Effects of SCH23390 and Raclopride on a Run-Climb-Run Behavioral Task in Rats

Ruey-Ming Liao[1], Jian-You Lin[1], Ruey-Kuang Cheng[1] and Jui-Jung Liao[2]

[1] Department of Psychology
National Cheng-Chi University
Taipei, Taiwan, ROC
and
[2] First Division of Neurosurgery
Department of Surgery
Chung Gung Memorial Hospital
Taoyuan, Taiwan, ROC

Abstract

The present study was designed to compare the putative differential behavioral consequences of treatment with SCH23390 (a selective dopamine D1 receptor blocker) and raclopride (a selective dopamine D2 receptor blocker) by employing a run-climb-run (RCR) behavioral task of different lengths. Rats were trained to traverse an uncovered floor alleyway (150 cm), climb a vertical rope (70 or 130 cm), and run across an upper board (100 cm) to access water for the reinforcement. At doses of 0.05, 0.10 and 0.15 mg/kg administered intraperitoneally 60 min before the behavioral session, both SCH23390 and raclopride significantly increased the total time to complete the tasks in a dose-related fashion. Microstructural analysis on the RCR behavioral performance revealed that the most apparent impairment induced by either drug was observed as the subject shifted motion from the end of the floor alleyway to the rope when hopping or to initiate climbing. However, the motion shift from climbing to running on the upper board was significantly impaired by raclopride, but not by SCH23390. Surprisingly, neither SCH23390 nor raclopride affected the climbing response itself. Running responses on the floor alleyway board were significantly disrupted by raclopride, whereas those on the upper board were significantly disrupted by SCH23390. Deficits induced by both drugs were more profound for the longer compared to the shorter rope, and were most notably shown at the transition area from running to climbing. These data indicate that both dopamine D1 and D2 receptors are involved in the RCR behavior performance. The results also suggest that the cost of motoric demand for behavioral performance is important for evaluating of the effects of drugs blocking dopamine receptors.

Key Words: dopamine, D1 receptor, D2 receptor, motor, motivation, switching

Introduction

Dopaminergic receptor antagonists have been shown to reduce operant responses to reinforcers such as food (2, 26, 30, 31), water (13, 16, 18, 20), sex (8), drugs with abuse potential (3), and electrical stimulation of certain areas of the brain (9, 15, 23). In an attempt to address the common element among these different effects, the anhedonia hypothesis states that the administration of neuroleptic drugs via blocking dopamine (DA) receptors blunts the hedonic value of rewards (35). Alternatively, neuroleptic-induced reductions in operant responses have been attributed to a motor deficit related to blocking the dopaminergic pathway of extrapyramidal motor systems (6, 7). Separating the anhedonic and motor effects of DA receptor blockade has been problematic when using the response rate as the sole measure of behavioral

Corresponding Author: Dr. Ruey-Ming Liao, Department of Psychology, National Cheng-Chi University, Taipei 116, Taiwan,ROC; Fax: 886-2-29390644; E-mail: rmliao@nccu.edu.tw
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impairment in traditional operant tasks (5, 10). It now seems clear that numerous behavioral effects produced by traditional neuroleptic drugs are more integrated and complicated than originally thought (29). One difficulty in interpreting the operant deficits of DA receptor blockade is due to multiple behavioral components involved in the operant responses *continuously* being exerted in a traditional (i.e., fixed-ratio) schedule of reinforcement. To overcome this issue, a run-climb-run (RCR) behavioral task was developed by Fowler and Senyuz (12) to examine how the running/climbing motion conducted in a style of *discrete* trials was affected by DA receptor blockade. Using haloperidol, a non-selective DA D2 receptor blocker, their data provide convergent evidence consistent with previous findings of neuroleptic operant deficits. However, contrast to what expected, the drug did not affect rope-climbing speed more than horizontal running speed. While haloperidol significantly disrupted the RCR behavioral performance by slowing the speeds on the floor, the rope, and the upper-board segments, such impairments were not dissociative on the RCR task when different rope lengths were used (12). Because the subjects tested for the dose-response function on the RCR task with the shorter rope occurred 70 days prior to that with the longer rope in that study. We speculated that observing no distinctive drug effects on the RCR task with different rope lengths might have resulted from 1) the drug effects on the RCR task with different rope lengths being evaluated in separate phases, and 2) the sequential order of using the shorter and longer rope in that study. The present investigation, therefore, was designed to examine more extensively the effects of selective DA antagonists on the RCR task; we were particularly interested in preventing the aforementioned confounding effects by testing a rat's RCR performance with different rope lengths arranged in a counterbalanced fashion under DA receptor blockade. Furthermore, the times to complete five different segments of the RCR task were measured instead of just three segments (floor, rope, and board) used in the study of Fowler and Senyuz (12). As reported in the present study, the times recorded in these two extra segments specifically reflect the transitional motion as the subject shifted from running to climbing and vice versa. SCH23390 and raclopride were chosen because of their selectivity in respectively antagonizing the D1 and D2 subtypes of DA receptors. These two drugs were administered in the same dose range for the RCR behavioral task, so that their effects could be directly compared. The dose range applied in the present work had a low potential to produce complete akinesia or catalepsy, and was referenced to previous work from this and other laboratories (18, 22, 32)

