Pharmacology Biochemistry and Behavior, Vol. 41, pp. 707-713, 1992

0091-3057/92 $5.00 + .00

Effects of Yohimbine and Idazoxan on Motor Behaviors in Male Rats

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Received 22 April 1991

BOWES, M. P., R. H. PETERS, W. J. KERNAN, JR. AND D. L. HOPPER. *Effects of yohimbine and idazoxan on motor behaviors in male rats.* PHARMACOL BIOCHEM BEHAV **41**(4) 707-713, 1992.—Yohimbine, an α_2 adrenergic antagonist, facilitates copulatory behaviors in male rats. This facilitation may reflect nonspecific activation of behavior rather than a more selective activation of copulatory behaviors. The present experiments assessed the effects of yohimbine on locomotor behaviors at a dose (2.0 mg/kg) known to facilitate sexual behaviors. Experiment 1 used a computer pattern-recognition system to classify motor behaviors into specific acts and act groups. Male albino rats were tested in three conspecific conditions: estrous female, anestrous female, or no conspecific. Yohimbine decreased locomotor activity in all three conspecific conditions. Experiment 2 examined the effects of yohimbine (2.0 mg/kg) and amphetamine (1.0 mg/kg) on locomotor behavior in a photocell-equipped activity measurement system. Amphetamine increased and yohimbine decreased locomotor activity. Experiment 3 used the computer pattern-recognition system to compare the effects of yohimbine and idazoxan, another α_2 adrenergic antagonist, on motor behaviors. Yohimbine and idazoxan both decreased activity but produced different patterns of behavioral change. The facilitatory effects of yohimbine on copulatory behaviors at a dose of 2.0 mg/kg are apparently not mediated by nonspecific activation of behavior.

Yohimbine Idazoxan Rats Pattern recognition Motor behavior

THE copulatory behaviors of male rats are modulated by excitatory dopaminergic and inhibitory serotonergic systems (4,12). Although various pharmacological manipulations of noradrenergic systems have had little effect on copulatory behaviors, recent research has suggested that yohimbine increases sexual motivation in male rats (9-11,37).

Yohimbine, an α_2 adrenergic antagonist, elevates norepinephrine (NE or noradrenergic) activity, presumably by autoreceptor blockade (2,20,24,32). Diffuse noradrenergic projections of the locus coeruleus (LC) are believed to mediate arousal (5). The LC contains the highest density of noradrenergic neurons in the brain and 70% of total brain NE (38). α_2 adrenergic receptors have been identified on LC cells (7). Yohimbine may increase activity in LC neurons, increase general arousal, and thereby increase copulatory behaviors. Alternatively, NE mechanisms may modulate copulatory behaviors more directly. The medial preoptic area, richly innervated by NE projections, has been implicated in the control of male copulatory behaviors (21,33).

If the effects of yohimbine on copulatory behaviors can be attributed to nonspecific arousal, then yohimbine may similarly increase other behaviors. The present research examined the effects of yohimbine on motor behaviors at dose and temporal parameters that facilitate copulatory behaviors. Activity measurements were obtained with a recently developed computer pattern-recognition system and a conventional method based on photocell interruptions. In addition, the effects of yohimbine on motor behaviors were compared with those of idazoxan, another α_2 adrenergic antagonist.

Yohimbine potentiates a variety of behaviors including head-twitch and seizure thresholds (23,34), acoustic startle (14,15,27), sensitivity to a stressor (13), conditioned defensive burying (47), conditioned avoidance responding (18), and bar-pressing previously inhibited by clonidine (48) or aversive conditioning (44). Yohimbine also influences locomotor behavior, but with considerable variability in behavioral outcomes. Yohimbine may increase or decrease locomotor activity depending upon a number of factors including dose, route

Portions of this research were included in a master's thesis submitted by the first author to Iowa State University, and were presented at the annual meeting of the Midwestern Psychological Association, May 2-4, 1991, Chicago.

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of administration, behavioral measure, and injection-to-test interval (8,25,35,42,49,50–52). Experiment 1 assessed the effects of yohimbine on locomotor behavior using dose and temporal parameters known to increase copulatory behaviors.

