Proc. Natl. Acad. Sci. USA
Vol. 84, pp. 2101–2105, April 1987
Psychology

Cerebellar GABAergic processes: Evidence for critical involvement in a form of simple associative learning in the rabbit

(classical conditioning/nictitating membrane response/bicuculline methiodide/picrotoxin)

LAURA A. MAMOUNAS*†, RICHARD F. THOMPSON*, AND JOHN MADDEN IV‡

*Department of Psychology, Stanford University, Stanford, CA 94305; and ‡Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305

Contributed by Richard F. Thompson, November 17, 1986

ABSTRACT **Converging evidence from electrophysiological recording and lesion studies suggests an essential role for the cerebellum in classical conditioning of the nictitating membrane response in the rabbit. The present study begins to delineate within this structure neurotransmitter systems that appear critical for the expression of this form of simple associative learning. Experiments reported here demonstrate that microinfusion of γ-aminobutyric acid (GABA) antagonists (either bicuculline methiodide or picrotoxin) into specific areas of the medial dentate/lateral interpositus nuclei or into the cerebellar cortex of lobule HVI can selectively and reversibly abolish conditioned responding, while leaving the unconditioned reflex response intact. The results are consistent with the suggestion that GABAergic synapses play an essential role in the circuitry that mediates the conditioned response.**

Experimental evidence suggests an essential role for the dentate/interpositus nuclei of the cerebellum in a form of simple associative learning, classical conditioning of the rabbit nictitating membrane (NM) response. Work in Thompson's laboratory (1–4) initially demonstrated that discrete lesions of the medial dentate/lateral interpositus region, or the superior cerebellar peduncle, could selectively disrupt acquisition, retention, and relearning of this associative task. These observations were subsequently confirmed by others (5); the critical nuclear region appears to be the anterior lateral interpositus (6, 7). Moreover, electrophysiological analysis revealed that training-induced modifications in neural activity, which precede and model the conditioned response, develop in this region and in localized regions of the cerebellar cortex during learning (8, 9). These observations suggest that some neural modification critical for the acquisition and retention of this associative task may be located within the cerebellar circuitry (10).

As a preliminary step in elucidating potential synaptic circuitry subserving classical conditioning of the NM response, a series of pharmacological studies was initiated. Such analysis not only circumvents the difficulties intrinsic to ablation/lesion experimental approaches but also may provide an initial characterization of critical neurotransmitter systems. Noting that an extensive literature indicates that intrinsic cerebellar neurons appear to be predominantly GABAergic (11), these initial experimental manipulations were directed at determining whether microinfusion of γ-aminobutyric acid (GABA) antagonists within select regions of the cerebellum could effect retention of this form of simple associative learning.

MATERIALS AND METHODS

Thirty-five male New Zealand albino rabbits (*Oryctolagus cuniculus*), weighing 2–3 kg at the beginning of the experiment, were used. Animals were individually housed with ad lib access to food and water.

Surgical Procedures. Animals were anesthetized with Halothane, and a cannula/electrode assembly was implanted into either the left dentate/interpositus or fastigial deep nuclei of the cerebellum using both stereotaxic coordinates and electrophysiological monitoring. The cannula/electrode assembly consisted of three components; a 26-gauge stainless steel guide cannula, a 33-gauge internal stylet (Plastic Products, Roanoke, VA), and a recording electrode. The internal stylet extended 1.25 mm beyond the tip of the external cannula. The electrode was cemented immediately adjacent to the guide cannula and extended 0.5 mm ventral to the tip of the internal stylet.

The skull was positioned with lambda 1.5 mm ventral to bregma. The stereotaxic coordinates for dentate/interpositus nuclei placements were 4.75 ± 0.25 mm lateral to the midline, 0.6 ± 0.1 mm anterior and 14.0 ± 0.5 mm ventral to the skull bone at lambda. Coordinates for fastigial nuclei placements were 1.5 ± 0.1 mm lateral, 0.5 ± 0.1 mm anterior, and 14.9 ± 0.1 mm ventral. The cannula/electrode assembly and a head stage, designed to accommodate the air puff/micropotentiometer systems, were then secured to the skull with screws and dental acrylic.