Materials and Methods

Subjects

The subjects were male Wistar rats, with average body weights of approximately 250 g upon receipt (Breeding Center of Experimental Animals, National Taiwan University Hospital, Taipei). After 10 days of adaptation (food and water *ad libitum*), the rats were maintained on a water deprivation regimen such that 5 min of access to tap water in the home cage occurred no sooner than 30 min after the end of each daily experimental session. The rats were monitored and kept at 85% of their pre-experimental body weight. Food pellets were continuously available in each home cage. Training and/or test sessions were administered at the same time each day during the light portion of the vivarium's 12/12-h light-dark cycle, with lights on at 0700 h.

Drugs

SCH23390 hydrochloride and raclopride l-tartrate purchased from Research Biochemical Inc. (Natick, MA, USA) were separately dissolved in 0.9% saline and prepared into 0.05, 0.10, and 0.15 mg/ml concentrations. Injections of the drug and vehicle were administered intraperitoneally (IP) at a constant volume of 1 ml/kg of body weight, 1 h before the commencement of a behavioral session.

Apparatus

The apparatus consisted of three major parts: a horizontal runway on the floor, a vertical rope, and an elevated runway board. The horizontal runway (15 cm W, 30 cm H, 150 cm L) on the floor was made from a piece of plywood with acrylic walls. An area of 15 by 30 cm was set as the start segment into which the subject was gently placed to initiate each trial. The elevated board was constructed from a piece of plywood (20 by 100 cm) which was affixed horizontally against the wall 130 cm above the floor. Four pieces of rubber mat (1 by 20 cm each) glued in a line were separated by 2 cm

on one end of the elevated board, while a metal cup 2.5 cm in diameter and 1 cm deep was placed at the other end of this board. The end of the elevated runway board with the metal cup was blocked off with plywood. A vertical rope, made of 3-cm-diameter hemp 130 cm long, intersected the floor runway perpendicularly at a point 100 cm from the beginning of the floor runway segment (20 cm from the end of the floor board). Thus, the bottom end of the rope was suspended a negligible distance from the floor runway. The height of the elevated board could be adjusted to 130 or 70 cm to correspond to the length of the rope, when using the longer or shorter ropes (see the procedure).

For conducting microstructural analysis of RCR behavior, the apparatus was divided into five segments to represent distinct components of this behavior in addition to the aforementioned start segment. The first segment covered 80 cm of the runway on the floor board to represent the floor running response. The second segment, representing a transition response from running to grasping the rope, covered the last 40 cm of floor runway and the bottom 40 cm of the rope. The third segment representing the rope-climbing response covered 80 cm of the middle section of the rope for the longer rope, and only 20 cm for the shorter rope. The fourth segment covered the top 10 cm of rope and the beginning area (20 by 20 cm) of the elevated board to represent another transitional response in which motion was shifted from climbing to running. The fifth segment covered the 80-cm runway of the elevated board to represent the running response immediately after climbing. A stopwatch (Casio, HS-30W) was used to time the subject passing the end mark of each of these five segments in every trial.

Procedure

At the beginning of the experiment, rats were trained to perform the RCR behavior with the longer rope (130 cm) by completing the five segments in a reverse sequence, i.e., the rat was first trained to perform the terminal response of licking 0.3 ml of tap water from the metal cup on the end of the elevated board. The subject was then placed farther and farther from the metal cup as training progressed. Subsequently, the experimenter released the subject from the fourth segment of the RCR apparatus. After the subject had successfully climbed onto the board from this position, the rat was then placed progressively further down the third segment eventually to the first segment. The rat was allowed 10 s of access to the reward when completing each trial. Each daily session consisted of seven trials with a 60-s intertrial interval. The subject was returned to its home cage during the intertrial interval. In each squad, six home cages were moved in a cart from the animal colony to the testing room and remained there while the training or experiment was being conducted. The criterion for determining the baseline was defined as less than a 10% variation in the mean total time for completing the task for three consecutive sessions. About 90 sessions were required for each subject to reach a stable baseline performance. The shorter rope (70 cm) was then used for three sessions. Subsequently, subjects were separated into two groups (n=7 each) to receive either SCH23390 or raclopride treatment. Each drug was administered in four separate doses while repeating the RCR task using both the longer and shorter ropes. The sequences of using the longer or shorter rope were counterbalanced across subjects within each drug-treated group.