Kernan and associates developed a computer pattern-recognition system to analyze spontaneous locomotor behavior in rats (26,28–30). A computer is programmed to identify five major acts; standing, sitting, rearing, walking, and lying down. It also recognizes eight behavioral modifiers that can occur concurrently with the major acts (e.g., head turn, washing face). Various combinations of acts and modifiers yield 19 behavioral act classifications. The number of initiations and the total duration of each independent behavioral act are measured. In addition, the total distance traveled during the behavioral test session provides a measure of general activity sensitive to a drug manipulation (amphetamine) known to increase locomotor behavior (29,40).

If yohimbine's effects are relatively specific to copulatory behaviors, then yohimbine may differentially influence patterns of activity depending on the conspecific paired with a yohimbine-treated animal. Specifically, activity may be higher in the presence of an inaccessible estrous female than in the presence of an inaccessible anestrous female. Male rats were paired with either no conspecific, an inaccessible nonestrous female, or an inaccessible estrous female.

The purpose of Experiment 2 was to obtain converging evidence on the effects of a 2.0-mg/kg dose of yohimbine on motor activity. The procedures used to measure activity in Experiment 1 were based on a sophisticated computer analysis of behavior patterns in contrast with more typical but less sophisticated procedures such as recording the frequency of photocell interruptions. This experiment evaluated the effects of yohimbine using this more typical procedure. In addition to saline and yohimbine conditions, an amphetamine condition (1.0 mg/kg) was included to demonstrate that the photocell apparatus was sensitive to a drug manipulation that increases locomotor activity (40).

In Experiment 3, the effects of yohimbine were compared with those of idazoxan. Idazoxan is a compound that has been described as both more selective and more potent than yohimbine as an α_2 adrenergic antagonist (19,22,23,45,46), although this characterization may not be entirely accurate (16,17,34,41,45,46). It has been reported that idazoxan binds to α_2 receptors with less affinity than yohimbine by approximately a factor of 5 (32). Idazoxan potentiates male copulatory behavior (45,46). Unpublished data from our laboratory suggest that idazoxan facilitates copulatory behavior at 10 mg/kg, a dose higher than the facilitory dose for yohimbine. Thus, whereas idazoxan appears to be more selective than yohimbine, the relative potencies of the two drugs remain in question.

The purpose of Experiment 3 was to compare the effects of idazoxan and yohimbine on motor activity. Idazoxan may increase general activity level, thereby making any behavior, including copulatory behaviors, more likely. Alternatively, idazoxan may act to modulate copulatory behaviors more directly. The experiment also provided a replication for the effects of yohimbine observed in Experiment 1.

In addition to the behavioral measures described in Experiment 1, a parameter known as the K-function was computed for each act and for each pair of acts (29). The K-function describes the distribution of each act in time (known as time-distribution analysis), indicating whether the occurrences of each act are more clustered or more dispersed in time as a function of the experimental manipulation. The K-function also describes the temporal relationship between pairs of acts in time (known as time-sequence analysis). Acts do not occur in isolation; rather, they are performed in a structured order. The order of acts may be independent or may be determined by the occurrence of a preceding act. The K-function calculations in the form of time-sequence analysis assess sequences of acts and their relationships. The time-sequence analysis is at least partly independent of the time-distribution analysis; that is, the results of the time-sequence calculations are not predictable by the time-distributions of the acts (29). Time-distribution and time-sequence analyses may also be computed for the behavioral modifiers and combined act classifications. Thus, in addition to providing a measure of total activity level this pattern-recognition system allows independent analysis of four separate aspects of locomotor behavior: number of initiations for each act, total time engaged in each act, the distribution of each act in time, and the temporal relationships between pairs of acts (29).

METHOD

Subjects

Male Sprague-Dawley albino rats were obtained at 25–35 days of age from Laboratory Animals Resources, College of Veterinary Medicine, Iowa State University. Animals were housed in groups of five to six until the beginning of the experiment and were individually housed thereafter. Subjects were housed in a temperature-controlled environment (22–24°C) and maintained on a reversed 12 L:12 D cycle with lights off at 0800 h. Food (Simonsen 1525 rat/mice diet) and water were available ad lib except during testing. Behavioral testing began when the rats were 80–90 days of age. Twenty males were used in Experiment 1, 10 in Experiment 2, and 120 in Experiment 3.