General Training and Testing Procedures. Animals were given 1 week to recover from surgery before training was initiated. Standard training procedures for classical conditioning of the rabbit NM response have been described (12). Briefly, training consisted of short-delay classical conditioning with a tone conditioned stimulus (CS; 1 kHz, 85 dB, 350 msec) and a corneal air puff unconditioned stimulus directed to the left eye (US; pressure, 2.1 N/cm^2; 100 msec coterminate with the CS). Each daily training session consisted of 13 blocks of trials. A block of trials contained one CS alone test trial followed by eight paired CS–US trials. Trials were delivered every 20–40 sec (mean, 30 sec). Conditioned and unconditioned responses (CR, UR) were determined by calculating the peak NM response amplitude (expressed in mm) during these CS and US periods, respectively. A CR was defined as an extension of the NM of at least 0.5 mm within the CS period. Animals were trained until they exhibited at least a 95% CR proficiency in a given training session. Thus, animals typically received a total of four to six training sessions before drug testing sessions were initiated.

Microinfusion Protocol. On the day of testing, a four-block baseline measurement of behavior was obtained immediately prior to drug administration. After baseline conditioning, the internal stylet was removed and replaced with an internal cannula connected to a microsyringe via polyethylene tubing.

The publication costs of this article were defrayed in part by page charge payment. This article must therefore be hereby marked "*advertisement*" in accordance with 18 U.S.C. §1734 solely to indicate this fact.

Abbreviations: CS, conditioned stimulus; US, unconditioned stimulus; CR, conditioned response; UR, unconditioned response; NM, nictitating membrane; GABA, γ-aminobutyric acid.

†Present address: Department of Neuroscience, The Johns Hopkins University School of Medicine, Baltimore, MD 21205.

The internal cannula was identical in dimension to the internal stylet. Appropriate compounds dissolved in a 0.75-μl vol of Ringer's solution (final pH 7.4) were infused at a constant rate over a 60-sec period. To allow adequate time for diffusion of substances, a 5-min period intervened between completion of the microinfusion and resumption of behavioral testing. Animals were then tested for an additional 9–18 blocks, as determined by the particular study.

A 4-day intertest interval was maintained to minimize possible tachyphylaxis due to prior drug administration. In preliminary experiments using this protocol, no apparent loss of drug efficacy was observed over successive drug testing sessions. Animals were typically tested over a particular drug regime once. Throughout each testing session, neural activity was recorded in an area immediately adjacent to the infusion site using a chronically implanted multiple-unit electrode.

Experimental Designs. A series of four studies was used to assess the effects of microinfusion of either GABAergic or glycinergic antagonists into the left dentate/interpositus nuclei on the classically conditioned NM response. A within-subjects design was used in each study. An initial study assessed the effects of the GABA antagonist bicuculline methiodide. With each animal receiving a randomized dose sequence, 13 animals were administered three doses of bicuculline methiodide (1.5, 0.75, and 0.38 nmol) and the vehicle (0.75 μl of Ringer's solution) over four testing sessions.

A second study determined the effect of the GABA antagonist picrotoxin. With the sequence of dose administration randomized, 11 animals each received three doses of picrotoxin (0.75, 0.38, and 0.19 nmol) and the vehicle over four testing sessions.

A third study examined the relative effects of the glycine antagonist strychnine on NM behavior. Six animals that had demonstrated behavioral sensitivity to 1.5 nmol of bicuculline methiodide in the initial study were used in the present experiment. Animals were determined to be "sensitive" if the CR peak amplitude was reduced by >90% for three blocks postinfusion during the initial study. In the present study, each of these animals was tested with a counterbalanced sequence of drug administrations with 1.5 nmol of bicuculline methiodide, 1.5 nmol of strychnine, and the vehicle administered over three testing sessions.