Statistics

The mean time to complete a trial was measured, and the average amount of time to complete each segment of the RCR task was also determined. A 3-way mixed design analysis of variance (ANOVA), with one between-subjects factor (drug) and two within-subjects factors (rope length and dose), was computed on data depicted in each figure. Due to the lack of significant main effect of drug revealed from the results of 3-way ANOVA's (see below), a two-way repeated ANOVA was computed for each dependent variable in order to assess the effects of each drug treatment on the RCR tasks with different rope lengths. The Scheffe test was used for post hoc comparison to specify differences revealed by significant ANOVA's. A probability level of $p<0.05$ was taken as significant in all tests.

Results

At the baseline level, the subject performed the RCR behaviors smoothly or continuously across the floor alleyway, up the rope, and across the upper board with no stops between the start and the end where the reinforcer was obtained. The mean total time to complete the RCR behaviors with the longer rope was

about two- fold longer than that with the shorter rope. These qualitative observations were also true for most drug treatments in the present study. In other words, each subject was able to complete all seven trials of a session despite having injections of vehicle or drug. However, three subjects of the SCH23390-treated group failed to complete all seven trials when challenged with the highest dose (0.15 mg/kg) in the RCR task with the longer rope. These three subjects adequately responded to the RCR task in only the first 4 or 5 trials, but failed to complete the subsequent 3 or 2 trials. It should be noted that such failures were not observed in these three subjects given the highest dose of SCH23390 in the RCR task with the shorter rope. To prevent the total omission of data from affecting the strength of the statistical analysis, we averaged only the times from the completed trials to represent the performance of those three subjects under that specific treatment.

The mean times to complete the RCR task with the longer or shorter rope under drug treatment with SCH23390 or raclopride are shown in Fig. 1. A 3-way ANOVA revealed significant main effects of rope length, $F(1,12)=66.732$, $p<0.01$, and dose, $F(3,36)=13.623$, $p<0.01$, as well as a significant interaction of rope length and dose, $F(3,36)=11.853$, $p<0.01$. Additionally, the results of a 2-way ANOVA applied to the SCH23390 data in the upper panel of Fig. 1 confirmed that all three effects were statistically significant: for rope length, $F(1,6)=32.35$, $p<0.01$; for dose, $F(3,18)=9.52$, $p<0.01$; and for the rope-by-dose interaction, $F(3,18)=8.283$, $p<0.01$. Post hoc comparisons found that the times for subject to complete the RCR task with longer rope were significantly more than that with shorter rope at 0.1 mg/kg ($p<0.05$) and 0.15 mg/kg ($p<0.01$) of SCH23390. For raclopride data in the lower panel of Fig. 1, the results of a 2-way ANOVA revealed significant effects for rope length, $F(1,6)=39.34$, $p<0.01$; for dose, $F(3,18)=4.6$, $p<0.05$; and for the rope-by-dose interaction, $F(3,18)=3.86$, $p<0.05$. Post hoc comparisons found that the times for subject to complete the RCR task with longer rope were significantly more than that with shorter rope at 0.15 mg/kg of raclopride ($p<0.01$).

The times to complete segment 1 in the RCR task with the longer or shorter rope under drug treatment with SCH23390 or raclopride are shown in Fig. 2. A 3-way ANOVA revealed significant main effects of rope length, $F(1,12)=9.234$, $p<0.05$, and dose, $F(3,36)=5.195$, $p<0.01$, as well as a significant interaction of rope length and dose, $F(3,36)=4.138$, $p<0.05$. As in the upper panel of

