Effects of 5-Hydroxytryptamine on Neuronal Activities in the Rat Dorsolateral Septal Nucleus

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Summary: The ionic channels and signal transduction pathways underlying the 5-hydroxytryptamine (5-HT)-induced hyperpolarization in neurons of the rat dorsolateral septal nucleus (DLSN) were examined by using intracellular and voltage-clamp recording techniques. Application of 5-HT (1-50 μ M) caused a hyperpolarizing response associated with a decreased membrane resistance in DLSN neurons. The hyperpolarization induced by 5-HT was blocked by Ba^{2+} (1 mM) but not by tetraethylammonium (TEA, 3 mM), glibenclamide (100 μ M) and extracellular Cs^+ (2 mM). 8-Hydroxy-di-n-propylamino tetralin (8-OH-DPAT; 3 μ M), a selective agonist for the 5-HT_{1A} receptor, mimicked 5-HT in producing the hyperpolarization. The 5-HT hyperpolarization was blocked by NAN-190 (5 μ M), a 5-HT_{1A} receptor antagonist. CP93129 (100 μ M), a 5-HT_{1B} receptor agonist, and L-694-247 (100 μ M), a 5-HT_{1B/1D} receptor agonist, also produced hyperpolarizing responses. The order of agonist potency was 8-OH-DPAT $\gg$ CP93129 $\geq$ L-694-247. ($\pm$)-2,5-Dimethoxy-4-iodoamphetamine hydrochloride (DOI, 100 μ M), a 5-HT₂ receptor agonist, and RS67333 (100 μ M), a 5-HT₄ receptor agonist, caused no hyperpolarizing response. The voltage-clamp study showed that 5-HT caused an outward current ($I_{5\text{-HT}}$) in a concentration-dependent manner. $I_{5\text{-HT}}$ was associated with an increased membrane conductance. $I_{5\text{-HT}}$ reversed the polarity at the equilibrium potential for K^+ calculated by the Nernst equation. $I_{5\text{-HT}}$ showed inward rectification at membrane potentials more negative than -70 mV. Ba^{2+} (100 μ M) blocked the inward rectifier K^+ current induced by 5-HT. $I_{5\text{-HT}}$ was irreversibly depressed by intracellular application of guanosine 5'-O-(3-thiotriphosphate)(GTP- γ S) but not by guanosine 5'-O-(2-thiodiphosphate) (GDP β S). These results suggest that in rat DLSN neurons activation of 5-HT_{1A} receptors causes a hyperpolarizing response by activating mainly the inward rectifier K^+ channels through a GTP-binding protein.

Key words lateral septum, 5-HT, hyperpolarization, 5-HT_{1A} receptors, G-protein, GIRK channel, outward rectifier K^+ channel

INTRODUCTION

The lateral septum is the largest nuclear mass of the septal area which is known to be an integrated part of the limbic system in the rat brain. The principal neurons in the lateral septum receive a major neuronal projection from hippocampal CA1 and CA3 neurons and in turn send efferents to hypothalamic and amygdaloid areas [1-4]. The lateral septal neurons also receive serotonergic input from medial and dorsal raphe nuclei [5,6]. In vitro autoradiography

has demonstrated that 5-hydroxytryptamine (5-HT) receptors, especially 5-HT_{1A} receptors, are localized with the highest density in the lateral septum and the hippocampus [7-11]. Molecular cloning has established that 5-HT_{1A} receptors belong to the superfamily of GTP binding protein (G-protein)-coupled receptor [12-16]. A family of cDNA cloning subunits of the pertussis toxin (PTX)-sensitive G-protein activates the inward rectifier K^+ (GIRK) channels in neuronal cells [17,18]. Coexistence with the rat brain GIRK3 and other subunits in *Xenopus* oocytes give

Received for publication June 29, 1998

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rise to prominent current which is enhanced by stimulation of co-expressed 5-HT_{1A} receptors [19]. Sim et al. [20] have demonstrated high level of 5-HT_{1A}-stimulated [³⁵S]GTP γ S binding in the lateral septum. *In situ* hybridization revealed a substantial distribution of GIRK1-4 mRNA in the rat lateral septum [21]. Electrophysiological studies have shown that 5-HT produces hyperpolarizing responses in neurons of the dorsolateral septal nucleus (DLSN) [22-24]. The purpose of the present study is to examine the properties of the K⁺ channels and signal transduction system underlying the 5-HT-induced hyperpolarization in DLSN neurons.

