Brain Research, 309 (1984) 309–316
Elsevier

BRE 10302

Autoreceptor-Mediated Changes in Dopaminergic Terminal Excitability: Effects of Increases in Impulse Flow

JAMES M. TEPPER, STEPHEN J. YOUNG and PHILIP M. GROVES

University of California, School of Medicine, Department of Psychiatry, M-003, La Jolla, CA (U.S.A.)

(Accepted February 14th, 1984)

Key words: dopamine — autoreceptor — antidromic stimulation — excitability — conduction — substantia nigra — impulse flow

The effect of spontaneous and stimulation-induced alterations in impulse flow on the antidromic excitability of nigrostriatal dopaminergic neurons were investigated in urethane-anesthetized rats. Terminal excitability was found to be inversely related to the rate of spontaneous activity of nigral neurons. Conditioning stimulation applied to dopaminergic axons in the medial forebrain bundle was found to decrease terminal excitability, but axonal conditioning stimulation was without effect on antidromic responses evoked from the medial forebrain bundle. Decreases in terminal excitability induced by medial forebrain bundle stimulation could be blocked by local infusions of haloperidol into the region of the terminal fields, suggesting that the effect was receptor-mediated. These results are consistent with the proposal that nigrostriatal dopaminergic neurons may modulate the impulse-dependent release of dopamine from striatal nerve terminals as a function of firing rate by autoreceptor-mediated alterations in the electrical properties of the terminal membrane.

INTRODUCTION

We have previously demonstrated that pharmacological stimulation of autoreceptors located on the terminals of central catecholamine neurons by systemic administration or local infusions of direct- or indirect-acting catecholamine agonists leads to a reduction in the excitability of these terminals, determined by measuring the current necessary to activate neurons antidromically from their terminal fields in neostriatum or frontal cortex[3,4,11,12,19]. These effects can be blocked or reversed by the administration of appropriate antagonists: phentolamine or yohimbine in the case of noradrenergic neurons[11,13] and haloperidol, sulpiride or fluphenazine in the case of dopaminergic neurons[3,17,19]. These data suggest that the autoinhibition of transmitter release in central catecholamine neurons[2,7,9,14,18,20] is associated with a decrease in excitability of the nerve terminal region. The decreased excitability has been interpreted as arising from an autoreceptor-mediated hyperpolarization and/or alteration in ionic conductance of the terminal membrane[3,4,11,17,19].

Although the autoinhibition phenomenon has been well-characterized through biochemical studies on transmitter release, the contribution of this phenomenon to the in situ functioning of catecholamine neurons remains unclear. There are data indicating that the neuroleptic-induced facilitation of dopamine release from striatal terminals in vitro increases with the frequency of the electrical stimulus used to evoke the release[6,10]. These results suggest that the amount of transmitter released from dopamine terminals per nerve impulse may vary with the rate of impulses reaching the terminal. At high rates of firing, the terminal autoreceptors may be expected to be stimulated to a greater degree than when cells are firing slowly, due to increased concentrations of dopamine in the synaptic region, hence autoinhibition would be more pronounced. If this is so, dopaminergic terminal excitability, which is decreased as a function of autoreceptor stimulation[3,4,19], should be decreased at high rates of impulse traffic compared to lower rates of firing. This phenomenon may have special signifi-

Correspondence: P. M. Groves, University of California at San Diego School of Medicine, Department of Psychiatry, M-003, La Jolla, CA 92093, U.S.A.

cance with respect to nigral dopaminergic unit function inasmuch as these neurons typically exhibit a firing pattern consisting of short series (100–500 ms) of repetitive firing at frequencies of 8-15 Hz embedded within a background of slower, more random or 'occasional' neuronal activity[1,21].

In the present experiments, the effects of spontaneous and stimulation-induced alterations in impulse flow on the terminal excitability of nigrostriatal dopaminergic neurons were studied. Our results indicate that dopaminergic terminal excitability varies inversely with the spontaneous rate of firing of the neuron. Stimulation of dopaminergic axons in the medial forebrain bundle (MFB) induced transient decreases in terminal excitability which were prevented by local striatal infusions of haloperidol. When excitability was tested from axons in the MFB following conditioning stimuli applied to the terminal fields, these decreases in antidromic excitability did not occur, suggesting that the effects of impulse flow on terminal excitability were due to the activation of autoreceptors constrained to the terminal regions of the axon and not due to a 'subnormal period' of axonal excitability which has been shown to result from increased impulse flow in other central axons[15,16].

METHODS

The subjects for these experiments were male Sprague–Dawley rats weighing between 285 and 400 g at the time of recording. Details of the surgical preparation have been reported previously[19]. Briefly, animals were anesthetized with urethane (ethyl carbamate, 1.3 g/kg i.p.), and mounted in a stereotaxic frame according to König and Klippel[8]. Following the completion of surgery, animals were immobilized with gallamine triethiodide (15 mg/kg i.v. followed by 40 mg/kg i.p., supplemented as necessary) and respired on a Harvard Apparatus Rodent Respirator at 75–80 strokes/min.

