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AMPA, Kainic Acid, and N-Methyl-D-Aspartic Acid Stimulate Locomotor Activity After Injection Into the Substantia Innominata/Lateral Preoptic Area

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SHREVE, P E AND N J URETSKY *AMPA, kainic acid, and N-methyl-D-aspartic acid stimulate locomotor activity after injection into the substantia innominata/lateral preoptic area* PHARMACOL BIOCHEM BEHAV **34**(1) 101–106, 1989 —The substantia innominata/lateral preoptic area (SI/LPO) is a subpallidal region which has been shown to regulate the hypermotility produced by drugs acting in the nucleus accumbens Evidence has been presented that the SI/LPO contains glutamatergic nerve terminals and receptors for excitatory amino acids The purpose of this study was to determine the effects of the activation of excitatory amino acid receptors in the SI/LPO on locomotor activity following the direct injection of excitatory amino acids into this brain site It was found that the bilateral injection of α-amino-3-hydroxy-5-methyl-isoxazole-4-propionate (AMPA), kainic acid, and N-methyl-D-aspartic acid into the SI/LPO produced marked dose-dependent stimulations of locomotor activity which resembled the effects of these agents after their injection into the nucleus accumbens The effect, however, was bell-shaped in that at high doses, the locomotor activity values decreased from their peak values The coinjection of γ-glutamylaminomethylsulfonate (GAMS) with AMPA into the SI/LPO was found to inhibit the hypermotility response to AMPA at doses that were unable to produce a significant inhibition of the hypermotility responses to kainic acid or N-methyl-D-aspartic acid The injection of 6,7-dinitroquinoxaline-2,3-dione (DNQX) into the SI/LPO inhibited the hypermotility responses to AMPA or kainic acid while having no significant inhibitory effect on N-methyl-D-aspartic acid stimulated locomotor activity The injection of D-α-aminoadipic acid into the SI/LPO produced a significant inhibition of the hypermotility response produced by N-methyl-D-aspartic acid at a dose that did not produce a significnt inhibition of the hypermotility response produced by AMPA These results suggest that the activation of specific excitatory amino acid receptors in the SI/LPO mediates the locomotor activity produced by AMPA, kainic acid, and N-methyl-D-aspartic acid

Excitatory amino acids Locomotor activity Substantia innominata Lateral preoptic area Nucleus accumbens

THE substantia innominata/lateral preoptic area (SI/LPO) is a subpallidal region which receives a large GABAergic projection from the nucleus accumbens (11, 16, 17, 21), a region of the forebrain that has been postulated to be involved in the integration of motivational and motor behavior (15,18) The inhibition of this GABAergic pathway appears to be involved in the stimulation of locomotor activity produced by the actions of various drugs in the nucleus accumbens (10). Thus, it has been shown that the stimulation of locomotor activity produced by the activation of opioid (28), dopamine (16, 25, 27, 28), and excitatory amino acid (24) receptors in the nucleus accumbens can be inhibited by the injection of GABA or muscimol into the SI/LPO. In addition to the effects of muscimol, the injection of picrotoxin, an inhibitor of endogenous GABA, into the SI/LPO has been shown to stimulate locomotor activity (16, 24, 26) Therefore, GABAergic synapses in this subpallidal region appear to regulate locomotor activity stimulated by mechanisms in the nucleus accumbens.

In addition to the presence of GABA, an inhibitory neurotransmitter, glutamate, an excitatory neurotransmitter, is also found in the SI/LPO Thus, autoradiographic studies have shown that this region contains a high concentration of excitatory amino acid binding sites that are thought to represent receptors for glutamic acid (8,19). Furthermore, synaptosomes prepared from the SI/LPO possess high-affinity uptake sites for L-glutamate and D-aspartate and can release glutamate in a calcium-dependent manner in response to depolarization (1) Based on a recent neuroanatomical study which utilized ^{3}H-D-aspartate as a selective retrograde tracer, the cells of origin of these glutamate terminals appear in part to be located in the amygdala, a region of the limbic system (7). While the functional effects of glutamate in the SI/LPO are not known, it is possible that glutamate, an excitatory amino acid, may serve to directly or indirectly oppose the inhibitory actions of