MATERIALS AND METHODS

Coronal slices containing the lateral septal nucleus were obtained from the rat brain in a manner described previously [25]. Male Wistar rats, 80-150 g, were killed by decapitation and their brains were rapidly removed and immersed for 8-10 s in a cooled artificial cerebrospinal fluid (ACSF 4-6 °C) that was pre-bubbled with 95% O₂-5% CO₂. Transverse slices (500 μ m in thickness) were cut with a Vibroslice (Campden Instruments) and left to recover for one hour in oxygenated ACSF at room temperature (22-24 °C). The slice was then transferred to a chamber and submerged in ACSF at 32-33 °C. The composition of the ACSF was as follows (in mM): NaCl, 117; KCl, 4.7; CaCl₂, 2.5; MgCl₂, 1.2; NaHCO₃, 25; NaH₂PO₄, 1.2 and d-glucose, 11 (pH 7.4 and 295-305 mOsm). Recording of the membrane potential of DLSN neurons was made with a microelectrode filled with 3 M K-acetate. The tip resistance of microelectrodes was 100-140 M Ω . Under voltage-clamp, membrane currents were obtained with an Axoclamp-2A amplifier using discontinuous single electrode voltage clamp (dSEVC) mode at a sampling rate of 2-5 kHz and gain of 0.8 nA/mV. The head stage output was continuously monitored. The current-voltage (I-V) relationship was obtained by applying a ramp command potential from holding potentials of -75 mV to -140 mV to -40 mV and back to the holding potentials at a rate of approximately 0.2 V/s. The membrane voltage and current were monitored continuously with a pen-writing recorder and memory oscilloscope (Nihon-Kohden, RTA-1100). The pClamp software program (Axon Instruments) operating on an IBM-AX computer (Gateway 2000) was used to analyze the membrane currents. All drugs except glibenclamide were dissolved in the Krebs solution. Glibenclamide and

L-694-247 were dissolved in DMSO and added to the Krebs solution, where the final concentration of DMSO was 0.1% which had no direct effect on DLSN neurons. Of the drugs used, 5-HT creatinine phosphate, guanosine 5'-O-(3-thiotriphosphate)(GTP- γ S), guanosine 5'-O-(2-thiodiphosphate) (GDP β S), NAN-190 and glibenclamide were purchased from Sigma (St Louis, MO). Tetrodotoxin (TTX) and tetraethylammonium chloride were purchased from Wako Pure Chemical Industries, Ltd. ($\pm$)-2,5-Dimethoxy-4-iodoamphetamine hydrochloride (DOI) and 8-hydroxy-di-n-propylamino tetralin (8-OH-DPAT) were purchased from RBI (Natick, MA). RS67333, CP93129 and L-694-247 were from TOCRIS. All experiments were carried out at a temperature of 30-32 °C. Each experimental value is presented as the mean $\pm$ SE (standard error of the mean) and was analyzed by Student's *t*-test.

RESULTS

Effects of 5-HT on membrane properties of DLSN neurons

Neurons in the rat DLSN had a resting membrane potential of -70 ± 3 mV ($n=45$) and input resistance of 132 ± 11 M Ω ($n=45$). Bath-application of 5-HT (10 μ M) caused a hyperpolarizing response with amplitude of 14 ± 3 mV in 76 neurons (84%) out of 91 neurons (an example is shown in Fig. 1). The remaining 5 (6%) neurons showed no obvious changes in the resting membrane potential during the application of 5-HT. The rate of firing of spontaneous action potentials was markedly reduced during the 5-HT hyperpolarization. Voltage-current relationship (V-I) curve was constructed by application of rectangular current pulses with a duration of 300 msec (Fig. 1B). 5-HT (100 μ M) decreased the slope of the V-I curve, suggesting a decreased input resistance (Fig. 1C). The 5-HT hyperpolarization reversed polarity at -82 mV in this particular neuron (Fig. 1C). The reversal potential obtained from 7 neurons was -96 ± 6 mV.

