANN, U. Serotonin 
reduces synaptic excitation of principal cells in the superficial layers of 
rat hippocampal-entorhinal cortex combined slices. *Neurosci. Lett.* 190: 

SCHMITZ, D., EMPSON, R. M., GLOVELI, T., AND HEINEMANN, U. Serotonin 
blocks different pattern of low Mg2+-induced epileptiform activity in 
entorhinal cortex, but not hippocampus. *Neuroscience* 76: 449–458, 
1997a.

SCHMITZ, D., EMPSON, R. M., AND HEINEMANN, U. Serotonin reduces inhibi-
tion via 5-HT1A receptors in area CA1 of rat ventral hippocampal slices 

SCHMITZ, D., GLOVELI, T., EMPSON, R. M., DRAGUHN, A., AND HEINEMANN, U. 
Serotonin reduces synaptic excitation in the superficial medial entorhi-
 nal cortex of the rat via a presynaptic mechanism. *J. Physiol. (Lond.)* 

SEGUAT, M. Serotonin attenuates a slow inhibitory postsynaptic potential 

STEWARD, O. AND SCOVILLE, S. A. Cells of origin of entorhinal cortical 
afferents to the hippocampus and fascia dentata of the rat. *J. Comp. 

TEJANI-BUTT, S. M., YANG, J., AND PAVLYK, A. C. Altered serotonin trans-
porter sites in Alzheimer’s disease raphe and hippocampus. *Neuroreport* 