GABA in this subpallidal region on locomotor activity

The purpose of the present study was to determine the actions of the excitatory amino acids, α-amino-3-hydroxy-5-methyl-isoxazole-4-propionate (AMPA), kainic acid, and N-methyl-D-aspartic acid, on locomotor activity following their direct injection into the SI/LPO These amino acids were studied because they have been shown to be agonists at different excitatory amino acid receptors Our results show that AMPA, kainic acid, and N-methyl-D-aspartic acid elicited marked stimulations of locomotor activity and the effect of each compound could be distinguished by administering excitatory amino acid antagonists

METHOD

Surgical Procedure

Male Sprague-Dawley rats (Harlan Sprague-Dawley, Indianapolis, IN), weighing 150–190 g, were lightly anesthetized with a halothane/oxygen mixture and placed in a stereotaxic apparatus (David Kopf Instruments, CA) A midline incision was made in the scalp and holes were drilled on each side of the skull to facilitate bilateral injections into the substantia innominata/lateral preoptic area (SI/LPO) The coordinates for the SI/LPO were 6 8 mm anterior to the intraaural line, 1 8 mm lateral to the sagittal suture, and 2 0 mm above the intraaural line (13) The needle of a 10 μl Hamilton syringe (Hamilton Co , Reno, NE) was then inserted into the previously drilled holes Drugs or vehicle were injected in a 0 5 μl volume at a rate of 0 5 μl/min The needle was left in place for an additional 1 min to allow for diffusion of the solution After the injection, the needle was removed and the incision was sutured and swabbed with 5% (w/v) lidocaine ointment

Monitoring Locomotor Activity

After the injections into the SI/LPO, the anesthesia was turned off and the animals recovered from anesthesia within 5 min After recovery, the animals were placed in motor activity cages (Opto Varimex-Minor, Columbus Instruments, OH) and allowed 10 min to adapt to the cages The motor activity cages contained 12 × 12 infra-red beams passing a height of 5 cm from the bottom of the cage through a ventilated Plexiglas box measuring 42 cm square and 20 cm high Ambulatory movement was recorded as the number of times two consecutive beams, 3 5 cm apart, were interrupted per hour Each animal was injected once and the locomotor activity was recorded for a one-hour interval The data were collected and printed by a Columbus digital counter The animals were observed for convulsions rearing, or any other nonambulatory behavior during all recording sessions All testing was done between 8 00 a m and 4 00 p m in an isolated environmental room, maintained at a temperature of 22 ± 1°C Prior to the day of the experiment, the animals were housed, four to a cage, in an air-conditioned room kept at 20–21°C with an automatic light-dark cycle (light on 6 00 a m –6 00 p.m)

Histology

After each experiment, the rats were decapitated and their brains rapidly removed and fixed in a 10% formalin solution for 48 hours Frozen sections (80 μ thick) were sliced using a Cryo-Cut Microtome (American Optical Corp , Buffalo, NY) to check the location of the injection needle When the tips of the needle tracks were found to be outside of the SI/LPO, solutions containing excitatory amino acids did not stimulate locomotor activity and the locomotor activity recordings of these animals were not used for the study Figure 1 shows the injection sites for AMPA, kainic acid, or N-methyl-D-aspartic acid in the SI/LPO that were effective and ineffective in stimulating locomotor activity AMPA, kainic acid, or N-methyl-D-aspartic acid were found to be ineffective when at least one of the two injection sites in an animal were outside the SI/LPO