Effects of 5-HT receptor agonist and antagonist in DLSN neurons

8-OH-DPAT (3 μ M), a selective agonist for the 5-HT_{1A} receptor [26-32], produced a hyperpolarizing response associated with a decreased membrane resistance (Fig. 2A). It has been shown that NAN-190 is a relatively selective antagonist for the 5-HT_{1A} receptor [29]. NAN-190 (10 μ M) produced no significant change in the membrane potential in DLSN

Fig. 1. Effect of 5-HT on passive membrane properties of DLSN neurons. A: a pen-writer recording of 5-HT-induced hyperpolarization in a DLSN neuron. A horizontal bar indicates the period of bath-application of 5-HT (10 μM). Downward deflections indicate electrotonic potentials produced by application of cathodal current pulses with duration of 500 ms. Upward deflections indicate spontaneous action potentials. B: expanded records of electrotonic potentials produced by injection of anodal and cathodal current pulses with duration of 500 ms. C: voltage-current relationship obtained before (○) and during application of 5-HT (□). All data were obtained from records (A).

TABLE 1.
Effects of 5-HT-receptor agonists and antagonists on rat septal neurons

Agonists and antagonist		receptor type	hyperpolarizations
Agonists			
5-HT	(10 μM)	—	14 ± 3 mV (n=8)
8-OH-DPAT	(3 μM)	5-HT _{1A}	7 ± 3 mV (n=6)
CP93129	(10 μM)	5-HT _{1B}	no effect
	(100 μM)	—	11 mV (n=1)
L-694-247	(10 μM)	5-HT _{1D/1B}	no effect
	(100 μM)	—	8 ± 3 mV (n=3)
DOI	(100 μM)	5-HT ₂	no effect
RS67333	(100 μM)	5-HT ₄	no effect
Antagonist			
NAN-190	(3 μM)	5-HT _{1A}	block

8-OH-DPAT: 8-hydroxy-di-n-propylamino tetralin; DOI: (±)-2,5-Dimethoxy-4-iodoamphetamine hydrochloride

Fig. 2. Effects of an agonist (A) and an antagonist (B) for 5-HT receptors on DLSN neurons. A: effects of 8-OH-DPAT ($3\mu\text{M}$) and 5-HT ($10\mu\text{M}$) on the same neuron. The drugs were applied to the ACSF during the period indicated by horizontal bars. B: blockade of the 5-HT-induced hyperpolarization by NAN-190. The 5-HT hyperpolarizations were recorded in the absence (top) and presence (bottom) of NAN-190 ($10\mu\text{M}$). The horizontal bars indicate the period of application of 5-HT.

neurons. The hyperpolarization induced by 5-HT ($10\mu\text{M}$) was blocked by NAN-190 ($10\mu\text{M}$) (Fig. 2B). CP93129 ($10\mu\text{M}$), a 5-HT_{1B} receptor agonist [33,34], and L-694-247 ($10\mu\text{M}$), a 5-HT_{1B/1D} receptor agonist [35], did not produce hyperpolarization in DLSN neurons. When the concentration was increased to $100\mu\text{M}$, CP93129 and L-694-247 produced hyperpolarization in DLSN neurons. The order of agonist potency was 8-OH-DPAT $\gg$ CP93129 $\geq$ L-694-247.

DOI ($100\mu\text{M}$), a 5-HT₂ receptor agonist [30,36], produced no hyperpolarizing response in DLSN neurons. RS67333 ($100\mu\text{M}$), a 5-HT₄ receptor agonist [37], had no ability to hyperpolarize the DLSN neurons. These results are summarized in Table 1.

Effects of channel blockers on the 5-HT hyperpolarization

Tetraethylammonium (TEA, 3 mM), a blocker for the delayed rectifier K⁺ current [38], did not depress the hyperpolarization induced by 5-HT (Fig. 3A). Cs⁺ (1 mM), a blocker for non-selective cation channels (Q-current, [39]), did not depress the hyperpolarization induced by 5-HT (Fig. 3B). Ba²⁺ has been known to block several K⁺ currents in neuronal membrane [40-44]. The rate of spontaneous action potential was markedly increased in a ACSF containing Ba²⁺ (1 mM). The 5-HT hyperpolarization was depressed by $70 \pm 5\%$ ($n=12$) by Ba²⁺ (Fig. 3C). Glibenclamide ($100\mu\text{M}$), a blocker for the ATP-sensitive K⁺ channels [45,46], did not block the 5-HT hyperpolarization (Fig. 3D). The 5-HT hyperpolarization of DLSN neurons was not depressed, when Ca²⁺ was removed from the ACSF. It is well known that intracellular Cs⁺ blocks K⁺ channels in a non-selective manner [47]. In the present study, Cs⁺ was injected to DLSN neurons by applying outward DC current through intracellular microelectrode. Cs⁺-treated DLSN neurons had an action potential with a prolonged plateau on the falling phase. The 5-HT hyperpolarization was reduced in DLSN neurons that had been injected by Cs⁺.