Electrical stimulation

The electrical stimuli for conditioning and testing of terminal and axonal excitability were delivered through bipolar stainless steel, enamel-coated wires approximately 200 μm in diameter with a tip separation of approximately 100 μm. The in vitro impedance of these electrodes was typically 30 KΩ at 500 Hz.

The electrical stimuli consisted of single monophasic pulses of durations ranging from 20 to 750 μs at current intensities between 0.3 and 4.0 mA. Each channel of the stimulator (Grass S-88) was coupled to the desired stimulating electrode through a stimulus isolation unit (Grass SIU-5). Stimulating electrodes were individually calibrated before each experiment by measuring stimulating current in situ and were monitored periodically throughout all experiments to control for possible changes in electrode conductance.

Excitability testing

The general paradigm for testing the terminal excitability of single dopaminergic nigrostriatal neurons has been described in detail in a previous report[19]. Briefly, extracellular recordings of single substantia nigra neurons antidromically activated from neostriatum and MFB were obtained by conventional means, and identified as dopaminergic, based on previously published electrophysiological criteria[5,21].

The 'thresholds' for neostriatal or MFB stimulation, defined as the minimum stimulating current, delivered at a constant duration that was sufficient to elicit the antidromic response on 100% of the noncollision trials, were determined from counterbalanced series of current increments and decrements, with steps approximately equal to 10% of the threshold value. A zero point was determined as the maximum stimulating current that failed to evoke any antidromic responses, and intermediate currents which yielded intermediate frequencies of antidromic response were also presented. Between 25 and 150 stimuli were presented at each current setting in a series.

For testing the effects of increased impulse traffic on striatal terminal excitability, one channel of the stimulator was configured as the 'test' channel, and was set to the neostriatal threshold for each particular neuron, and stimuli were delivered at a rate of 1/s. The second channel was configured as the 'conditioning' channel, and stimulating currents were set to 1.5–2.0 times the threshold for eliciting antidromic responses from the MFB. The conditioning stimulus was delivered after the test stimulus with a fixed delay of 25 ms and consisted of a 750 ms train of single shocks to the MFB within which from 0 to 10 stimuli/s were delivered. A fixed delay of 225 ms followed the

conditioning train. In order to test the effects of increased impulse flow on MFB antidromic excitability, the roles of the neostriatal and MFB electrodes were reversed so that the neostriatal electrode was used to condition the axon antidromically while excitability testing was performed from the MFB. In all cases, the ability of the conditioning stimulus to initiate axonal action potentials and thus condition the axon was verified by observation of the antidromic response induced by the stimulus at the recording site in the substantia nigra. In a few cases, haloperidol (1 μM, 0.3125 μl) was locally infused into the striatal terminal regions of dopaminergic neurons as described elsewhere[11,19], and the effects of MFB conditioning stimulation re-determined.

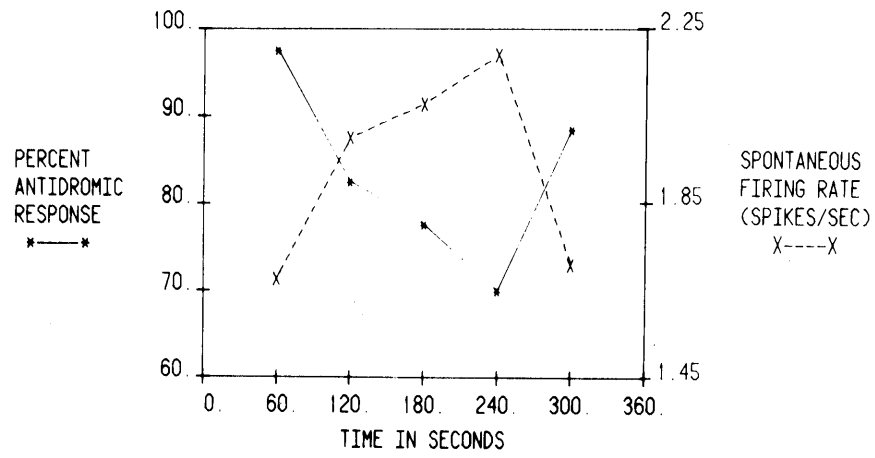

Fig. 1. Relationship between spontaneous firing rate and threshold, illustrated for one representative neuron. Right ordinate: firing rate in spikes/s. Left ordinate: probability of obtaining an antidromic response. Neostriatal stimulus current was set to 1.3 mA and firing rates and percent antidromic response were calculated for one minute epochs, and plotted against time. Firing rate and threshold exhibit a tight inverse dependence.