A fourth study assessed the relative effects of bicuculline methiodide on the ipsilateral vs. contralateral NM response. Seven animals with cannula placed in the left deep nuclei region were initially trained and then tested (1.5-nmol dose of bicuculline methiodide) on the NM ipsilateral to the infusion cannula (left NM). Training was then shifted to the eye contralateral to the infusion cannula by directing the air puff to the right cornea. All animals rapidly learned to elicit CRs on the right NM and were trained 2 additional days—exhibiting 95% CR proficiency. On the following day, the right NM response was tested with the same dose of bicuculline methiodide used in the previous test of the left side. Training was then shifted back to the original ipsilateral side for three daily training sessions. On the next day, animals were retested on the left side.

A final study examined the effects of microinfusion of GABA antagonist bicuculline methiodide into the left fastigial nuclei on the NM response ipsilateral to the site of infusion. Using a randomized dose sequence, four animals each received 1.5 nmol of bicuculline methiodide and the vehicle over two testing sessions.

At the completion of each experiment, cannulae placements were determined by using histological procedures previously described (6).

RESULTS

Histological Reconstruction of Infusion Sites. Histological reconstruction of cannulae tip placements marked the apparent sites of drug infusion for each animal. Each infusion site was graphically characterized by its relative sensitivity to GABA antagonists (Fig. 1). Relative sensitivity for each site was determined by assessing the magnitude of the diminution/abolition of the CR peak amplitude following microinfusion of either 1.5 nmol of bicuculline methiodide or 0.75 nmol of picrotoxin depending on the particular experimental assignment of the animal. Subsequent group analysis indicated that most sensitive sites were located within 0.5 mm of the rostral half of the medial dentate/lateral interpositus region, ranging within this structure from 0.5 to 1.5 mm rostral to lambda. These anatomical boundaries are consistent with the areas reported as the most effective sites for abolishing the CR in the lesion/ablation studies (1–9). Only animals with cannula placements within these anatomical boundaries were

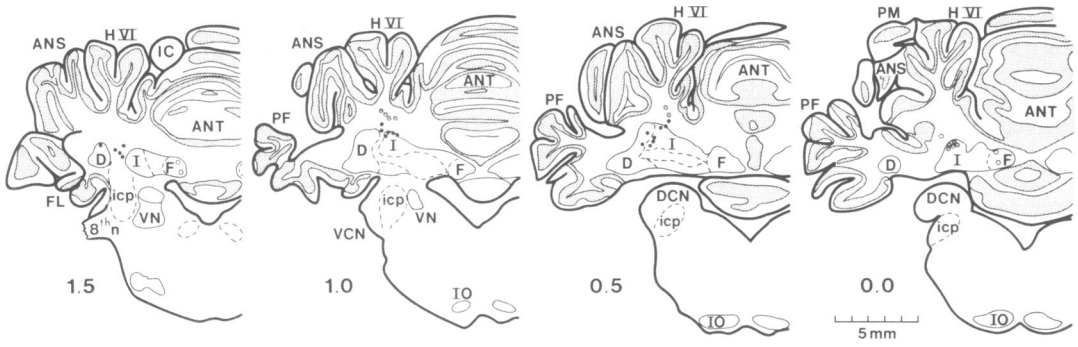

FIG. 1. Histological reconstruction of infusion sites graphically characterized by relative sensitivity to GABA antagonists. Deep nuclei sites: solid circles indicate marked diminution/abolition (an average 97% ± 2% reduction relative to baseline CR amplitude) for the corresponding sites (n = 19). Collectively, these sites lie within 0.5 mm of the rostral half of the medial dentate/lateral interpositus region, ranging within this structure from 0.5 to 1.5 mm rostral to lambda bone suture. Shaded circles indicated partial diminution of the CR (an average 50% ± 7% reduction relative to baseline CR amplitude) in the posterior region of the medial dentate/lateral interpositus (n = 5). Open circles indicate no apparent effect on the CR relative to baseline CR amplitude at infusion sites within the fastigial nucleus (n = 4). Distal white matter: infusion sites in the distal overlying white matter ranged from partial diminution to no apparent effect reflected in the corresponding shaded and open circles (n = 4%). This reduction averaged 28% ± 4% relative to baseline CR amplitude. Numbers in lower left of each reconstruction indicate distance (in mm) anterior to lambda when the skull is oriented with lambda positioned 1.5 mm ventral to bregma. ANS, ansiform lobes; ANT, anterior lobe; D, dentate nucleus; DCN, dorsal cochlear nucleus; HVI, lobule HVI (of Larsell); F, fastigial nucleus; FL, flocculus; 8th n, nerve of the eighth nucleus; IC, inferior colliculus; icp, inferior cerebellar peduncle; I, interpositus nucleus; IO, inferior olive; PF, paraflocculus; PM, paramedian lobe; VCN, ventral cochlear nucleus; VN, vestibular nucleus.