5-HT-induced outward current in DLSN neurons

Under voltage-clamp condition, 5-HT ($1\text{--}50\mu\text{M}$) caused an outward current ($I_{5\text{-HT}}$) in DLSN neurons (Fig. 4A). A current-voltage relationship (I-V curve) was constructed using a ramp command potential that held the membrane potential at values from -140 to -40mV (Fig. 4B). TTX ($1\mu\text{M}$) was added to the ACSF to block the action potential. 5-HT increased the slope of the I-V curve at all holding membrane potentials, indicating an increased membrane conductance during $I_{5\text{-HT}}$. The effect of 5-HT in producing the outward current in DLSN neurons was concentration-dependent (Fig. 4C). The minimum effective concentration of 5-HT was $1\mu\text{M}$. This concentration produced the outward current with amplitude of approximately 10 pA. At a concentration of $50\mu\text{M}$, 5-HT caused the maximum response with amplitude of $230 \pm 18\text{pA}$ ($n=6$). The half-maximum response (EC_{50}) of $I_{5\text{-HT}}$ was produced by $2\mu\text{M}$ 5-HT.

Fig. 3. Effect of K⁺-channel blockers (TEA, CsCl, BaCl₂ and glibenclamide) on the 5-HT hyperpolarizations. Horizontal bars indicate the period of bath-application of 5-HT. Each blocker was applied to the bath 5-10 min before application of 5-HT. Note that Ba²⁺ (1 mM) depressed the 5-HT hyperpolarization.

I_{5-HT} was recorded at several membrane potentials (Fig. 5A). When DLSN neurons were hyperpolarized, I_{5-HT} decreased in amplitude and finally reversed the polarity. In 7 neurons, the reversal potential of I_{5-HT} was -90 ± 4 mV in the normal ACSF (containing 4.7 mM K⁺). The reversal potential of I_{5-HT} was also recorded from DLSN neurons superfused with an external solution containing 1, 9.7 or 20 mM K⁺ (Fig. 5B). The reversal potential was shifted to -125 ± 3 mV (n=5), -72 ± 2 mV (n=6) and -42 ± 2 mV (n=7) in 1, 10 and 20 mM K⁺ solution, respectively. Figure 5C shows the relationship between the reversal potential of I_{5-HT} and the concentration of extracellular K⁺. The slope of this curve was 54 mV, suggesting that I_{5-HT} reversed polarity at

the equilibrium potential for K⁺ calculated by the Nernst equation. Interestingly, the K⁺ conductance which links to 5-HT receptors seems voltage-dependent, because I_{5-HT} increased in amplitude at hyperpolarizing membrane potentials in high K⁺ solutions (Fig. 5B).

The properties of the 5-HT-activated K⁺ channels in DLSN neurons were examined by using the I-V curve. In the absence of 5-HT, an almost linear I-V curve was produced by the ramp command potential in DLSN neurons. In contrast, the 5-HT-induced membrane conductance was markedly increased at potentials more negative than -70 mV (Fig. 6A). The net I_{5-HT} was obtained by subtraction of the control I-V curve from that recorded during the application of

Fig. 4. Outward currents produced by 5-HT in DLSN neurons. A: a pen-writing record of 5-HT-induced outward current (I_{5-HT}) in a DLSN neuron. Membrane conductance was measured by ramp command potentials before, during and after application of 5-HT. B: current-voltage relationship obtained before and during the application of 5-HT ($10 \mu M$). These curves are based on the data shown in record (A). C: concentration-response relationship of 5-HT obtained from 4-11 neurons for each point. Vertical lines indicate the SE of the mean. The data were fitted to a modified Michaelis-Menten equation by using the least-squares fitting: $I = (I_{max} \cdot C^n) / (C^n + EC_{50}^n)$, where I was the drug-induced current, I_{max} was the maximum response, C was the concentration of 5-HT, EC_{50}^n was the concentration that produced the half-maximum response and n was the Hill coefficient.