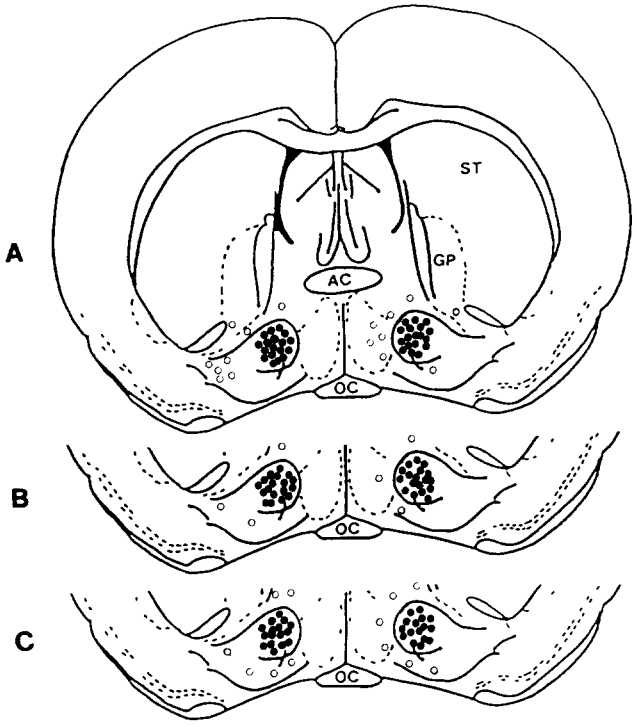

FIG 1 Injection sites of AMPA, kainic acid, or N-methyl-D-aspartic acid in the SI/LPO These sites represent the tips of the needle tracks Closed circles in diagrams A, B, and C refer to sites that produced a significant stimulation of locomotor activity in response to AMPA, kainic acid, or N-methyl-D-aspartic acid injected into the SI/LPO respectively, open circles were sites that were located outside the SI/LPO and that did not produce a significant hypermotility response The locomotor activity of animals with injection sites outside the SI/LPO was not included in this study Adapted from (13) Abbreviations AC, anterior commissures, GP, globus pallidus, OC, optic chiasm, ST, striatum

Drugs

The following compounds were purchased from Sigma Chemical Co (St Louis, MO) N-methyl-D-aspartic acid, kainic acid, and D-α-aminoadipic acid α-Amino-3-hydroxy-5-methyl-isoxazole-4-propionate (AMPA) was purchased from Research Biochemicals Inc (Natick, MA) 6,7-Dinitroquinoxaline-2,3-dione (DNQX) and γ-glutamylaminomethylsulfonate (GAMS) were obtained from Tocris Chemicals (Essex, England)

N-Methyl-D-aspartic acid was dissolved in saline and adjusted to pH 7 4 with 1 N NaOH All other drugs were dissolved in phosphate buffer (pH = 7 5) The doses shown refer to the amount injected on each side of the SI/LPO For the studies on the antagonistic action of GAMS and D-α-aminoadipic acid, AMPA and kainic acid were administered at doses that produced a similar degree of locomotor activity Although this level of locomotor activity could not be achieved with N-methyl-D-aspartic acid, the highest dose which did not elicit seizure activity was utilized for

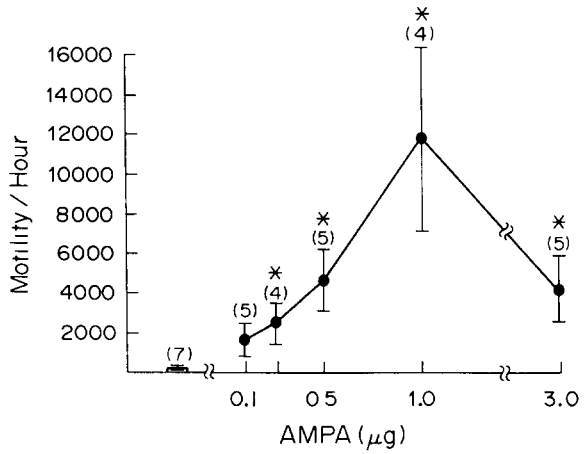

FIG 2 Effect of AMPA on locomotor activity after bilateral injection into the SI/LPO A solution of AMPA or vehicle was injected in a 0 5 μl volume and the animals were placed in motor activity cages and locomotor activity recorded for 1 hour Each point represents the mean ± S E M for the number of observations in parentheses Kruskal-Wallis analysis of variance H = 17 62, $p<0$ 05 *$p<0$ 05 with respect to vehicle (Mann-Whitney U-test)

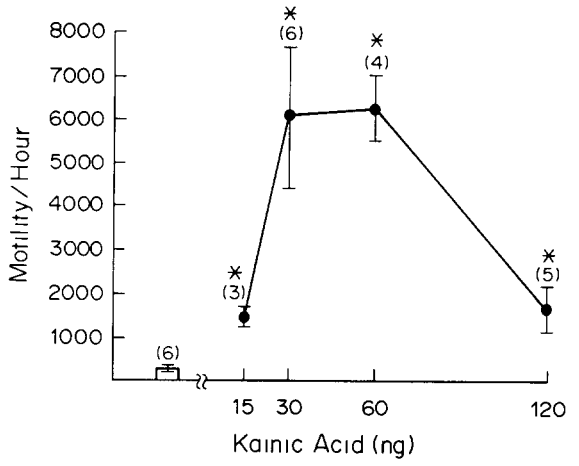

FIG 3 Effect of kainic acid on locomotor activity after bilateral injection into the SI/LPO A solution of kainic acid or vehicle was injected in a 0 5 μl volume and the animals were placed in motor activity cages and locomotor activity recorded for 1 hour Each point represents the mean ± S E M for the number of observations in parentheses Kruskal-Wallis analysis of variance H = 18 98, $p<0$ 05 *$p<0$ 05 with respect to vehicle (Mann-Whitney U-test)

these studies Control animals were injected with an equal volume (0 5 μl) of saline or phosphate buffer