used to determine the drug–dose relationship of these antagonists or the effects of bicuculline methiodide on the ipsilateral vs. contralateral NM response (study 1, 8 of 13 animals had such placements; study 2, 7 of 11 animals; and study 4, 4 of 7 animals). In contrast, the remaining animals with cannula placements in more posterior regions of the medial dentate/lateral interpositus region, as well as animals with cannula placements located more distal to the deep nuclei in the overlying white matter, displayed drug effects either less effective or totally ineffective in reducing the CR peak amplitude. Furthermore, microinfusion of bicuculline methiodide into the fastigial nucleus, including areas at lambda, and 1.5 mm rostral to lambda produced no apparent effect on the CR.

Effects of GABA Antagonists on NM Response. Microadministration of bicuculline methiodide into the medial dentate/lateral interpositus region produced a significant diminution/abolition of the CR peak amplitude. This effect was dose dependent and, at the highest dose administered (1.5 nmol), markedly reduced or completely abolished the CR for 3–4 blocks postinfusion (Fig. 2). A two-way analysis of variance (drug treatment × postdrug block of trials) with repeated measures over both factors confirmed these observations, showing significant dose [$F(3,21) = 11.88$; $P < 0.001$], block [$F(10,70) = 9.70$; $P < 0.001$], and dose–block interaction [$F(30,210) = 4.85$; $P < 0.001$] effects. Post hoc analysis showed that the three drug dose levels were reliably different from vehicle during the first two blocks postinfusion (blocks 5–6). The NM peak amplitude for the highest dose level remained significantly different from vehicle control levels until the end of the testing session (blocks 12–15). In contrast to the effect on the CR, bicuculline methiodide produced no apparent effect on the amplitude of the UR.

Analysis of multiple unit activity, recorded near the infusion site during testing, revealed no obvious abnormalities in background unit firing following drug infusion when compared to either preinfusion neural activity or activity following behavioral recovery. Note that the learning-induced increase in neuronal discharge in the CS period was reversibly abolished in parallel with the behavioral CR (Fig. 3).

Microinfusion of picrotoxin into this region, as in the case of bicuculline methiodide, produced a significant dose-dependent diminution/abolition of the CR peak amplitude (Fig. 4). A two-way analysis of variance yielded significant dose [$F(3,18) = 10.45$; $P < 0.001$], block [$F(17,102) = 3.90$; $P < 0.001$], and dose–block interaction [$F(51,306) = 5.32$; $P < 0.001$] effects. Post hoc analysis revealed that both the 0.75- and 0.38-nmol (but not the 0.19-nmol) dose levels were significantly different from the vehicle during the initial blocks postinfusion (blocks 5–11). The NM peak amplitude for the highest dose level remained significantly different from vehicle control levels until the end of the testing session (blocks 19–22). As observed with bicuculline methiodide infusions, picrotoxin produced no apparent effect on the UR amplitude.

A second series of studies (not detailed here) assessed the effects of infusion of these GABA antagonists into the cerebellar cortex of lobule HVI on the NM response. Results from a representative animal from these studies are displayed in Fig. 5. The results show that microinfusion of picrotoxin

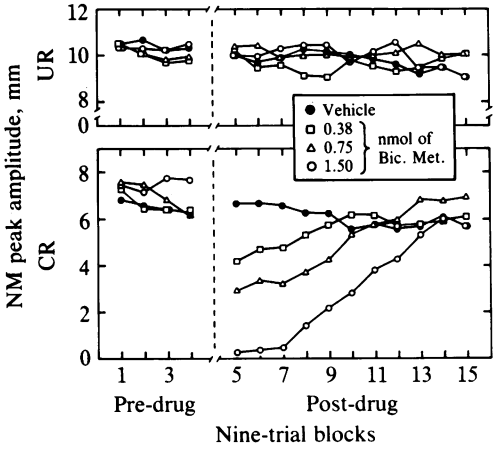

FIG. 2. Mean UR (*Upper*) and CR (*Lower*) peak amplitudes (expressed in mm) during 4 blocks of preinfusion baseline conditioning (blocks 1–4) and 11 blocks following microinfusion (blocks 5–15) of either bicuculline methiodide (Bic. Met.) or the vehicle into the dentate interpositus.