RESULTS

Relations between spontaneous activity and threshold

Occasionally, neurons were encountered for which it was not possible to obtain a stable baseline measure of threshold. In some of these cases it was noted that the level of spontaneous activity was not constant, and seemed to vary inversely with terminal excitability. This phenomenon is illustrated for one such cell in Figure 1. Data for this figure were obtained by setting the neostriatal stimulating current to a value that elicited an average antidromic response probability of about 80%. The stimulus was left at this setting and several minutes of data were collected. This epoch was subdivided into 60 s bins, and within each bin the percent antidromic response and spontaneous firing rate were calculated. The right ordinate in Fig. 1 represents the spontaneous firing rate of the cell in spikes/s (dashed line). The left ordinate represents terminal excitability expressed in terms of the percent antidromic response (solid line). It can be seen that over the course of 6 min the terminal excitability and spontaneous firing rate display a strong inverse relationship. It should be noted that not all instances of unstable thresholds could be accounted for in this manner, as some 'unstable' cells displayed very constant firing rates.

In addition to being responsive to relatively prolonged changes in firing rate (over the course of many seconds or minutes), dopaminergic terminal excitability was affected by relatively brief events in the millisecond range. It was a common observation that current settings which appeared to be at threshold for 'normal' or 'random' inter-burst periods of firing (which sometimes lasted for minutes), became subthreshold during periods of spontaneous bursting activity during which the 'instantaneous' firing rate can reach 12–15 spikes/s[1,21]. Upon cessation of the burst, recovery ensued over a period of 1–2 s, dependent on the duration and frequency of the repetitive firing.

Furthermore, the probability of obtaining an antidromic response was markedly reduced by the occurence of spontaneous spikes within 5 ms prior to the start of the collision interval. This phenomenon was only apparent when stimulus currents were carefully adjusted to be just at threshold, in agreement with results we have previously obtained[17].

Stimulation-induced impulse flow and terminal and axonal excitability

Increases in the rate of impulses reaching the terminal fields of dopamine neurons elicited by stimulation of nigrostriatal axons in the MFB led to decreases in terminal excitability. Fig. 2 illustrates the phenomenon for one typical cell. The stimulus paradigm is illustrated schematically in Fig. 2A. Fig. 2B shows 5 traces, each taken from a single stimulus delivery from the neostriatum in the absence of any stimulation from the MFB. The neostriatal stimulus is 1.57 mA, which was at threshold as indicated by the presence of an antidromic response, denoted by the arrow, following each stimulus artifact. In