Statistics

Data were expressed as the mean and standard error of the mean (SEM) The effects of drugs and saline treatment were evaluated statistically using the nonparametric Kruskal-Wallis one-way analysis of variance followed by the one-tailed Mann-Whitney U-test, with a level of $p<0$ 05 being considered significant

RESULTS

Effect of AMPA, Kainic Acid, and N-Methyl-D-Aspartic Acid on Locomotor Activity in the Rat

The bilateral injection of either AMPA (0 1–1 μg), kainic acid (15–60 ng), or N-methyl-D-aspartic acid (1–2 5 μg) into the SI/LPO produced a dose-dependent increase in locomotor activity (Figs 2, 3, and 4 respectively) At these doses, rats exhibited periods of intense prolonged coordinated locomotor activity similar to that observed when these agents were injected into the nucleus accumbens While the movements of the rats were vigorous, they were also controlled Thus, the rats avoided obstacles placed in their path and never ran into the cage walls. AMPA (1 μg) produced the greatest hypermotility response which was 65 times greater than the response of saline-treated animals Kainic acid (60 ng) and N-methyl-D-aspartic acid (2 5 μg) were less effective, producing maximum hypermotility responses which were only 25 and 12 times greater than the responses of control animals respectively Higher doses of AMPA (3 μg), kainic acid (120 ng), and N-methyl-D-aspartic acid (5 μg) induced tremors and labored breathing which appeared to interfere with the hypermotility response and may account for the reduction in locomotor activity at these doses

Effect of GAMS on AMPA-, Kainic Acid-, and N-Methyl-D-Aspartic Acid-Stimulated Locomotor Activity in the Rat

γ-Glutamylaminomethylsulfonate (GAMS) has been characterized as a selective antagonist of the effects of quisqualic acid in the nucleus accumbens (23) The purpose of this experiment was to determine the effect of GAMS on AMPA-, kainic acid-, and N-methyl-D-aspartic acid-stimulated locomotor activity after bilateral injection into the SI/LPO. GAMS (1 and 25 μg) was coadministered with AMPA (0 5 μg), kainic acid (30 ng), and N-methyl-D-aspartic acid (2.5 μg) into the SI/LPO For this study, AMPA and kainic acid produced comparable levels of locomotor activity while the hypermotility response elicited by N-methyl-D-aspartic acid was only one third of that produced by AMPA and kainic acid (Fig 5) GAMS (1 μg) produced a significant 82% inhibition of AMPA-stimulated locomotor activity, whereas this

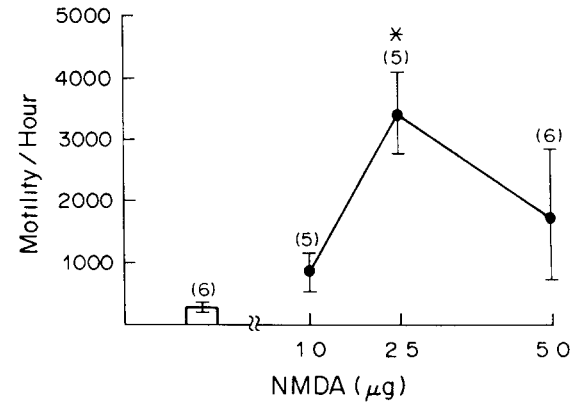

FIG 4 Effect of N-methyl-D-aspartic acid on locomotor activity after bilateral injection into the SI/LPO A solution of N-methyl-D-aspartic acid or vehicle was injected in a 0 5 μl volume and the animals were placed in motor activity cages and locomotor activity recorded for 1 hour Each point represents the mean ± S E M for the number of observations in parentheses Kruskal-Wallis analysis of variance H = 9 86, $p<0$ 05 *$p<0$ 05 with respect to vehicle (Mann-Whitney U-test)