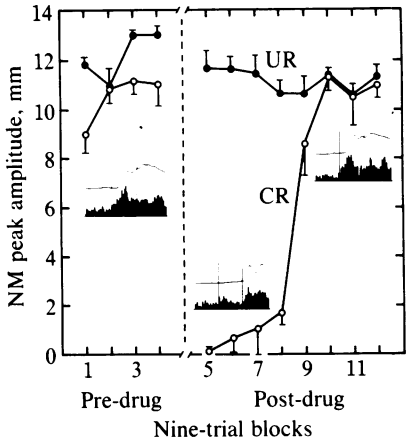

FIG. 3. Example of the effects of microinjection of bicuculline methiodide into the medial dentate/lateral interpositus region on the ipsilateral NM response and multiple unit neural activity during a testing session. ● and ○, peak amplitude of UR and CR, respectively. (*Left*) Mean NM response amplitude during four blocks of pre-drug baseline conditioning. (*Right*) Mean NM response amplitude for eight blocks following microinfusion of 1.5 nmol of bicuculline methiodide. (*Insets*) Upper trace in each histogram represents the averaged NM response; lower trace depicts the corresponding medial dentate/lateral interpositus multiple unit peristimulus histogram. The bin width is 9 msec. The first vertical line in each histogram indicates tone onset; the second vertical line indicates air puff onset. The pre-drug histogram is an average of blocks 2, 3, and 4; the post-drug histogram is an average of blocks 5, 6, and 7. The rightmost histogram is an average of blocks 10, 11, and 12.

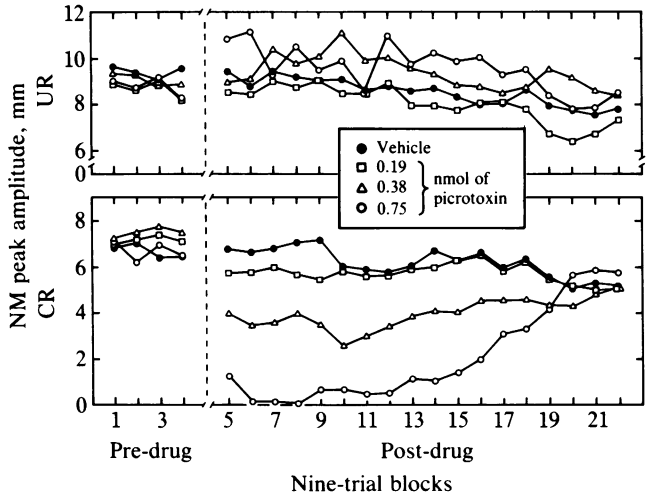

FIG. 4. Mean UR (*Upper*) and CR (*Lower*) peak amplitudes (expressed in mm), during 4 blocks of preinfusion baseline conditioning (blocks 1–4) and 18 blocks following microinfusion (blocks 5–22) of either picrotoxin or the vehicle into the dentate interpositus.

(0.75 nmol) into the cerebellar cortex in the deeper layers of the mid to rostral region of lobule HVI (of Larsell) also selectively and reversibly abolishes the CR, leaving the UR intact.

Effects of Strychnine on the NM Response. In contrast to the effects of GABA antagonists, the glycine antagonist strychnine produced no apparent effect on NM CRs or URs relative to vehicle when infused into the dentate/interpositus region of the cerebellum (Fig. 6).