5-HT. The net I_{5-HT} showed a marked inward rectification in 45% of the neurons (Fig. 6B). In the remaining 55% of the neurons, I_{5-HT} was less sensitive to the membrane potential (Figs 6C and D). Ba^{2+} , at the relatively low concentration of $100-200 \mu M$, has been reported to selectively block the inward rectifier K^+ current in central neurons [48]. In DLSN neurons Ba^{2+} ($100 \mu M$) depressed the inward rectifier I_{5-HT} (Fig. 7). These results suggest that 5-HT hyperpolarizes the DLSN neurons by activating the inward rectifier K^+ currents.

Contribution of G-protein to I_{5-HT}

GTP γ S ($10 mM$) was applied to the intracellular space by diffusion from an intracellular microelectrode. 5-HT ($10 \mu M$) was applied to the superfusing solution 5 min after insertion of the microelectrode. 5-HT produced a hyperpolarization that did not recover. The membrane potential was continuously shifted to a hyperpolarizing potential, even when 5-HT was removed from the superfusing solution, probably because of diffusion of GTP γ S into the

Fig. 5. Reversal potentials of I_{5-HT} . A: I_{5-HT} was recorded at various holding potentials. The neuron was held at two different potentials by using hyperpolarizing voltage commands. Holding potentials are shown at the left of records. B: the relationships between the amplitude of I_{5-HT} and the holding voltage. I_{5-HT} was obtained in the presence of 1.0 (Δ), 4.7 ($\blacksquare$), 9.7 ($\circ$) or 20 ($\square$) mM K^+ . Lines were fitted by eye. C: reversal potentials of I_{5-HT} plotted against the concentration of external K^+ . Each point is the mean of data from 4-6 cells. Vertical lines represent SE of mean.

intracellular space. Further repeated applications of 5-HT at intervals of 20 min caused no hyperpolarization (Figs 7A and C). GDP β S (3 mM) was also applied to the intracellular space of DLSN neurons by diffusion from an intracellular microelectrode. However, the 5-HT hyperpolarization was not depressed by injection GDP β S in DLSN neurons for more than 50 min (Figs 7B and D).

DISCUSSION

The present study showed that 5-HT caused a

hyperpolarizing response, associated with increased membrane conductance, in DLSN neurons. 8-OH-DPAT (3 μ M), a 5-HT_{1A} receptor agonist, also produced a hyperpolarizing response in DLSN neurons. Although CP93129 and L-694-247, 5-HT_{1B/1D} agonists, also produced hyperpolarizing responses, these drugs were less potent than 5-HT. Agonists for the 5-HT₂ receptor, DOI (100 μ M) and the 5-HT₄ receptor agonist, RS67333 (100 μ M) caused no hyperpolarizing response in DLSN neurons. The hyperpolarization induced by 5-HT (10 μ M) was almost completely depressed by NAN-190 (500 nM), an antago-

Fig. 6. Current-voltage relationships (I-V curves) from two different DLSN neurons (A, B and C, D) constructed using ramp command potentials. The membrane potential was initially held at -70 mV. A: I-V curves were taken in the absence (control) and presence of 5-HT ($10\mu\text{M}$). B: net $I_{5\text{-HT}}$ obtained by subtraction of the I-V curve for 5-HT from the control curve in (A). C: I-V curves were obtained in the absence and presence of 5-HT ($10\mu\text{M}$). D: net $I_{5\text{-HT}}$ calculated for the curves shown in C.

nist for the 5-HT_{1A} receptor subtype. These results suggest that the 5-HT_{1A} receptors are mainly responsible for the hyperpolarization in neurons of the DLSN.

Under voltage-clamp condition, 5-HT ($1\text{-}50\mu\text{M}$) caused an outward current ($I_{5\text{-HT}}$) associated with an increased membrane conductance. $I_{5\text{-HT}}$ reversed polarity at the equilibrium potential for K^+ calculated by the Nernst equation. Intracellular Cs^+ has been

known to block K^+ channels in a non-selective manner [47]. Injection of Cs^+ in the intracellular space of DLSN neurons depressed the 5-HT hyperpolarization. The 5-HT hyperpolarization was not blocked by extracellular Cs^+ , a blocker for non-selective cation channels that are activated at hyperpolarizing membrane potentials (Q-current, [39]). The delayed rectifier K^+ channel and ATP-sensitive K^+ channels may not be responsible for the

Fig. 7. Effect of Ba²⁺ (100 μ M) on the membrane current of a DLSN neuron. A: the 5-HT-induced inward rectifier K⁺ current was obtained from I-V curves taken before and during the application 5-HT (10 μ M). B: the 5-HT-induced current in the presence of Ba²⁺. Note that Ba²⁺ depressed not only the amplitude of I_{5-HT} but also inward rectifier properties.