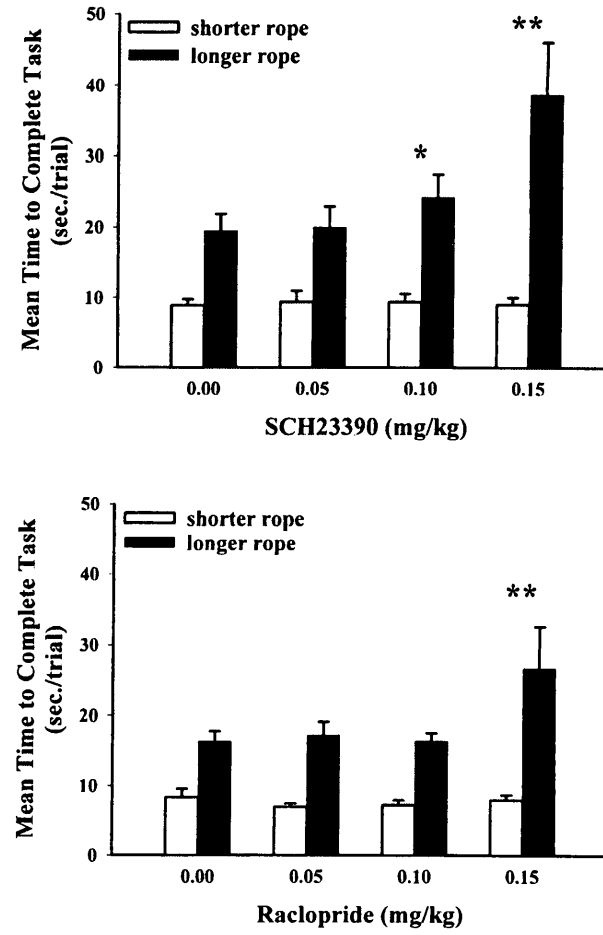

Fig. 1. Total times (mean ± 1 S.E.M.) to complete the entire RCR task using a longer or shorter rope under drug treatment with SCH23390 (upper panel) or raclopride (lower panel). * $p<0.05$ and ** $p<0.01$, differences between longer and shorter rope at the indicated dose level based on Scheffe tests that followed ANOVA.

Fig. 2, SCH23390 produced no significant effect on the tests of a 2-way ANOVA ($p>0.05$). All three tests in this ANOVA were marginally significant, $F(1,6)=4.32$, $p=0.083$ for rope length, $F(3,18)=3.01$, $p=0.0573$ for dose, and $F(3,18)= 3.13$, $p=0.0513$ for the rope-by-dose interaction. Regarding the raclopride data in the lower panel of Fig. 2, the results of a 2-way ANOVA revealed significant effects for rope length and dose, $F(1,6)=39.34$, $p<0.01$, and $F(3,18)=4.6$, $p<0.05$, respectively. The rope-by-dose interaction was not significantly verified.

The times to complete segment 2 for the motion of shifting from floor-running to rope-climbing in the RCR task with the longer or shorter rope under drug treatment with SCH23390 or raclopride are shown in Fig. 3. A 3-way ANOVA revealed significant main effects of rope length, $F(1,12)=28.843$, $p<0.01$, and dose, $F(3,36)=11$.

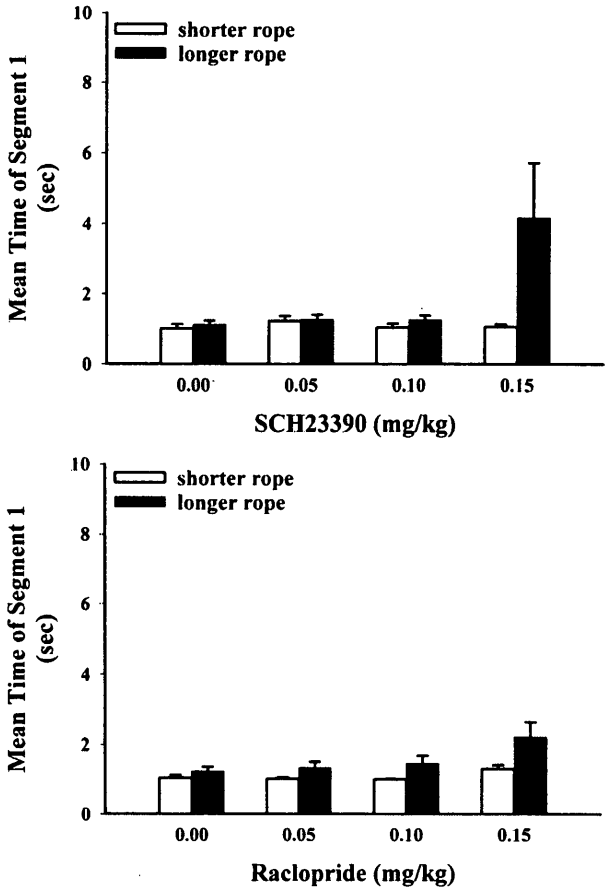

Fig. 2. Times for completing segment 1 (running on the floor alleyway) of the RCR task using a longer or shorter rope under drug treatment with SCH23390 (upper panel) or raclopride (lower panel). Each bar represents the mean ± 1 S.E.M..