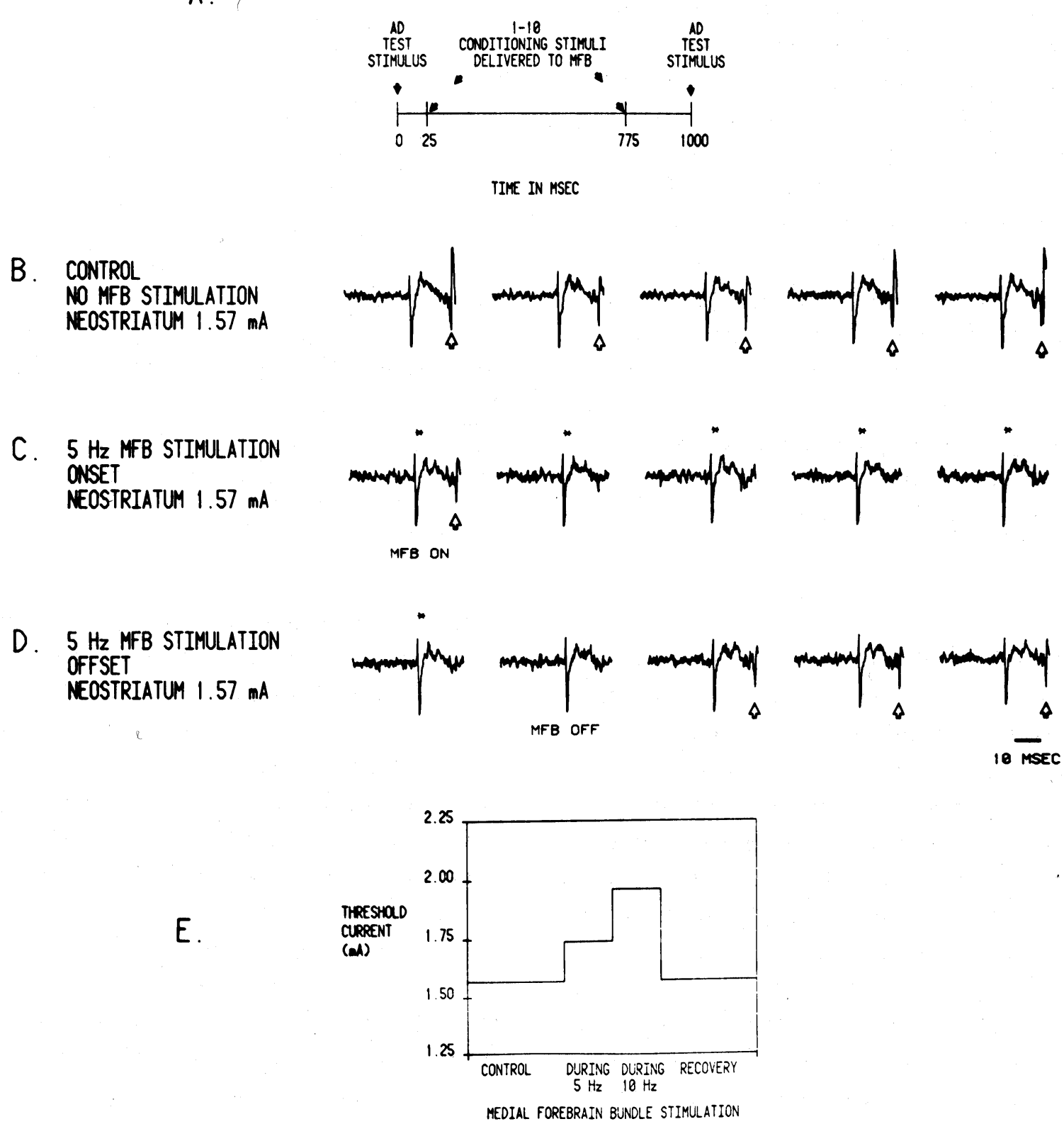

Fig. 2. Effects of stimulus-induced alterations in the rate of impulse traffic on dopaminergic terminal excitability. A: stimulus paradigm. 25 ms following the presentation of the neostriatal testing stimulus at 1 Hz, from 1 to 10 conditioning stimuli were applied to the MFB, in a 750 ms window. B: prior to MFB stimulation, 1.57 mA elicits an antidromic response (arrow) from every stimulus. C: following the onset of 5 Hz MFB conditioning pulses (asterisk), terminal excitability decreases and the antidromic response disappears. Note that the response is still present following the first MFB conditioning train. D: following the cessation of MFB stimuli, excitability recovers to pre-stimulation values. Note that the response does not reappear to the first neostriatal stimulus presentation following cessation of MFB conditioning stimuli, but has returned by the second. E: effect of MFB stimulus frequency on neostriatal threshold for the neuron described above.

Fig. 2C, the neostriatal test stimuli are presented following conditioning of the axon with 750 ms trains at 5 Hz, applied to the MFB. The antidromic response is still present on the first test trial after the initiation of the MFB stimulus, but cannot be evoked at this current following the first trial. In Fig. 2D the last MFB stimulus is indicated by the last asterisk. The response does not reappear immediately upon the first neostriatal stimulus after the cessation of the MFB conditioning stimuli, but returns by the time the second post-MFB neostriatal stimulus is presented, 1 s later. Fig. 2E plots the measured threshold for this neuron following the MFB conditioning trials as a function of conditioning stimulus frequency. Note that the threshold increases with stimulus frequency, and that complete recovery is evident following ces-

sation of the conditioning stimulus. A total of 16 neurons was tested for their response to MFB conditioning stimuli at frequencies ranging from 1 to 10 Hz. All 16 responded with a decrease in excitability. The duration of the decreased excitability varied with the frequency and duration of the conditioning stimulus from a minimum of about 250 ms up to a maximum of several seconds following 10 s of conditioning at 10 Hz.

The degree to which MFB conditioning stimulation reduces the excitability of the dopamine terminal depends on the baseline rate of spontaneous discharge of the neuron. This relationship is illustrated in Fig. 3. Here the percent response during 3 Hz MFB conditioning stimuli to a stimulus current set at the threshold for each neuron prior to conditioning is plotted against the baseline spontaneous firing rate of the cell. There is a significant positive correlation between firing rate and antidromic response probability at 3 Hz ($r = 0.667$, df = 15, $P < 0.05$). If the MFB stimulating current was adjusted to be just below the threshold for eliciting action potentials, stimulation of the MFB did not alter neostriatal terminal excitability, indicating that the phenomenon was dependent upon the passage of impulses down the axon.

The decrease in excitability following conditioning stimulation of the axon is a phenomenon that occurs only at the terminal region of the axon. If the roles of the neostriatal and MFB conditioning and testing electrodes were reversed, so that excitability was measured from the MFB while sending conditioning pulses down from the terminal region, no change in MFB excitability could be detected, even at stimulation frequencies as high as 10 Hz. This is illustrated for one typical neuron in Fig. 4. Each trace is the superimposition of 5 single sweeps. The left column of traces illustrates changes in the excitability of the terminal regions following orthodromic conditioning from the MFB. In Fig. 4A, 1.85 mA is the neostriatal threshold. During the application of MFB conditioning stimuli at 5 Hz (1.5 × threshold), the excitability of the terminal is markedly reduced and antidromic responding occurs on only one of the 5 stimulus presentations, as shown in Fig. 4B. Fig. 4C shows the antidromic responses elicited by the MFB conditioning stimulus, demonstrating that the conditioning stimulus was initiating action potentials along the