Effects of Bicuculline Methiodide on the Ipsilateral vs. Contralateral NM Response. Microinfusion of bicuculline methiodide into the left dentate/interpositus region selectively abolishes conditioned NM responding ipsilateral to the infusion cannula (Fig. 7). However, this same manipulation produces no apparent alteration during testing of the contralateral (right NM) CR. Animals were initially tested on the NM response ipsilateral to the infusion cannula (left NM). The results were consistent with previous experiments and demonstrated the characteristic selective reduction/abolition of the CR postinfusion. Testing of the contralateral NM response, however, produced no apparent change in NM peak amplitude. A retest of the ipsilateral NM response produced a selective abolition as was initially observed. A two-way analysis of variance performed on the CR amplitudes of these three treatments yielded significant treatment [$F(2,6) = 33.44$; $P < 0.001$], block [$F(10,30) = 11.85$; $P < 0.001$] and treatment–block interaction [$F(20,60) = 3.65$; $P < 0.001$] effects. Post hoc comparisons revealed no significant difference between the two left NM measures at any block, but both were reliably different from the right NM measure during the first 10 blocks postinfusion (blocks 5–14, but not block 15). Separate analysis of variance revealed that the UR peak amplitude was not reliably altered by any of these manipulations.

DISCUSSION

A wealth of experimental evidence suggests that the interpositus region of the cerebellum is an essential neuronal substrate involved in classical conditioning of the rabbit NM response (1–9). The present series of experiments extends these observations and suggests a critical role for GABAergic processes in enabling the expression of the CR. Microinfusion of GABA antagonists (either bicuculline methiodide or picrotoxin) into this region produced a complete and reversible abolition of the conditioned NM response. These effects are dose dependent and can be selective to the CR, with the unconditioned reflex response remaining unaffected. When strychnine was tested in the same animals (at equimolar doses that reliably produced complete and selective abolition of CRs by GABA antagonists), there was no apparent difference in either the animals' CR or UR measures or in gross behavioral manifestations relative to pre-drug baseline behavior. Such results suggest the pharmacological specificity of these drug effects on the CR.

Histological reconstruction of infusion sites confirmed the anatomical specificity of these effects, showing that the rostral portion of the medial dentate/lateral interpositus

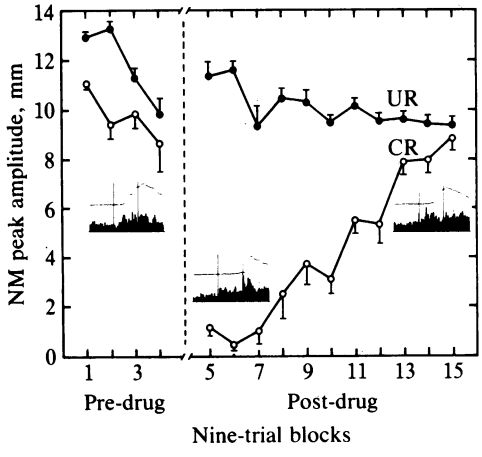

FIG. 5. Example of the effects of microinfusion of picrotoxin into the region of lobule HVI (of Larsell) on the ipsilateral NM response and multiple unit neural activity during a testing session. ● and ○, peak amplitude of UR and CR, respectively. (*Left*) Mean NM response amplitude during four blocks of pre-drug baseline conditioning. (*Right*) Mean NM response amplitude for eight blocks following microinjection of 0.75 nmol of picrotoxin. (*Insets*) Upper trace in each histogram represents the averaged NM response; lower trace depicts the corresponding lobule HVI (of Larsell) multiple unit peristimulus histogram. The bin width is 9 msec. The first vertical line in each histogram indicates tone onset; the second vertical line indicates air puff onset. The pre-drug multiple unit histogram is an average of blocks 2, 3, and 4; the post-drug histogram is an average of blocks 5, 6, and 7. The rightmost histogram is an average of blocks 13, 14, and 15.