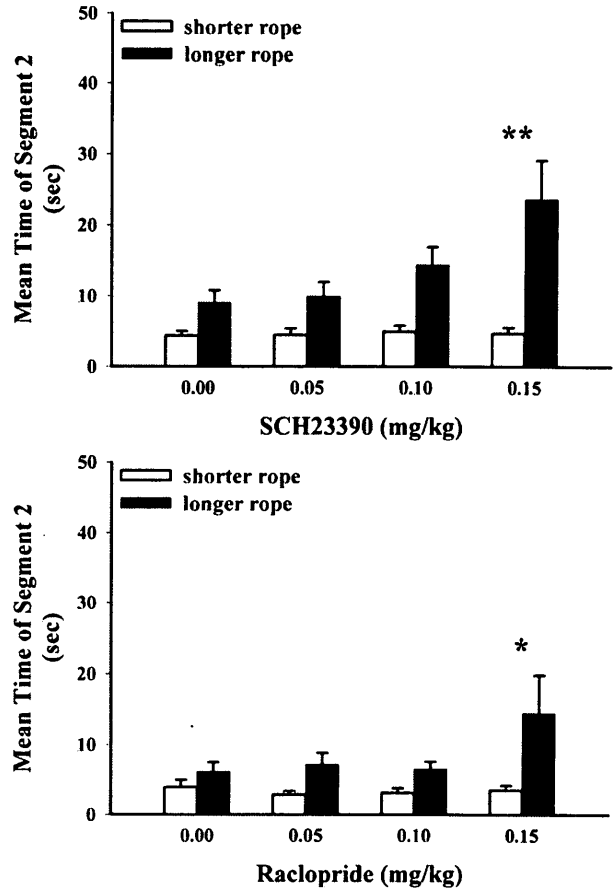

Fig. 3 Times for completing segment 2 (shifting motion from running to climbing) of the RCR task using a longer or shorter rope under drug treatment with SCH23390 (upper panel) or raclopride (lower panel). Each bar represents the mean ± 1 S.E.M.. * $p<0.05$ and ** $p<0.01$, differences between longer and shorter rope at the indicated dose level based on Scheffe tests that followed ANOVA.

686, $p<0.01$, as well as a significant interaction of rope length and dose, $F(3,36)=10.148$, $p<0.01$. Additionally, the results of a 2-way ANOVA applied to the SCH23390 data in the upper panel of Fig. 3 confirmed that all three tests were statistically significant: for rope length, $F(1, 6)=18.43$, $p<0.01$; for dose, $F(3,18)=9.49$, $p<0.01$; and for the rope-by-dose interaction, $F(3,18)=7.57$, $p<0.01$. Post hoc comparisons found that the times for subject spent to complete this segment in the RCR task with longer rope were significantly more than that with shorter rope at 0.15 mg/kg of SCH23390 ($p<0.01$). Regarding the raclopride data in the lower panel of Fig. 3, the results of a 2-way ANOVA revealed significant test results for rope length, $F(1,6)=10.43$, $p<0.05$; for dose, $F(3,18)=3.44$, $p<0.05$; and for the rope-by-dose interaction, $F(3,18)=3.18$, $p<0.05$. Post hoc comparisons found that the times for subject spent to complete this segment in the RCR task with longer rope were significantly more than that with shorter rope at 0.15 mg/kg of raclopride ($p<0.05$).

The times of segment 3 consisting of just rope climbing in the RCR task with the longer or shorter rope under drug treatment with SCH23390 or raclopride are shown in Fig. 4. A 3-way ANOVA revealed significant main effects of rope length, $F(1,12)=228.097$, $p<0.01$, and dose, $F(3,36)=3.346$, $p<0.05$. Neither the main effect of drug nor any of the interactions was significantly confirmed. Additionally, for the data of SCH23390 in the upper panel of Fig. 4, the results of a 2-way ANOVA revealed only a significant effect on rope length, $F(1,6)=131.7$, $p<0.01$. Neither dose nor the rope-by-dose interaction was significantly verified. Similarly, only a significant effect of rope length was significantly confirmed by a 2-way ANOVA for the data of raclopride as shown in the lower panel of Fig. 4, $F(1,6)=101.3$, $p<0.01$.