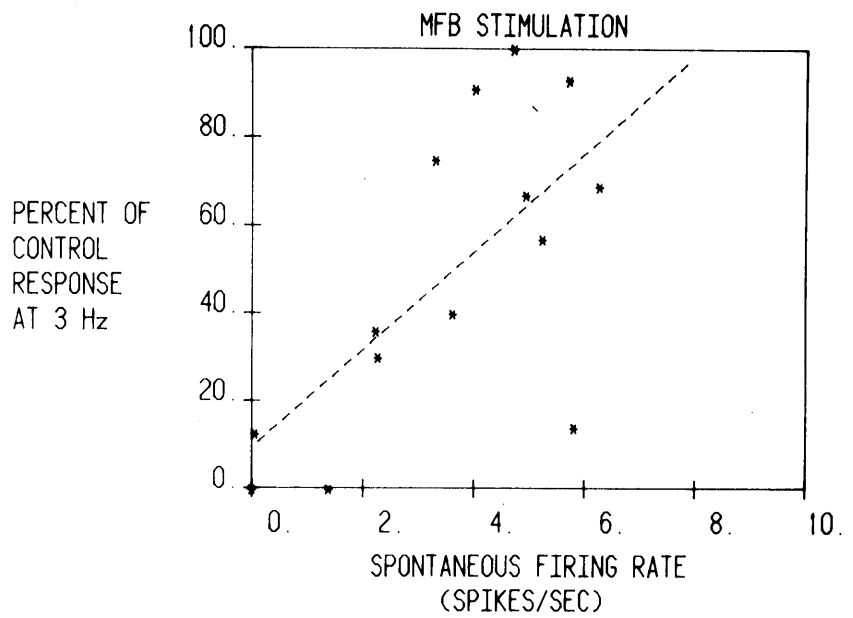

Fig. 3. Relationship between MFB stimulation-induced decreases in terminal excitability and pre-stimulation firing rate. The ordinate represents the percent antidromic response during 3 Hz MFB stimulation to neostriatal stimulus currents which are at threshold in the absence of MFB stimulation. The resulting correlation attains statistical significance ($r = 0.667$, df = 15, $P < 0.05$).

axon. The right column of traces illustrates data obtained from the same neuron when testing excitability from the MFB electrode while conditioning stimuli were applied at the terminal. In Fig. 4D it can be seen that 0.4 mA is the pre-conditioning threshold for antidromic responses evoked from the MFB. Stimulation of the terminal at 5 Hz (1.5 × threshold) fails to alter the MFB threshold (Fig. 4E) despite the fact that the neostriatal conditioning stimulus is driving the axon at 5 Hz, as illustrated in Fig. 4F.

In three cases, haloperidol was infused into the neostriatal stimulating site in an attempt to block the MFB-induced decrease in terminal excitability. In these cases, the decreased excitability seen during MFB stimulation was partially or totally blocked, as illustrated in Fig. 5. All traces are the superimposition of 5 single sweeps. In the first trace, 0.84 mA is seen to be at threshold for eliciting antidromic responses from the neostriatum. Following trains of 3 Hz conditioning stimuli delivered to the MFB, the excitability of the terminal is reduced, and antidromic responses appear on only 3 of the 5 trials although the current is unchanged, as shown in Fig. 5B. Note that the latency to the antidromic responses that are present is prolonged, and that, whereas all responses are full spikes in the control condition (Fig. 5A), following MFB conditioning stimulation the soma-dendritic component of the spike fails in 2 cases. In Fig. 5C the MFB stimulus is presented at 5 Hz, and no antidrom-