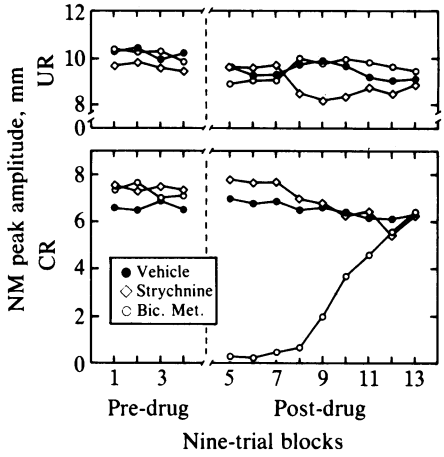

FIG. 6. Mean UR (*Upper*) and CR (*Lower*) peak amplitudes (expressed in mm) during four blocks of preinfusion baseline conditioning (blocks 1–4) and nine blocks following microinfusion (blocks 5–13) of either bicuculline methiodide (Bic. Met.) or strychnine, both at 1.5 nmol, or the vehicle into the dentate interpositus.

Histological reconstruction of infusion sites confirmed the anatomical specificity of these effects, showing that the rostral portion of the medial dentate/lateral interpositus

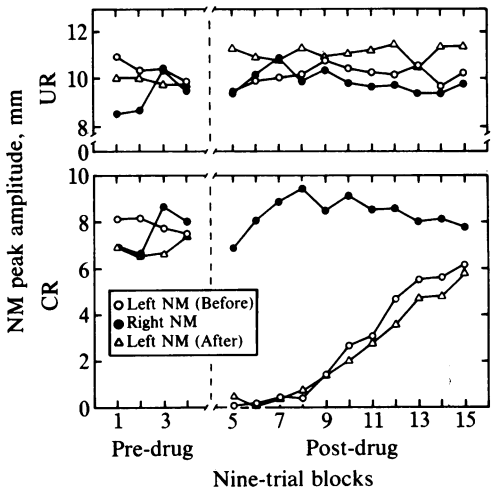

FIG. 7. Mean UR (*Upper*) and CR (*Lower*) peak amplitudes (expressed in mm) during 4 blocks of preinfusion baseline conditioning (blocks 1–4) and 11 blocks following microinfusion (blocks 5–13) of bicuculline methioidide (1.5 nmol) into the left medial dentate/lateral interpositus region. Response measures were obtained over three testing sessions, initially on the NM ipsilateral to the infusion sites (Before), then on the NM contralateral (i.e., right side), and finally on the original ipsilateral NM (After).

region is the most effective site of infusion. Cannula placements in either the more caudal dentate/interpositus region or in more distal areas in the overlying white matter, were either considerably less effective or completely ineffective in disrupting CRs. Placements within the adjacent fastigial nuclei were also ineffective. These observations extend the initial lesion experiments (1–9).

Electrophysiological analysis following drug infusion indicated no substantial change in background unit firing when compared to unit activity prior to infusion or following behavioral recovery. This suggests the GABA antagonists were probably not affecting conditioned behavior by producing abnormal patterns of unit discharge (13). Nonetheless, one could still argue that infused GABA antagonists did not produce direct effects on CR circuitry but worked through indirect means. For example, blockage of inhibitory processes by bicuculline methiodide or picrotoxin in selective regions could result in neuronal activation and release of neurotransmitter substances that ultimately produce effects at distal sites. In fact, Obata and Takeda (14) have observed that stimulation of the cerebellum can induce about a 3-fold increase in the amount of GABA released into the ventricular perfusate, presumably through the activation of GABAergic neurons with terminals within the cerebellar deep nuclei and adjacent to the fourth ventrical. Our results, obtained from testing the eye contralateral to the infusion site, however, would argue against this possibility. Specifically, bicuculline methiodide infusion was ineffective in disrupting the contralateral CR. This suggests that the drug acts by affecting localized structures ipsilateral to the site of infusion rather than by altering the animal's general state of arousal. These observations, coupled with the anatomical specificity of the effect, would also argue that these substances were not diffusing into the general circulation and producing their effects distally.