Stimulus Females

In Experiment 1, four female rats between 80 and 90 days of age served as conspecifics. Ovariectomies were performed under Chloropent anesthesia (Fort Dodge Laboratories, Inc.; 3 ml/kg, IP) at least 2 wk prior to test sessions. Two of the females were always used as conspecifics on estrous conspecific trials and the other two were always used on nonestrous conspecific trials. Estrus was induced with estradiol benzoate (5 μg,SC, 48 and 24 h before test sessions) and progesterone (0.5 mg,SC, 4–6 h before test sessions) in a 0.1 ml sesame oil vehicle. Estrous females were screened for sexual receptivity with sexually vigorous nonexperimental males prior to behavioral testing and always displayed proceptive behaviors (3) and vigorous lordosis prior to use as conspecifics. Females employed on nonestrous trials never received hormone treatment following ovariectomy and were therefore in continuous anestrus. Conspecifics were housed in a separate room isolated from the experimental males during the entire experiment.

Apparatus

In Experiments 1 and 3, the observational environment consisted of a clear Plexiglas box divided in half by a Plexiglas partition with exterior walls slanted to minimize glare. The box may be described as trapezoidal at the top and bottom with the two trapezoids separated by a vertical distance of 23.5 cm. The top trapezoid had parallel sides 42 and 32 cm in length separated by 24 cm. The parallel sides of the bottom

trapezoid were 52.5 and 40 cm long, separated by 31 cm. A common wall between the two compartments had six 1.2-cm holes, allowing the animals to see and smell each other. Two videocameras monitored the test environment from a distance of about 1 m, one camera oriented horizontally, the other vertically. The Plexiglas compartment was located in a small, isolated room used only for these experiments. Uniform dim red illumination throughout the test area allowed good contrast between the albino animals and a black background behind the test chamber. A preliminary experiment using albino rats as subjects confirmed that yohimbine (2.0 mg/kg) increased copulatory behaviors in this strain (6). Previous work with yohimbine used hooded rats exclusively. Hooded rats cannot be used as subjects in the pattern-recognition apparatus.

In Experiment 2, a maze in the shape of a figure-eight was used to measure locomotor behavior (39). The maze consisted of alleys (10 cm wide × 10 cm high) interconnected at a midpoint. The overall dimensions of the maze were 76 cm × 60 cm. Eight photocells recorded passage of an animal through the maze. Activity counts were recorded automatically by a microcomputer.

Drugs used were yohimbine hydrochloride (Sigma Chemical Co.), *d*-amphetamine sulfate (Sigma Chemical Co.), idazoxan (generously provided by Reckitt and Hull, Coleman, England), and normal saline.

Procedure

Experiment 1. Each of 20 experimental animals served in each combination of conspecific (three levels) and drug (two levels) conditions. On each test day, only one type of conspecific was used to avoid contaminating the test chamber with a variety of potentially different odor cues. Ten animals were tested each day during the first half of the dark cycle. Each subject was tested every other day. The order of conspecific presentation was randomized over days. On the first three trials, animals received either yohimbine (2.0 mg/kg, IP) or saline. In the second three trials, drug conditions were reversed.

Each behavioral test session lasted 15 min. The two computer-controlled cameras sampled each test session once per second, dividing the 15-min session into 900 discrete segments of two "frames" (horizontal and vertical). The data consisted of either 0 or 1 for each pixel depending on whether the signal level exceeded a discriminator level. A computer pattern-recognition program was used to classify these data into the five major body positions and eight modifiers.

The data were analyzed as a 2 × 3 factorial experiment (drug × conspecific) with both factors repeated. The drug condition main effect (effect of yohimbine on motor behavior) and the drug × conspecific interaction (differential yohimbine effects as a consequence of conspecific) were of principal interest. The main effect of conspecific was of no interest and the results of its analysis are not reported.