The times to complete segment 4 for the motion of

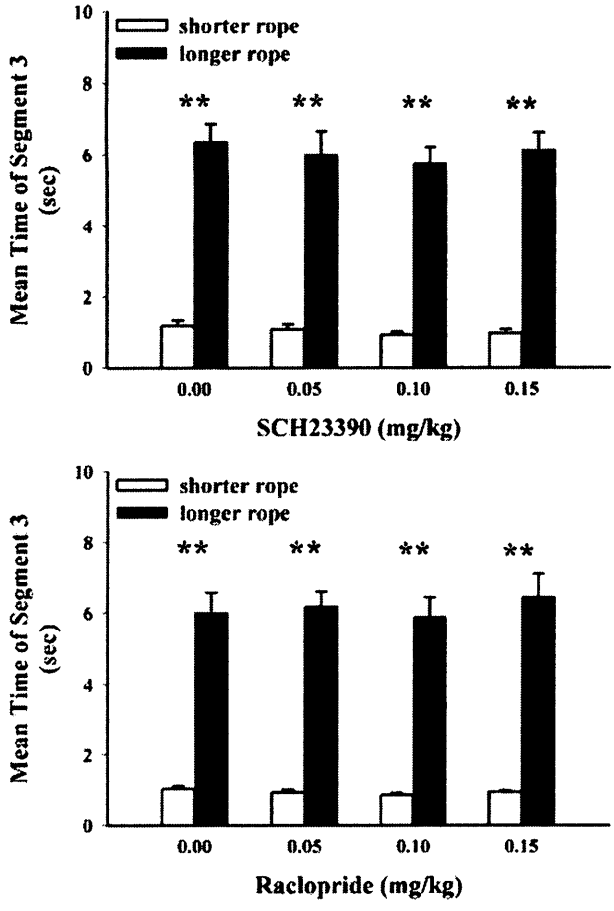

Fig. 4. Times for completing segment 3 (rope-climbing) of the RCR task using a longer or shorter rope under drug treatment with SCH23390 (upper panel) or raclopride (lower panel). Each bar represents the mean ± 1 S.E.M.. ** $p<0.01$, differences between longer and shorter rope at the indicated dose level based on Scheffe tests that followed ANOVA.

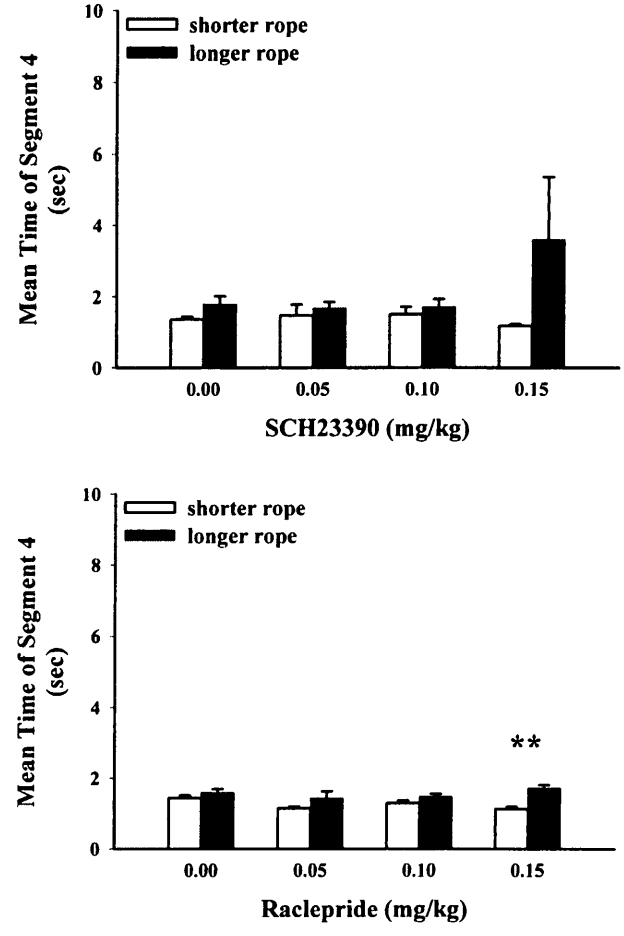

Fig. 5. Times for completing segment 4 (shifting motion from climbing to running on the upper board) of the RCR task using a longer or shorter rope under drug treatment with SCH23390 (upper panel) or raclopride (lower panel). Each bar represents the mean ± 1 S.E.M.. ** $p<0.01$, difference between longer and shorter rope at the indicated dose level based on Scheffe tests that followed ANOVA.

shifting from rope-climbing to running in the RCR task with the longer or shorter rope under drug treatment with SCH23390 or raclopride are shown in Fig. 5. None of the main effects or interactions from the results of a 3-way ANOVA was significant. As shown in the upper panel with data for SCH23390, none of the three tests was significantly confirmed by an additional 2-way ANOVA ($p>0.1$). In contrast, the results of a 2-way ANOVA for the data of raclopride in the lower panel revealed significant effects for rope length, $F(1, 6)=12.03$, $p<0.05$; for dose, $F(3,18)=3.396$, $p<0.05$; and for the rope-by-dose interaction, $F(3,18)=3.584$, $p<0.05$. Post hoc comparisons found that the times for subject spent to complete this segment in the RCR task with longer rope were significantly more than that with shorter rope at 0.15 mg/kg of raclopride ($p<0.01$).

The times to complete segment 5 of running on the upper board in the RCR task with the longer or shorter rope under drug treatment with SCH23390 or raclopride are shown in Fig. 6. A 3-way ANOVA significantly confirmed the main effect of rope length, $F(1,12)=10.32$, $p<0.01$, but not the other tests. Additionally, only a significant effect of dose was confirmed by a 2-way ANOVA for the data of SCH23390 as shown in the upper panel of Figure 6, $F(3,18)=5.187$, $p<0.05$. Regarding the data of raclopride shown in the lower panel, none of the three tests was significantly confirmed by a 2-way ANOVA ($p>0.05$).