The results are consistent with the position that blockage of ongoing GABA transmission within specific regions of the dentate/interpositus can produce selective diminution/abolition of the CR. However, the present technique will not allow us to differentiate between the various GABAergic processes within the dentate/interpositus—both the intrinsic neurons and the well-characterized Purkinje cell input to the deep nuclei are known to be GABAergic, and, thus, blockage of either of these GABAergic inputs could result in the observed modification of behavior following drug administration. Note that microinfusions of GABA antagonists into the cerebellar cortex of lobule HVI, one of several regions exhibiting learning-induced alterations in neuronal activity (9), also selectively abolish the conditioned NM response, implicating a role for cerebellar cortex as well (Fig. 5) (see also refs. 15 and 16). It must be stressed that disruption of the CR by GABA antagonists could be due to alterations of synaptic processes within the essential circuitry rather than direct action on the memory trace.

Interestingly, Roberts (17) suggested disinhibition by GABAergic processes as a mechanism of learning. While the precise function of these GABAergic synaptic processes in this form of learning is not known, the present results do provide a basis for further analysis into their potential involvement in neuronal plasticity during learning.

The authors are grateful to Daniel Cervone, Deborah Haley, David McCormick, and Bruce Quinn for their comments on earlier drafts of this manuscript. Special thanks to Drs. Thomas H. Brown and Eugene Roberts for their valuable criticisms, Professor Wally I. Welker for his expert guidance on cerebellar anatomical issues, Carol Dizack for preparation and drawing of the histological plates, Terry P. Stewart for photographic reproductions, and Humberto Garcia for surgical assistance. We are indebted to Professor Jack D. Barchas for his encouragement and support. This research was supported in part by National Institute of Mental Health Training Grant 1T32 MH 17047-01 to L.A.M.; National Science Foundation Grant BNS-81-17115, Office of Naval Research Grant N00014-83-K-0238, and a grant from The McKnight Foundation to R.F.T.; and National Institute of Mental Health Grant MH-23861 to Professor Jack D. Barchas. J.M. held the Peggy R. and Albert K. Orschel Fellowship in Behavioral Neurochemistry.

1. McCormick, D. A., Lavond, D. G., Clark, G. A., Kettner, R. E., Rising, C. E. & Thompson, R. F. (1981) *Bull. Psychon. Soc.* **18(3),** 103–105.
2. Lavond, D. G., McCormick, D. A., Clark, G. A., Holmes, D. T. & Thompson, R. F. (1981) *Physiol. Psychol.* **9(4),** 335–339.
3. McCormick, D. A., Clark, G. A., Lavond, D. G. & Thompson, R. F. (1982) *Proc. Natl. Acad. Sci. USA* **79,** 2731–2735.
4. Lincoln, J. S., McCormick, D. A. & Thompson, R. F. (1982) *Brain Res.* **242,** 190–193.
5. Yeo, C. H., Hardiman, M. J. & Glickstein, M. (1985) *Exp. Brain Res.* **60,** 87–98.
6. Clark, G. A., McCormick, D. A., Lavond, D. G. & Thompson, R. F. (1984) *Brain Res.* **291,** 125–136.
7. Lavond, D. G., Hembree, T. L. & Thompson, R. F. (1984) *Brain Res.* **326,** 179–182.
8. McCormick, D. A. & Thompson, R. F. (1984) *Science* **223,** 296–299.
9. McCormick, D. A. & Thompson, R. F. (1984) *J. Neurosci.* **4,** 2811–2822.
10. Thompson, R. F. (1986) *Science* **233,** 941–947.
11. Ito, M. (1984) *The Cerebellum and Neural Control* (Raven, New York).
12. Berger, T. W. & Thompson, R. F. (1978) *Brain Res.* **145,** 323–346.
13. Bisti, S., Iosif, G., Marchesi, G. F. & Strata, P. (1971) *Exp. Brain Res.* **14,** 24–37.
14. Obata, K. & Takeda, K. (1969) *J. Neurochem.* **16,** 1043–1047.
15. Yeo, C. H., Hardiman, M. J. & Glickstein, M. (1985) *Exp. Brain Res.* **60,** 99–113.
16. Lavond, D. G., Steinmetz, J. E., Yokaitis, M. H., Lee, J. & Thompson, R. F. (1986) *Soc. Neurosci. Abstr.* **12,** 753.
17. Roberts, E. (1980) in *Antiepileptic Drugs: Mechanisms of Action*, eds. Glaser, G. H., Penny, J. K. & Woodbury, D. M. (Raven, New York), pp. 667–713.