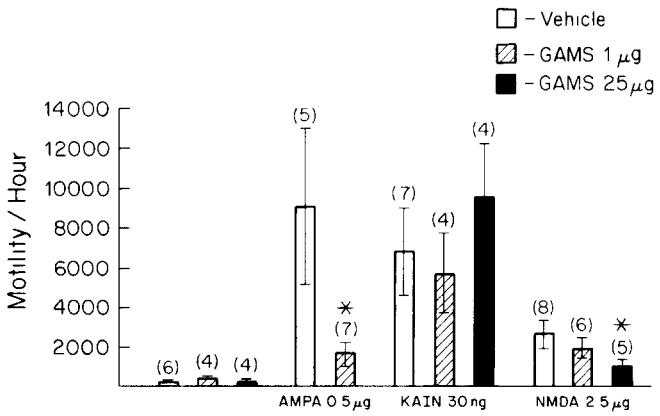

FIG 5 Effect of GAMS on AMPA-, kainic acid-, and N-methyl-D-aspartic acid-stimulated locomotor activity after bilateral injection into the SI/LPO A solution of AMPA (0 5 μg), kainic acid (30 ng), or N-methyl-D-aspartic acid (2 5 μg) with or without GAMS (1–25 μg) was injected in a 0 5 μl volume and the animals were placed in motor activity cages and locomotor activity recorded for 1 hour Each point represents the mean ± S E M for the number of observations in parentheses Kruskal-Wallis analysis of variance H = 2 38, $p<0$ 05 for the control experiment, H = 7 2, $p<0$ 05 for the AMPA experiment, H = 1 8, $p>0$ 05 for the kainic acid experiment, H = 4 53, $p = 0$ 05 for the N-methyl-D-aspartic acid experiment *$p<0$ 05 with respect to vehicle controls (Mann-Whitney U-test)

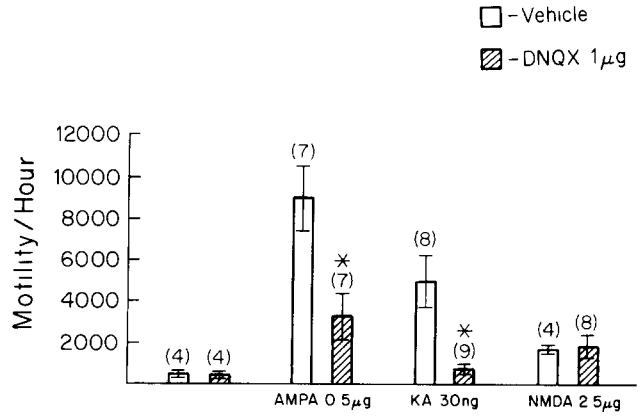

FIG 6 Effect of DNQX on AMPA-, kainic acid-, or N-methyl-D-aspartic acid-stimulated locomotor activity after bilateral injection into the SI/LPO A solution of AMPA (0 5 μg), kainic acid (30 ng), or N-methyl-D-aspartic acid (2 5 μg) with or without DNQX (1 μg) was injected in a 0 5 μl volume and the animals were placed in motor activity cages and locomotor activity recorded for 1 hour Each point represents the mean ± S E M for the number of observations in parentheses *$p<0$ 05 with respect to vehicle controls

dose of GAMS did not produce a significant inhibition of either kainic acid (16%) or N-methyl-D-aspartic acid (25%) A further increase in the dose of GAMS to 25 μg with kainic acid and N-methyl-D-aspartic acid produced no inhibition and a significant 62% inhibition respectively GAMS, administered alone at these doses, did not produce a statistically significant effect on locomotor activity

Effect of DNQX on AMPA-, Kainic Acid-, and N-Methyl-D-Aspartic Acid-Stimulated Locomotor Activity in the Rat

6,7-Dinitroquinoxaline-2,3-dione (DNQX) has recently been characterized as a selective quisqualic acid receptor antagonist on the basis of ^{3}H-AMPA binding studies (9) The purpose of this experiment was to determine the effect of DNQX on AMPA-, kainic acid-, and N-methyl-D-aspartic acid-stimulated locomotor activity after bilateral injection into the SI/LPO DNQX (1 μg) was coadministered with either AMPA (0 5 μg), kainic acid (30 ng), or N-methyl-D-aspartic acid (2 5 μg) into the SI/LPO AMPA alone produced the greatest hypermotility response which was two and five times greater than kainic acid and N-methyl-D-aspartic acid respectively (Fig 6) DNQX (1 μg) produced a significant 64% and 84% inhibition of AMPA- and kainic acid-stimulated locomotor activity respectively However, this dose of DNQX did not significantly effect the hypermotility response elicited by N-methyl-D-aspartic acid The administration of DNQX alone did not produce a significant effect on locomotor activity

Effect of D-α-Aminoadipic Acid on AMPA- and N-Methyl-D-Aspartic Acid-Stimulated Locomotor Activity in the Rat