Discussion

The purpose of the current study was to assess the effects of selective DA receptor antagonists (D1 or D2) on RCR behavioral tasks. Regarding general adverse

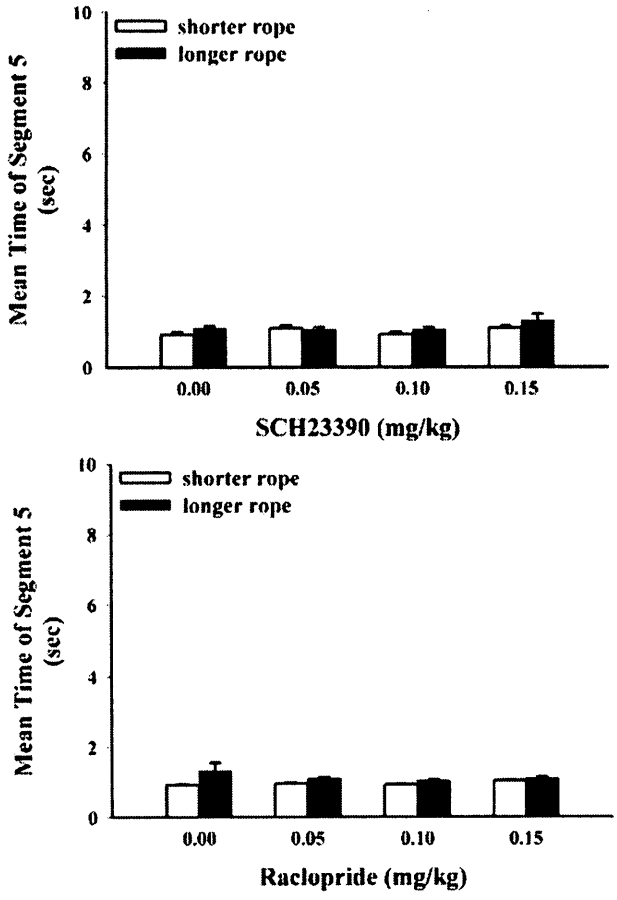

Fig. 6. Times for completing segment 5 (running on the upper board) of the RCR task using a longer or shorter rope under drug treatment with SCH23390 (upper panel) or raclopride (lower panel). Each bar represents the mean ± 1 S.E.M..

effects, both SCH23390 and raclopride significantly increased the mean time to complete the RCR trial in a dose-related manner. Further microstructural analysis of the data for the five segments within the RCR trial showed differential patterns of anomalous behavior produced by SCH23390 and raclopride.

The adverse effects of SCH23390 and raclopride on the RCR task in the present work were similar to those reported in a previous study using the same agents (32). However, we observed no maldirected jumping phenomenon induced by raclopride as reported in that work. The different dose ranges of raclopride employed in these two studies may explain the lack of raclopride-induced jumping reaction in the present work. The doses of raclopride (0.12-1.00 mg/kg) used in the study of Senyuz and Fowler (32) were much higher than the doses (0.05-0.15 mg/kg) used in the present study by about six- fold. The current results with no severe motoric deficits, including cataleptic reactions, fit the purpose of the dose range of DA receptor blockers applied in the present work.

A significant interaction of dose with rope length was found for both SCH23390 and raclopride in the present study. These results indicate that the magnitudes of behavioral impairment on the RCR task under drug treatment differed between the use of the longer or shorter rope. For both SCH23390 and raclopride (shown in Fig. 1), the drug-induced behavioral changes on the RCR task with the shorter rope were almost negligible, while those with the longer rope appeared more strongly as the dose increased. The data reported here agree with the kinetic requirement hypothesis based on the assumption of different efforts required for completing the RCR tasks with a longer or shorter rope, presumably a greater effort required for the RCR task with the longer rope and less effort required with the shorter rope. The kinetic requirement hypothesis of the behavioral effects of neuroleptics argues that those responses which are relatively more demanding in a motoric sense should be disrupted by neuroleptic treatment to a greater degree than those less demanding (7). In reviewing evidence from previous work to support this hypothesis, the class of behaviors more sensitively affected by neuroleptics is related to a operant-like behavior repertoire rather than a reflexive-like one (1, 7, 16, 18, 20, 21). In contrast to previous studies that used two different tasks, the present work manipulated a parameter (of rope-length) within one behavioral task to evaluate the effects of DA receptor antagonists. In conversely considering the lower effort required to complete the RCR task with the shorter rope, it is possible that increasing the reward value of the reinforcer for this type of goal-directed behavior would also be resistant to the behavior-suppressed effects produced by DA receptor antagonists. Although there is no direct evidence from the RCR behavioral task to support this argument, a previous study using intracranial self-stimulation in the medial forebrain bundle showed that the decreased response induced by SCH23390 was significantly reversed by increasing the stimulation frequency for reward enhancement (17).