The following measures were recorded: 1) the total distance traveled during the test session, 2) number of initiations for each behavioral classification, and 3) total time spent in each behavioral classification.

Experiment 2. Twenty minutes prior to each test session, each rat received a 1-ml/kg IP injection of either isotonic saline, yohimbine (2.0 mg/kg), or *d*-amphetamine sulfate (1.0 mg/kg). Drugs were dissolved in distilled water and prepared immediately before behavioral testing. Test duration for each animal was 1 h. Order of presentation of the three conditions was randomized for each animal. Tests were conducted under dim red illumination at 4- to 5-day intervals. The number of activity counts for each of the three conditions were analyzed using a repeated-measures analysis of variance (ANOVA).

Experiment 3. Experimental animals (12 per group) received an IP injection (1 ml/kg) of either yohimbine (2.0 mg/kg) or idazoxan (0.3, 1.0, 3.0, or 10.0 mg/kg). Twenty min following injection, each animal was placed in the test compartment for 15 min. Each animal was tested only once and at only one dose level. In Experiment 1, each subject received each drug treatment in the presence of a conspecific in the adjoining chamber. In this experiment, the adjoining compartment was occupied by a saline-treated male control animal (0.15 M, 1 ml/kg, $n = 60$).

Dependent variables in this experiment were 1) number of initiations of each act, 2) total time for each act, 3) total distance traveled during the test session, 4) number of initiations for each combined act, 5) total time for each combined act, 6) distribution of acts in time, 7) distribution of act pairs in time, 8) distribution of combined acts in time, and 9) distribution of pairs of combined acts in time. Number of initiations, total time, and total distance traveled were analyzed using Dunnet's multiple-comparison procedure (31), simultaneously comparing each of the five experimental groups with control subjects.

Computation of K-functions involves computer-intensive statistical techniques to calculate variance. An estimate of the false-positive error rate of the K-function analysis was obtained by comparing two groups of untreated subjects ($n = 12$ per group). The false-positive error rate for these K-function analyses was approximately 10% for the major acts and modifiers and less than 4% for the combined acts. These values were used in analyses of the K-function calculations. In the time-sequence and time-distribution analyses, any act with an average number of initiations per animal below 10 was dropped from the analysis. For each of the experimental groups, the number of behaviors labeled as changed by the pattern-recognition program is counted. Using the false-positive error rate determined previously and the summed binomial probability distribution, the probability of obtaining this number of significant differences by chance may be determined (29).

RESULTS

Experiment 1

Overall activity. The total distance traveled during the behavioral session was used as an index of locomotor activity. Yohimbine significantly decreased locomotor activity, $F(1,95) = 5.67, p < 0.0192$. The conspecific × drug interaction was not significant. Thus, the dose of yohimbine (2.0 mg/kg) that facilitates copulatory behavior significantly decreased the total distance traveled in each conspecific condition.

A summary of the analysis of the specific components of locomotor behavior is presented in Table 1. None of the conspecific × drug interactions were significant, and the conspecific main effect was of no particular interest; the data presented in Table 1 were therefore collapsed over conspecific conditions. This pattern-recognition procedure generated 38 behavioral measures; consequently, only differences with p values less than 0.01 were considered significant in this portion of the analysis. Of the 38 measures, 13 were significant at $p < 0.01$, with a description as follows.

Five major acts. Each of the five major acts (standing,

TABLE 1

ACTIVITY MEASURES CHANGED ($p < 0.01$) BY ADMINISTRATION OF YOHIMBINE (2.0 mg/kg; $n = 20$)