D-α-Aminoadipic acid, an antagonist of the N-methyl-D-aspartic acid subtype of excitatory amino acid receptors, has been shown to selectively inhibit the hypermotility responses to N-methyl-D-aspartic acid in the nucleus accumbens (5) In this study, D-α-aminoadipic acid (10 μg) was coadministered with AMPA (0 5 μg) and N-methyl-D-aspartic acid (2 5 μg) into the SI/LPO AMPA and N-methyl-D-aspartic acid produced significant increases in locomotor activity as compared to vehicle controls although the hypermotility response to AMPA was over four times greater than the response to N-methyl-D-aspartic acid (Fig 7) D-α-Aminoadipic acid produced a significant 58% inhibition of N-methyl-D-aspartic acid-stimulated locomotor activity but did not produce a statistically significant inhibition of AMPA-stimulated locomotor activity D-α-Aminoadipic acid, administered alone, did not produce a statistically significant effect on locomotor activity

DISCUSSION

The major finding of this study is that the direct injection of the excitatory amino acids, AMPA, kainic acid, and N-methyl-

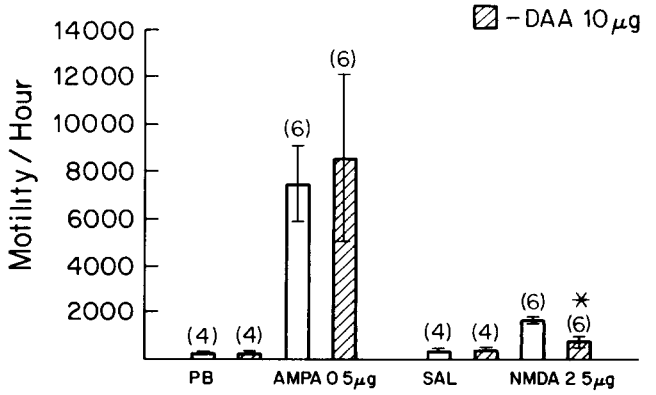

FIG 7 Effect of D-α-aminoadipic acid on AMPA- or N-methyl-D-aspartic acid-stimulated locomotor activity after bilateral injection into the SI/LPO A solution of AMPA (0 5 μg) or N-methyl-D-aspartic acid (2 5 μg) was injected in a 0 5 μl volume and the animals were placed in motor activity cages and locomotor activity recorded for 1 hour Each point represents the mean ± S E M for the number of observations in parentheses *$p<0$ 05 with respect to vehicle controls

D-aspartic acid into the SI/LPO produced a bell-shaped response consisting of marked dose-dependent increases in locomotor activity followed by a decrease from the peak value at the higher doses These hypermotility responses to AMPA and N-methyl-D-aspartic acid were selectively inhibited by excitatory amino acid receptor antagonists suggesting that the responses are mediated by the activation of specific excitatory amino acid receptors These results suggest that excitatory amino acid neurotransmission in the SI/LPO is involved in the stimulation of coordinated locomotor activity

Studies were designed to determine the involvement of non-N-methyl-D-aspartic acid receptors in the SI/LPO in stimulating locomotor activity DNQX has recently been described as a potent competitive non-N-methyl-D-aspartic acid receptor antagonist based on its ability to selectively inhibit ^{3}H-AMPA and ^{3}H-kainic acid binding, while being a much weaker inhibitor of the binding of ^{3}H-CPP, an N-methyl-D-aspartic acid receptor antagonist (9) In the present study DNQX (1 μg) produced a significant 64% and 84% inhibition of AMPA- and kainic acid-stimulated locomotor activity respectively, while producing no significant effect on N-methyl-D-aspartic acid-stimulated loocmotor activity. These results, which are in agreement with the inhibitory effects of DNQX on the responses to AMPA and kainic acid in electrophysiological studies (9), suggest that the activation of non-N-methyl-D-aspartic acid receptors in the SI/LPO produces a stimulation of locomotor activity