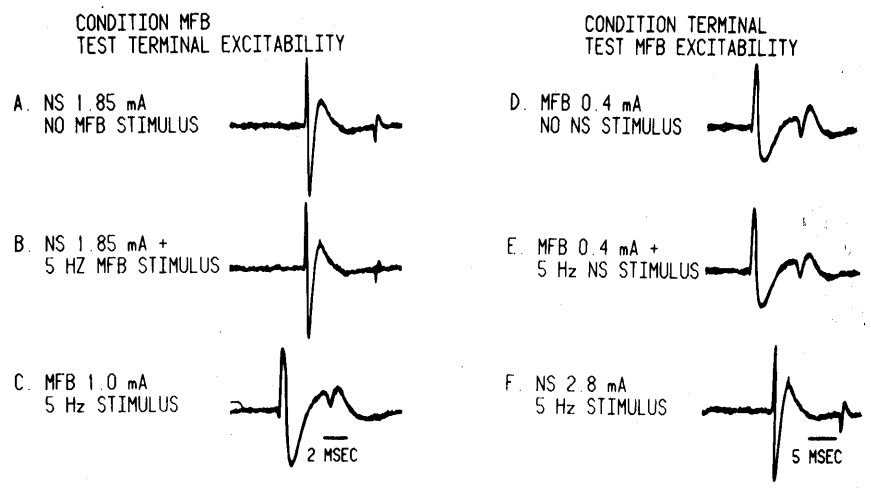

Fig. 4. Comparison of the effects of stimulation-induced alterations in impulse flow on terminal and axonal excitability. Each trace is the superimposition of 5 single sweeps. A: a neostriatal stimulus current of 1.85 mA is at threshold in the absence of MFB conditioning stimuli. B: during the presentation of 5 Hz MFB stimulation, terminal excitability is reduced, and a response is obtained on only 1 of the 5 trials. C: illustration of the antidromic response elicited by the 5 Hz MFB stimulus, demonstrating that it was stimulating the axon. D: excitability is now tested from the MFB electrode while the neostriatal electrode is used to condition the axon antidromically. In the absence of neostriatal stimuli, 0.4 mA is at threshold for MFB stimulation. E: during 5 Hz striatal stimulation, there is no change in the antidromic excitability of the MFB. F: antidromic responses elicited by the neostriatal conditioning stimulus showing that, despite the lack of effect, the axon was being successfully stimulated by the neostriatal conditioning stimuli. The 5 ms calibration marker applies to A, B and F. The 2 ms marker applies to C, D and E.

ic responses are elicited from striatum. After cessation of the MFB stimulus, complete recovery of the pre-stimulation threshold ensues, illustrated in Fig. 5D. Note that the latency recovers to the pre-conditioning value as well, but that some responses now consist of the initial segment spike only. Following an infusion of 1 μM haloperidol into the neostriatal stimulating site, excitability increases slightly and the threshold drops to 0.76 mA. All antidromic responses now consist of full spikes. Application of the MFB conditioning stimulus is now unable to induce a decrease in terminal excitability in this neuron, and the latency remains unchanged, as shown in Fig. 5E.

DISCUSSION

We have observed that spontaneous changes in dopaminergic terminal excitability take place which are often time-locked to alteratons in the rate of spontaneous discharge of nigrostriatal neurons. This finding indicates that terminal excitability in dopamine neurons displays sufficient plasticity to respond to transient fluctuations in the rate of impulses reaching the striatal dopaminergic terminals.

Increases in the rate of impulses reaching the terminals of nigrostriatal neurons induced by stimulation of the MFB over a physiologically relevant range of frequencies and durations led to pronounced decreases in terminal exitability. These decreases in excitability were quantitatively and qualitatively similar to those seen following local striatal infusions or