Measure	Change	Saline (mean ± SE)	Yohimbine (mean ± SE)
Acts and modifiers: Number of initiations			
Rear	Decrease	23.7 ± 1.4	15.9 ± 1.6
Blank	Increase	134.9 ± 1.9	143.7 ± 2.7
Groom	Decrease	19.9 ± 2.1	12.4 ± 1.8
Head turn	Increase	56.0 ± 1.1	67.3 ± 1.6
Acts and modifiers: Total time (seconds)			
Stand	Increase	587.7 ± 10.8	664.1 ± 10.5
Sit	Decrease	125.3 ± 11.2	89.0 ± 8.9
Rear	Decrease	66.3 ± 4.2	42.0 ± 4.6
Groom	Decrease	45.6 ± 6.1	23.7 ± 4.2
Head turn	Increase	65.0 ± 1.5	78.5 ± 2.0
Combined acts: Initiations			
Groom	Decrease	17.2 ± 1.9	9.7 ± 1.5
Combined acts: Total time (seconds)			
Groom	Decrease	38.0 ± 5.5	16.9 ± 3.2
Groom/explore	Decrease	37.8 ± 3.2	29.0 ± 3.0
Attention	Increase	464.3 ± 11.4	519.8 ± 10.3

sitting, rearing, walking, and lying down) generated 2 behavioral measures (total number of initiations of each act and total time engaged in each act) yielding a total of 10 behavioral measures. Significant yohimbine effects were obtained for four measures. Yohimbine decreased number of rearings, total time rearing, and total time sitting and increased time standing. With one exception (time standing), this pattern of changes is consistent with a decrease in overall activity level. None of the conspecific × drug interactions were significant.

Eight modifiers. Each of the modifiers is an act that can cooccur with one of the five major acts. The modifiers are groom, head turn, look, sniff, smell, turn, wash face, and blank (no concurrent activity). As with the five major acts above, two parameters were measured for each modifier: number of initiations and total time. For the 16 measures, 5 significant drug effects were observed. Yohimbine decreased grooming (number of initiations and total time), and increased head turning (number of initiations and total time) and a blank category (no concurrent activity; number of initiations). Again, none of the conspecific × drug interactions were significant.

Combined acts. Each act and modifier may be classified into one of three categories of combined acts, arbitrarily labeled groom, attention, and explore. If an act and its concurrent modifier are from two different categories, the combined classification for that frame is a combination of the two, for example, groom/attention. There are six possible combined acts: groom, attention, explore, groom/attention, groom/explore, and explore/attention. The number of initiations and total time were measured for the combined acts. Significant drug effects were observed for 4 of these 12 measures. Yohimbine decreased number of initiations of grooming and total time for grooming and groom/explore. An increase was observed for total time of the combined act labeled attention. None of the conspecific × drug interactions were significant.

Experiment 2

ANOVA revealed significant differences among groups in the number of photocell interruptions, $F(2,18) = 17.73, p < 0.0001$. The mean number of photocell interruptions for the saline, yohimbine, and *d*-amphetamine conditions were 933.5, 694.1, and 1743.6, respectively. Posthoc comparisons revealed a significant increase in locomotor activity for the *d*-amphetamine condition, $t(18) = 8.76, p < 0.0001$, and a significant decrease in locomotor activity for the yohimbine condition, $t(18) = 2.59, p < 0.02$.

Experiment 3

Overall activity. As in Experiment 1, the total distance traveled was used as an index of general activity level. Idazoxan at a dose of 10.0 mg/kg significantly decreased locomotor activity ($p < 0.01$); comparisons at the three lower dose levels were not significant. Thus, the dose of idazoxan (10.0 mg/kg) that facilitates copulatory behaviors significantly decreased locomotor activity as measured by total distance traveled in the 15-min behavioral test session. In contrast to Experiments 1 and 2, yohimbine failed to significantly decrease locomotor activity.

Acts and modifiers. A summary of the analysis of specific components of motor activity is presented in Table 2. The pattern-recognition procedure generated 38 behavioral measures; consequently, only differences with p value less than 0.01 were considered significant. Significant changes were observed for 19 of the 38 behavioral measures. For each of the five major acts (standing, sitting, etc.) the number of initiations and total time were measured. Significant drug effects were observed for 7 of the 10 measures. As with the major acts, each modifier (blank, groom, etc.) produces two behavioral measures: number of initiations and total time. Significant drug effects were obtained for 6 of the 16 behavioral measures. Yohimbine significantly increased number of head turns, consistent with the yohimbine-induced increase in Experiment 1. This outcome contrasts with the effect of the large dose of idazoxan (10.0 mg/kg), which significantly decreased this same behavioral measure. Yohimbine also significantly increased the total time of the modifier head turn, again consistent with the effects of yohimbine obtained in Experiment 1.