The effects of excitatory amino acids in the SI/LPO were also determined in the presence of GAMS which has been described as a potent, but nonselective, antagonist of kainic acid and quisqualic acid receptor subtypes (6) based upon electrophysiological studies (3, 4, 12) However, despite its ability to inhibit the electrophysiological effects of AMPA and kainic acid, recent studies have shown that GAMS is a very weak inhibitor of both ^{3}H-AMPA and ^{3}H-kainic acid binding (9,20) suggesting that GAMS does not block AMPA and kainic acid receptors In the present study, GAMS at a dose of 1 μg produced a marked (82%) inhibition of AMPA-stimulated locomotor activity while having no significant effect on kainic acid- and N-methyl-D-aspartic acid-stimulated locomotor activity The selective effect of GAMS in inhibiting AMPA-induced responses is in agreement with the results of a previous study which showed that GAMS selectively inhibited the hypermotility responses to AMPA and quisqualic acid in the nucleus accumbens at doses that were ineffective in inhibiting the responses to kainic acid and N-methyl-D-aspartic acid (23) Although the mechanism for the selectivity of GAMS in the SI/LPO and nucleus accumbens is currently not known, these results suggest that the hypermotility response to AMPA in the SI/LPO is mediated by a different mechanism than that produced by kainic acid or N-methyl-D-aspartic acid and are consistent with the actions of AMPA at a separate receptor

Similarly, the hypermotility response produced by the direct injection of N-methyl-D-aspartic acid into the SI/LPO seems to be selectively mediated by the activation of N-methyl-D-aspartic acid receptors. D-α-Aminoadipic acid has been shown in electrophysiological (2,14), binding (22), and behavioral (5,23) studies to be a selective antagonist of the N-methyl-D-aspartic acid receptor. In the present study D-α-aminoadipic acid, at a dose that produced a significant 58% inhibition of N-methyl-D-aspartic acid-induced locomotor activity, did not significantly inhibit AMPA-induced locomotor activity Although this result is consistent with a selective inhibition of the effects of N-methyl-D-aspartic acid, the stimulation of locomotor activity produced by the maximally effective dose of N-methyl-D-aspartic acid (2.5 μg) was three to four times less than that produced by a low dose of AMPA (0 5 μg) It is therefore possible that the greater stimulation of locomotor activity produced by AMPA may be more difficult to antagonize than the smaller effect produced by N-methyl-D-aspartic acid While this possibility can not be excluded, the greater hypermotility response to AMPA was selectively inhibited by GAMS and DNQX at doses that had no significant effect on the smaller response to N-methyl-D-aspartic acid suggesting that the size of the hypermotility response is not a factor in determining the selectivity of inhibition. Furthermore, we have found in a previous study (23) that the dose of D-α-aminoadipic acid used in the present study selectively inhibited the hypermotility response elicited by N-methyl-D-aspartic acid but had no significant effect on that produced by AMPA in the nucleus accumbens Therefore, these results suggest that activation of N-methyl-D-aspartic acid receptors in the SI/LPO leads to the stimulation of locomotor activity

The results from previous studies have suggested that the stimulation of locomotor activity produced by drugs acting in the nucleus accumbens is mediated by a decrease in GABAergic neurotransmission in the SI/LPO These results taken together with the present observations suggest that both the inhibition of GABAergic neurotransmission and the stimulation of glutamatergic (excitatory amino acid) neurotransmission in the SI/LPO can produce a stimulation of coordinated locomotor activity Therefore, since neuronal mechanisms in the nucleus accumbens have been implicated in goal-oriented behavior (15), excitatory amino acid as well as GABAergic mechanisms in the SI/LPO may function to regulate this behavior

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REFERENCES

1 Davies, S W , McBean, G J , Roberts, P J A glutamatergic innervation of the nucleus basalis/substantia innominata Neurosci Lett 45 105–110, 1984
2 Davies, J , Watkins, J C Selective antagonism of amino acid-induced synaptic excitation in the cat spinal cord J Physiol (Lond) 297 621–635, 1979
3 Davies, J , Evans, R H , Jones, A W , Smith, D A S , Watkins, J C Differential activation and blockade of excitatory amino acid receptors in the mammalian and amphibian central nervous system Comp Biochem Physiol 72C 211–224, 1982
4 Davies, J , Watkins, J C Depressant action of γ-D-glutamylaminomethyl sulfonate (GAMS) on amino acid-induced and synaptic excitation in the cat spinal cord Brain Res 327 113–120, 1985
5 Donzanti, B A , Uretsky, N J Antagonism of the hypermotility response induced by excitatory amino acids in the rat nucleus accumbens Naunyn Schmiedebergs Arch Pharmacol 325 1–7, 1984
6 Fagg, G E L-Glutamate, excitatory amino acid receptors and brain function Trends Neurosci 8 207–210, 1985
7 Fuller, T A , Russchen, F T , Price, D L Sources of presumptive glutamatergic/aspartergic afferents to the rat ventral striatopallidal region J Comp Neurol 258 317–338, 1987
8 Halpain, S , Wieczorek, C M , Rainbow, T C Localization of L-glutamate receptors in rat brain by quantitative autoradiography J Neurosci 4 2247–2258, 1984
9 Honore, T , Davies, S N , Drejer, J , Fletcher, E J , Jacobsen, P , Lodge, D , Nielsen, F E Quinoxalinediones Potent competitive non-NMDA glutamate receptor antagonists Science 241 701–703, 1988
10 Jones, D L , Mogenson, G J Nucleus accumbens to globus pallidus GABA projections subserving ambulatory activity Am J Physiol 283 R63–R69, 1980
11 Jones, D L , Mogenson, G J Nucleus accumbens to globus pallidus