5-HT hyperpolarization, because TEA and glibenclamide did not block the 5-HT hyperpolarization. Ca²⁺-activated K⁺ current does not seem to be involved in the current underlying the 5-HT hyperpolarization, because the outward current induced by 5-HT was not blocked by removal of Ca²⁺ from either the external or internal solution [24,44]. In DLSN neurons, the net I_{5-HT} showed inward rectifi-

cation at potentials more negative than -70 mV. Ba²⁺ (100 μ M), known to be a blocker for the inward rectifier K⁺ current [48], depressed the inward rectifier K⁺ current produced by 5-HT.

I_{5-HT} was irreversibly reduced by intracellular injection of GTP γ S but not by GDP β S in DLSN neurons. Several studies have reported that 5-HT_{1A} receptors are coupled to the inward rectifier K⁺ channels through a G-protein in neurons of the dorsal raphe nucleus [40,43,44]. Interestingly, injection of GDP β S into the cells produced no or relatively weak inhibition of I_{5-HT} in neurons of the hippocampus and the dorsal raphe nucleus [44,49]. Katayama et al. [44] have reported that 5-HT_{1A} receptors are coupled to a G-protein which is resistant to GDP β S. The G-protein which mediates I_{5-HT} in DLSN neurons may belong to a GDP β S-resistant type. Previous reports have suggested that the G-protein coupled to the 5-HT receptor is PTX-sensitive (Gi and/or Go) in dorsal raphe nucleus neurons [40,41,50]. Further experiments are needed, however, to clarify whether a PTX-sensitive G-protein is involved in the 5-HT_{1A} receptor-mediated activation of the inward rectifier K⁺ current in rat DLSN neurons.

As an integrated part of the limbic system, the septum plays an important role in the control of a variety of physiological and behavioral processes related to higher cognitive functions, emotions and stress, as well as autonomic regulation. It is of particular interest that the 5-HT_{1A} receptor has been implicated in depression, anxiety and panic disorder [26-28,30-32,51]. The principal neurons in the lateral septum receive a massive hippocampo-septal projection which contains axons of CA1 and CA3 pyramidal neurons, and in turn send efferents to the hypothalamic and amygdaloid area [1-4]. The principal neurons in the lateral septum contain γ -aminobutyric acid (GABA) and participate in local inhibitory circuits within the lateral septum, via their axon collaterals [3]. Stimulation of GABAergic neurons in the lateral septum evoked inhibitory postsynaptic potentials (IPSPs) [52]. The present study showed that 5-HT completely depressed the spontaneous firing activity of principal neurons in the lateral septum. The inhibition of GABAergic neurons may lead to disinhibition of excitatory synaptic transmission in the lateral septum. Supporting this hypothesis, 5-HT has been reported to depress the IPSPs in DLSN neurons [24]. An extracellular study has shown that the excitatory component of the field potentials in the lateral septum evoked by electrical stimulation of fimbrial fibers, was increased by

Fig. 8. Effects of GTP γ S (10 mM) and GDP β S (3 mM) on the 5-HT hyperpolarization obtained from two different DLSN neurons. A and B: sample records of the 5-HT hyperpolarizations obtained from neurons treated with GTP γ S (A) and GDP β S (B). 5-HT hyperpolarizations were recorded 5, 10 and 20-40 min after insertion of the microelectrode. C and D: ordinate indicates the amplitude of the 5-HT hyperpolarization. The 5-HT hyperpolarization recorded 5 min after insertion of the microelectrode is taken as control (100%).

ionophoretic application of 5-HT, whereas the inhibitory component was diminished [53]. Recently, we also observed that 5-HT enhanced the excitatory postsynaptic potential (EPSP) in the DLSN (unpublished observation). These reports, together with the present study, suggest that serotonergic neurons facilitate excitatory synaptic transmission in the hippocampus-septum pathway by depressing the GABAergic inhibitory circuit.

ACKNOWLEDGMENTS: I am most grateful to Professors K. Oizumi and T. Akasu for their useful suggestion and continuous encouragement during the present study. The author also thanks Drs. H. Hasuo and M. Tsurusaki for their helpful comments. This work was supported by The Ishibashi Research Fund and a Grant-in-Aid for Scientific Research

from the Ministry of Education, Science, Sports and Culture of Japan.

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