TABLE 2

ACTIVITY MEASURES CHANGED ($p < 0.01$) BY ADMINISTRATION OF YOHIMBINE (2.0 mg/kg) AND IDAZOXAN (3.0 AND 10.0 mg/kg; $n = 12$ PER CONDITION)

Measure	Yohimbine 2.0	Idazoxan 3.0	Idazoxan 10.0
Acts and modifiers: Number of initiations			
Stand			−
Rear	−	−	−
Walk			−
Lie down			+
Blank			−
Head turn	+		−
Smell			−
Turn			−
Acts and modifiers: Total time			
Rear	−	−	−
Walk			−
Lie down			+
Head turn	+		−
Turn			−
Combined acts: Initiations			
Explore			−
Attention			−
Exp/att			−
Combined acts: Total time			
Explore			−
Exp/att			−
Groom/att			+

+ and − indicate significant increase and decrease from controls ($n = 60$), respectively.

Combined acts. Significant changes in the combined acts were obtained only in the high-dose (10.0 mg/kg) idazoxan condition for 6 of the 12 behavioral measures (see Table 2).

K-Function analyses: Acts and modifiers. Two acts (walk and lie down) and three modifiers (look, sniff, and wash face) were excluded from the analysis for the idazoxan 10.0 group because the average number of initiations was less than 10 for either the experimental or control groups. Thirty-four time-sequence or time-distribution analyses were subsequently performed. Of these, 11 were significantly changed. Assuming that 1) these 34 analyses are independent, 2) the false-positive rate is 10%, and 3) an approximately binomial distribution describes the number of "real" changes, then the summed binomial distribution can be used to calculate the probability that the changes observed are due to chance (29). The p value for the idazoxan 10.0 group resulting from this calculation is equal to 0.0003, suggesting that the number of behavioral changes observed is probably not attributable to chance. For the other groups (idazoxan 3.0, 1.0, 0.3, and yohimbine) the p values obtained were all greater than 0.05. Time distributions for idazoxan 10.0 were significantly different for the following acts and modifiers: stand, sit, walk, smell, and turn. Time sequences were significantly different for the following pairs of acts and modifiers: stand/walk, walk/stand, head turn/turn, smell/head turn, turn/groom, and turn/head turn.

K-Function analyses: Combined acts. Thirty-six time-sequence or time-distribution analyses for the idazoxan 10.0 group met the criteria for analysis (none were excluded); 11 were classified as significantly different. The false-positive rate for the combined classifications was about 4%. Again, the summed binomial distribution can be used to calculate the probability that this number of changes is consistent with the null hypothesis. The p value for this calculation is less than 0.0001. For the other groups, all p values were greater than 0.05, consistent with the time-distribution and time-sequence analyses of the acts and modifiers. Time distributions and sequences were significantly different for the idazoxan 10.0 combined acts or pairs of acts including explore, attention, explore/attention, and attention/grooming.

DISCUSSION

Experiment 1 used a sophisticated computer pattern-recognition system to assess the effects of yohimbine on motor behaviors at dose and temporal parameters that facilitate copulatory behaviors. The results of this experiment indicate that yohimbine diminished rather than increased motor behaviors measured by this procedure. The overall level of locomotor activity, measured by the total distance traveled during the observational session, was reduced in yohimbine-treated animals. When individual acts, modifiers, and combined acts were examined, the general picture was also one of decreased motor activity. For example, decreases were observed for rearing and grooming. Increases were observed for standing and for the blank modifier, indicating that animals were spending more time standing in place performing no concurrent activities. The decrease in sitting may appear anomalous; however, this act is probably inversely correlated with the act stand such that an increase in standing necessitates a decrease in sitting. The other apparently anomalous finding was an increase in head turning. The overall pattern of activity that emerges is one of increased standing and head turning, coupled with a decrease in grooming and total distance traveled. The increase in the occurrence of the combined act attention was probably due to the fact that standing, blank, and head turning are three of the five acts that are members of this combined classification.