Different degrees of drug-induced impairment on the RCR task with a longer or shorter rope being manipulated in the present work were not observed in a previous study using haloperidol (12). The administered drugs differed between these two studies. While SCH23390 and raclopride are selective D1 and D2 receptor antagonists, respectively, haloperidol is now known to be a non-selective D2 receptor antagonist. Thus, haloperidol produced significant dose-related impairment of RCR behavior with a short rope in that previous work in which effects might have resulted from

the drug blocking D2 receptors in combination with other receptors (including D1), especially when the highest dose of 0.32 mg/kg was administered. If this is the case, we would expect to observe the adverse effects on behavioral performance of the RCR task even with the short rope when given a combination of SCH23390 and raclopride at less-effective doses. Consistent with this idea, the present work demonstrates negative results for both SCH23390 and raclopride on the RCR task with the shorter rope. Further, in terms of DA receptor blocking effects on the RCR task using the shorter rope, differences between the present study and that previous work (12) may be due to experimental procedures in addition to the different DA receptor antagonists applied. In the present work, the dose-response effects evaluated with the RCR task using a long and short rope for each drug treatment were obtained by arranging RCR tasks with two rope lengths in a counterbalanced manner, and these data were completely collected in a single phase. In addition, subjects in this study were first trained to reliably perform the RCR task with the longer rope and then they were exposed to the same task with the shorter rope for three sessions shortly before being challenged with drug injection. The success of manipulating rope length for the present RCR task can be confirmed by the significant effects of testing rope length from ANOVA results. Thus, the subject responded to the RCR task with different motoric efforts as each rope length was introduced.

Analysis of the microstructural data of the five segments within the RCR performance revealed one of the striking results from the present study. Neither SCH23390 nor raclopride affected the rope-climbing itself (segment 3). The duration for the transition from floor-running to rope-climbing (segment 2) was significantly increased by drug treatment, the effect of which was aggravated by the longer rope. These results indicate that initial preparation for or commencement of rope-climbing was apparently impaired by DA receptor blockade. Once the rat began climbing (segment 3), this on-going response was not significantly affected by the drug. This type of deficit of motoric initiation has been reported from clinical observation in neuroleptic-treated patients (28, 33). The capability to shift motions with distinct characteristics is an essential need in exerting the RCR behavior especially in segments immediately before and after climbing the rope. By employing the modified operant chamber, this type of shifting capability is also needed to repeatedly complete motion components such as lever-pressing and head-entry into a muzzle for obtaining a reinforcer. Latencies between each of those components significantly increased in rats with 6-hydroxydopamine lesions in the striatum (19) or with DA receptor blockade (11, 14). One common characteristic related to behavioral switching can be drawn from the tasks used in these aforementioned studies and the present work. These data, therefore, indicate that the disruption of behavioral switching can be induced by DA receptor blockade and lesions of striatal areas. In agreement with previous work using different behavioral paradigms (4, 25), the present study of RCR task support a hypothesis addressing that the mesotelencephalic DA systems play an important role in behavioral switching. Accordingly, the tonic levels of DA activity can be positively correlated to the likelihood of switching between alternative sources of behavioral reaction (24, 27). In the present RCR task, another shifting capability was essential for the motion exerted in segment 4. Raclopride significantly produced motoric deficits as seen by the increased duration of segment 4, while SCH23390 produced no such impairment. The latter non-significant result might be due to our exclusion of some missing data from the statistical analysis (as described in Results). One should therefore be conservative when interpreting the distinctive effects between these two drugs on this specific behavioral component. Nevertheless, current data separating the RCR behavioral performance into five segments for microstructural analysis should provide more meaningful information than that reported previously (12, 32).

Although SCH23390 and raclopride tended to produce similar effects on the second and third segments of present RCR task, there were distinctive effects between these two drugs on other segments. For instance, raclopride but not SCH23390 was found to disrupt running in the first segment of the floor alleyway as well as in the transition from climbing to running in the fourth segment. In contrast, SCH23390 significantly impaired running (for the reward) in the final segment of the RCR task. In reviewing the duration data across the five segments of the RCR task, these results reflect some distinct reactions to SCH23390 and raclopride and support the hypothesis of different functions existing between DA D1 and D2 receptor subtypes. Further, these D1 and D2 receptors may interact to somewhat different extents for mediating similar behavioral performance (34).

In conclusion, both SCH23390 and raclopride significantly disrupted the RCR behavioral performance by increasing the time to complete task in a dose-related manner. However, such impairment was diminished as the cost of motoric demands was

reduced in the RCR task when a shorter rope was introduced. Further analysis based on the duration data for the five segments within the RCR trial indicates that DA D1 and D2 receptors may be involved to different extents as revealed by the microstructural patterns of these anomalous behaviors being differentially produced by SCH23390 and raclopride.

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