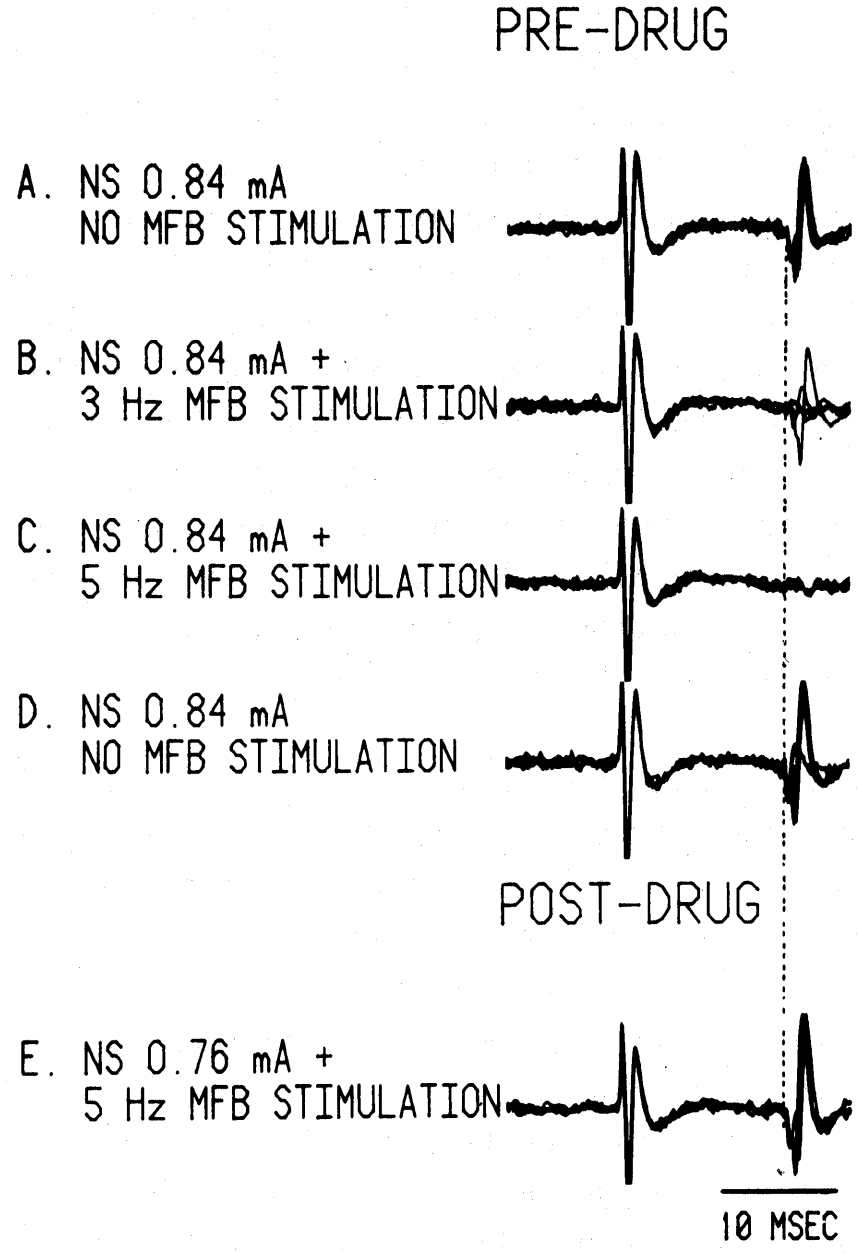

Fig. 5. MFB stimulation-induced decreases in terminal excitability are sensitive to blockade by neostriatal infusions of haloperidol. All traces are the superimposition of 5 single sweeps. A: in the absence of MFB conditioning, 0.84 mA is at threshold. B: during 3 Hz MFB conditioning, terminal excitability is reduced, and responses are observed on only 3 of the 5 sweeps. Note that, whereas all responses prior to the onset of conditioning consisted of full initial segment–soma-dendritic spikes, during MFB stimulation 2 of the 3 antidromic responses consist of initial spike spikes only, and that the latency to all responses is clearly increased. C: during 5 Hz MFB conditioning, no antidromic responses occur. D: recovery of antidromic excitability following the cessation of the MFB conditioning stimuli. E: following a local infusion of haloperidol, the threshold is reduced to 0.76 mA, and 5 Hz MFB conditioning is completely without effect on terminal excitability.

systemic administration of apomorphine or amphetamine which we have attributed to an autoreceptor-mediated hyperpolarization and/or alteration in ionic conductance of the terminal membrane[3,4,19]. As was the case with the drug-induced decreases in excitability, increases in antidromic latency were accompanied by impulse-dependent decreases in excitability which may be attributable to increased activation time resulting from an autoreceptor-mediated hyperpolarization or alteration in conductance near the site of antidromic impulse initiation.

The decreases in terminal excitability following axonal conditioning were probably not due to a non-specific 'subnormal period' of axonal excitability due simply to the passage of action potentials, as described by Swadlow and others[15,16]. This is indicated by the observation that reversing the stimulation paradigm so that excitability was measured from the MFB following antidromic conditioning of the axon from the terminal region failed to alter thresholds from the MFB. Thus, increases in impulse flow alone do not decrease excitability in nigrostriatal axons. Furthermore, in all three cases, striatal infusions of haloperidol were able to block the conditioning-induced decreases in terminal excitability, demonstrating that increased impulse flow alone does not reduce excitability, even at the terminal regions. We have previously shown that local infusions of apomorphine into the MFB do not alter antidromic excitability from this region[19], suggesting that axonal autoreceptors are constrained to the terminal regions of dopamine neurons. These results are all consistent with the idea that activity-dependent decreases in terminal excitability are due to increased autoreceptor stimulation secondary to increased release of dopamine from nerve terminals.

This interpretation is supported by the correlation obtained between the effects of MFB conditioning stimuli on threshold and the pre-stimulation firing rate of the neuron. In addition, neostriatal thresholds during MFB stimulation were observed to be directly related to the frequency of the conditioning stimuli. This finding is in good agreement with other results showing that the sensitivity of dopaminergic terminals to facilitation of evoked transmitter release by dopamine receptor blocking agents is increased at higher rates of electrical stimulation[6,10]. Consistent with this, infusions of dopamine antagonists cause much larger increases in terminal excitability in rapidly firing neurons than in slowly firing cells, while agonists decrease excitability more in slowly firing neurons than in cells with a high rate of spontaneous activity[19]. These results suggest that the level of autoinhibition, or autoinhibitory 'tone', in dopaminergic nerve terminals in striatum is not constant, but varies with firing rate over a time domain in the tens or hundreds of milliseconds.

The relationship between the rate of impulse activity and terminal excitability suggests that autoinhibition is more pronounced at higher rates of firing. Since autoinhibition acts to reduce the total amount of transmitter released[9,14,19], these data suggest that as firing rate increases, either tonically or phasically as within a burst, the total amount of dopamine released by each action potential in nigrostriatal neurons is reduced compared to release evoked by single action potentials at lower rates of firing.

ACKNOWLEDGEMENTS

This research was supported, in part, by Grant DA 02854 and Research Scientist Development Award DA 00079 (to P.M.G.) from the National Institute on Drug Abuse.