The effects of yohimbine did not depend on the conspecific with which subjects were paired. No significant conspecific × drug interactions were observed for any of the behavioral measures. The absence of a drug × conspecific interaction may reflect the fact that copulatory behaviors are more directly controlled by cues not present in this activity chamber (e.g., direct access to the female).

These findings are in general agreement with those of other researchers (8,25,35) who have shown that yohimbine, at some dose and temporal parameters, reduces activity level. In addition, the present research has demonstrated that yohimbine, at a dose (2.0 mg/kg) that increases copulatory behaviors, decreases locomotor behaviors.

Consistent with the finding of Experiment 1, yohimbine decreased locomotor activity in the figure-eight maze (Experiment 2). The significant increase in photocell interruptions following the administration of amphetamine indicates that the behavioral measures obtained in this apparatus were sensitive to a drug manipulation (amphetamine) that increases locomotor activity.

Idazoxan, at a dose of 10.0 mg/kg, facilitates copulatory behavior and, like yohimbine, significantly decreased activity indexed by total distance traveled during a 15-min behavioral test session (Experiment 3). When the individual acts, modifiers, and group acts were examined, the results suggested a

general decrease in motor activity for the idazoxan 10.0 group. For example, the number of initiations of stand, sit, and walk decreased whereas the number of initiations of lie down significantly increased.

Yohimbine (2.0 mg/kg) produced fewer behavioral changes than in Experiment 1. The changes observed for yohimbine in this experiment were consistent with the results of Experiment 1; a significant decrease in the act rearing and increase in the act modifier head turning were observed in both experiments. The difference in the number of significant behavioral changes observed may reflect the different designs of the two experiments. In Experiment 1, a more powerful within-subjects design was used. In Experiment 3, a between-subjects design was adopted to avoid any potential confound produced by multiple exposures to the test apparatus.

Experiment 3 also used K-function calculations to analyze the temporal patterning of behavioral acts and the temporal relationships between act pairs. Test methods that are insensitive to temporal patterning may miss significant behavioral effects when the number of initiations or total time for a given act are not changed but the pattern of activity is changed. Thus, several time distributions and time sequences were significantly modified by idazoxan (10.0 mg/kg) but not by yohimbine (2.0 mg/kg).

The results of the present experiments suggest that both yohimbine and idazoxan, at dose levels that significantly increase copulatory behaviors, decrease motor activity. Yohimbine and idazoxan do not, however, influence components of locomotor activity in the same manner. For example, yohimbine significantly increased head turning, whereas idazoxan significantly decreased this act. Idazoxan (10.0 mg/kg) significantly disrupted the temporal patterning of a number of behaviors; yohimbine (2.0 mg/kg) did not affect these behavioral measures. Despite the characterization of both of these drugs as α_2 adrenergic antagonists, the mechanisms of action of these drugs on components of locomotor behavior may be dissimilar. Yohimbine, in addition to its α_2 adrenergic properties, also affects dopamine (1,36) and serotonin (23,34,35,43) neurotransmission; idazoxan also affects dopamine neurotransmission, although to a lesser extent than yohimbine (17).

A general purpose of this series of experiments was to contribute to an understanding of the mechanisms mediating yohimbine's potentiation of copulatory behaviors. Substantial evidence now documents yohimbine's facilitory effect on copulatory behaviors (9–11, 37). Yohimbine may have some selective facilitory effects on neural circuits regulating copulatory behaviors. Yohimbine has in fact been described as a "prosexual" drug (32). Alternatively, yohimbine may increase dominant responses observed in particular test environments. If yohimbine nonspecifically potentiates behaviors, then an increase in locomotor behavior would be anticipated. The present experiments demonstrated that yohimbine at a dose of 2.0 mg/kg did not increase locomotor activity as measured by two different procedures. These results suggest that the facilitory effects of α_2 adrenergic antagonists on copulatory behaviors are not associated with a generalized increase in locomotor behaviors.

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