GABA projection electrophysiological and iontophoretic investigations Brain Res 188 93–105, 1980
12 Jones, A W , Smith, D A S , Watkins, J C Structure activity relations of dipeptide antagonists of excitatory amino acids Neuroscience 13 573–581, 1984
13 Konig, J R F , Klippel, R A The rat brain A stereotaxic atlas of the forebrain and lower parts of the brainstem New York Krieger, 1963
14 McLennan, H , Lodge, D The antagonism of amino induced excitation of spinal neurons in the cat Brain Res 169 83–90, 1979
15 Mogenson, G J , Jones, D L , Yim, C Y From motivation to action Functional interface between the limbic system and the motor system Prog Neurobiol 14 69–97, 1980
16 Mogenson, G J , Nielsen, M A Evidence that an accumbens to subpallidal GABAergic projection contributes to locomotor activity Brain Res Bull 11 309–314, 1983
17 Mogenson, G J , Swanson, L W , Wu, M Neural projection from the nucleus accumbens to globus pallidus, substantia innominata, and lateral preoptic-lateral hypothalamic area an anatomical and electrophysiological investigation in the rat J Neurosci 3 189–202, 1983
18 Mogenson, G J , Yim, C Y Electrophysiological and neuropharmacological-behavioral studies of the nucleus accumbens implications for its role as a limbic-motor interface In Chronister, R , DeFrance, J F , eds The neurobiology of the nucleus accumbens Brunswick Haer Institute, 1980 210–229
19 Monaghan, D T , Cotman, C W Distribution of N-methyl-D-aspartate sensitive L^{3}H-glutamate binding sites in rat brain J Neurosci 5 2909–2919, 1985
20 Murphy, D E , Snowhill, E W , Williams, M Characterization of quisqualate recognition sites in rat brain tissue using DL^{3}H-α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) and a filtration assay Neurochem Res 12 775–782, 1987
21 Nauta, W J H , Smith, G P , Faull, R L M , Domesick, V B Efferent connections and nigral afferents of the nucleus accumbens septi in the rat Neuroscience 3 385–410, 1978
22 Olverman, H J , Jones, A W , Watkins, J C [^{3}H]-D-2-amino-5-phosphonopentanoate as a ligand for N-methyl-D-aspartate receptors in the mammalian central nervous system Neuroscience 26(1) 1–15, 1988
23 Shreve, P E , Uretsky, N J Role of quisqualic acid receptors in the hypermotility response produced by the injection of AMPA into the nucleus accumbens Pharmacol Biochem Behav 30 379–384, 1988
24 Shreve, P E , Uretsky, N J Effect of GABAergic transmission in the subpallidum on the hypermotility response to the intraaccumbens administration of excitatory amino acids and picrotoxin Neuropharmacology, in press
25 Swerdlow, N R , Koob, G F The neural substrates of apomorphine-stimulated locomotor activity following denervation of the nucleus accumbens Life Sci 35 2537–2544, 1984
26 Swerdlow, N R , Koob, G F Lesion of the dorsomedial nucleus of the thalamus, medial prefrontal cortex, and pedunculopontine nucleus effects on locomotor activity mediated by nucleus accumbens-ventral pallidal circuitry Brain Res 412 233–243, 1987
27 Swerdlow, N R , Swanson, L W , Koob, G F Substantia innominata Critical link in the behavioral expression of mesolimbic dopamine stimulation in the rat Neurosci Lett 50 19–24, 1984
28 Swerdlow, N R , Vaccarino, F J , Amalric, M , Koob, G F The neural substrates for the motor-activating properties of psychostimulants A review of recent findings Pharmacol Biochem Behav 25 233–248, 1986