REFERENCES

1 Bunney, B. S., Walters, J. R., Roth, R. H. and Aghajanian, G. K., Dopaminergic neurons: effect of antipsychotic drugs and amphetamine on single cell activity, *J. Pharmacol. exp. Ther.*, 185 (1973) 560–571.
2 De Langen, C. D. J., Hogenboom, F. and Mulder, A. H., Presynaptic noradrenergic α-receptors and modulation of [^{3}H]noradrenaline release from rat brain synaptosomes, *Europ. J. Pharmacol.*, 60 (1979) 79–89.
3 Groves, P. M., Fenster, G. A., Tepper, J. M., Nakamura, S. and Young, S. J., Changes in dopaminergic terminal excitability induced by amphetamine and haloperidol, *Brain Res.*, 221 (1981) 425–431.
4 Groves, P. M. and Tepper, J. M., Neuronal mechanisms of action of amphetamine. In I. Creese (Ed.), *Stimulants: Neurochemical, Behavioral, and Clinical Perspectives,* Raven Press, New York, 1983, pp. 81–129.
5 Guyenet, P. G. and Aghajanian, G. K., Antidromic identification of dopaminergic and other output neurons of the rat substantia nigra, *Brain Research,* 150 (1978) 69–84.
6 Hoffman, I. S. and Cubeddu, L. X., Rate and duration of stimulation determine presynaptic effects of haloperidol on dopaminergic neurons, *J. Neurochem.*, 39 (1982) 585–588.

7 Kamal, L. A., Arbilla, S. and Langer, S. Z., Presynaptic modulation of the release of dopamine from the rabbit caudate nucleus: differences between electrical stimulation, amphetamine and tyramine, *J. Pharmacol. exp. Ther.*, 216 (1981) 592–598.
8 König, J. F. R. and Klippel, R. A., *The Rat Brain: a Stereotaxic Atlas of the Forebrain and Lower Part of the Brain Stem,* Williams and Wilkins, Baltimore, 1963.
9 Langer, S. Z., Presynaptic receptors and their role in the regulation of transmitter release, *Brit. J. Pharmacol.,* 60 (1977) 481–497.
10 Lehman, J. and Langer, S. Z., The pharmacological distinction between central pre- and post-synaptic dopamine receptors: Implications for the pathology and therapy of schizophrenia. In M. Kohsaka, T. Shohmori, Y. Tsukada and G. L. Woodruff (Eds.), *Advances in Dopamine Research — Advanc. Biosci., Vol. 37,* Pergamon Press, Oxford, 1982, pp. 25–39.
11 Nakamura, S., Tepper, J. M., Young, S. J. and Groves, P. M., Neurophysiological consequences of presynaptic receptor activation: Changes in noradrenergic terminal excitability, *Brain Research,* 226 (1981) 155–170.
12 Nakamura, S., Tepper, J. M., Young, S. J. and Groves, P. M., Changes in noradrenergic terminal excitability induced by amphetamine and their relation to impulse traffic, *Neuroscience,* 7 (1982) 2217–2224.
13 Ryan, L. J., Tepper, J. M., Young, S. J. and Groves, P. M., Comparison of amphetamine dose–response effects on presynaptic terminal and somatodendritic regions of noradrenergic locus coeruleus neurons, submitted.
14 Starke, K., Presynaptic receptors, *Ann. Rev. Pharmacol. Toxicol.,* 21 (1981) 7–30.
15 Swadlow, H. A., Kocsis, J. D. and Waxman, S. G., Modulation of impulse conduction along the axonal tree. *Ann. Rev. Biophys. Bioengng.,* 9 (1980) 143–179.
16 Swadlow, H. A. and Waxman, S. G., Activity-dependent variations in the conduction properties of central axons. In S. G. Waxman (Ed.), *Physiology and Pathobiology of Axons,* Raven Press, New York, 1978, pp. 191–202.
17 Takeuchi, H., Young, S. J. and Groves, P. M., Dopaminergic terminal excitability following the arrival of the nerve impulse: the influence of amphetamine and haloperidol, *Brain Research,* 245 (1982) 47–56.
18 Taube, H. D., Starke, K. and Borowski, E., Presynaptic receptor systems on the noradrenergic neurons of rat brain, *Naunyn-Schmiedeberg's Arch. Pharmacol.,* 299 (1977) 123–141.
19 Tepper, J. M., Nakamura, S., Young, S. J. and Groves, P. M., Autoreceptor-mediated changes in dopaminergic terminal excitability: effects of striatal drug infusions, *Brain Reserach,* 309 (1984) 317–333.
20 Westfall, T. C., Perkins, N. A. and Paul, C., Role of presynaptic receptors in the synthesis and release of dopamine in the mammalian central nervous system. In S. Z. Langer, K. Starke and M. L. Dubocovich (Eds.), *Presynaptic Receptors — Advanc. Biosci.,* Pergamon Press, New York, 1978, pp. 243–248.
21 Wilson, C. J., Young, S. J. and Groves, P. M., Statistical properties of neuronal spike trains in the substantia nigra: cell types and their interactions, *Brain Research,* 36 (1977) 243–260.